The SAGE Encyclopedia of CANCER AND SOCIETY

Second Edition
SAGE was founded in 1965 by Sara Miller McCune to support the dissemination of usable knowledge by publishing innovative and high-quality research and teaching content. Today, we publish more than 850 journals, including those of more than 300 learned societies, more than 800 new books per year, and a growing range of library products including archives, data, case studies, reports, and video. SAGE remains majority-owned by our founder, and after Sara's lifetime will become owned by a charitable trust that secures our continued independence.
The SAGE Encyclopedia of
CANCER
AND
SOCIETY

Second Edition

Edited by
Graham A. Colditz
Siteman Cancer Center, Washington University School of Medicine
Contents

Volume 1
List of Articles vi
Reader’s Guide xiv
About the Editor xxii
List of Contributors xxiii
Introduction xxx
Chronology xxxiii

Articles
A 1 D 331
B 119 E 379
C 199 F 447

Volume 2
List of Articles vi
Reader’s Guide xiv

Articles
G 477 M 719
H 521 N 793
I 573 O 849
J 627 P 879
K 643 R 967
L 657

Volume 3
List of Articles vi
Reader’s Guide xiv

Articles
S 1013 W 1297
T 1135 X 1329
U 1203 Y 1333
V 1271 Z 1341

Glossary 1345
Resource Guide 1373
Index 1483
List of Articles

A
Abbott Laboratories (United States)
Acrylic Rubber and Fibers
Adrenocortical Carcinoma
Adrenocortical Carcinoma, Childhood
Advertising
Aerospace Industry
Afghanistan
Age
AIDS-Related Cancers
Albert Einstein Cancer Center
Alcohol
Algeria
Allergan (United States)
Alternative Therapy: Diet and Nutrition
Alternative Therapy: Herbs, Vitamins, and Minerals
Alternative Therapy: Manual Healing and Physical Touch
Alternative Therapy: Mind, Body, and Spirit
Alternative Therapy: Pharmacological and Biological Treatment
American Academy of Pediatrics, Section on Hematology/Oncology
American Association for Cancer Education
American Association for Cancer Research
American Brain Tumor Association
American Cancer Society
American College of Gastroenterology
American College of Radiation Oncology
American Joint Committee on Cancer
American Lung Association
American Psychosocial Oncology Society
American Society for Radiation Oncology
American Society of Clinical Oncology
American Society of Hematology
American Society of Pediatric Hematology/Oncology
Amgen (United States)
Anal Cancer
Angola
Antibiotics
Anticancer Drugs
Argentina
Asbestos
Asian Diet
Aspirin
Assisted Suicide
Association for the Cure of Cancer of the Prostate
Association of Cancer Online Resources
Association of Community Cancer Centers
Association of Freestanding Radiation Oncology Centers
Association of Oncology Social Work
Association of Pediatric Hematology/Oncology Nurses
Astellas Pharma (Japan)
AstraZeneca (United Kingdom)
Australia
Austria
Automobiles
Azerbaijan

B
Bangladesh
Barbara Ann Karmanos Cancer Institute
Battery Acid
Belarus
Belgium
Benin
Bereavement Issues
Beta-Carotene
Bicycles
Bile Duct Cancer, Extrahepatic
Biologic Therapy
Bladder Cancer
Bladder Cancer, Childhood
Bolivia
Bonadonna, Gianni
Bone Cancer, Osteosarcoma/Malignant Fibrous Histiocytoma
Bone Marrow Transplants
Brain Stem Glioma, Childhood
Brain Tumor, Adult
Brain Tumor, Cerebellar Astrocytoma, Childhood
Brain Tumor, Cerebral Astrocytoma/Malignant Glioma, Childhood
Brain Tumor, Childhood
Brain Tumor, Medulloblastoma, Childhood
Brain Tumor, Supratentorial Primitive Neuroectodermal, Childhood
Brain Tumor, Visual Pathway and Hypothalamic Glioma, Childhood
Brazil
Breast Cancer
Breast Cancer, Male
Breast Cancer, Sociocultural Differences and Breast Cancer and Pregnancy
Bristol-Myers Squibb (United States)
Broad-Spectrum Ultraviolet (UV) Radiation
Bronchial Adenomas/Carcinoids, Childhood
Bulgaria
Burkina Faso

Burma (Myanmar)
Burundi

C
Calcium
California Blood Bank Society
Cambodia
Cameroon
Canada
Canadian Association of Medical Oncologists
Canadian Association of Pharmacy in Oncology
Canadian Cancer Society
Canadian Red Cross
Canadian Society of Surgical Oncology
Canadian Urologic Oncology Group
Cancer Association of South Africa
Cancer Communication
Cancer Council Australia
Cancer Drugs, Cost and Benefits of Cancer Therapy Evaluation Program
Candlelighters Childhood Cancer Foundation
Carcinoid Cancer Foundation
Carcinoid Tumor, Childhood
Carcinoid Tumor, Gastrointestinal
Carcinoma of Unknown Primary
Careers
Caregivers
Celebrities and Cancer
Celgene (United States)
Cell Phones
Central African Republic
Central Nervous System Lymphoma, Primary
Cervical Cancer
Chad
Chao Family Comprehensive Cancer Center
Chemical Industry
Chemoprevention
Chemotherapy
Childcare and Cancer Risk
Childhood Brain Tumor Foundation
Childhood Cancers
Chile
China
Chlorine
Chloroform
City of Hope
Clinical Trials
Clothing
Coal Industry
Cold Spring Harbor Laboratory
Colombia
Colon Cancer
Colorectal Cancer, Childhood
Comprehensive Cancer Center of Wake Forest University
Congo, Democratic Republic of Cosmetics
Cost of Therapy
Costa Rica
Côte d'Ivoire
COX-2 Inhibitors
Croatia
Cuba
Czech Republic

D
Daiichi Sankyo (Japan)
Daily Life
Dana-Farber Cancer Institute
Danish Cancer Society
DDT
Denmark
Deodorizers
Detergents
Developing Countries
Diesel Exhaust
Diet and Nutrition
Disability
Disinfectants and Antiseptics
Disparities Within Nations (Elimination of Cancer)
Dominican Republic
Drugs
Duke Cancer Institute
Dyes and Pigments

E
Ecuador
Education
Egypt
Eisai (Japan)
El Salvador
Electrical Industry
Electronics
Eli Lilly and Company (United States)
Embalming Fluids
Endometrial Cancer
Environmental Justice and Cancer
Environmental Tobacco Smoke
Ependymoma, Childhood
Eritrea
Esophageal Cancer
Esophageal Cancer, Childhood
Estrogen, Steroidal
Ethiopia
Europa Donna, the European Breast Cancer Coalition
European Association for Cancer Research
European CanCer Organisation
European Cancer Prevention
European School of Oncology
European Society for Therapeutic Radiology and Oncology
European Society of Mastology
European Society of Surgical Oncology
Ewing’s Family of Tumors
Exercise
Experimental Cancer Drugs
Explosives
Extracranial Germ Cell Tumor, Childhood
Extragonadal Germ Cell Tumor

F
Family Size
Finland
Flame Retardant
Flavoring Agents
Food Additives
Food and Drug Administration
Forest Labs (United States)
Fox Chase Cancer Center
France
Fred & Pamela Buffett Cancer Center
Fred Hutchinson Cancer Research Center
Freon
Future of Cancer

G
Gallbladder Cancer
Gasoline
Gene Therapy
Genentech
Genetics
Genzyme (United States)
Georgia
Germany
Gestational Trophoblastic Tumor
Ghana
<table>
<thead>
<tr>
<th>Glass Industry</th>
<th>International Cancer Alliance for Research and Education</th>
</tr>
</thead>
<tbody>
<tr>
<td>GlaxoSmithKline (United Kingdom)</td>
<td>International Committee of the Red Cross</td>
</tr>
<tr>
<td>Global Health Issues and Cancer</td>
<td>International Myeloma Foundation</td>
</tr>
<tr>
<td>Government</td>
<td>International Psycho-Oncology Society</td>
</tr>
<tr>
<td>Greece</td>
<td>International Society for Cutaneous Lymphomas</td>
</tr>
<tr>
<td>Green, Adele</td>
<td>International Society for Experimental Hematology</td>
</tr>
<tr>
<td>Gregoire, Christine</td>
<td>International Society for Preventive Oncology</td>
</tr>
<tr>
<td>Guatemala</td>
<td></td>
</tr>
<tr>
<td>Guinea</td>
<td></td>
</tr>
<tr>
<td>H</td>
<td></td>
</tr>
<tr>
<td>H. Lundbeck (Denmark)</td>
<td>International Society of Nurses in Cancer Care</td>
</tr>
<tr>
<td>Haemophilia Society (United Kingdom)</td>
<td>International Society of Paediatric Oncology</td>
</tr>
<tr>
<td>Hair Dye</td>
<td>International Society on Thrombosis and Haemostasis</td>
</tr>
<tr>
<td>Haiti</td>
<td>Intraocular Melanoma</td>
</tr>
<tr>
<td>Head and Neck Cancer</td>
<td>Iran</td>
</tr>
<tr>
<td>Health Advocacy</td>
<td>Iraq</td>
</tr>
<tr>
<td>Healthy People</td>
<td>Ireland, Republic of</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>Ireland (Ohio) Cancer Center</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>Irish Cancer Society</td>
</tr>
<tr>
<td>Hepatocellular (Liver) Cancer, Adult (Primary)</td>
<td>Islet Cell Carcinoma (Endocrine Pancreas)</td>
</tr>
<tr>
<td>Hepatocellular (Liver) Cancer, Childhood (Primary)</td>
<td>Israel</td>
</tr>
<tr>
<td>Herbert Irving Comprehensive Cancer Center</td>
<td>Italy</td>
</tr>
<tr>
<td>Herbicide</td>
<td></td>
</tr>
<tr>
<td>History of Cancer</td>
<td></td>
</tr>
<tr>
<td>Holden Comprehensive Cancer Center at the University of Iowa</td>
<td></td>
</tr>
<tr>
<td>Honduras</td>
<td></td>
</tr>
<tr>
<td>Hong Kong Anti-Cancer Society</td>
<td></td>
</tr>
<tr>
<td>Hospice Care</td>
<td></td>
</tr>
<tr>
<td>Hospitals</td>
<td></td>
</tr>
<tr>
<td>HPV Vaccination</td>
<td></td>
</tr>
<tr>
<td>Hungary</td>
<td></td>
</tr>
<tr>
<td>Huntsman Cancer Institute</td>
<td></td>
</tr>
<tr>
<td>Hypopharyngeal Cancer</td>
<td></td>
</tr>
<tr>
<td>Hypothalamic and Visual Pathway Glioma, Childhood</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td></td>
</tr>
<tr>
<td>Immigrant Populations</td>
<td></td>
</tr>
<tr>
<td>India</td>
<td></td>
</tr>
<tr>
<td>Indonesia</td>
<td></td>
</tr>
<tr>
<td>Infection</td>
<td></td>
</tr>
<tr>
<td>Insecticides</td>
<td></td>
</tr>
<tr>
<td>Insurance</td>
<td></td>
</tr>
<tr>
<td>International Agency for Research on Cancer</td>
<td></td>
</tr>
<tr>
<td>International Association for the Study of Lung Cancer</td>
<td></td>
</tr>
<tr>
<td>International Association of Cancer Registries</td>
<td></td>
</tr>
<tr>
<td>J</td>
<td></td>
</tr>
<tr>
<td>Japan</td>
<td></td>
</tr>
<tr>
<td>Japan Lung Cancer Society</td>
<td></td>
</tr>
<tr>
<td>Japanese Cancer Association</td>
<td></td>
</tr>
<tr>
<td>Japanese Gastric Cancer Association</td>
<td></td>
</tr>
<tr>
<td>Japanese Society for Therapeutic Radiology and Oncology</td>
<td></td>
</tr>
<tr>
<td>Jet and Rocket Fuels</td>
<td></td>
</tr>
<tr>
<td>Jimmy Fund</td>
<td></td>
</tr>
<tr>
<td>Johnson &amp; Johnson (United States)</td>
<td></td>
</tr>
<tr>
<td>Jordan</td>
<td></td>
</tr>
<tr>
<td>K</td>
<td></td>
</tr>
<tr>
<td>Kaposi’s Sarcoma</td>
<td></td>
</tr>
<tr>
<td>Kazakhstan</td>
<td></td>
</tr>
<tr>
<td>Kenya</td>
<td></td>
</tr>
<tr>
<td>Kidney (Renal Cell) Cancer</td>
<td></td>
</tr>
<tr>
<td>Kidney Cancer, Childhood</td>
<td></td>
</tr>
<tr>
<td>Kidney Cancer Association</td>
<td></td>
</tr>
<tr>
<td>Kimmel Cancer Center</td>
<td></td>
</tr>
<tr>
<td>Kyrgyzstan</td>
<td></td>
</tr>
<tr>
<td>L</td>
<td></td>
</tr>
<tr>
<td>Laos</td>
<td></td>
</tr>
<tr>
<td>Laryngeal Cancer</td>
<td></td>
</tr>
</tbody>
</table>
List of Articles

Laryngeal Cancer, Childhood
Latitude
Lead
Leukemia, Acute Lymphoblastic, Adult
Leukemia, Acute Lymphoblastic, Childhood
Leukemia, Acute Myeloid, Adult
Leukemia, Acute Myeloid, Childhood
Leukemia, Chronic Lymphocytic
Leukemia, Chronic Myelogenous
Leukemia, Hairy Cell
Leukemia & Lymphoma Society
Libya
Liver Cancer, Adult (Primary)
Liver Cancer, Childhood (Primary)
Lombardi Comprehensive Cancer Center
Lung Cancer, Non–Small Cell
Lung Cancer, Small Cell
Lymphoma, AIDS-Related
Lymphoma, Burkitt’s
Lymphoma, Hodgkin’s, Adult
Lymphoma, Hodgkin’s, Childhood
Lymphoma, Hodgkin’s, During Pregnancy
Lymphoma, Non-Hodgkin’s, Adult
Lymphoma, Non-Hodgkin’s, Childhood
Lymphoma, Non-Hodgkin’s, During Pregnancy
Lymphoma, Primary Central Nervous System
Lymphoma Research Foundation of America

M
Madagascar
Malawi
Malaysia
Mali
Malignant Fibrous Histiocytoma of Bone/Osteosarcoma
Marketing, Drug
Marketing, Hospitals and Clinics
Massachusetts Medical Society
Massey Cancer Center
Mayo Clinic Cancer Center
Mayo Clinic Cancer Center, Jacksonville
Mayo Clinic Cancer Center, Scottsdale
Meat, Cooking
Meat Processing
Media
Medicare and Medicaid
MedImmune (United States)
Melanoma
Melanoma, Intraocular (Eye)
Memorial Sloan Kettering Cancer Center
Menarche, Early
Merck (Germany)
Merck & Co. (United States)
Merkel Cell Carcinoma
Mesothelioma, Adult Malignant
Mesothelioma, Childhood
Mexico
MIT Center for Cancer Research
Moldova
Morocco
Mozambique
Mozambique
Multiple Endocrine Neoplasia Syndrome, Childhood
Multiple Myeloma/Plasma Cell Neoplasm
Mycosis Fungoides
Myelodysplastic Syndromes
Myelodysplastic/Myeloproliferative Diseases
Myeloma, Multiple
Myeloproliferative Disorders, Chronic

N
Nasopharyngeal Cancer
Nasopharyngeal Cancer, Childhood
National Alliance of Breast Cancer Organizations
National Cancer Institute
National Cancer Policy Board
National Cancer Registrars Association
National Childhood Cancer Foundation
National Marrow Donor Program
Natural Causes of Cancer
Nepal
Netherlands
Netherlands Cancer Institute
Netherlands Hemophilia Patients Society
Neuroblastoma
Neutrons
New Zealand
Nicaragua
Nickel Compounds
Niger
Nigeria
Nixon, Richard (War on Cancer)
North American Association of Central Cancer Registries
North Korea
Norway
Novartis Group (Switzerland)
Novo Nordisk (Denmark)
Nuclear Industry

O
Obesity
Occupational Therapy
Ohio State University Comprehensive Cancer Center
OHSU Knight Cancer Institute
Oncology Nursing Society
Ono Pharmaceutical (Japan)
Oral Cancer, Childhood
Oral Cavity Cancer, Lip and
Organisation of European Cancer Institutes
Oropharyngeal Cancer
Ovarian Cancer, Childhood
Ovarian Epithelial Cancer
Ovarian Germ Cell Tumor
Ovarian Low Malignant Potential Tumor

P
Pain and Pain Management
Paint
Pakistan
Pancreatic Cancer
Pancreatic Cancer, Childhood
Pancreatic Cancer, Islet Cell
Paper Industry
Papua New Guinea
Paraguay
Paranasal Sinus and Nasal Cavity Cancer
Parathyroid Cancer
Passive Smoking
Penile Cancer
Perfume
Perlmutter Cancer Center
Peru
Pesticides
Pfizer (United States)
Pharmaceutical Industry
Phaeochromocytoma
Philippines
Photodynamic Therapy
Physical Therapy
Pineoblastoma and Supratentorial Primitive Neuroectodermal, Childhood
Pinkel, Donald
Pituitary Tumor
Plasma Cell Neoplasm/Multiple Myeloma
Plastics Industry

Pleuropulmonary Blastoma
Poland
Polishes
Pollution, Air
Pollution, Water
Portugal
Poverty
Prostate Cancer
Proton Therapy
Psychosocial Care/Support
Purdue University Center for Cancer Research

R
Radiation
Radiation, Gamma
Radiation, Ionizing
Radiation Therapy
Raloxifene
Rectal Cancer
Religion
Religion: Jewish Women and Cancer Risk
Religion: Meditation and Risk
Religion: Preventability Versus Preordained
Religion: Use of Interventions
Retinoblastoma
Rhabdomyosarcoma, Childhood
Roche Group (Switzerland)
Romania
Rosenberg, Barnett
Roswell Park Cancer Institute
Russia
Rwanda

S
Salivary Gland Cancer
Salivary Gland Cancer, Childhood
Salk Institute for Biological Studies
Sanford-Burnham Medical Research Institute
Sarcoma, Ewing's Family of Tumors
Sarcoma, Soft Tissue, Adult
Sarcoma, Soft Tissue, Childhood
Sarcoma, Uterine
Sarcoma Foundation of America
Saudi Arabia
Screening
Screening, Access to
Sedentary Occupations
Selenium
Senegal
Serbia
Sex
Sézary Syndrome
Shire UK
Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins
Sierra Leone
Singapore
Singapore Cancer Society
Siteman Cancer Center
Skin Cancer, Childhood
Skin Cancer, Melanoma
Skin Cancer, Non-Melanoma
Skin Carcinoma, Merkel Cell
Skipper, Howard E.
Slovakia
Small Intestine Cancer
Smokeless Tobacco
Smoking and Society
Smoking Cessation
Society of Gynecologic Oncology
Society of Surgical Oncology
Solar Radiation
Solvents
Somalia
South Africa
South Korea
Spain
Squamous Neck Cancer With Occult Primary, Metastatic
Sri Lanka
St. Jude Children’s Research Hospital
Stainless Steel
Statistics
Stomach (Gastric) Cancer
Stomach (Gastric) Cancer, Childhood
Stress
Sudan
Sun Exposure (Australia)
Sunlamps or Sunbeds, Exposure to Sunscreen
Surgery
Survivors of Cancer
Survivors of Cancer, Families of Sweden
Switzerland
Syria

T
Taisho Pharmaceutical (Japan)
Taiwan
Tajikistan
Takeda Pharmaceutical (Japan)
Tamoxifen
Tanzania
Taxation
Technology, Imaging
Technology, New Therapies
Terry, Luther
Testicular Cancer
Textile Dyes
Thailand
Thymoma, Childhood
Thymoma and Thymic Carcinoma
Thyroid Cancer
Thyroid Cancer, Childhood
Tobacco in History
Tobacco Smoking
Tobacco-Related Exposures
Togo
Town Plans
Toxic Mold
Transportation
Trichopoulos, Dimitrios
Trophoblastic Tumor, Gestational
Tunisia
Turkey
Turkish Society of Haematology
Turkmenistan

U
Uganda
Ukraine
Ultraviolet A Radiation
Ultraviolet B Radiation
Ultraviolet C Radiation
Ultraviolet Radiation Related Exposures
Union for International Cancer Control
United Arab Emirates
United Kingdom
United States
University of Alabama at Birmingham Comprehensive Cancer Center
University of California, Davis, Comprehensive Cancer Center
University of California, Los Angeles, Jonsson Comprehensive Cancer Center
University of California, San Francisco, Helen Diller Family Comprehensive Cancer Center
University of Chicago Medicine Comprehensive Cancer Center
Alternative Treatments and Therapies
Alternative Therapy: Diet and Nutrition
Alternative Therapy: Herbs, Vitamins, and Minerals
Alternative Therapy: Manual Healing and Physical Touch
Alternative Therapy: Mind, Body, and Spirit
Alternative Therapy: Pharmacological and Biological Treatment

Associations by Cancer Type
American Brain Tumor Association
American College of Gastroenterology
American Lung Association
Association for the Cure of Cancer of the Prostate
Candlelighters Childhood Cancer Foundation
Carcinoid Cancer Foundation
Childhood Brain Tumor Foundation
International Myeloma Foundation
Kidney Cancer Association
Lymphoma Research Foundation of America
National Alliance of Breast Cancer Organization
National Childhood Cancer Foundation
National Marrow Donor Program
Sarcoma Foundation of America
Yul Brynner Head and Neck Cancer Foundation (Head and Neck Cancer Alliance)

Associations: Others
American Academy of Pediatrics, Section on Hematology/Oncology
American Association for Cancer Education
American Association for Cancer Research
American Brain Tumor Association
American College of Radiation Oncology
American Joint Committee on Cancer
American Psychosocial Oncology Society
American Society for Radiation Oncology
American Society of Hematology
American Society of Pediatric Hematology/Oncology
Association of Community Cancer Centers
Association of Freestanding Radiation Oncology Centers
Association of Oncology Social Work
Association of Pediatric Hematology/Oncology Nurses
California Blood Bank Society
Canadian Association of Medical Oncologists
Canadian Association of Pharmacy and Oncology
Canadian Cancer Society
Canadian Red Cross
Canadian Society of Surgical Oncology
Canadian Urologic Oncology Group
Cancer Association of South Africa
Danish Cancer Society
Europa Donna, the European Breast Cancer Coalition
European Association for Cancer Research
European Cancer Organisation
European CanCer Prevention
European Society for Therapeutic Radiology and Oncology
European Society of Mastology
European Society of Surgical Oncology
Haemophilia Society (United Kingdom)
Hong Kong Anti-Cancer Society
International Agency for Research on Cancer
International Association for the Study of Lung Cancer
International Association of Cancer Registries
International Committee of Red Cross
International Myeloma Foundation
International Psycho-Oncology Society
International Society for Cutaneous Lymphomas
International Society for Preventive Oncology
International Society of Experimental Hematology
International Society of Nurses in Cancer Care
International Society of Paediatric Oncology
International Society on Thrombosis and Haemostasis
Irish Cancer Society
Japan Lung Cancer Society
Japanese Cancer Association
Japanese Gastric Cancer Association
Japanese Society for Therapeutic Radiology and Oncology
Lymphoma Research Foundation of America
National Alliance of Breast Cancer Organizations
National Cancer Policy Board
National Cancer Registrars Association
National Marrow Donor Program
Netherlands Hemophilia Patients Society
North American Association of Central Cancer Registries
Oncology Nursing Society
Organization of European Cancer Institutes
Society of Gynecology Oncologists
Society of Surgical Oncology
Turkish Society of Haematology
Union for International Cancer Control
World Health Organization

Business of Cancer
Abbott Laboratories (United States)
Allergan (United States)
Amgen (United States)
Astellas Pharma (Japan)
AstraZeneca (United Kingdom)
Bristol-Myers Squibb (United States)
Celgene (United States)
Cost of Therapy
Daiichi Sankyo (Japan)
Eisai (Japan)
Eli Lilly & Co. (United States)
Forest Labs (United States)
Genentech
Genzyme (United States)
GlaxoSmithKline (United Kingdom)
H. Lundbeck (Denmark)
Johnson & Johnson (United States)
Marketing, Drug
Marketing, Hospitals and Clinics
MedImmune (United States)
Merck (Germany)
Merck & Co. (United States)
Novartis Group (Switzerland)
Novo Nordisk (Denmark)
Ono Pharmaceutical (Japan)
Pfizer (United States)
Roche Group (Switzerland)
Shire UK
Taisho Pharmaceutical (Japan)
Takeda Pharmaceutical (Japan)

Cancer Around the World
Afghanistan
Algeria
Angola
Argentina
Australia
Austria
Azerbaijan
Bangladesh
Belarus
Belgium
Benin
Bolivia
Brazil
Bulgaria
Burkina Faso
Burma (Myanmar)
<table>
<thead>
<tr>
<th>Country</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burundi</td>
<td>Mali</td>
</tr>
<tr>
<td>Cambodia</td>
<td>Mexico</td>
</tr>
<tr>
<td>Cameroon</td>
<td>Moldova</td>
</tr>
<tr>
<td>Canada</td>
<td>Morocco</td>
</tr>
<tr>
<td>Central African Republic</td>
<td>Mozambique</td>
</tr>
<tr>
<td>Chad</td>
<td>Nepal</td>
</tr>
<tr>
<td>Chile</td>
<td>Netherlands</td>
</tr>
<tr>
<td>China</td>
<td>New Zealand</td>
</tr>
<tr>
<td>Colombia</td>
<td>Nicaragua</td>
</tr>
<tr>
<td>Congo, Democratic Republic</td>
<td>Niger</td>
</tr>
<tr>
<td>Costa Rica</td>
<td>Nigeria</td>
</tr>
<tr>
<td>Côte d’Ivoire</td>
<td>North Korea</td>
</tr>
<tr>
<td>Croatia</td>
<td>Norway</td>
</tr>
<tr>
<td>Cuba</td>
<td>Pakistan</td>
</tr>
<tr>
<td>Czech Republic</td>
<td>Papua New Guinea</td>
</tr>
<tr>
<td>Denmark</td>
<td>Paraguay</td>
</tr>
<tr>
<td>Dominican Republic</td>
<td>Peru</td>
</tr>
<tr>
<td>Ecuador</td>
<td>Philippines</td>
</tr>
<tr>
<td>Egypt</td>
<td>Poland</td>
</tr>
<tr>
<td>El Salvador</td>
<td>Portugal</td>
</tr>
<tr>
<td>Eritrea</td>
<td>Romania</td>
</tr>
<tr>
<td>Ethiopia</td>
<td>Russia</td>
</tr>
<tr>
<td>Finland</td>
<td>Rwanda</td>
</tr>
<tr>
<td>France</td>
<td>Saudi Arabia</td>
</tr>
<tr>
<td>Georgia</td>
<td>Senegal</td>
</tr>
<tr>
<td>Germany</td>
<td>Serbia</td>
</tr>
<tr>
<td>Ghana</td>
<td>Sierra Leone</td>
</tr>
<tr>
<td>Greece</td>
<td>Singapore</td>
</tr>
<tr>
<td>Guatemala</td>
<td>Slovakia</td>
</tr>
<tr>
<td>Guinea</td>
<td>Somalia</td>
</tr>
<tr>
<td>Haiti</td>
<td>South Africa</td>
</tr>
<tr>
<td>Honduras</td>
<td>South Korea</td>
</tr>
<tr>
<td>Hungary</td>
<td>Spain</td>
</tr>
<tr>
<td>India</td>
<td>Sri Lanka</td>
</tr>
<tr>
<td>Indonesia</td>
<td>Sudan</td>
</tr>
<tr>
<td>Iran</td>
<td>Sweden</td>
</tr>
<tr>
<td>Iraq</td>
<td>Switzerland</td>
</tr>
<tr>
<td>Ireland, Republic of</td>
<td>Syria</td>
</tr>
<tr>
<td>Israel</td>
<td>Taiwan</td>
</tr>
<tr>
<td>Italy</td>
<td>Tajikistan</td>
</tr>
<tr>
<td>Japan</td>
<td>Tanzania</td>
</tr>
<tr>
<td>Jordan</td>
<td>Thailand</td>
</tr>
<tr>
<td>Kazakhstan</td>
<td>Togo</td>
</tr>
<tr>
<td>Kenya</td>
<td>Tunisia</td>
</tr>
<tr>
<td>Kyrgyzstan</td>
<td>Turkey</td>
</tr>
<tr>
<td>Laos</td>
<td>Turkmenistan</td>
</tr>
<tr>
<td>Madagascar</td>
<td>Uganda</td>
</tr>
<tr>
<td>Libya</td>
<td>Ukraine</td>
</tr>
<tr>
<td>Malawi</td>
<td>United Arab Emirates</td>
</tr>
<tr>
<td>Malaysia</td>
<td>United Kingdom</td>
</tr>
</tbody>
</table>
United States  Uzbekistan  Venezuela  Vietnam  Yemen  Zambia  Zimbabwe  

**Cancer in Society**  

**Known or Suspected Carcinogens/Causes of Cancer**  
Acrylic Rubber and Fibers  Aerospace Industry  Age  Alcohol  Antibiotics  Anticancer Drugs  Battery Acid  Broad-Spectrum Ultraviolet (UV) Radiation  Chemical Industry  Chemotherapy  Chloroform  Coal Industry  DDT  Deodorizers  Detergents  Diesel Exhaust  Disinfectants and Antiseptics  Dyes and Pigments  Electrical Industry  Embalming Fluids  Environmental Tobacco Smoke  Estrogen, Steroidal  Experimental Cancer Drugs  Explosives  Family Size
Flame Retardant
Flavoring Agents
Freon
Gasoline
Genetics
Glass Industry
Hair Dye
Hepatitis B
Hepatitis C
Herbicide
Immigrant Populations
Infection
Insecticides
Jet and Rocket Fuels
Latitude
Lead
Meat, Cooking
Natural Causes of Cancer
Neutrons
Nickel Compounds
Nuclear Industry
Obesity
Paint
Paper Industry
Passive Smoking
Perfume
Pesticides
Pharmaceutical Industry
Plastics Industry
Polishes
Radiation, Gamma
Radiation, Ionizing
Smokeless Tobacco
Solar Radiation
Solvents
Stainless Steel
Sunlamps or Sunbeds, Exposure to
Textile Dyes
Tobacco-Related Exposures
Tobacco Smoking
Toxic Mold
Ultraviolet A Radiation
Ultraviolet B Radiation
Ultraviolet C Radiation
Ultraviolet Radiation Related Exposures
Vinyl
War Gases and Chemicals
Water Treatment
Wax and Soap
Wood Dust
Wood Preserver
X-Rays

**Major Cancer Associations**
American Association for Cancer Research
American Cancer Society
American Society of Clinical Oncology
Association of Cancer Online Resources
Association of Community Cancer Centers
Cancer Therapy Evaluation Program
International Cancer Alliance for Research and Education
Massachusetts Medical Society
National Cancer Institute
National Cancer Registrars Association
Union for International Cancer Control
World Health Organization

**Major Hospitals and Treatment Centers**
Albert Einstein Cancer Center
Barbara Ann Karmanos Cancer Institute
Chao Family Comprehensive Cancer Center
City of Hope
Cold Spring Harbor Laboratory
Comprehensive Cancer Center of Wake Forest University
Dana-Farber Cancer Institute
Duke Cancer Institute
Fox Chase Cancer Center
Fred & Pamela Buffett Cancer Center
Fred Hutchinson Cancer Research Center
Herbert Irving Comprehensive Cancer Center
Holden Comprehensive Cancer Center at the University of Iowa
Huntsman Cancer Institute
Ireland (Ohio) Cancer Center
Jimmy Fund (DFCI)
Kimmel Cancer Center
Lombardi Comprehensive Cancer Center
Massey Cancer Center
Mayo Clinic Cancer Center
Mayo Clinic Cancer Center, Jacksonville
Mayo Clinic Cancer Center, Scottsdale
Memorial Sloan-Kettering Cancer Center
MIT Center for Cancer Research
National Cancer Institute
Ohio State University Comprehensive Cancer Center
OHSU Knight Cancer Institute
Purdue University Center for Cancer Research
Roswell Park Cancer Institute
Salk Institute for Biological Studies
Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins
Siteman Cancer Center
St. Jude Children’s Research Hospital
University of Alabama at Birmingham
Comprehensive Cancer Center
University of California, Davis, Comprehensive Cancer Center
University of California, Los Angeles, Jonsson Comprehensive Cancer Center
University of California, San Francisco, Helen Diller Family Comprehensive Cancer Center
University of Chicago Medicine Comprehensive Cancer Center
University of Colorado Cancer Center
University of Hawai’i Cancer Center
University of Michigan Comprehensive Cancer Center
University of Minnesota Masonic Cancer Center
University of New Mexico Cancer Research and Treatment Center
University of North Carolina Lineberger Comprehensive Cancer Center
University of Pittsburgh Cancer Institute
University of Southern California Norris Comprehensive Cancer Center
University of Texas MD Anderson Cancer Center
University of Virginia Cancer Center
University of Wisconsin Carbone Cancer Center
Vanderbilt-Ingram Cancer Center
Vermont Cancer Center
Wistar Institute
Yale Cancer Center

Prevention
Aspirin
Beta-Carotene
Calcium
Chemoprevention
COX-2 Inhibitors
Raloxifene
Screening
Screening, Access to
Selenium
Smoking Cessation

Tamoxifen
Taxation
Vaccines
Vitamins

Treatments and Therapies
Biologic Therapy
Bone Marrow Transplants
Cancer Drugs, Cost and Benefits of Chemotherapy
Clinical Trials
Gene Therapy
Hospice Care
Pain and Pain Management
Photodynamic Therapy
Proton Therapy
Radiation Therapy
Surgery

Types of Cancer
Adrenocortical Carcinoma
Adrenocortical Carcinoma, Childhood
AIDS-Related Cancers
Anal Cancer
Bile Duct Cancer, Extrahepatic
Bladder Cancer
Bladder Cancer, Childhood
Bone Cancer, Osteosarcoma/Malignant Fibrous Histiocytoma
Brain Stem Glioma, Childhood
Brain Tumor, Adult
Brain Tumor, Cerebellar Astrocytoma, Childhood
Brain Tumor, Cerebral Astrocytoma/Malignant Glioma, Childhood
Brain Tumor, Medulloblastoma, Childhood
Brain Tumor, Supratentorial Primitive Neuroectodermal, Childhood
Brain Tumor, Visual Pathway and Hypothalamic Glioma, Childhood
Breast Cancer
Breast Cancer, Male
Breast Cancer and Pregnancy
Bronchial Adenomas/Carcinoids, Childhood
Carcinoid Tumor, Childhood
Carcinoid Tumor, Gastrointestinal
Carcinoma of Unknown Primary
Central Nervous System Lymphoma, Primary
Cervical Cancer
Childhood Cancers
Colon Cancer
<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Cancer Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorectal Cancer, Childhood</td>
<td>Multiple Endocrine Neoplasia Syndrome, Childhood</td>
</tr>
<tr>
<td>Endometrial Cancer</td>
<td>Multiple Myeloma/Plasma Cell Neoplasm</td>
</tr>
<tr>
<td>Ependymoma, Childhood</td>
<td>Mycosis Fungoides</td>
</tr>
<tr>
<td>Esophageal Cancer</td>
<td>Myelodysplastic Syndromes</td>
</tr>
<tr>
<td>Esophageal Cancer, Childhood</td>
<td>Myelodysplastic/Myeloproliferative Diseases</td>
</tr>
<tr>
<td>Ewing’s Family of Tumors</td>
<td>Myeloma, Multiple</td>
</tr>
<tr>
<td>Extracranial Germ Cell Tumor, Childhood</td>
<td>Myeloproliferative Disorders, Chronic</td>
</tr>
<tr>
<td>Extragonadal Germ Cell Tumor</td>
<td>Nasopharyngeal Cancer</td>
</tr>
<tr>
<td>Gallbladder Cancer</td>
<td>Nasopharyngeal Cancer, Childhood</td>
</tr>
<tr>
<td>Gestational Trophoblastic Tumor</td>
<td>Neuroblastoma</td>
</tr>
<tr>
<td>Head and Neck Cancer</td>
<td>Oral Cancer, Childhood</td>
</tr>
<tr>
<td>Hepatocellular (Liver) Cancer, Adult (Primary)</td>
<td>Oral Cavity Cancer, Lip and Oropharyngeal Cancer</td>
</tr>
<tr>
<td>Hepatocellular (Liver) Cancer, Childhood (Primary)</td>
<td>Ovarian Cancer, Childhood</td>
</tr>
<tr>
<td>Hypopharyngeal Cancer</td>
<td>Ovarian Epithelial Cancer</td>
</tr>
<tr>
<td>Hypothalamic and Visual Pathway</td>
<td>Ovarian Germ Cell Tumor</td>
</tr>
<tr>
<td>Glioma, Childhood</td>
<td>Ovarian Low Malignant Potential Tumor</td>
</tr>
<tr>
<td>Intraocular Melanoma</td>
<td>Pancreatic Cancer</td>
</tr>
<tr>
<td>Islet Cell Carcinoma (Endocrine Pancreas)</td>
<td>Pancreatic Cancer, Childhood</td>
</tr>
<tr>
<td>Kaposi's Sarcoma</td>
<td>Pancreatic Cancer, Islet Cell</td>
</tr>
<tr>
<td>Kidney Cancer, Childhood</td>
<td>Paranasal Sinus and Nasal Cavity Cancer</td>
</tr>
<tr>
<td>Kidney (Renal Cell) Cancer</td>
<td>Parathyroid Cancer</td>
</tr>
<tr>
<td>Laryngeal Cancer</td>
<td>Penile Cancer</td>
</tr>
<tr>
<td>Laryngeal Cancer, Childhood</td>
<td>Pheochromocytoma</td>
</tr>
<tr>
<td>Leukemia, Acute Lymphoblastic, Adult</td>
<td>Pineoblastoma and Supratentorial Primitive Neuroectodermal, Childhood</td>
</tr>
<tr>
<td>Leukemia, Acute Lymphoblastic, Childhood (Primary)</td>
<td>Pituitary Tumor</td>
</tr>
<tr>
<td>Leukemia, Acute Myeloid, Adult</td>
<td>Plasma Cell Neoplasm/Multiple Myeloma</td>
</tr>
<tr>
<td>Leukemia, Acute Myeloid, Childhood</td>
<td>Pleuropulmonary Blastoma</td>
</tr>
<tr>
<td>Leukemia, Chronic Lymphocytic</td>
<td>Prostate Cancer</td>
</tr>
<tr>
<td>Leukemia, Chronic Myelogenous</td>
<td>Rectal Cancer</td>
</tr>
<tr>
<td>Leukemia, Hairy Cell</td>
<td>Retinoblastoma</td>
</tr>
<tr>
<td>Liver Cancer, Adult (Primary)</td>
<td>Rhabdomyosarcoma, Childhood</td>
</tr>
<tr>
<td>Liver Cancer, Childhood (Primary)</td>
<td>Salivary Gland Cancer</td>
</tr>
<tr>
<td>Lung Cancer, Non–Small Cell</td>
<td>Salivary Gland Cancer, Childhood</td>
</tr>
<tr>
<td>Lung Cancer, Small Cell</td>
<td>Sarcoma, Ewing’s Family of Tumors</td>
</tr>
<tr>
<td>Lymphoma, AIDS-Related</td>
<td>Sarcoma, Soft Tissue, Adult</td>
</tr>
<tr>
<td>Lymphoma, Burkitts</td>
<td>Sarcoma, Soft Tissue, Childhood</td>
</tr>
<tr>
<td>Lymphoma, Hodgkin’s, Adult</td>
<td>Sarcoma, Uterine</td>
</tr>
<tr>
<td>Lymphoma, Hodgkin’s, Childhood</td>
<td>Sézary Syndrome</td>
</tr>
<tr>
<td>Lymphoma, Hodgkin’s, During Pregnancy</td>
<td>Skin Cancer, Childhood</td>
</tr>
<tr>
<td>Lymphoma, Non-Hodgkin’s, Adult</td>
<td>Skin Cancer, Melanoma</td>
</tr>
<tr>
<td>Lymphoma, Non-Hodgkin’s, Childhood</td>
<td>Skin Cancer, Non-Melanoma</td>
</tr>
<tr>
<td>Lymphoma, Non-Hodgkin’s, During Pregnancy</td>
<td>Skin Carcinoma, Merkel Cell</td>
</tr>
<tr>
<td>Lymphoma, Primary Central Nervous System</td>
<td>Small Intestine Cancer</td>
</tr>
<tr>
<td>Malignant Fibrous Histiocytoma of Bone/Osteosarcoma</td>
<td>Squamous Neck Cancer With Occult Primary, Metastatic</td>
</tr>
<tr>
<td>Melanoma</td>
<td>Stomach (Gastric) Cancer</td>
</tr>
<tr>
<td>Melanoma, Intraocular (Eye)</td>
<td>Stomach (Gastric) Cancer, Childhood</td>
</tr>
<tr>
<td>Merkel Cell Carcinoma</td>
<td></td>
</tr>
<tr>
<td>Mesothelioma, Adult Malignant</td>
<td></td>
</tr>
<tr>
<td>Mesothelioma, Childhood</td>
<td></td>
</tr>
<tr>
<td>Testicular Cancer</td>
<td>Urethral Cancer</td>
</tr>
<tr>
<td>--------------------------------------------------------</td>
<td>-------------------------------------------------------</td>
</tr>
<tr>
<td>Thymoma, Childhood</td>
<td>Uterine Cancer, Endometrial</td>
</tr>
<tr>
<td>Thymoma and Thymic Carcinoma</td>
<td>Uterine Sarcoma</td>
</tr>
<tr>
<td>Thyroid Cancer</td>
<td>Vaginal Cancer</td>
</tr>
<tr>
<td>Thyroid Cancer, Childhood</td>
<td>Visual Pathway and Hypothalamic Glioma, Childhood</td>
</tr>
<tr>
<td>Trophoblastic Tumor, Gestational</td>
<td></td>
</tr>
<tr>
<td>Unknown Primary Site, Cancer of, Childhood</td>
<td>Vulvar Cancer</td>
</tr>
<tr>
<td>Unknown Primary Site, Carcinoma of, Adult</td>
<td>Waldenström’s Macroglobulinemia</td>
</tr>
<tr>
<td>Unusual Cancers of Childhood</td>
<td>Wilms’ Tumor</td>
</tr>
<tr>
<td>Ureter and Renal Pelvis, Transitional Cell Cancer</td>
<td>Women’s Cancers</td>
</tr>
</tbody>
</table>
About the Editor

Graham A. Colditz, M.D., Dr.PH, is Niess-Gain Professor of Surgery, and associate director of Prevention and Control at the Siteman Cancer Center, Washington University School of Medicine, in St. Louis, Missouri. He received his B.Sc., MBBS, and M.D. from the University of Queensland, Australia, and his doctorate in public health from the Harvard University School of Public Health.

From 1996 to 2006, Colditz was the principal investigator of the Nurses’ Health Study, one of the largest prospective investigations of factors that influence women’s health. He founded the Growing Up Today study (GUTS), which focuses on the diet and lifestyle of 16,883 adolescents. His epidemiologic research addresses issues of etiology and potential for prevention of chronic diseases, largely among women. He continues to pursue approaches to the translation of epidemiologic data to improve risk stratification and tailor prevention messages and screening strategies.

After 23 years at Harvard University, Colditz joined the Washington University School of Medicine, where he is now chief of the Division of Public Health Sciences in the Department of Surgery. He also serves as program director for the School of Medicine’s Master of Population Health Sciences degree.

With a commitment to identifying preventable causes of chronic disease among women and adolescents, Colditz continues to study benign breast disease and other markers for risk of breast cancer. He leads studies of adolescent diet, activity, and growth in relation to risk of benign lesions as well as invasive breast cancer. Colditz developed the award-winning Your Disease Risk Web site, which communicates tailored prevention messages to the public. He has published over 950 peer-reviewed publications, six books, and contributed to six reports for the Institute of Medicine, National Academy of Sciences.

Colditz has served in numerous leadership roles. He was the editor-in-chief of the journal Cancer Causes and Control and has contributed to reports of the U.S. Surgeon General on Tobacco and Health. He has served on several committees for the National Academy of Science and is a member of the Board of Scientific Advisors of the National Cancer Institute, among others.

In October 2006, on the basis of professional achievement and commitment to public health, Colditz was elected to membership of the Institute of Medicine, an independent body that advises the U.S. government on issues affecting public health. In 2011, he was awarded the American Cancer Society Medal of Honor for cancer control research. In 2012, he received the AACR-American Cancer Society Award for Research Excellence in Cancer Epidemiology and Prevention. In 2014, he was the recipient of the ASCO-American Cancer Society award and lecture.
List of Contributors

Maysa Abu-Khalaf
Yale Cancer Center
Lalatendu Acharya
Purdue University
Samuel Ojima Adejoh
University of Lagos
Amber Afzal
Independent Scholar
Mohamad Reza Aghanoori
Shiraz University of Medical Sciences
Ainur Akilzhanova
Nazarbayev University
Kenneth B. Alexander
Independent Scholar
Ali Al-Jumaili
University of Iowa
Gordon Alley-Young
Kingsborough Community College
Samantha Armstrong
Indiana University School of Medicine
Jin R. Baker
Health and Food Institute
Poonam Bala
Cleveland State University and University of South Africa
Poonam Balani
Independent Scholar
Paula K. Baldwin
Western Oregon University
Linda Barley
York College, University of New York
Barbara A. Barton
Western Michigan State University
Joan Beder
Yeshiva University
Kourosh Beroukhim
David Geffen School of Medicine at UCLA
Arundhati Bhattacharyya
Bhairab Ganguly College,
West Bengal State University
Anca Nicoleta Birzescu
Bowling Green State University
Jessica Bodoh-Creed
California State University, Los Angeles
Sarah E. Boslaugh
Saint Louis University
Kathryn Bouskill
Emory University
Andrew Robert Branagan
Yale Medical School
Brent Braveman
University of Texas MD Anderson Cancer Center
Benjamin Wilson Brewer
University of Colorado, Denver
Sherri Brown
Case Western Reserve University
William J. Brown
Regent University
Claudio Butticè
Independent Scholar
Leon James Bynum
Columbia University
Whitney Cann
Independent Scholar
John M. Carethers
University of Michigan, Ann Arbor
Catherine Cassara
Bowling Green State University
Melany Chambers
Georgia State University
Yung-Chia Chen
Kaohsiung Medical University
Liang Chen
Nanyang Technological University
Felix O. Chima
Prairie View A&M University
Mahati Chittem
Indian Institute of Technology Hyderabad
Elisia L. Cohen
University of Kentucky
Holly Cole-Hawkins
University of Bristol
Hope Comer
Old Dominion University
Alberto Costa
European School of Oncology
Jaslynn Cuff
North Carolina Central University
Karim Daliri
Shiraz University of Medical Sciences
George Dion Daniel
University of North Carolina at Wilmington
Rachel Diana Davidson
University of Wisconsin–Milwaukee
Lenna Dawkins-Moultin
Texas A&M University
Gary T. Deimling
Case Western Reserve University
David Delulius
Duquesne University
Ann Del Bianco
York University
Joseph Dewey
Broward College
Anh-Vu Do
University of Iowa
Catherine A. Dobris
Indiana University–Purdue University
Constance M. Dolecki
Independent Scholar
Eamon Duffy
Yale School of Medicine
David Dunning
University of Nebraska Medical Center
Arthur Durazo
University of California, Merced
Emad Abdulhamid Eddokali
Independent Scholar
Christopher Edwards
Duke University Medical Center
Sothy Eng
Comparative International Education
Ezgi Eyüboglu
Maltepe University
Navid Ezra
Indiana University School of Medicine
Natalia Fernández Diaz-Cabal
Free University of Barcelona
Cindy Ferraino
Independent Scholar
Diane Ferrero-Paluzzi
Iona College
Courtney Vail Fletcher
University of Portland
Michael Fox
Independent Scholar
Marcos E. García-Ojeda
University of California, Merced
Sean Geary
University of Iowa
Sana Ghafoor
Independent Scholar
Aubrey Gilbert
Harvard Medical School
Joy V. Goldsmith
University of Memphis
Ellen L. Goode
Mayo Clinic College of Medicine
William B. Grant
Sunlight, Nutrition, and Health Research Center
Tiarra Green
North Carolina Central University
Matthew J. Gritter
Angelo State University
Terje Grønning
University of Oslo
Jessica Smartt Gullion
Texas Woman’s University
Emily Joy Haas
National Institute for
Occupational
Safety and Health
Carin Halper
Independent Researcher
Chelsea Halstead
University of Portland
Lynn Marie Hamilton
Independent Scholar
Emily Hammad
University of Colorado Denver
Jessica Anne Hammer
Independent Scholar
Zachary Hargis
Old Dominion University
Joy L. Hart
University of Louisville
Katharine J. Head
Indiana University-Purdue
University Indianapolis
Thomas L. Head
Edith Cowan University
James R. Hebert
University of South Carolina
Trina Henry
University of Texas MD Anderson
Cancer Center
Steven Charles Hertler
College of New Rochelle
Justina D. Higgins
Independent Scholar
LaBarron K. Hill
Duke University Medical Center
Lisa Hines
Wichita State University
Servando Z. Hinojosa
University of Texas–Rio
Grande Valley
Shirley S. Ho
Nanyang Technological University
Denise Hooks-Anderson
Saint Louis University
Elaine Hsieh
University of Oklahoma
Sherry C. Huang
University of California,
San Diego
Anne Hubbell
New Mexico State University
Andrew Jon Hund
United Arab Emirates University
Jessica A. Hutchins
Independent Scholar
Nicholas T. Iannarino
University of Michigan–Dearborn
Godfrey Ilonzo
Independent Scholar
Qurratulain Muhammad Iqbal
Heart and Vascular Institute
Nicholas Reed Iverson
Albert Einstein College of Medicine
Margret Jaeger
UMIT University for Health Sciences,
Medical Informatics and Technology
Constance J. Jeffery
University of Illinois at Chicago
Huei Wang Anna Jeng
Old Dominion University
Jakob Daniel Jensen
University of Utah
Vinit K. Jha
Old Dominion University
Ami P. Jhaveri
Yale Smilow Cancer Center
Keith R. Johnson
Oakton Community College
David Jourabchi
University of California,
Los Angeles
School of Dentistry
Natanel Jourabchi
Johns Hopkins School of Medicine
René Julyan
Independent Scholar
Boaz Kahana
Cleveland State University
Eva Kahana
Case Western Reserve University
Hagop Kantarjian
University of Texas MD Anderson
Cancer Center
David Keleti
Independent Scholar
Sarah Kelleher  
*Duke University Medical Center*

Amanda Kenny  
*La Trobe University Rural Health School*

Abigail Keys  
*Duke University Medical Center*

Saami Khalifian  
*Johns Hopkins School of Medicine*

Ghulam Ishaq Khan  
*Columbia University*

Behnoush Khorsand  
*University of Iowa*

Ivana K. Kim  
*Harvard Medical School*

Susan Knox  
*Europa Donna, the European Breast Cancer Coalition*

Betsy Kohler  
*North American Association of Central Cancer Registries*

Melinda Krakow  
*University of Utah*

Gary L. Kreps  
*George Mason University*

Bill Kte’pi  
*Independent Scholar*

Christopher Kubajak  
*University of Kentucky College of Medicine*

Rohit Kumar  
*University Hospitals of South Manchester*

Brett Rodrique Labbe  
*Bowling Green State University*

Johanne I. Laboy  
*North Carolina State University*

Chervin Lam  
*Purdue University*

Walter Landers  
*Independent Scholar*

Mark Laudenslager  
*University of Colorado, Denver*

Edmund W. J. Lee  
*Nanyang Technological University*

Joseph H. Lee  
*Sergievsky Center/Taub Institute, Columbia University*

Anthony F. Lemieux  
*Georgia State University*

Lara Lengel  
*Bowling Green State University*

Bridget Lepore  
*Kean University*

Simmons Lessell  
*Harvard Medical School*

Youqing Liao  
*Nanyang Technological University*

Donald W. Light  
*Rowan University School of Osteopathic Medicine*

Susan Lilly  
*University of Texas MD Anderson Cancer Center*

Ingrid Marie Lizzarraga  
*University of Iowa*

Héctor E. López-Sierra  
*Inter American University of Puerto Rico*

Kim Lorber  
*Ramapo College of New Jersey*

Tamikia Lott  
*Old Dominion University*

Jennette Lovejoy  
*University of Portland*

L. L. Lundin  
*Independent Scholar*

Natalia Luxardo  
*University of Buenos Aires/CONICET*

Annette D. Madlock Gatison  
*Southern Connecticut State University*

Marifel Malacara  
*University of Texas MD Anderson Cancer Center*

Haylee Massaro  
*Independent Scholar*

Marifran Mattson  
*Purdue University*

Steve McCabe  
*Independent Scholar*

Philip McCallion  
*State University of New York, Albany*

Andrea McDonald  
*Texas A&M University*

Kimberly McFarland  
*University of Nebraska Medical Center*

Trudy M. Mercadal  
*Florida Atlantic University*

Heather Mernitz  
*Tufts University*

Laurie Michaels  
*University of Toledo*
List of Contributors

Shari Parsons Miller
Independent Scholar

Steven E. Mischler
National Institute for Occupational Safety and Health

Anirban P. Mitra
University of Southern California

Sheetal A. Mitra
Children’s Hospital Los Angeles

Manoranjan Mohanty
University of the South Pacific

Thomas Moors
London Medical School

Janice Marie Moreland
Nationwide Children’s Hospital

Jennifer J. Moreland
Nationwide Children’s Hospital

Kelly Morrison
Michigan State University

Vadim P. Moskvin
Indiana University–Purdue University Indianapolis

Katie Moss
Independent Scholar

Malik Muhammad
Synthesis Behavioral Medicine PLLC

Shizuo Mukai
Harvard Medical School

Lauro A. Munoz
University of Texas MD Anderson Cancer Center

William N. Myhill
Burton Blatt Institute at Syracuse University

Laura Nabors
University of Cincinnati

Keerty Nakray
Jindal Global Law School

Nima Nassiri
David Geffen School of Medicine at UCLA

Denese M. Neu
National Louis University-Chicago

Patricia Neville
University of Bristol

Kathleen Nhakomwa-Cassidy
Coventry University

Keisha N. O’Garo
Duke University Medical Center

Eva Olariu
University of Kentucky College of Medicine

Barbara Cook Overton
Louisiana State University

Burcu Ozdemir
Ankara University

Manisha Pahwa
Occupational Cancer Research Centre

Jong Y. Park
Moffitt Cancer Center

Jan Pascal
La Trobe University Rural Health School

Krunal Patel
Independent Scholar

Courtney Peasant
Duke University Medical Center

William M. Peaster
Independent Scholar

Prema P. Peethambaram
Mayo Clinic College of Medicine

David Petechuk
Independent Scholar

Sheila Peuchaud
American University in Cairo

James E. Phelan
Department of Veterans Affairs

Daniel Webster Phillips
Lindsey Wilson College

Samuel Xavier Pimienta Rodríguez
Universidad Estatal de Cuenca

Christine M. Platt
University of Memphis

John Pritchard III
Independent Scholar

John Michael Quinn
University of Illinois at Chicago

Rosellen Reif
Duke University Medical Center

Anthony J. Roberto
Arizona State University

Lorna Rogahn
Independent Scholar

Robin L. Rohrer
Seton Hill University

Jaroslaw Richard Romaniuk
Case Western Reserve University

Aliasger K. Salem
College of Pharmacy, University of Iowa

Tim Sannes
University of Colorado, Denver

Paul Richard Saunders
Canadian College of Naturopathic Medicine
Stephen T. Schroth  
_Towson University_
Carol Scott-Conner  
_University of Iowa_
Gail Seymour  
_Tennessee Department of Human Services_
Chryslee Sherrill  
_Lindsey Wilson College_
Mark D. Sherry  
_University of Toledo_
Kelly Shimabukuuro  
_Moores UCSD Cancer Center_
Michael J. Simonton  
_Northern Kentucky University_
Kelsey W. Snapp  
_University of Kentucky College of Medicine_
Kristine Song  
_University of Kentucky College of Medicine_
Narketta Sparkman  
_Old Dominion University_
Lisa L. Sparks  
_Chapman University_
Brad St. Martin  
_University of Kentucky College of Medicine_
Jeannie Mager Stellman  
_Columbia University_
Steven D. Stellman  
_Columbia University_
Walter Scott Stepanenko  
_University of Toledo_
Victor B. Stolberg  
_Essex County College_
Daniele Struppa  
_Chapman University_
Sonia L. Sugg  
_University of Iowa Hospitals & Clinics_
Corey Helm Swartz  
_University of Texas MD Anderson Cancer Center_
Whitney Szmodis  
_Lehigh University_
Sharon A. Takiguchi  
_Nurse Consultant_
Olusegun Moses Temilola  
_University of Lagos_
Sachiko Terui  
_University of Oklahoma_
Dinah Adjo Tetteh  
_Bowling Green State University_

Ashland Thompson  
_Synthesis Behavioral Medicine_
Kyle L. Thompson  
_Appalachian State University_
David P. Tracer  
_University of Colorado Denver_
Jay Trambadia  
_Duke University Medical Center_
Paige Mayleen True  
_California State University, Monterey Bay_
Yvonne Valdecanas  
_University of Texas MD Anderson Cancer Center_
Rhea U. Vallente  
_Prevention Genetics, LLC_
Ton van Helvoort  
_Independent Scholar_
Rakesh Verma  
_Yale University_
Cecilia Vindrola-Padros  
_London South Bank University_
Mark Vrabel  
_Oncology Nursing Society_
Krishna Subhash Vyas  
_University of Kentucky College of Medicine_
Anna Wagstaff  
_CancerWorld_
Brandy Harris Wallace  
_University of Maryland, Baltimore County_
Michael J. Walsh  
_University of Illinois at Chicago_
Guoyu Wang  
_University of Oklahoma_
Xiang-Dong Wang  
_Tufts University_
Courtney Ward  
_North Carolina Central University_
Andrea Waylen  
_University of Bristol_
Adele Weiner  
_Metropolitan College of New York_
Jessemte L. Welsh  
_University of Iowa Hospitals & Clinics_
Robert West  
_Hospice of the Bluegrass_
Salli Whisman  
_Hospice of the Bluegrass_
Andrew J. Widener  
_University of Texas Medical School at Houston_
Fay V. Williams
  Northern Caribbean University
Eric Wood
  Hawthorn University
Mary Wood
  Duke University Medical Center
Jody A. Worley
  University of Oklahoma
Alan Yaghoubian
  David Geffen School of Medicine at UCLA
Vivianne Yang
  University of Texas MD Anderson Cancer Center
Daniel Yazdi
  David Geffen School of Medicine at UCLA
Minzhi Ye
  Case Western Reserve University
Melda N. Yildiz
  Kean University
Yoshihiro Yonekawa
  Harvard Medical School
Stephen M. Yoshimura
  University of Montana
Brigitte Yuille
  B. Y. Communications Worldwide
Tara Michele Zrinski
  Northampton Community College
Introduction

More than 12 million people were diagnosed with cancer worldwide in 2012, and more than 8 million people die from cancer each year. There is overwhelming evidence that lifestyle factors impact cancer risk and that positive, population-wide changes can significantly reduce the cancer burden. What drives the distribution of these modifiable risk factors and what slows our progress to improving the patterns of risk in our society? Broader social and political forces are a major component and are addressed in this encyclopedia. Not only do health care providers and regulatory approaches each have a role, but in addition individual behavior changes can substantially reduce the burden of cancer in our society. For example, how we design our cities and towns and how governments regulate and tax tobacco and alcohol sales all play a part in the risk of cancer in society.

Current epidemiologic evidence links behavioral factors to a variety of diseases, including the most common cancers diagnosed in the developed world—lung, colorectal, and breast cancer, for example. These cancers account for 50 percent of the cancers diagnosed in high-income countries. Tobacco causes some 30 percent of cancer, lack of physical activity 5 percent, obesity 20 percent, diet 10 percent, alcohol 3 to 5 percent, viral infections 5 to 7 percent, and excess sun exposure 3 percent. In low- and middle-income countries, infections account for more than 23 percent of new cases of cancer. Because of the tremendous impact of modifiable factors on cancer risk, especially for the common cancers, it has been estimated that at least 50 percent of cancers are preventable. Currently, in the United States, not all risk factors are really distributed across race and social class. Thus, we not only address the causes of cancer in this encyclopedia but we also have entries on the relation between race and ethnicity and cancer risk. Because race and social class also co-vary with occupation and environmental exposures, these areas are also addressed in detail.

Exposures at work have been related to cancer risk throughout history—from chimney sweeps and exposure to soot, to asbestos miners, to blast furnace operators. Many of these exposures have been reduced in Western society by regulations that reduce harm in the workplace. Within occupations, many different agents are still generated by manufacturing processes. These are described, and are related to occupations that give rise to carcinogens as they help produce the trappings of modern society. As regulations work to protect the West, are we simply exporting the manufacturing, occupational exposure, and cancer risk?

Trends in risk factors should also be considered when assessing the potential for cancer
prevention. To bring about dramatic reductions in cancer incidence, widespread lifestyle changes are necessary. Which strategies will likely work and how we can achieve these goals are further areas we must consider. To reduce the risk of disease in the population, substantial benefits can be achieved by a small reduction of risk for all members of society rather than just focusing on the high-risk group. Medical interventions can also reduce risk, and these are discussed in detail.

When population-wide approaches to cancer prevention are considered, one must address the etiologic process, which covers a different time course and sequence from coronary heart disease. Although cardiovascular disease is the endpoint of the chronic process of atherosclerosis, treatment focuses on the reversal and subsequent prevention of the acute thrombotic process of myocardial infarction. Cancer, on the other hand, is the result of a long process of accumulating DNA damage, leading ultimately to the clinical detectable lesion such as in situ and invasive cancer. For example, studies of the progression in colon cancer from the first mutation to invading malignancy suggest that DNA changes accumulate over a period of at least 40 years. The goal of cancer prevention is to arrest this progression; different interventions interrupt carcinogenesis at different points in the process.

Age is the dominant factor that drives cancer risk; for all major malignancies, risk rises markedly with age. The importance of age is exemplified by the fact that the aging U.S. population, together with projected population growth, will result in a doubling of the number of cases diagnosed annually by the year 2050, assuming that incidence rates remain constant. With this estimated growth in cancer from 1.3 million to 2.6 million new cases per year, it is expected that both the number and proportion of older persons with cancer will also rise dramatically. Entries in this encyclopedia help place this increase in cancer in context.

Population-wide prevention strategies for cancer do work. For example, reductions in lung cancer rates in the United States mirror changes in smoking patterns, with marked decreases seen first in young men, then older men, and finally in women. In fact, lung cancer mortality has fallen by over one-third since 1991. Introduction of the Papanicolaou test for cervical cancer in the 1950s was followed by a dramatic decline in cervical cancer in those countries that made widespread screening available. The decline in Australian melanoma mortality for those born after 1950 is an additional example of effective intervention at the population level. Behavior change is possible and offers great potential for cancer prevention. The recommendations for cancer risk reduction include reducing tobacco use, increasing physical activity, maintaining a healthy weight, improving diet, limiting alcohol, avoiding excess sun exposure, utilizing safe sexual practices and vaccination against the human papillomavirus (HPV) infection, and obtaining routine cancer screening tests. Vaccination against the hepatitis B infection also protects against liver cancer. Emerging science in the prevention of cancer through drugs and vaccines in the past 20 years adds to our opportunities for prevention. They must also be considered as a prevention priority at a local, national, and international level. What are the barriers beyond costs that would limits access to these new preventive strategies for those most at risk of cancer?

The Encyclopedia
Over 600 entries, written for this second edition (90 percent of which are new articles) by experts from an incredible diversity of fields, is a first step to understanding the emerging knowledge and the burden of cancer in different countries, on cancer causes, strategies for prevention, placing these in the context of societal underlying forces that respond or ignore the role of industry and social structure driving the burden of cancer in society. The volume brings together an enormous range of topics, from causes of cancer, the biologic processes and treatment strategies, the places where treatment is delivered, and to organizations working to advance knowledge and conquer cancer. Together these entries provide a sweeping array of insightful perspectives that will be useful for students encountering issues in cancer causes and prevention, for those organizations and providers who are not yet aware of the scope of the problem, and those training in the many disciplines that relate to the challenges of addressing cancer in its full societal context.

The encyclopedia was designed to include a vast range of different types of entries. This gives
the reader the scope of the cancer problem and includes, what the editors believe, an integrated vision of cancer society. By bringing these entries together in one encyclopedia, we helped place in context the issue of cancer in society and provide a resource that will be useful for readers from around the world. By providing increase for many countries, we also offer the opportunity to compare and contrast the state of cancer and the potential for prevention that fairly substantially from region to region.

The authors have included sample cancer incidence rates from many country articles from the International Agency for Research on Cancer (IARC). Readers are encouraged to visit the IARC Web site, www.iarc.fr, for more information.

We live in a time when the cancer burden is rising globally, and the majority of cancers are diagnosed in low- and middle-income countries with less access to diagnosis and treatment. Yet advances in understanding the potential for prevention and the impact of social structures on the underlying risk of disease rapidly inform strategies to reduce the burden around the world. The editors hope the second edition of *The SAGE Encyclopedia of Cancer and Society* helps map out the lessons from past victories and strategies that can be applied to understand the problem and minimize the burden as we move forward.

Graham A. Colditz
*Editor*
ca. 3000 B.C.E.: The first known mention of cancer in the written record, in the Edwin Smith Papyrus; written in ancient Egypt, it describes surgical procedures including using cauterization to treat breast cancer.

ca. 400 B.C.E.: Hippocrates uses the term carcinos to describe tumors; the term is derived from the Greek work for crab, and refers to the pattern of blood vessels, resembling the claws of a crab, observed on tumors.

168 C.E.: The Roman physician Galen discusses the prevention and treatment of cancer; he suggests that food and climate were both related to the occurrence of cancer, and that cancer could be treated by surgery or cauterization.

1675: The Dutch scientist Anton van Leeuwenhoek uses a microscope to examine many natural objects, and publishes descriptions of cells and bacteria.

1713: The Italian physician Bernardino Ramazzino observes that nuns have a relatively high rate of breast cancer, and a low rate of cervical cancer, a discovery later understood to be related to hormones.

1761: The English botanist John Hill publishes “Cautions Against the Immoderate Use of Snuff,” perhaps the first publication linking tobacco and cancer; he notes that nasal polyps occurred in patients who used nasal snuff.

1775: In an early example of occupational medicine, the English physician Percival Pott noted scrotal cancer was common among chimney sweeps, and connects the disease to their exposure to soot.

1779: The first hospital dedicated to treating cancer is created in Reims, France.

1798: In the United States, the Marine Hospital Service is created, marking an early instance of federally funded public health and medical care.

1836: Opening of the Library of the Office of the Surgeon General of the Army, which later becomes the National Library of Medicine.

1887: The Laboratory of Hygiene is established at the Marine Hospital in Staten Island, New York; it is a precursor of the Centers for Disease Control and Prevention.

1889: The English surgeon Steven Paget notes non-random patterns in breast cancer metastasis, which he explains through his “seed and soil” theory, arguing that specific tumor cells (seeds) will only grow in certain organs (the soil).
1890: The German pathologist David Paul von Hansemann describes the mitotic figures of 13 carcinoma samples, and hypothesized that the observed aberrations caused the abnormal amounts of chromatin found in the cells.

1890: The American physician William Stewart Halstead pioneers the radical mastectomy as a treatment for breast cancer in the United States. (it was already in use in France); Halstead was also noted for his role in developing the residency system of physician training in the United States.

1901: French scientist Pierre Curie suggests the idea that tumors could be treated by putting a source of radiation directly into the tumor; an approach that later came to be known as brachytherapy.

1903: The Austrian chemist Richard Adolf Zsigmond'y develops the ultramicroscope, making it possible to study objects below the wavelength of light; he is awarded the Nobel Prize in Chemistry in 1925.

1903: Radium is first used to treat skin cancer in two patients; this pioneers the way for radiation therapy to use many types of cancer, including breast, prostate, and cervical tumors.

1909: The American biologist Paul Ehrlich suggests that the immune system normally suppressed the development of tumors in the body.

1910: The viral theory of cancer receives support when the American physician Francis Peyton Rous successfully induces tumors in chickens by injecting them with the cells of tumors from other chickens.

1913: The American Society for the Control of Cancer is founded in New York City by a group of businessmen and physicians; it is later renamed the American Cancer Society.

1915: The American biologist Thomas Hunt Morgan demonstrates that the somatic mutation theory of cancer, which was originally proposed by the German biologist Theodor Boveri, is in fact correct.

1922: The U.S. Public Health Service establishes a Cancer Investigations Laboratory at Harvard Medical School.

1933: The Women’s Field Army joins the fight against cancer, raising money and educating people about the disease.

1937: U.S. president Franklin Roosevelt signs the National Cancer Institute Act, legislation creating the National Cancer Institute, with a budget of $400,000 for the first year.

1938: The German physicist Ernst Ruska develops the electron microscope, improving resolution; he is awarded the Nobel Prize in Physics in 1986.

1939: Charles Brendon Huggins, while studying prostate cancer and androgen in dogs, discovers that hormones were influential in the growth of some types of cancer.

1939: Gordon Ide and colleagues suggest that tumors might produce a substance fostering the creation of new blood vessels; their work is based on observing the growth of transplanted tumors in rabbits. Later research by Melvin Greenblatt and Philippe Shubik demonstrates that transplanted tumors cause blood vessels to proliferate even when a Millipore filter is used to create a physical barrier.

1940: In August, the first issue of the Journal of the National Cancer Institute is published.

1945: In Science: The Endless Frontier, Vannevar Bush argues for increased federal government funding for science and technology while allowing the community of scientists to be self-governing, without government interference.

1946: Led by the philanthropist Mary Lasker, the American Cancer Society begins a research program with a budget of $1 million.

1946: At the National Institutes of Health, the Research Grants Office is created to operate a program of fellowships and extramural research grants; it is later renamed the Division of Research Grants.

1947: The Nuremberg Code is developed following evidence of Nazi abuse of humans, including prisoners, in the name of scientific research; it sets a precedent in establishing ethical guidelines for human research.

1947: The physician and researcher Sidney Farber, working with funding from the American Cancer Society, develops the first successful chemotherapy treatment for cancer. Farber successfully treats a 4-year-old leukemia patient with aminopterin and later reports on additional cases of remission in a disease that at the time normally resulted in death soon after diagnosis.

1948: The National Cancer Institute begins a program of grants to medical, osteopathic, and medical schools to improve the training of professionals in cancer diagnosis, research, and treatment.

1948: The fight against cervical and uterine cancer is strengthened when the American Cancer Society advocates for widespread use of the Pap smear, a screening test developed by the physician Georgios Papanikolaou.

1949: The U.S. Food and Drug Administration approves nitrogen mustard for the treatment of Hodgkin’s lymphoma, the first chemotherapeutic treatment approved for cancer.

1950: American researchers Ernst Wynder and Evarts Graham publish a case-control study that shows an association between tobacco smoking and lung cancer.

1951: In the United Kingdom, the Medical Research Council begins the British Doctors Study, which will continue until 2001; among other results, this study provides strong evidence that smoking tobacco is a risk for the development of lung cancer.

1953: At the University of Chicago, the Argonne Cancer Research Hospital begins operation; it is the first facility dedicated to using radioactive isotopes to diagnose and treat disease.

1953: James Watson and Francis Crick discover the helical structure of DNA, a scientific breakthrough for which they are awarded the Nobel Prize in 1962.

1954: Eugene Goldwasser, working at the University of Chicago, explains the basic working principles of erythropoietin; in 1977, he becomes the first person to isolate erythropoietin.

1955: The National Cancer Institute creates the Clinical Trials Cooperative Group Program, a network facilitating cancer research and clinical trials.

1956: Arthur von Hippel, working at the Massachusetts Institute of Technology, coins the term molecular engineering and develops many of the key concepts in the field.

1958: Combination chemotherapy (using multiple drugs together) is demonstrated by scientists at the National Cancer Institute (part of the National Institutes of Health) as a successful approach to treating leukemia; this approach becomes common in chemotherapy in the future.

1959: Physicist Richard Feyman delivers the lecture “There’s Plenty of Room at the Bottom” at an American Physical Society meeting in California; it is considered by many to be the first discussion of technology at the atomic scale.

1960: Discovery of the chromosomal abnormality called the “Philadelphia chromosome” (because it was discovered by Peter Nowell and David Hungerford, researchers working in Philadelphia) that is linked to many leukemias; this abnormality later becomes the focus of one of the first targeted cancer drugs, Gleevec.

1961: The American biologist Rachel Carson publishes Silent Spring, a highly influential book pointing out the health dangers of human exposure to DDT and other toxins; this book plays a key role in coalescing the environmental movement.
1961: The National Cancer Institute establishes a Laboratory of Viral Oncology to investigate the role of viruses in cancer.

1964: In the United States, the Surgeon General publishes a report that concludes that cigarette smoking bears a causal relationship to lung cancer in men, with an effect greater than all other factors combined.

1964: The World Medical Association publishes the Declaration of Helsinki, an influential statement of research ethics in medical research; it has been revised multiple times, with the 2006 revision being the sixth.

1965: Vincent DeVita and colleagues develop the MOPP (mechlorethamine, vincristine, procarbazine, and prednisone) chemotherapy regime, which has a cure rate of around 50 percent, becomes standard treatment until replaced by the ABVD (doxorubicin, belomycin, vinblastine, and darcarbacine) regime in the 1970s.

1966: Peyton Rous is awarded the Nobel Prize for Physiology or Medicine for his work in identifying the role played by viruses in some kinds of cancer.

1966: Henry Beecher publishes an article in the New England Journal of Medicine identifying a number of unethical medical studies and claimed that they showed a systematic pattern of abuse rather than isolated incidents.

1966: Charles Brenton Huggins, a Canadian-born American physician, is awarded the Nobel Prize for Physiology or Medicine for his work demonstrating that hormones could be used to treat some cancers.

1967: The USPHS (U.S. Public Health Service) Hospital is created in Baltimore to conduct integrated laboratory and clinical research on cancer.

1967: The FOBT (fecal occult blood test) is introduced as a simple method to screen patients for colorectal cancer; two more elaborate techniques, colonoscopy and flexible sigmoidoscopy, are also introduced within a few years, and together these methods contributed to a significant reduction in mortality from colorectal cancer.

1968: Elwood V. Jensen develops a test for the presence of estrogen receptors in breast cancer cells, later concluding that about a third of breast cancer cells contain the receptors.

1970s: The use of asbestos in construction decreases as scientific studies demonstrate a link between asbestos exposure and particular cancers.

1971: Judah Folkman and colleagues announce the discovery of a tumor angiogenic factor (TAF) and hypothesize that if TAF activity could be blocked, the growth of malignancies might also be prevented.

1971: Total mastectomy, which involves removing less tissue than radical mastectomy, is demonstrated to be equally effective in treating breast cancer in the early stages.

1971: On December 23, U.S. President Richard Nixon signs the National Cancer Act, authorizing and funding the National Cancer Institute to create new research and treatment facilities, award research grants, and otherwise spur the War on Cancer.

1972: Janet Rowley, working at the University of Chicago, pioneers the recognition of the genetic basis of cancer with her discovery of a chromosomal abnormality in leukemia.

1972: Computerized tomography (CT) scanning is developed by the British engineer Godfrey Hounsfield and South African physicist Allan Comack. CT scans are first used on the head (the first clinical application is used to diagnose a woman with a suspected brain tumor) but are later used for all parts of the body.

1973: A study reveals that mammography is the best tool for finding early-stage breast cancer.

1973: In the United States, eight institutions are recognized as Comprehensive Cancer Centers (CCCs); the number of CCCs increases over the years, to 37 as of 2000.
1973: John Ulmann and Donald Ferguson demonstrate that staging laparotomy, the surgical examination of part of the body, is useful in the evaluation of Hodgkin’s disease.

1974: William Summerlin, a researcher at the Sloan Kettering Cancer Institute, admits fraud in his research on skin grafts; Summerlin claimed to have successfully grafted skin from unrelated animals but in fact had colored the grafts with ink.

1974: The National Cancer Institute awards funds to state health departments to screen low-income women for cervical cancer.

1975: Dr. Bernard Fisher and Dr. Gianni Bonadonna demonstrate that adjuvant chemotherapy—using chemotherapy after surgery—is effective in treating drug cancer.

1975: In the United States, the Cancer Information Service is created to educate health professionals, patients, and the public about cancer.

1975: The Australian philosopher Peter Singer publishes Animal Liberation, arguing against speciesism, the belief that some species (e.g., humans) are more important and should have greater rights than other species (e.g., animals, including those used for lab research).

1976: The first Great American Smokeout is held in California, encouraging smokers to quit for at least one day; the program proves successful and becomes an annual, nationwide event.

1976: The first oncogene, src, is discovered by Harold E. Varmus and J. Michael Bishop.

1977: A clinical trial demonstrates that advanced testicular cancer can be treated by a combination of cisplatin, vinblastine, and bleomycin.

1977: Studies demonstrate that breast-conserving surgery, in which only the tumor but not the entire breast is removed, is as effective in treating early-stage breast cancer as mastectomy (removing the entire breast), if followed by radiation therapy.

1978: The U.S. Food and Drug Administration approves cisplatin as a chemotherapeutic drug for cancer.

1979: The National Commission for the Protection of Human Subject of Biomedical and Behavioral Research publishes the Belmont Report, which sets out principles and guidelines to govern the treatment of human subjects. The core principles of the Belmont Report are beneficence, justice, and respect for the person, while procedures specified include informed consent, risk and benefit assessment, and subject selection.

1980: The U.S. Supreme Court rules, in Diamond v. Chakrabarty, that life forms (in this particular case, a genetically modified bacterium) can be patented.


1981: The U.S. Food and Drug Administration approves a vaccine for hepatitis B, a disease that is strongly associated with liver cancer.

1981: The Centers for Disease Control and Prevention forms a Task Force on Kaposi’s Sarcoma and Opportunistic Infections to investigate a cluster of illnesses caused by what was later determined to be acquired immunodeficiency syndrome (AIDS).

1981: Gerd Binnig and Heinrich Rohrer, working in Zurich, develop the scanning tunneling microscope, an instrument that allows scientists to create images of individual atoms; they are awarded the Nobel Prize in Physics in 1986 for this achievement.

1981: The National Cancer Institute begins the Biological Response Modifiers Program to develop therapeutic agents that may alter biological responses relevant to cancer and to conduct clinical trials of such agents.

1982: Total mesorectal excision provides a new treatment option for patients with rectal cancer;
prior to this time, the standard treatment was colostomy, the removal of the colon, and the use of a colostomy bag for the rest of the patient’s life.

1982: Aline van Pel and Thierry Boon find that mice can be vaccinated against cancer with mutagenized cancer cells, giving them specific immunity to spontaneous tumors.

1983: The National Cancer Institute creates the R. A. Bloch International Cancer Information Center, housing information programs for scientists and health professionals.

1986: Gerd Binnig, Christoph Gerber, and Calvin Quate develop the atomic force microscope, which allows scientists to view and manipulate materials as small as fractions of a nanometer.

1986: The first tumor suppressor gene, Rb, is discovered by Stephen H. Friend and colleagues.

1986: The U.S. Food and Drug Administration approves a PSA (prostate-specific antigen) test for prostate cancer screening, adding a new tool to the fight against the most common type of cancer in men.

1986: The World Health Organization issues guidelines on the adequate treatment of pain for cancer patients, addressing common worries about addiction, tolerance, and abuse connected with opioid drugs.

1986: U.S. cities begin to ban indoor smoking after the U.S. Surgeon General declares that second-hand smoke is a carcinogen.

1986: Tamoxifen, a drug originally produced from the yew tree, is used to treat breast cancer in conjunction with surgery.

1988: The first Consortium Cancer Center in the United States is created by a grant from the National Cancer Institute, supporting research into cancer prevention, control, epidemiology, and clinical trials at three historically black universities: Charles R. Drew University of Medicine and Science, Meharry Medical College, and Morehouse School of Medicine.

1989: Epoetin Alpha is approved to stimulate the production of red blood cells, addressing the problem of anemia that is often a side effect of chemotherapy.

1990: The California Supreme Court rules, in Moore v. Regents of the University of California, that researchers can claim intellectual property rights in a cell line developed from an individual’s tissue but that the individual does not have property rights to the tissue.

1990: Michelle Le Beau and Janet Rowley use fluorescence in situ hybridization (FISH) to map chromosome dislocation, a method now commonly used to diagnose leukemia and lymphoma.

1991: In the United States, childhood vaccination for hepatitis B becomes routine, resulting in a 98 percent decline of acute hepatitis B among children age 15 and under; in the long term, substantial reduction is also expected in liver cancer, a disease strongly associated with hepatitis B.

1991: In the first attempt at treating cancer with human gene therapy, patients with melanoma are treated with tumor-infiltrating lymphocytes modified by the addition of a gene for tumor necrosis.

1991: The U.S. Food and Drug Administration approves Ondansetron to prevent vomiting, a common side effect of chemotherapy and radiation.

1991: The National Cancer Institute and the nonprofit organization Produce for Better Health begin the Five-a-Day program, which is a public health campaign encouraging Americans to eat at least five servings of fruits and vegetables each day.

1992: The technique of sentinel lymph node biopsy, which involves removing the lymph node closest to a primary tumor, offers a method to assess the spread of cancer without invasive surgery.

1992: Paclitaxel is approved by the U.S. Food and Drug Administration to treat advanced ovarian cancer; it is later discovered to be useful for treating breast cancer as well.
1994: Dr. Roger Poisson, a researcher at the University of Montreal and a member of the National Surgical Adjuvant Breast and Bowel Project, is found to have been enrolling ineligible women in breast cancer trials and maintaining false records to cover up the deception.

1994: The BRCA1 gene, implicated in about 25 percent of breast cancers in women under age 30, is discovered by researchers at the National Institute of Environmental Health Sciences.

1994: Victor DeNobel and Paul Mele, who work at the tobacco company Philip Morris, testify before U.S. Congress about suppressed research demonstrating the addictive properties of nicotine; this testimony leads to a $206 billion settlement between 46 states and the tobacco companies; some of the funds are devoted to antismoking campaigns.

1994: Ralph Weichselbaum and Samuel Hellman propose the existence of “oligometastases,” which is an intermediate state in cancer between not having spread at all and having spread extensively.

1995: The Centers for Disease Control and Prevention reports that the cancer death rate in the United States fell by 2.6 percent between 1991 and 1995, the first time cancer mortality rates declined since the 1930s (when recordkeeping began).

1995: Kunio Doi, working at the University of Chicago, pioneers the clinical use of a computer-assisted system to read mammograms.

1995: A group of religious leaders and ethicists protest the patenting of human body tissue, plants, and animals.

1997: The American Cancer Society begins operating a call center, proving information to cancer patients and their families every day, around the clock.

1998: Results from the Breast Cancer Prevention Trial show that the drug tamoxifen can be effective in preventing breast cancer—women taking tamoxifen had 45 percent fewer diagnoses of breast cancer than the women in the control group.


1998: A large-scale prevention trial finds that a moderate dose of Vitamin E reduces the incidence of prostate cancer, as well as prostate cancer deaths, among male smokers.

1998: Tamoxifen is approved for prophylactic use for women at high risk for breast cancer after a clinical trial shows it reduces the risk of breast cancer in women with a family history of breast cancer or with the BRCA1 and BRCA2 genetic mutations that are associated with a higher risk of breast cancer.

1998: The benefits of neoadjuvant therapy, in which chemotherapy is used before surgery to shrink tumors before they are surgically removed, is shown to allow many patients to have breast-conserving surgery (removing only the tumor) rather than mastectomy.

1999: The risks of human subjects research comes to public attention after a research subject, Jessie Gelsinger, dies during an experiment on human gene therapy conducted at the University of Pennsylvania.

2000: Brian Duker develops the first successful molecularly-targeted cancer drug, Gleevec, which is used to treat myelogenous leukemia.

2000: Radon exposure is associated with lung cancer in the Iowa Radon Lung Cancer Study, raising awareness about the risks of long-term exposure to radon in the home.

2000: Research using microarray technology finds that non-Hodgkin’s lymphoma is actually two
diseases, helping to explain why some patients respond to chemotherapy and others do not.

2000: The Special Populations Networks for Cancer Awareness Research and Training program is created in the United States to address the unequal burden of cancer in particular subpopulations.

2001: Gleevec is approved by the U.S. Food and Drug Administration to treat chronic myelogenous leukemia after three months of review, the fastest approval on record. The same year, Gleevec is shown to be effective against gastrointestinal stromal tumor, a rare type of abdominal tumor.

2002: Helen Davies and colleagues publish research in Nature identifying a faulty BRAF gene as present in many cancers, including over half of all malignant melanomas.

2002: In the United Kingdom, the Cancer Research Campaign and the Imperial Cancer Research Fund merge to form Cancer Research UK, the world's largest independent cancer research organization.

2002: John Crispino, working at the University of Chicago, discovers that the development of leukemia in Down syndrome children is linked to a gene defect.

2002: The National Cancer Institute begins the National Lung Screening Trials to test the efficacy of two methods for screening current and former smokers for lung cancer: chest X-rays and spiral computed tomography.

2003: Results from the Million Woman Study indicate that the current use of hormone replacement therapy (HRT) increases the incidence of breast cancer as well as increasing breast cancer mortality.

2003: The Human Genome Project, a 13-year collaboration among researchers in seven countries, announces that they have completed mapping the DNA in the human genome; the results are made freely available to the international scientific community.

2003: Research published in the New England Journal of Medicine shows that taking aspirin daily is associated with a reduction in the risk of colorectal polyps among people at high risk for colorectal cancer.

2003: British researchers publish research demonstrating that combining chemotherapy and radiotherapy improves outcomes in treating the most common type of pediatric brain tumor, medulloblastoma.

2003: Researchers at Rice University develop gold nanoshells that can be used in the discovery, diagnosis, and treatment of breast cancer.

2003: Eugenia E. Calle and colleagues publish research in the New England Journal of Medicine demonstrating a strong relationship between obesity and many types of cancer, and estimates that if Americans maintained a healthy weight, 90,000 cancer-related deaths annually could be avoided.

2004: The Alliance for Nanotechnology in Cancer is created to integrate nanotechnology into basic and applied cancer research, including supporting the development of nanomaterials and nanoscale devices for cancer detection and treatment.

2004: Avastin (bevacizumab) becomes the first approved anti-angiogenic drug, a type of drug that treats cancer by blocking the growth of blood vessels that feed tumors.

2004: University of Chicago researcher Olufunmilayo Olopade, studying women with breast cancer in North America, Nigeria, and Senegal, discovers that women with African ancestry, as compared to women of European ancestry, are more likely to be diagnosed with an aggressive form of breast cancer; in 2005 she receives a MacArthur Foundation “genius grant.”

2004: Results from a large trial funded by Cancer Research UK involving people with operable pancreatic cancer indicate that using chemotherapy after surgery helps delay or prevent recurrence.
2004: The Environmental Protection Agency strengthens its rules regarding human subjects research with children and pregnant women following public criticism of the Children’s Environmental Exposure Research Study (CHEERS).

2004: The 50-year follow-up study of the British Doctors Study finds that prolonged cigarette smoking caused death 10 years earlier than among non-smokers, based on results from men born between 1910 and 1930; the study also shows that cessation of smoking reduces this risk substantially.

2005: In the United States, the National Human Genome Research Institute and the National Cancer Institute announce the Cancer Genome Atlas Project, whose first goal is to create an atlas of the genomes of lung and ovarian cancer and glioblastoma.

2005: Results from the Women’s Health Study finds that supplemental vitamin E does not reduce the incidence of cancer among women.

2005: The National Institutes of Health (NIH) in the United States strengthens its policies intended to prevent conflict of interest, including barring NIH researchers from consulting with or holding stock in pharmaceutical and biotechnology companies.

2005: The National Cancer Institute creates the Community Networks Program to provide education, research, and training aimed at reducing cancer disparities among underserved populations.

2005: The Childhood Cancer Survivors Study reveals that survivors of childhood cancer suffer from many health concerns later in life, including scarring of the lungs, other types of cancer, and heart trouble.

2005: Eric Pohlman, a professor at the University of Vermont, pleads guilty to falsifying results in numerous scientific grants and research articles; in 2006, he becomes the first person in the United States to be sentenced to prison for research fraud.

2006: The U.S. Food and Drug Administration approves Gardasil, a vaccine to prevent infection with human papillomavirus (HPV), associated with cervical cancer; Gardisil is approved for girls and women ages 9 to 26.

2006: In the United Kingdom, the Network of Experimental Cancer Medicine Centres opens, with the goal of moving new treatments into clinical trials and practice quickly.

2006: In the United States, the National Community Cancer Centers Program Pilot begins operation with the goal of improving cancer care in local communities as well as reducing cancer health disparities and increasing access to prevention and screening services.

2007: Results from the United Kingdom (UK) QUASAR clinical trial of chemotherapy for bowel cancer demonstrates that chemotherapy improves survival for people with less advanced cancer.

2008: Greg Karczmar, Suzanne Conzen and colleagues develop a procedure using magnetic resonance image (MRI) to detect very early breast cancer in mice.

2008: Hans Schreiber demonstrates that, in mice, killing nonmalignant cells surrounding a tumor can prevent spread of the tumor.

2009: Early results from the UK Collaborative Trial of Ovarian Cancer Screening finds that screening women with both a blood test and ultrasound produces more accurate results than ultrasound alone, perhaps because the blood test helps to rule out harmless cysts picked up through ultrasound scans.

2009: Ezra Cohen discovers that grapefruit juice enhances the effectiveness of rapamycin, allowing patients to take lower dosages of the drug.

2009: In the United States, the Family Smoking Prevention and Tobacco Control Act allows the Food and Drug Administration to regulate tobacco products, and creates a Tobacco Products Scientific Advisory Committee to advise the Department of Health and Human Services.

2009: Results from the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial casts
doubt on whether routine screening for prostate cancer reduces mortality, and suggests that screening also leads to overdiagnosis and treatment of cancers unlikely to be life threatening.

2009: The Prevent All Cigarette Trafficking Act prohibits tobacco products from being sent through the U.S. mail.

2010: Results from the National Lung Screening Trial indicate that annual screening by computerized tomography (CT) scan of smokers and former smokers reduces the risk of death from lung cancer; this is the first lung cancer screening program successful in reducing mortality.


2011: An international research team identifies a new oncogene, ZNF703, which is believed to accelerate the development of breast cancer.

2011: The Sunbeds Regulation Act in the United Kingdom bars people under the age of 18 from using tanning beds, associated with the development of skin cancer.

2012: The American Cancer Society and the National Cancer Institute report that the number of Americans living with cancer has increased four-fold since 1971, from 3 million to 13.7 million.

2013: On August 23, Song-Yi Park and colleagues announce results from the Multiethnic Cohort Study showing that, for women, increased consumption of fruits and vegetables is associated with a lower incidence of invasive bladder cancer.

2013: In the September issue of the *Texas Public Health Journal*, researchers report that cancer is the most common cause of death for Hispanics living in Texas.

2013: On November 6, Alastair Sutcliffe and colleagues report research based on children born in the United Kingdom as a result of in vitro fertilization, finding that they are no more likely than other children to develop cancer.

2013: On December 20, *Science* announces that cancer immunotherapy has been selected as the breakthrough of the year.

2014: On February 14, Cancer Research UK publishes a report and makes available two online interactive maps allowing the comparison of the incidence and mortality from cancer globally.

2014: On April 17, a clinical trial studying the effectiveness of personalized treatment for lung cancer is announced by Cancer Research UK, AstraZenica, and Pfizer.

2014: On June 26, Martin Widschwendter and colleagues announce the discovery of a genetic marker or “switch” observable in blood samples associated with increased risk for breast cancer, suggesting the possibility that a simple blood test may be available in the future to help predict the likelihood of noninherited breast cancer.

2014: On July 11, Min Yu and colleagues report in *Science* that they successfully isolated breast cancer cells in patients’ bloodstreams, including cells carrying the “seed” of metastasis.

2014: In October, the International Agency for Research on Cancer added several recommendations, including for girls to get the HPV (human papillomavirus) vaccine and for mothers to breastfeed.

2014: In December, Jan Durmanski and colleagues at Uppsala University in Sweden reported research linking smoking with the loss of Y chromosomes from the blood cells in men. In addition, the researchers found that the loss of Y chromosomes from at least one fifth of an individual’s blood cells was associated with almost four times the risk of developing certain cancers.

2015: According to estimates by the American Cancer Society, approximately 1.66 million new cancer cases are expected to occur in the United States in 2015; this estimate does not include noninvasive cancers or basal cell or squamous cell
skin cancers. In addition, about 589,430 Americans are expected to die of cancer in 2015.

2015: In January, England’s National Health Service removed nine cancer drugs from the list of treatments it will pay for, based on the high cost of the drugs relative to the value they provide to patients. At the same time, NHS England reduced the number of conditions for which several other drugs were an approved treatment, reducing the total number of treatment options by 25.

2015: In February, the World Health Organization (WHO) announces that cancers are among the leading worldwide causes of illness and death, with about 14 million new cases of cancer and 8.2 million deaths due to cancer, occurring in 2012. In addition, the WHO reports that the number of new cancer cases per year is expected to rise to 22 million within the next 20 years.

2015: In March, Takaaki Hirotsu and colleagues at Kyushu University report that roundworms were able to correctly identify individuals with cancer, based on urine samples in Petri dishes, with 96 percent accuracy.

Sarah E. Boslaugh
Saint Louis University
Abbott Laboratories (United States)

Abbott is a global company specializing in diagnostics, medical devices, nutritionals, and branded generic pharmaceuticals. Its headquarters are in Abbott Park, Illinois, but it operates in more than 130 countries, and the most recent data show revenue in excess of $20 billion. Abbott has products that are designed specifically to help in diagnosis for cancer patients. Abbott’s history goes back to its founder, Wallace Calvin Abbott, who created the Abbott Alkaloidal Company in 1888. The key innovation that propelled Abbott Alkaloidal to success was the development of a technology that allowed the separation of the active principle of a medicinal plant to deliver it in the form of small pills, which in turn allowed more consistent dosages for patients.

As the company very successfully expanded and grew, its core businesses now focuses on branded generic pharmaceuticals, diagnostics, medical devices, and nutritional products, and its business model organizes it along the following divisions: animal health (anesthesia, animal diets, and other veterinary products), diabetes care (monitoring devices for glucose levels as well as therapeutic products), diagnostics (including a significant number of products in hematology, immunodiagnostic, oncology, and clinical chemistry—famously, in 1984, Abbott developed the first human immunodeficiency virus [HIV] blood screening test), branded generic pharmaceuticals (significant presence in markets outside the United States, including developed and developing markets), medical optics (treatments and equipment for cataract surgery and laser eye surgery as well as drops and solutions), molecular medicine (analysis of DNA, RNA, and proteins at the molecular level), human nutrition (products for babies as well as for adults), and finally vascular technologies (endovascular and coronary technologies developed by Abbott include, for example, the first bioresorbable coronary stents and a first-in-class, catheter-based treatment for mitral regurgitation). Both the diagnostics and molecular divisions have significant interest for oncological patients and their care providers.

Abbott produces a variety of medical devices, diagnostics, and nutritional products. Diagnostic products are very relevant to oncologists in addition to some of the nutritional products (such as Ensure) that may find applications with cancer patients who are struggling to get the required nutrition while in therapy.

Abbott’s molecular division has explored many ideas for the development of a variety of diagnostic tests. Of particular interest is work in the oncology area. Abbott’s work in this direction fits within the current push toward personalized medicine, which requires doctors to be in a position to assess the
specific proteomic and genomic characteristics of the patient’s tumor to identify which patients may be eligible for new, targeted therapies. The genetic origin for many tumors (especially solid tumors) can be detected with fluorescence in situ hybridization (FISH) probe technology.

This technology was developed in the early 1980s, and it is used to detect the presence of specific DNA sequences on chromosomes. By using fluorescent probes that bind only to the targeted areas of the chromosomes, doctors can visualize the bound (or detected areas) using fluorescence microscopy. In this way, this technology can help detect appropriate genetic targets in tissues and determine whether specific mutations or genetic alterations exist.

Abbott has developed numerous products that utilize this technology. The first example is the UroVysion Bladder Cancer Kit, which uses urine only to support an initial diagnosis of bladder cancer; the kit and its accessories also can be used to monitor disease progression (or lack of) and detect disease recurrence. Another example, relevant for women diagnosed with breast cancer, is the PathVysion HER-2 DNA probe kit, which accurately assesses the patient’s HER-2 status, thus providing crucial information to help the doctor select the most appropriate therapy, such as Herceptin (trade name for the monoclonal antibody Trastuzumab, which interferes with the HER-2 receptor). Patients with non–small cell lung cancer (NSCLC) may be tested for the Vysis ALK Break Apart FISH Probe Kit, which may help physicians identify those patients who might respond to the kinase inhibitor crizotinib. Crizotinib, under the trade name of Xalkori, is now the standard of care for NSCLC patients whose tumors test positive for the ALK gene rearrangement (ALK+). While ALK+ patients represent a small percentage of all NSCLC patients (3–5 percent), clinical studies have shown many patients on Xalkori experience improved outcomes.

Daniele Struppa
Chapman University

See Also: Bladder Cancer; Breast Cancer; Lung Cancer, Non–Small Cell.

Further Readings
fall into two principle families of polymers—the omopolymere and a copolymer—each offering valuable properties that provide resistance to deteriorating during extreme temperatures.

Acrylic fiber is also produced from a polymer and is a synthetic fiber that commonly resembles the texture of wool in both look and texture. Because acrylic fibers are lightweight and tend to be soft, they can be found commonly in carpets, home furnishings, and some clothing as a less-expensive alternative to more-expensive natural textiles such as cashmere and cotton. These acrylic fibers are popular for the textile industry and consumers because they are resistant to general deterioration and damage caused by pests, such as moths, chemicals, and oils. Acrylic fibers also are very popular for craftspersons who knit or crochet as their properties lend themselves to holding up during washing and fabric dyeing. Many credit the company DuPont with creating the first synthetic, acrylic fibers in the early 1940s, although they were not mass manufactured until a decade later.

The main ingredient in most acrylic fibers is acrylonitrile, also known as vinyl cyanide, which is considered a carcinogen, as classified by the International Agency for Research on Cancer, linked to causing breast cancer—and also brain, lung, and bowel cancers—as well as negatively affecting and targeting the central nervous system. Acrylonitrile is not a naturally occurring chemical and is produced by mixing propylene with ammonia and oxygen (amnomoxidation) in the presence of a catalyst; this is known as the Sohio process. Acrylonitrile is colorless, extremely volatile, and flammable and does not occur naturally. In addition to its use in the manufacture of acrylic fibers, plastics, resins, and synthetic rubbers, acrylonitrile is also used to produce other chemicals, such as acrylamide, adiponitrile, and carbon fiber. Acrylonitrile is a known toxin. Occupational exposure to acrylonitrile over an extended period can cause effects such as headache, chest pains, insomnia, fatigue, a general unwell feeling, and increased irritability.

Without proper protective equipment and measures, acrylonitrile can be absorbed through the skin, ingestion, and inhalation. A carcinogen is defined as any substance that causes cancer in living tissues, and the process of cancer developing in living tissues is referred to as carcinogenesis, oncogenesis, or tumorigenesis. Basically, this process is when a living, normal cell is transformed into a cancerous cell that then divides in an uncontrollable manner and forms a malignant mass, or neoplasm. Researchers and medical professionals typically classify carcinogens by their structure or chemical as a way to differentiate among known carcinogens and the way they behave; however, all chemical carcinogens have the ability to directly or indirectly change the DNA structure of living tissue.

Acrylonitrile is also a mutagen, which is a physical or chemical agent that changes the genetic material, usually DNA, of an organism or living tissue and, therefore, increases the chances and frequency of occurrence of mutations. A carcinogen can be or not be a mutagen.

The following is a list of common chemicals that can be considered carcinogenic that are used in the production of acrylic rubber and fibers:

- Accelerators
- Oils (process and extender)
• Antioxidants
• Organic vulcanizers
• Antiozonants
• Pigment blends
• Anti-tack agents
• Plasticizers
• Chemical by-products
• Reinforcing agents
• Curing fumes
• Resins
• Extenders
• Solvents
• Fillers

Recent research has primarily focused on the occupational exposure people working in these respective industries suffer from coming into contact with solvents and chemicals used in the development of acrylic rubber and fibers, with specific research studies focusing on the potential linkage between exposure and breast cancers and cervical cancers. However, scientific data exist that indicate individuals working in these manufacturing industries have died due to various cancers, such as bladder, stomach, lung, hematopoietic, and others, after being exposed to the solvents and chemicals used to develop acrylic and rubber products. In addition to cancer, other health effects experienced by workers in these manufacturing industries include adverse respiratory, dermatological, and reproductive effects.

The U.S. Occupational Safety and Health Act of 1970 calls for the industry’s need to standardize its protective measures and take action to improve work conditions to limit workers’ exposure to known carcinogens. As a result, the Occupational Safety and Health Administration (OSHA) has reported that the acrylic rubber and fiber industries have not adequately tested the chemicals for carcinogenicity and toxicity, advocates for a need to reexamine the health effects that exposure to these chemicals has on workers, and proposes more research be conducted on ways to prevent exposure to these carcinogens. Specifically, OSHA calls for more research in the following areas in the face of a lack of data:

• Evaluation of hazardous exposures
• Epidemiologic, toxicologic, and industrial hygiene studies

• Assessment of control measures
• Epidemiologic research
• Collection of injury data
• Evaluation of health and safety programs
• Identification of compounds or groups of substances

See Also: Breast Cancer; Colon Cancer; Lung Cancer, Small Cell; Stomach (Gastric) Cancer.

Further Readings


Adrenocortical Carcinoma

Adrenocortical carcinoma, adrenal cortex cancer, or adrenal cortical carcinoma is a cancer of the cortex of the adrenal gland. The adrenal gland is an endocrine gland near the kidneys, responsible for producing hormones in response to stress and trauma and for assisting kidney function. Humans have two adrenal glands, one proximate to each kidney: The right adrenal gland is triangular, while the left is semilunar, with each located above its respective kidney. They are small, weighing only about four grams each and surrounded by connective and fatty tissues. Their small size accounts for the high probability of metastasis as there is not much tissue for the cancer to consume before it moves beyond the gland. The cortex of the adrenal gland is responsible for the production of corticosteroid and androgen hormones, such as androgens, aldosterone, and cortisol.

Adrenocortical carcinoma is rare, with about one case per million people per year, with patients predominantly in two clusters: children under five and adults in their 30s. The five-year survival rate is between 20 and 35 percent.

Because it affects the adrenal gland, a number of hormonal syndromes can occur in adrenocortical carcinoma patients. Cushing’s syndrome results from excessive cortisol, for instance, resulting in weight gain, especially in the face and trunk, a moon face from excessive fat pads around the face, excessive perspiration, thinning of the skin and mucous membranes due to the rapid weight gain stretching them (and resulting stretch marks on the trunk, buttocks, and legs), dry and brittle hair or hair loss, and increased facial hair growth. In extreme cases, the endocrine system may be thrown off and cause insomnia, impotence, or female infertility. Memory and mood problems are common, and the patient is more prone to acne, fungal infections of the skin, and the development of adult-onset diabetes.

Another possible complication, Conn syndrome, is caused by excessive aldosterones, which can affect almost every kind of cell in the body but especially sodium and potassium channels. As a result, excessive aldosterone can lead to increased intracellular potassium and increased sodium reabsorption throughout the intestines, resulting in constipation, muscle cramps, elevated blood pressure from sodium retention, and headaches from electrolyte imbalances.

Hormonal imbalances can lead even to abnormal virilization, the process by which biological sex differences develop. When virilization occurs in adults, it typically refers to a long-term hormonal imbalance causing the development of characteristics of the opposite sex; in women, this may mean thinning hair, increased facial hair, increased muscle strength, enlargement of the clitoris, deepening of the voice, and fertility problems, while in men, it can include the development of breasts, impotence, and a decrease in body hair. Male patients with adrenocortical carcinoma actually may experience a combination of these symptoms—for instance, an increase in facial and body hair and deepening of the voice but the development of female breasts—as the body converts excess androgen to estrogen and the patient thus suffers from an overabundance of both sex hormones.

Adrenocortical carcinoma tends to present differently in children than adults. Though both are likely to experience Cushing’s syndrome, adults are more likely to experience Cushing’s alone, while children usually experience it in conjunction with virilization. Children also may experience early-onset puberty as a result of the hormonal imbalance, which may be the first sign of something wrong.

The etiology of adrenocortical carcinoma is not well understood. Certain hereditary diseases increase the risk, including Li-Fraumani syndrome (which increases risk for several cancers), Beckwith–Weidemann syndrome (an overgrowth disorder resulting in large babies with large tongues and low blood sugar), and Carney complex (noted by dark spots on the skin and tumors in several organs).

Early symptoms can include a lump, pain, or feeling of fullness in the abdomen, but in more than half of cases, the tumor is a functioning one that impacts hormonal production, resulting in one of the syndromes above. In nonfunctioning tumors, there may be no symptoms until the tumor is late stage.

The tumor is usually discovered and identified through radiology, and blood and urine tests can uncover hormonal imbalances. Biopsies of tumors usually are not performed, but a pathologist will confirm the cancer diagnosis after surgery removing
Adrenocortical Carcinoma, Childhood

Adrenocortical carcinoma (ACC) is a rare but often malignant neoplasm found most commonly in children. These tumors are chiefly identified by the presence of virilization, the excessive production of sex hormones and often are selective for androgens. These adrenocortical hormone secretions that are strongly upregulated above normal baseline values are found most commonly in female pediatric patients under the age of five. The constellation of clinical symptoms may all suggest Cushing’s syndrome or other paraneoplastic processes. The result of excessive hormone production includes physical asymmetry and growth disorders, including precocious puberty. Germ-line mutations in key tumor suppressor genes, such as p53, have been readily associated with ACC.

The classical clinical presentation of ACC is a female, pediatric patient exhibiting poor growth velocity, signs of virilization, accompanied by acne, puberache, and macroclitoris. These patients also may exhibit additional steroid hormone disorders, including glucocorticoid excess. Patients may have a family history of Li-Fraumeni syndrome or Beckwith–Weidemann syndrome. Germ-line mutations in TP53, affecting IGFII growth factor, have been associated with ACC. J. Fraumeni and J. Miller were the first to discover and document the familiar linkage through a nationwide retrospective analysis of children with ACC in 1967 (Else, 2012). Loss of p53 may be correlated to promote further genetic damage such as gain of function mutations in IGF2, for both are seen in malignant neoplasms. Other molecular factors may be at play, including stem and progenitor cells in the adrenals.

Population-based studies have revealed a carrier rate of a distinct mutation associated with ACC. The R337H mutation has been identified in 0.3 percent of the population of Southern Brazil and is found in the majority of pediatric ACC patients in this region. These pediatric patients present with the classical clinical symptoms at an earlier age of onset than those lacking the R337H mutation. Additionally, ACC may have been predicted to occur in one in every 455 live births in the region. R337H is one of the most common inherited mutations in southern and southeastern Brazil, with patients presenting with a constellation of malignant neoplasms. This same frequency of discovery has not been found in northern and northeastern Brazil.

Unlike in adults, histological features do not correlate with clinical outcome in pediatric patients. Nevertheless, compact cells with eosinophilic cytoplasm are common features of ACC tumor cells.
These cell nuclei demonstrate nuclear pleomorphic characteristics. Pathologic analyses reveal tumor masses that are large and browned, possessing cut surfaces and areas of focal necrosis and hemorrhage. Further microscopic evaluation reveals cells that may retain some characteristics of adrenal tissue but are significantly maligned or primary.

The presence of virilization supports evidence that pediatric adrenocortical neoplasms arise from within the fetal zone of the fetal adrenal cortex. The fetal adrenal gland rapidly grows through cell proliferation and angiogenesis at the gland periphery, cell migration, hypertrophy, and apoptosis. In terms of steroidogenesis, the fetal adrenal cortex is characterized by extensive production of dehydroepiandrosterone and its sulfate. After birth, the fetal zone rapidly involutes, followed by a decrease in androgen secretion. Following fetal zone regression, adult definitive zones arise from these definitive zones of the fetal adrenal. Disruption in these processes may promote ACC.

Childhood ACC cannot be distinguished by a specific prognostic indicator, including in R337H carriers. The loss of two functional alleles in the majority of all R337H-positive ACC is expected, however. Less than a quarter survival is predicted in patients with stage III and IV. Low survival is correlated to the R337H mutation as well as low-income status. Most of these children were found to be positive for germ-line R337H. Additionally, low family income status is also a predictor for poor prognosis as cancers are rarely found and options for appropriate treatment may not be available.

ACC diagnoses often precede poor prognosis, which is uncharacteristic of most adrenal cortex tumors. Five-year, disease-free survival for a complete resection of a stage I through III ACC is approximately 30 percent, while the most important prognostic factors are age of the patient and stage of the tumor. Poor prognostic factors include those commonly associated with malignant neoplasms, including high mitotic activity, local and distal invasion, mass of greater than 30 grams, diameter of greater than five centimeters, and failed or mutant p53 activity.

New treatments under investigation include targets to the IGF 1 complex. Figitumumab, an anti-IGF 1R monoclonal antibody has shown promising results; multikinase inhibitors, and growth factor blockers affecting epidermal growth factor and VEGF have also been shown to be effective therapeutic treatment options. These inhibitors retard tumor growth by interfering with processes of angiogenesis and tumor growth. They may also help to slow down the rate of metastasis.

Godfrey Ilonzo
Independent Scholar

See Also: Adrenocortical Carcinoma; Genetics; Surgery.

Further Readings

Advertising

New forms of advertising allow cancer centers and pharmaceutical companies to bypass gatekeepers such as physicians and regulatory commissions and appeal directly to consumers regarding cancer drugs and treatment options. The results have been manifold, from awareness and prevention of cancer to detection and diagnosis of its symptoms as well as treatment options and end-of-life decisions. This entry first discusses the nature and origins of cancer drug and treatment center advertisements then outlines responses to and regulations for these advertisements.
Types of Drug and Treatment Center Advertising

While cancer-related advertisements appear across many media outlets including print, radio and the Web, the most common forum for drug and treatment-center advertisements is television commercials. These television spots encourage patients to perform a behavior or express behavioral intent with regard to awareness, prevention, diagnosis, and long-term treatment of cancer. For instance, a recent advertising campaign by Pancreatic Cancer Action encourages people to see their doctor if they display symptoms of pancreatic cancer, one of the least known but most deadly of the common cancers. Also, many companies promote breast cancer awareness with advertisements for mammography or other breast-related services with sexual innuendoes or images of mastectomy scars.

In its first two years from 2001 to 2003, CURE magazine, a publication directed at cancer patients, survivors, and caregivers, published more than 50 advertisements for chemotherapy drugs such as Xeloda and Taxoetere, supportive agents such as Neulasta and Aloxi, hormonal agents such as Arimidex and Femara, and other targeted therapy drugs such as Bexxar and Tarceva. Other examples include a recent campaign by Pancreatic Cancer Action, which emphasized the severity of pancreatic cancer and the importance of early diagnosis by showing patients who wished they had more treatable forms of cancer. Similarly, a campaign for Neulasta, a prescription medication used to reduce the risk of infection in people receiving strong chemotherapy, featured cancer patients saying that, with Neulasta, they are ready to face chemotherapy. Also, a print advertisement that ran in the New York Times showed a man and woman climbing a mountain, with the man extending his arm to the women and helping her to the summit. The slogan read, “Prostate surgery so effective, even women can feel the difference.”

Also, many comprehensive cancer centers advertise the quality of physicians and efficacy of treatment through patient testimonials and emotional appeals. For instance, the MD Anderson Cancer Center’s Making Cancer History and University of Maryland Medical Center’s Life-Saving Mission manage their reputations through advertisements that emphasize comprehensive competence with individual attention, from early diagnosis to end-of-life decisions.

Origins and Efficacy of Advertising

Since the 1700s, when patent medications were first advertised in U.S. newspapers, direct-to-consumer advertisements for medications have formed the majority of newspaper revenues. In 1938, the passage of the Food, Drug, and Cosmetic Act gave the newly created Food and Drug Administration authority over the labeling of drugs and the Federal Trade Commission over the regulation of drug promotion and advertising. In 1962, the passage of the Kefauver–Harris Act required proof that all drugs were safe and effective and transferred the authority for oversight of promotional material to the Food and Drug Administration, which in turn, required that advertisements present both benefits and side effects of advertised drugs. Today, drug advertisers must present only a major statement of risks and provide adequate provision to a brief summary of these risks on the company’s Web site. These summaries include educational advertisements about medical issues, promotional advertisements with the name of a drug, and product-specific advertisements that outline the uses of a product and direct patients to other outlets for supplemental information.

The efficacy of advertising for cancer drugs and treatment centers depends on several factors. Socioeconomic (education, income, and employment), geographic (neighborhood and urbanicity), and sociodemographic (age, sex, race, and ethnicity) determinants, as well as factors such as social networks, social support, social capital, and health insurance, impact exposure and attention to cancer advertisements and external information seeking and processing. These communication inequalities lead to gaps in knowledge of treatment options and may also compromise the doctor–patient relationship and lead to patient dissatisfaction and lack of trust or low health literacy. All of these health communication issues may, in turn, lead to general health issues such as problematic health behaviors and under and overconsumption of health products. Together, all of these factors serve to exacerbate socioeconomic, geographic, and sociodemographic cancer outcomes.

Responses to Advertising

With this in mind, critics of cancer drugs and treatment center advertisements argue that the generalities in cancer drug and treatment center advertisements serve the interests of the pharmaceutical companies, not the patient, by building...
brand recognition among physicians rather than providing understandable information to patients. On one hand, advertisements do not educate patients thoroughly enough, require a high level of medical literacy that most patients lack, and promote overprescription that hampers treatment decisions. On the other, advertisements provide patients with information they would not otherwise have known, empower patients as participants in their own health care, and echo new models of patient-physician relationships centered on patient needs.

Proponents of cancer drug advertisements argue that they empower patients to play more of a role in their own treatment in an increasingly nonpaternal and patient-centered medical environment. Patients can take the general information provided in advertisements and contextualize their own situations so that they can be more knowledgeable and responsive when visiting their physician. For instance, a recent study showed that advertisements for the breast cancer drugs aromatase inhibitors led to a slight increase in total prescriptions for the drugs but only among women who had a medical use for them.

Cancer treatment center advertisements in particular have been criticized because, unlike the drugs themselves, they are not held to the highest levels of scientific scrutiny in their claims. They appeal to the emotions of the patients and fear of the disease with superlatives such as highest cure rate and lowest risk, which are not supported with any scientifically verifiable statistics. For many, these advertisements are evidence of a disconnect between cancer research and advertising of treatment options. While the Food and Drug Administration mandates that any claims in advertisements for cancer medicines must be substantiated with scientific proof, the Federal Trade Commission does not require such substantiation regarding claims for the efficacy of treatment centers. As a result, treatment centers may use superlative language to tell a story of miraculous (yet anomalous) survival through the most technologically advanced treatment options but with no evidentiary support.

For instance, a representative television advertisement for the MD Anderson Cancer Center in Houston, Texas, features cancer patients crossing out the word cancer for their Making Cancer History campaign. The advertisement then displays the company’s slogan, “When Cancer Strikes, We Strike Back,” with a number one ranking for cancer care by U.S. News and World Report. Similarly, the University of Maryland Medical Center’s Life-Saving Mission campaign features action shots of a group of physicians working collaboratively, with the following voiceover: “Good morning, cancer, watch your back. All these people mean you harm.” The advertisement emphasizes the collaborative approach of the center, in which physicians gang up on each person’s cancer individually. The advertisement ends with a group of doctors told to gather round, listen up, and make sure a patient lives to see his daughter’s marriage.

A 2012 study of more than 400 TV and magazine ads from more than 100 U.S. cancer centers in the Annals of Internal Medicine found that advertisements relied mainly on patient testimonials and emotional appeals that elicit hope for survival with few statistics or actual results. Such advertisements have been criticized for several reasons. In the case of breast cancer awareness, advertisements that seek to increase the number of women seeking mammograms may be funded largely by the companies that sell mammography equipment. Other advertisements may capitalize on the emotions of grieving and overwhelmed patients, contradict the relatively little progress made in combating cancer, and rest on the erroneous assumption that the decision about a cancer center will be a deciding factor in the patient’s life or death. For the advertisers, such emotional appeals are meant merely to manage the reputations of the centers and not to promote competition among cancer treatment centers or take advantage of vulnerable consumers.

David DeLuliiis
Duquesne University

See Also: Marketing, Drug; Marketing; Hospitals and Clinics; Media; Statistics.

Further Readings
Aerospace Industry

Employees of the aerospace industry face cancer risks from a variety of occupational sources. Workers who build and repair aircraft are exposed to many carcinogens, including asbestos, industrial solvents, rocket fuels, and rubbers. The pilots, flight crews, and astronauts who operate aircraft at altitude are exposed to ionizing radiation from cosmic rays and the sun. Ionizing radiation degrades genetic material and has been linked to a cancer incidence; however, aerospace employees can reduce their exposure to this radiation by limiting flight times and flying at low altitudes. Both aircraft manufacturers and operators are subject to the potentially carcinogenic effects of shift work, which disrupts the body's natural circadian rhythms.

From the 1940s through the 1980s, aircraft were manufactured using many parts made from asbestos. These included airplane brakes, insulation, glues, and epoxies. During this period, workers who assembled or repaired aircraft, as well as those who manufactured aircraft parts, risked exposure to carcinogenic asbestos. Asbestos was thought to be ideal for aircraft manufacturing because it is lightweight, offers efficient sound insulation, and is highly resistant to damage from friction, heat, and chemicals. However, asbestos releases particles into the air that can cause health problems when inhaled or swallowed. In the 1970s, asbestos was linked to lung cancer, esophageal cancer, and mesothelioma. Asbestos dust can become attached to clothing or other surfaces, causing aerospace workers and their loved ones to be exposed to the carcinogen. Although asbestos is no longer used to manufacture new aircraft, some older aircraft still contain parts made from asbestos. Aerospace workers continue to risk asbestos exposure during aircraft maintenance and retrofitting. When removing or replacing aircraft parts made from asbestos, workers can become exposed to carcinogenic asbestos dust.

Workers in the aerospace industry are exposed to carcinogenic industrial solvents, increasing their overall risk of kidney cancer, liver cancer, cervical cancer, prostate cancer, melanoma and non-Hodgkin's lymphoma. Studies have linked occupational exposure to mineral oil with increased instances of melanoma, stomach cancer, and esophageal cancer in aerospace workers. The aircraft manufacturing and repair industries regularly use the industrial solvent trichloroethylene (TCE) as a metal degreaser. TCE is a colorless, nonflammable liquid that is toxic to humans and believed to be a carcinogen. It was originally used as a general anesthetic in medicine and was also used as an inhaled analgesic during childbirth. Developed countries discontinued medicinal uses of TCE in the 1980s. Economic factors and government regulation have led to a decreasing industrial use of TCE in the United States since the 1970s. Studies show that TCE causes liver and kidney cancers in animals. Studies linking TCE to specific instance of human cancers are less conclusive because occupational TCE exposure tends to occur along with other known carcinogens.

Aerospace workers involved in the manufacture, testing, and repair of aircraft and rocket engines are exposed to cancer-causing substances called hydrazines, which are flammable, colorless liquids commonly used in rocket fuels. Aerospace workers can come in contact with hydrazines in the production of rocket fuels and while testing or repairing rocket engines. Studies have shown that exposure to hydrazines correlates to increased incidence of lung and colorectal cancers.

Manufacturing of rubber products used in the aerospace industry has been associated with increased incidence of lung cancer, bladder cancer, and leukemia. It is difficult to isolate the individual toxic substances that cause these cancers because the production of rubber involves a variety of potentially dangerous chemicals. Furthermore, as workers combine the materials that produce rubber, these substances undergo chemical reactions that can alter their structures and potentially change their carcinogenic qualities.

Airplane pilots, flight crews, and astronauts experience an elevated cancer risk from a number of sources, including interruption of circadian rhythms, radiation produced by airplane cockpit instruments, and ionizing cosmic radiation. Air travelers and airline employees flying at altitude are
exposed to ionizing radiation that penetrates the
Earth's atmosphere from space. Ionizing radiation
refers to high-energy particles emitted by radioac-
tive sources. These consist of subatomic particles
such as neutrons, protons, electrons, positrons, and
photons including both X-rays and gamma rays. The
subatomic particles interact with atoms in the body,
causing them to lose an electron or break apart the
nucleus. Humans become exposed to ionizing radia-
tion through contact with materials in the ground,
inhaled radon, radioactive substances within body
tissues, and galactic cosmic radiation. The Federal
Aviation Administration (FAA) acknowledged in
1994 that aircrews are at risk of cancer and other
health effects due to the effects of ionizing radiation.

Supernovae, or exploding stars, are believed to be
the primary source of ionizing radiation emanat-
ing from outer space. During a supernova event, the
core temperature of a dying compact star suddenly
rises, restarting the nuclear fusion reaction. This
destabilizes the star, resulting in an explosion that
propels radioactive particles through space. Solar
flares and other disturbances in the atmosphere of
the sun also produce radiation particles that reach
the Earth.

The FAA operates the Solar Radiation Alert
system in order to inform airlines about radiation
levels at specific altitudes. Alerts are distributed by
the National Oceanic and Atmospheric Adminis-
tration's Weather Wire Service and report radia-
tion conditions between the altitudes of 20,000 and
80,000 feet. Aircraft are recommended to avoid
prolonged flight times at the affected altitudes in
order to minimize the risk of exposure to ionizing
radiation within the atmosphere. Flying at night is
not an effective way to reduce the risk of radiation
from solar disturbances because the Earth's mag-
netic field disbands radioactive particles more or
less equally around the globe.

Long-distance flights at high altitudes expose
travelers and airline employees to the greatest risk
of negative health effects from ionizing radiation.
Flying shorter distances at lower altitudes reduces
this risk because the increased amount of air above
the aircraft acts as a shield against radiation. Addi-
tionally, flights at lower geographical latitudes
receive more shielding by the Earth's magnetic field.
Thus, the risk of radiation exposure is lowest on
short flights at low altitude close to the equator and
highest on long flights at high altitude nearer the
north or south poles.

Fatal cancers are the most common health effects
caused by exposure to ionizing radiation during
flight. Radiation damages DNA and disrupts cellular
metabolism, which can cause genetic mutations
and cancers. Parents who are exposed to high levels
of ionizing radiation can pass on genetic defects to
their children. Prior to conceiving a child, the par-
ents' reproductive genetic material may be dam-
aged by ionizing radiation. During pregnancy, both
the mother and the fetus are at risk of exposure to
ionizing radiation, which can cause a miscarriage or
lead to fatal cancers in the child.

Despite their increased exposure to ionizing
radiation, a study found that German commer-
cial airline pilots had a lower incidence of cancer
than the general population and a below-average
mortality rate. Researchers attributed these results
to the relatively high socioeconomic status of the
pilots as well as the nonsmoking environment in
which they work. Both of these variables contribute to lower rates of fatal cancers throughout the population. Additionally, pilots must meet stringent physical fitness standards, further contributing to their overall health. This study suggests that, while ionizing radiation can contribute to increased incidence of cancer in flight crews, it may not be the most important factor contributing to their risk of cancer mortality.

The carcinogenic effects of ionizing radiation remain one of the primary obstacles to long-distance space flight within the solar system, including proposed interplanetary missions to Mars or asteroids. Astronauts in low Earth orbit are protected from cosmic radiation by the Earth’s magnetosphere, making their risk of cancer relatively low. Beyond low Earth orbit, however, astronauts would be exposed to higher rates of ionizing radiation, greatly increasing their cancer risks. New shielding materials and propulsion technologies would be required to protect astronauts from ionizing radiation and reduce their time of exposure, but these have not yet been discovered. Researchers at the National Aeronautics and Space Administration (NASA) are investigating biomedical and pharmaceutical treatments that might prevent the cancerous effects of ionizing radiation exposure in astronauts. These could include mapping astronaut genomes to look for known cancer-causing mutations and then administering therapies as a preventative measure. Current research, however, remains limited to animal studies and genetic testing of astronauts is a controversial topic.

Workers in the aerospace manufacturing industry and airline flight crews who work during irregular hours experience disruptions in the sleep–wake cycle. This shift work, or work done outside the typical work day, has been shown to lead to increased incidence of cancers due to the disturbance of physiological cycles known as circadian rhythms. Melatonin produced by the body during the night has been shown to have anticancer effects; however, exposure to artificial light at night suppresses melatonin production. In 2007, the International Agency for Research on Cancer concluded that disruptions to circadian rhythms can increase the risk of cancer in humans. Disrupted circadian rhythms correlate with elevated rates of breast cancer, prostate cancer, and colorectal cancer. Flight crews who cross time zones in the course of their workday are especially affected.

Airport employees and air traffic controllers who work at night are also subject to the deleterious health effects of shift work.

Jessica A. Hutchins
Independent Scholar

See Also: Asbestos; Breast Cancer; Careers; Esophageal Cancer; International Agency for Research on Cancer; Jet and Rocket Fuels; Latitude; Lung Cancer, Non–Small Cell; Lymphoma, Non-Hodgkin’s, Adult; Melanoma; Neutrons; Prostate Cancer; Radiation, Gamma; Radiation, Ionizing; Solar Radiation; Solvents; Stomach (Gastric) Cancer; Transportation; X-Rays.

Further Readings
Afghanistan

The Islamic Republic of Afghanistan is a landlocked country in central-southern Asia with an arid to semiarid climate. Afghanistan has been invaded many times, and many great powers have battled for control of this territory, including the Timurids, Persians, Indians, Arabs, and British. In 1919, after three Anglo-Afghan wars, King Amanullah Khan declared Afghanistan a sovereign and independent country and began a modernization program. In 1973, Mohammed Daud seized power in a coup but was overthrown in 1978. The Soviet army invaded Afghanistan in December 1979 and propped up the People's Democratic Party, which had seized power in 1978. As part of the Cold War, the United States and the Soviet Union both funded conflict in Afghanistan with money, weapons, and equipment, and the Soviet invasion and the resulting civil war resulted in more than 1 million deaths and the creation of more than 6 million refugees who fled to the neighboring countries (mostly Iran and Pakistan).

Most of the recent history in Afghanistan saw the rise in power of the political-religious extremist movement of the Taliban, which imposed a brutal Islamic theocracy and committed many crimes against human rights, including systematically massacring civilians, forcing women into segregation, destroying many people's homes, and burning vast areas of fertile land. In 2001, the United States, together with the United Kingdom, launched Operation Enduring Freedom, allegedly in response to the September 11 terrorist attacks. Today, Afghanistan is one of the poorest nations in the entire world.

Decades of civil war and struggle have destroyed much of the Afghan health care system. Poverty, insufficient sanitation, and drought have exacerbated the problem, as has the exodus of health professionals. After Operation Enduring Freedom in 2001, the newly appointed Ministry of Public Health, with the help of foreign nations such as the United States, the United Kingdom, and France, did much to improve the health care system by building new clinics and hospitals, and in 2008, the fees charged for medical services were drastically reduced. However, most of the largest and better equipped medical facilities, many of which are military-controlled hospitals, are located in comparatively wealthy urban settings, such as Kabul, while poor rural communities have access only to lower quality services, often provided by poorly qualified personnel. Some efforts have been made by the government to educate the public about the importance of preventive health care, such as the establishment of a Breast Cancer Day, when volunteers from the Afghan Society Against Cancer distribute leaflets that teach women how to do a breast self-examination.

Afghanistan lacks a national cancer registry system, and specific cancer treatment facilities are not available, so people with the necessary resources often travel to neighboring countries (mostly India and Pakistan) to seek treatment. For these reasons, there are no conclusive statistics on the cancer burden, incidence, or mortality in Afghanistan. However, evidence from older and less comprehensive data sources (e.g., data collected from Afghan refugees in neighboring states or assistance camps, statistics provided by nongovernmental organizations, and research on foreign soldiers) indicates that among women, breast cancer is the most common, while among men, upper gastrointestinal tract (esophagus and stomach) cancer is the most common, followed by skin cancer and prostate cancer. Data on overseas military personnel deployed in Afghanistan show an alarmingly high risk of their developing prostate and breast cancer, possibly due to exposure to toxic substances such as depleted uranium (DU; used in ammunition and bombs).

Both sociocultural and environmental risk factors appear to play an important role in cancer incidence in Afghanistan. For instance, the high incidence of upper gastrointestinal tract cancer may be related to the dietary habits of the local populace, including the consumption of large quantities (up to 1 kilogram per day) of red meat barbecued over a wood fire. The elevated incidence of cancer in foreign soldiers may be related to chronic or continuous exposure to carcinogenic pollutants—from DU to chemicals from burn pits, kerosene-fueled pits used to incinerate all kinds of military waste. Burn pits are known to have released many known carcinogens, such as sodium dichromate, into the air, exposing thousands of
individuals to these toxic materials. The relationship between DU and elevated risk for cancer is controversial, but many peer-reviewed studies have found an elevated incidence of child/infant mortality and cancer in areas with high exposure due to military bombardment (e.g., Fallujah, Iraq). Many field tests performed by the Uranium Medical Research Center on the Afghan population in Jalalabad and Kabul shortly after Operation Enduring Freedom showed DU concentrations 400 to 2,000 percent above normal, and a significant amount of civilians examined suffered from symptoms of acute radiation poisoning.

Claudio Butticè
Independent Scholar

See Also: Breast Cancer; Poverty; Prostate Cancer; Radiation; Stomach (Gastric) Cancer

Further Readings


Age

Cancer incidence shows a clear relationship with age, with the highest rates among older individuals. For instance, according to statistics from the Surveillance, Epidemiology, and End Results (SEER) Program, for the years 2007–2011, age-adjusted cancer incidence rates in the United States for those age 65 and over were 2,095.8 per 100,000, compared to 223.8 per 100,000 for those under age 65. The age-adjusted death rate from cancer is also higher in older individuals: 994.3 per 100,000 for those age 65 and over compared to 55.1 per 100,000 for those under age 65, for the years 2007–2011. Despite this, less is known about this population than about younger populations with cancer. This reflects lower participation in clinical trials and poor understanding of the unique issues in aging and cancer, ability to tolerate treatments, the role of comorbidities and comorbidity management, and perhaps the use of inadequate assessments. Yet with greater longevity, older adults are likely to be survivors with cancer, may benefit from a different approach to both assessment and treatment, and above all, should be treated as individuals rather than as an age group.

Given projections of a United States population by 2030 of approximately 365 million, including 72 million older adults (at or more than 65 years), cancer incidence is expected to increase 45 percent overall to 2.3 million persons with a 67 percent increase in cancers among older adults, according to B. D. Smith and colleagues. This reflects both that tumors occur at a higher proportionate rate for people more than 65 and that, with longer survival rates, T. O. Blank and K. M. Bellizzi report, many of those whose cancer initially occurred at younger age are also present in this older group. These realities require consideration of links between aging and cancer, cancer prevention in older age, challenges for cancer assessment, cancer treatment in older age, survivorship in older age, and palliative and end-of-life care.

Links Between Aging and Cancer

Although rates of cancer increase with age, the nature of this relationship is still unclear, and it
is definitely not established that there is a causal sequence. It does appear that aging is related to greater susceptibility to the promotion of tumors probably because most cancers require time to develop, and molecular changes in tissue attributable to aging both increase readiness to be affected by carcinogens and reduce immunities. V. N. Anisimov advances three hypotheses: (1) higher incidence of cancers in older age reflects longer exposure to carcinogens, (2) age-related physiological change, particularly in the endocrine and immune systems, may create an environment that is increasingly favorable to both the initiation of neoplasms and the emergence and growth of previously latent malignant cells, and (3) higher onset reflects a combination of cumulative mutations, gene silencing, dysfunction in telomeres, and alterations in stromal milieu. Choosing among these hypotheses is further complicated because incremental growth in incidence is not uniform across types of cancer, describes R. A. DePinho.

Cancer Prevention in Older Age
Research on primary prevention, efforts to understand the clinical quality of life, and cost of care implications of health promotion, smoking cessation, and healthy lifestyle interventions for older adults is lacking and therefore is also not a major feature in intervention approaches, S. M. Miller and colleagues state. The long life in the development of many cancers has been an argument for the provision of secondary prevention strategies such as screening particularly, explains L. C. Walter and K. E. Covinsky, because there are likely to be identifiable molecular abnormalities even when cancers appear asymptomatic, and if diagnosed in early or preclinical stages there is a high rate of success in curative surgery. Yet there is less emphasis on screening in older patients, often attributed to responses to shorter life expectancy, concerns about tolerance for screening tests, and beliefs that screenings in younger years were sufficient. However, an increasing older age in populations is now well established, with those more than 90 years being the fastest-growing age group, W. He and M. N. Muenchrath have found. Given this increased longevity, there are recommendations for screenings for breast cancer for women deemed to have life expectancies of five or more years and for prostate cancer for men deemed to have life expectancies of ten or more years (i.e., for the majority of those over age 65) and for additional research to establish similar recommendations for other types of cancers, observe researchers. There are concerns that ageism and poor understanding of the potential to self-manage or be supported in cancer diagnosis and care has encouraged a lack of attention to screening in older adults and indeed to curative treatment, according to R. Yanick.

Challenges for Cancer Assessment
There are issues that traditional cancer assessment may not be sufficiently comprehensive and that standard measures such as the Eastern Cooperative Oncology Group (ECOG) and the Karnofsky performance status (KPS) measures may not be sensitive enough in older age. What is known is that, for older adults, there is a need to both measure and consider depressive symptoms, comorbidities (particularly those that may preclude use of treatment such as a specific chemotherapy drug or that may have a direct or indirect impact on the cancer itself), the accumulation of comorbidities, the level of functional reserve, and potential for toxicity given the likelihood of multiple medications. Reliance on instruments tested for sensitivity for older adults and use of comprehensive geriatric assessment protocols is particularly recommended, states M. Extermann.

Cancer Treatment in Older Age
There are challenges in older age that may mean that cancer treatment is more problematic. Specifically, past disease may influence current onset and readiness for the rigors of treatment, and the progression of cancer may be lower, recovery times may be longer, and there are higher levels of comorbidity which may influence choices in treatment, potential for complications, and likelihood of polypharmacy concerns, describe T. O. Blank and K. M. Bellizzi. Therapy approaches must also consider the potential consequences of reductions in the individual’s cardiovascular and pulmonary reserve, declines in renal function, increased peripheral neuropathy, reduced bone marrow reserve, declines in hormones, and gastrointestinal changes, explain M. Sehl, R. Sawhney, and A. Naeim. However, the biggest challenge for treatment is the lack of older adults in most clinical trials, which means that there is inadequate guidance on appropriate levels of dosing and insufficient
information on potential for intervention effectiveness, according to S. M. Lichtman, L. Balducci, and M. Aapro. For example, in treatment for older women with breast cancer, there is increasing recognition that there have been too few studies of therapy processes, comorbidities, and outcomes. There are also recommendations that trials particularly examine not only the impact of comorbidities but also the cognitive and quality-of-life effects of the treatments themselves. Greater attention is also suggested to physician communication strategies that promote patient choice or that convey ageism and their impact on outcomes as well as attention to the impact of perceived social support on treatment outcomes among a group more likely to live alone, points out M. Tallarico and colleagues. Regardless of research findings, these are areas in practice that require physician and other clinician attention.

There are similar issues with radiation therapy. Older adults are less likely to receive radiation therapy because of quality-of-life concerns or ability to cooperate with the procedures. Their tumors may be identified as less aggressive and therefore not suitable for radiation, and deficiencies in organ function may also be a barrier. Preexisting cardiac issues, devices such as pacemakers, and other comorbidities may be additional barriers. Impaired function and cognitive status and difficulties with transportation may also be construed as reasons why older adults with candidates may not be considered good candidates for radiation, M. K. Mell, L. J. Munt, T. Wasil, and colleagues agree. However, the clinical data available, while recognizing the need to pay attention to comorbidity and quality-of-life barriers, do not support that age in and of itself precludes the use of radiation therapy. What is clear is that more work is needed to better understand the clinical, behavioral, and social support criteria for intervention, whether for radiation therapy or other approaches, report B. Given and C. W. Given.

Survivorship in Older Age
Greater longevity for those with late onset cancers and increased survival of those with earlier onset concerns into older age both mean that cancer survival in old age is a greater reality and must be a feature of cancer responses. The limited data that is available suggests that, in survivorship, older adults may have more psychological issues as compared to those without cancer, but compared to younger cancer survivors, their issues are more likely to be physical with some risks for mobility impairments, which may mean they are no longer able to live independently, explain N. E. Avis and G. T. Deimling.

Palliative and End-of-Life Care
Given the challenges in assessment, the realities of comorbidities, the increased threats to quality of life, and barriers to treatment, treatment options include palliative as well as curative responses. Effective cancer care then requires that clinicians work with patients to better understand their desires and goals. To date, there are concerns that advanced care planning is too rarely undertaken or relies on surrogates who are not sufficiently informed of the patient's wishes, summarizes B. Saraiya and colleagues.

Philip McCallion
State University of New York, Albany

See Also: Clinical Trials; Hospice Care; Pain and Pain Management; Radiation Therapy.

Further Readings
AIDS-Related Cancers

AIDS-related cancers are those that are particularly prevalent in individuals either infected with the human immunodeficiency virus (HIV) or diagnosed with acquired immunodeficiency syndrome (AIDS).

AIDS-Defining Cancer

Three main forms of cancer have been identified as AIDS-defining cancers or malignancies. Kaposi’s sarcoma, non-Hodgkin lymphoma (NHL), and among female patients, cervical cancer are so closely identified with AIDS that the diagnosis of any one of these conditions in an HIV-positive patient signifies the transition from HIV infection to full-blown AIDS.

Kaposi’s sarcoma is rare among the general population; it is several thousand times more common among people infected with HIV. Similarly, NHL is some 70 times more likely to occur in an HIV-positive patient, and among female patients, cervical cancer occurs at least five times more commonly than in HIV-negative individuals.

These cancers occur with high frequency among those infected with HIV due to the oncogenic viruses that cause them. Human herpesvirus 8 is the pathogen responsible for Kaposi’s sarcoma; some subtypes of NHL are caused by Epstein-Barr virus; and human papillomavirus (HPV) is the cause of cervical cancer as well as other genito-urinary cancers.

Kaposi’s sarcoma was, along with pneumocystis pneumonia, one of the rare conditions whose sudden widespread appearance in the 1980s—the first description of AIDS-related Kaposi’s sarcoma appeared in 1981—led to the discovery of HIV and AIDS. While lesions due to Kaposi’s sarcoma can occur on any part of the body, a typical presentation of AIDS-associated Kaposi’s sarcoma includes cutaneous red or purple macules, usually on the upper body and the mucous membranes.
Kaposi’s sarcoma is most commonly transmitted through infected saliva.

NHLs are considered AIDS defining if they are either small noncleaved lymphomas or immunoblastic sarcomas, and they are lymphomas of B-cell or unknown immunologic phenotype; lymphomas of the brain are also deemed AIDS defining. NHLs are caused by, among other pathogens, Epstein-Barr virus; AIDS-related NHLs are the result of a compromised immune system, and a clear correlation exists between the extent of a patient’s immune suppression and the risk of comorbidity.

Cervical cancer among female AIDS patients is a result of infection by human papillomavirus. The risk of cervical intraepithelial neoplasia (CIN) in women with HIV is higher than among the general population; CIN is considered AIDS defining when it escalates into invasive cervical cancer. There is evidence of increased abnormality in Pap tests among HIV-positive women and that screening for cervical cancer by Pap smear is more reliable than by HPV DNA testing.

Because each of the three AIDS-defining cancers is caused primarily by an opportunistic infection, AIDS treatments that address immune suppression will also have an impact on cancers that are a consequence of AIDS—a shrinkage of lesions at the commencement of highly active antiretroviral therapy (HAART) is seen in more than 40 percent of Kaposi’s sarcoma patients, with incidence of NHL in particular among AIDS patients also reducing. HAART works by restoring a degree of immune function, enabling the infected patient to better fight the viruses responsible for these cancers.

Other AIDS-Related Cancers
In addition to the three AIDS-defining cancers, a range of other cancerous conditions are commonly comorbid with HIV and AIDS. Primary among these are cancers of the liver, anus, mouth, throat, lungs, testes, colon and rectum, and skin, as well as Hodgkin lymphoma and angiosarcoma. While these cancers are not caused by viruses opportunistically infecting patients with weakened immune systems, they are typically cancers that are strongly associated with risk factors that are commonly found among AIDS patients. Smoking, for example, is closely linked with cancers of the lungs, throat, and mouth; smoking is more common among HIV-positive patients than in the general population, and smoking, rather than HIV per se, is implicated in the increased incidence of these cancers. Similarly, there is a clear link between cancers of the liver, mouth, and throat and heavy alcohol consumption, which is also more common among patients with AIDS.

There is also evidence that the weakening of the immune system due to infection from HIV leads to a disruption in normal immune responses to very early malignancies.

Anal cancers are more common among AIDS patients; these cancers are primarily caused by human papilomavirus, but the prevalence among AIDS patients would appear to be due to the fact that male anal intercourse is a common means of transmission of both human papilloma and human immunodeficiency viruses.

Since the success of HAART has led to a reduction in the number of patients dying of AIDS at an early age from Kaposi’s sarcoma or non-Hodgkin’s lymphoma, AIDS has become a chronic condition with a significantly longer life expectancy, with the result that non-AIDS-defining cancers such as Hodgkin’s lymphoma and lung cancer have the opportunity to develop.

AIDS and Cancer Treatments
As AIDS is a weakening or failure of the immune system, patients with AIDS have specific considerations in terms of cancer treatments. In particular, chemotherapy and radiation therapy are, even in HIV-negative patients, harmful to the immune system. An additional complication is the interaction between the highly active antiretroviral therapies used to treat AIDS patients and the chemotherapies used to address their cancers. For example, both certain newer antiretroviral drugs and several cancer treatments are associated with long QT syndrome, itself implicated in sudden death from ventricular fibrillation.

Steve McCabe
Independent Scholar

See Also: Cervical Cancer; Kaposi’s Sarcoma; Lymphoma, Non-Hodgkin’s, Adult.

Further Readings
Albert Einstein Cancer Center

Affiliated with Yeshiva University, the Albert Einstein Cancer Center is a leader in basic and clinical research related to better understanding cancer and the human body’s response to it. Taking an interdisciplinary approach, the Albert Einstein Cancer Center combines talents from across Yeshiva University to better understand the origins of cancer and how best to detect, prevent, and treat it in patients. The Albert Einstein Cancer Center has also formed partnerships with private concerns to further research related to cancer. With its location in New York City, the Albert Einstein Cancer Center has played a significant role in providing health services to members of low-income groups from that city.

Background

Yeshiva University was founded in 1886 to provide education for Jewish students and to serve as a center for Judaic studies. Over the years, Yeshiva University has evolved into a major research university, with an endowment of more than $1 billion and serving more than 10,000 students. As Yeshiva University has evolved, it has increased its emphasis upon graduate education, adding a medical school and other programs related to the sciences. In order to advance these research efforts, in 1971, Yeshiva University established the Albert Einstein Cancer Center, which is a part of its Albert Einstein School of Medicine. The initial director of the Albert Einstein Cancer Center was Harry Eagle, a pathologist and physician who once was at the National Institutes of Health (NIH). The following year, the Albert Einstein Cancer Center was designated as one of the inaugural academic cancer research centers by the National Cancer Institute, an honor it has held continually since that time.

The Albert Einstein Cancer Center is comprised of more than 150 scientists and researchers who are drawn from 18 academic departments at the Albert Einstein College of Medicine. These researchers seek to foster basic, clinical, population, and translational research regarding a variety of types of cancer. This work is broadly concentrated on five separate but related areas, which include the following:

- Tumor microenvironment and metastasis
- Stem cells, differentiation, and cancer
- Experimental therapeutics
- Cancer epidemiology
- Colon cancer biology

This interdisciplinary research is supported by a series of 14 shared resource facilities that Yeshiva University has developed. These shared resource facilities provide laboratory space, clinical research services, and population technologies.

Research

Each of the Albert Einstein Cancer Center’s programs serves to find better methods to detect, prevent, and treat specific types of cancer. The Tumor Microenvironment and Metastasis program examines the interactions between cancer cells and their microenvironments so that physicians might better understand those determinants of the potential of tumor cells that allow them to invade surrounding tissues, penetrate blood vessels, and enter and grow in distant tissues. This work has focused upon better understanding the contribution of macrophage subpopulations to tumor progression and how growth factors and cytokine action regulate cell migration, dissemination, angiogenesis, and invasion of distant sites. Work has also focused upon how these studies can be translated into therapeutic results. The stem cells, differentiation, and cancer program brings together investigators working on B-cell leukemia and lymphomas with investigators that study myeloid malignancies. These researchers have been joined by scientists who focus on cancer stem cells so that basic science discoveries related to mechanisms of transcription (including histone and chromatin biology), lineage determination and differentiation, and splicing and translation at the biochemical and molecular levels can be made. This
work has led to a series of correlative and clinical therapeutic trials and to the identification of new targets for future drug development.

The Albert Einstein Cancer Center’s Experimental Therapeutics program has focused upon preclinical drug development. This work has concentrated upon examining transition-state inhibitors, novel microtubule-stabilizing agents, targeted drugs, antifolates, and a broad spectrum of biologicals. This work has proven especially beneficial to physicians working with and patients facing breast, gynecological, head and neck, and lung cancers. The cancer and epidemiology program has been organized in three separate areas, including those working on viral issues; hormonal, obesity, and inflammation concerns; and genetic and epigenetic matters. This work has led to new treatment options for patients and increased understanding of how best to direct future research endeavors. Finally, the biology of colon cancer program has used mouse models and strain crosses to increase understandings of genetic and environmental mechanisms that increase the risk for and development of intestinal cancer. This work has examined the role of inflammation on colon cancer and which treatments show the most promise for patients battling this disease.

Outreach
The Albert Einstein Cancer Center often works with the Montefiore Medical Center, a teaching hospital that is part of Yeshiva University. Located in Norwood, a working-class neighborhood in the Bronx, Montefiore Medical Center has established the Montefiore–Einstein Center for Cancer Care. At this center, researchers from the Albert Einstein Cancer Center engage in a variety of clinical research activities. Members of the clinical oncology services teams conduct these activities as part of multidisciplinary disease-focused teams. Phase I, II, and III clinical trials have embraced a wide spectrum of cancers and their specific stages. A clinical trials office has established specific procedures and services that have assisted with protocol development, regulatory affairs administration, and data management. The Albert Einstein Cancer Center provides scientific review and prioritization of all clinical trials before they are evaluated by the Yeshiva University Institutional Review Board (IRB). This extra level of review has helped to streamline the IRB process and to increase the rate at which proposed studies are approved.

The Bronx contains an unusually high concentration of individuals living below the federal poverty line. Indeed, this community has been identified as the poorest urban county in the United States. The Albert Einstein Cancer Center has made a commitment to improving the health and well-being of the Bronx population and has initiated several programs to help assist with this goal. To that end, the Albert Einstein Cancer Center has conducted treatment research that has focused on reaching a high proportion of ethnic and racial minority patients who are often underrepresented in cancer clinical trials. Epidemiological research conducted by the Albert Einstein Cancer Center has thus concentrated on certain factors that can contribute to the excess burden of cancer in low socioeconomic-status and minority communities, including obesity, viral infections, and comorbid illness. Behavioral and social scientists from the Albert Einstein Cancer Center have worked in conjunction with medical care providers and community partners to find ways to improve cancer outcomes in the Bronx and other areas, efforts that have improved the outcomes for those facing cancer.

Stephen T. Schroth  
*Towson University*

**See Also:** Drugs; Education; Future of Cancer; Hospitals; National Cancer Institute.

**Further Readings**

---

**Alcohol**

The International Agency for Research into Cancer (IARC), part of the World Health Organization (WHO), has classified alcohol as a Group 1
carcinogen since 1988. It is a known fact that cancer can occur when cells become damaged. In addition, it is known that alcohol can indeed damage cells and DNA. Alcohol also reduces the amount of folate in the blood. Folate is a B vitamin that cells need to create new DNA correctly. Alcohol may increase the risk of cancer by impairing the body’s ability to break down and absorb a variety of nutrients that may be associated with cancer risk. In the colon and rectum, bacteria can convert alcohol into large amounts of acetaldehyde, a chemical that has been shown to cause cancer in lab animals. Alcohol and its by-products can also damage the liver, leading to inflammation and scarring. As liver cells try to repair the damage, they can end up with mistakes in their DNA, which could lead to cancer.

Research shows that, the more a person drinks, the more his or her risk for certain cancers increases. Alcohol is a major contributor to cancer mortality; prevention of cancers associated with alcohol use includes limiting drinking. Education, screening, and brief counseling are ways to help decrease the risks associated with alcohol-related cancers.

Prevalence
According to the British Medical Journal, in Western Europe, a proportion of cases of cancer can be attributed to alcohol consumption, especially consumption higher than the recommended upper limits. Among men and women, 10 percent and 3 percent, respectively, of the incidence of total cancer was attributed to former and current alcohol consumption in selected European countries. A study published in 2013 in the American Journal of Public Health found that an estimated 18,178 to 21,284 alcohol-attributed deaths in the United States during 2009 amounted to 3.2 percent to 3.7 percent of all cancer deaths that year (accounting for an average of up to 19.1 years of potential life lost per death).

According to the WHO, alcohol is estimated to cause between 20 percent and 30 percent of esophageal and liver cancers worldwide. The impact of alcohol-related cancer is highest in North America and Europe and lowest in the Eastern Mediterranean and South East Asian regions. Of all deaths from cancers related to alcohol, approximately 30 percent occurred with a consumption of less than 1.5 drinks per day, thus indicating that there may be no safe consumption level at which there is no cancer risk.

Types of Cancers Associated With Alcohol
A meta-analysis of more than 200 studies assessing the links between alcohol and various types of cancer supports that alcohol consumption has been linked to an increased risk for various types of cancer including oral cavity, pharynx, larynx, esophagus, liver, colon, rectum, and in women, breast. The Lancet supported that evidence of a casual impact of average volume of alcohol consumption was found for these types of cancers.

While cirrhosis and aerodigestive cancers are generally seen with higher amounts, increases in incidence are seen at these low levels. The alcohol attribution rate for esophageal cancer is around 75 percent; lip, oral cavity, pharynx, and larynx cancers are around 45 percent; and liver cancer is around 15 percent. Usually, cirrhosis precedes liver cancer and often tends to shorten one’s life even before cancer sets in. According to the American Cancer Society, alcohol can also be connected to pancreatic cancer.

Alcohol can increase the level of hormones such as estrogen in the body. Unusually high levels of estrogen can be linked to breast cancer. An increase in breast cancer can be detected in women who drink one or more drinks per day.

Smoking and Alcohol Use: Double Trouble
People who smoke and drink multiply the risk for certain cancers because tobacco and alcohol work together to damage the cells of the body. For example, research suggests that alcohol makes it easier for the mouth and throat to absorb the cancer-causing chemicals in tobacco, making the risk of these cancers much larger compared to either drinking or smoking alone.

Alcohol Use and Cancer Treatment
According to the American Cancer Society, alcohol should be avoided during and after cancer treatment. Alcohol—even in very small amounts—can irritate mouth sores caused by some cancer treatments and can even make them worse. Alcohol can also interact with some drugs used during cancer treatment, which might increase the risk of harmful side effects. Although for those who have completed cancer treatment, the effects of alcohol on cancer recurrence risk are largely unknown in theory, it’s possible that alcohol use might raise the risk of recurrence.
Prevention

The study published in 2013 in the *American Journal of Public Health* was the first to quantify alcohol use in cancer death, identifying alcohol consumption as a leading cause of cancer deaths. The World Cancer Research Fund found that, in the United Kingdom, 51 percent of esophagus and 22 percent of breast cancers could have been prevented if everyone stopped drinking alcohol. Abstaining or cutting down on alcohol seem to be the best barriers against alcohol-related cancers and other problems. The American Institute for Cancer Research (AICR) provides the following prevention recommendations:

For cancer prevention, AICR recommends not to drink alcohol. However, our expert report recognizes that modest amounts of alcohol may have a protective effect on coronary heart disease. If you do drink alcohol, limit your consumption to no more than two drinks a day for men and one drink a day for women. The evidence that all types of alcoholic drinks increase the risk of a number of cancers is now stronger than it was in the mid-1990s.

The sooner prevention efforts begin, the better. For example, a pooled analysis of 13 case-control studies of cancer of the oral cavity and pharynx combined found that alcohol-associated cancer risk did not begin to decrease until at least 10 years after stopping alcohol drinking. Even 16 years after they stopped drinking alcohol, the risk of cancer was still higher for ex-drinkers than for nondrinkers.

Recommendations and Interventions

The prevalence and risk associated with alcohol and cancer is not well publicized. This is a problem and therefore an area of opportunity for the media, academia, health care providers, community advocates, and policy makers. Educators can use various platforms to inform students about the dangers of alcohol misuse. Early intervention is ideal as the sooner one hears a preventive message, the better. Health care providers have a perfect opportunity to make a difference in terms of prevention and intervention. Recommendations include integrating brief alcohol screenings such as the Alcohol Use Disorders Identification Test—Consumption (AUDIT-C) in primary care and in other points of entry in the health care system, including urgent care settings. The AUDIT-C, for example, is easy and quick to administer and gives a good indication of alcohol misuse.

Alcohol screening, followed by brief alcohol counseling interventions for patients who screen positive, has been found to decrease drinking. Research has shown that brief intervention is effective and essential. In fact, longer counseling sessions are not necessarily better. Five minutes of advice has been shown to be just as effective as 20 minutes. Brief intervention can be a one-time conversation or series of conversations between an at-risk drinker and a practitioner. The goals are to (1) help the drinker increase awareness of his or her alcohol use and its consequences and (2) encourage the person to create a plan to change his or her drinking behavior to stay within safe limits. The conversations are
typically 5 to 15 minutes, although they can last longer if needed. This is much more manageable for health care providers, who are often very busy with high patient workloads. It is not only time effective but cost-effective. One study of trauma patients in emergency departments and hospitals found a net savings of $89 in health care costs alone per patient screened and $330 for each patient offered an intervention.

Conclusions
Research has found that, the more a person drinks, the more the cancer risk increases. Proportions of cases of cancer can be attributed to alcohol consumption internationally. Alcohol consumption has been linked to an increased risk for various types of cancer including oral cavity, pharynx, larynx, esophagus, liver, colon, rectum, and in women, breast. People who smoke and drink multiply the risk for certain cancers. It’s possible that alcohol use after cancer treatment might raise the risk of recurrence if a person resumes drinking. Alcohol consumption is the number one preventable cause of cancer deaths. Prevention of cancers associated with alcohol use includes limiting drinking to no more, or less, than two drinks per day for men and less than one drink per day for women. Alcohol screening, followed by brief alcohol counseling interventions for patients who screen positive, has been found to decrease drinking and should be integrated into all levels of health care.

James E. Phelan
Department of Veterans Affairs

See Also: American Cancer Society; Breast Cancer; Colorectal Cancer, Childhood; Laryngeal Cancer; Liver Cancer, Adult (Primary); National Cancer Institute; Oral Cavity Cancer, Lip and; Oropharyngeal Cancer; Pancreatic Cancer.

Further Readings
American Institute for Cancer Research.


Algeria

Cancer in the north African nation of Algeria is one of the country’s leading causes of mortality and morbidity with roughly 30,000 new cases reported annually. The incidence of cancer is increasing due to growth of the population in the country, population aging, and the pervasiveness of tobacco smoking. The World Health Organization (WHO) GloboCan project reported, in 2008, that there were 28,736 cancer cases in Algeria. The GloboCan project predicted that the cases of cancer would
increase nearly 25 percent to 35,628 by 2015. The most common cancers in the nation are lung, breast, and prostate cancer, which together, account for more than 25 percent of new cancer cases annually. Treatment and management of other types of cancers, including Hodgkin’s disease, have seen considerable progress in Algeria, both in improvement in treatment outcomes and in reduction of long-term side effects.

During French colonial rule (1830–1962), Algerian medical practitioners were trained in European techniques, and health care in the nation came to be well regarded abroad. However, at the time of independence in 1962, it is reported that there were only 300 physicians and a faltering health care system. In the decades since independence, there has been discernable progress in enhancing and expanding the health care sector in Algeria to be one of the best across the African continent. Development has included education and training of doctors and other health care practitioners and the establishment of numerous health care facilities, including 13 university hospitals and research centers, 34 specialized hospitals, 460 polyclinics, 1,110 medical centers, and 3,600 small dispensaries and basic health care units, most with adequate practitioner staffing levels to serve the nation’s 34.9 million citizens.

In recent years, the Algerian health care system has continued to achieve a considerable level of development. Health care expenditures have also continued to increase; the WHO, in 2008, reported that the Algerian government spent more than 10 percent of its overall budget on health care. The gross domestic product (GDP) share of health expenditures has increased in the past decade from 4.1 percent in 2003 to 5.6 percent in 2009; however, this level is low given the vast needs of modernizing health care infrastructure and given that the epidemiological profile of Algeria is changing with increases in noncommunicable diseases such as cardiovascular diseases, diabetes, and cancer.

Most health services for Algerian citizens are provided by the public sector, although there does exist a small private sector in which approximately 20 percent of Algerian physicians practice.

The Algerian government established a national plan of information and communication technology use in the health care sector since 2002 to build connectivity and enhanced and expanded information dissemination to health care professionals and patients.

In 2010, the Ministère de l’Al Santé Algérien of the Algerian government launched a medical orientation plan to 2025 and allocated $28.5 billion to improve the health care infrastructure. Most notably, the plan includes the construction of 57 cancer treatment centers and 200 hospitals to increase health care access across the nation. This increase is important considering that Algeria is the largest country on the African continent, covering 919,595 square miles, and comprises vast rural areas populated by nearly one-third of the overall national population, who have been severely lacking in health infrastructure.

In January 2015, Abdelmalek Boudiah, the Algerian Minister of Health, announced several measures intended to improve health care in Algeria, including promotion of the use of generic drugs and the local production of pharmaceuticals, increasing the production of sera and vaccines by the Pasteur Institute of Algiers, and the creation of new centers to treat cancer. In May 2015, the Algerian Council of Ministers announced a new anticancer plan for the years 2015 to 2019, with funding amounting to about DZD 180 billion. Aspects of this plan include improved prevention, screening, and diagnostic services, modernization of existing facilities, and increased funding for oncology units and anticancer centers.

There are three strategic health and medical sites in Algeria, first, the capital city of Algiers, with expertise in heart disease; second, the northwestern city of Oran, specializing in oncology; and third, Blida, specializing in kidney research and care. However, there are several oncology research and treatment specialists in Blida, most notably at Le Centre Anti-Cancer de l'Hôpital Frantz Fanon de Blida, named for political theorist, activist, and social philosopher Frantz Fanon (1925–1961), who served as head of the psychiatric department of l'Hôpital Blida-Joinville from 1953 to 1956.

Along with the growing health care infrastructure, more generally, the cancer-specific health care infrastructure is developing. Noteworthy clinics with specialization in oncology and radiotherapy include the private Clinique Al Azhar in Dely-Ibrahim. In addition, at least 12 private-sector cancer diagnosis and treatment centers are in their planning stages, along with proposals to modernize existing cancer diagnosis and treatment centers.
and a plan to establish a National Cancer Care Institute in Oran. Medical equipment and particular medicines generally and specifically to diagnose and treat cancer may not be the newest available in Europe or the United States, and thus, some of Algeria’s health care network is in need of modernization, particularly in rural and remote areas.

Cancer specialists are members of international organizations such as le Congrès Nationale de la Société Française de Radiothérapie Oncologique (SFRO) in Paris, France, la Société Française de Cancérologie, la Fondation Française de Cancérologie Digestive, l’Association Internationale des Registres du Cancer, la Société Internationale de Chirurgie Hépato-Pancréato-Biliaire, la Fédération Pan-Arabe de Chirurgie, and the Arab Medical Association of Cancer. They have studied abroad at le Centre International de Recherche sur le Cancer in Lyon, France (CIRC—Lyon) and continued research partnerships with the International Agency for Research on Cancer in Lyon.

Relevant organizations within the nation include L’Association “El Fedjr” d’Aide aux Patients Atteints de Cancer, La Fondation Nationale pour la Recherche Médicale, La Société Algérienne d’Hématologie et de Transfusion Sanguine, Le Société Algérienne d’Oncologie Médicale in Blida.

Tobacco use continues to be an important risk factor for lung cancer in Algeria. A WHO study reported that 29 percent of adult men and 0.2 percent of women in Algeria use tobacco. Surgical procedures for lung cancer include lobectomy, bilobectomy, and pneumonectomy. Adjuvant chemotherapy is a standard treatment for patients with non-small cell lung cancer. The three-year survival rate for lung cancer reported in Algerian research is 22 percent. In addition, there is a relatively high risk for nasopharyngeal carcinoma in Algeria; rates of 5.4 in men and 1.9 in women are 10 times higher than incidence in Europe. Standard treatment of locally advanced undifferentiated nasopharyngeal carcinoma is chemotherapy followed by locoregional radiotherapy.

Cancer registries in Algeria, such as Le Registre des Tumeurs d’Alger, Institut National de Santé Publique, Le Pierre & Marie Centre Curie, Dept. of Medical Oncology, Algiers, and the Algeria Anti-Cancer Centre (CPMC) tumor registry; those of neighboring nations—Morocco, Tunisia, Libya, and Egypt—have increased in number from one to nine and cover at least 13 percent of the total regional population. Data from the registries is considered to maintain quality levels from acceptable to good, according to available indicators. The pattern of risk shown by North African cancer registries is exceptional in that the total cancer burden in the region ranges from one-third to one-half of what is observed in Western Europe. The overall incidence rate in men (world age standardized, per 100,000) ranges from 86.3 in Sétif, Algeria, to 156.1 in Garbiah, Egypt. The range is similar in women: 80.3 in Sétif, to 164.0 in the capital city of Algiers. Case mix and level of rates are quite homogeneous across the region. As mentioned, the most frequent cancers—lung, breast, and prostate—are consistent with those in Western Europe. The pattern of consistency between North Africa and Western Europe diverges entirely from that of sub-Saharan Central and Southern African countries, where infection-related cancers are predominant.

Lara Lengel
Catherine Cassara
Bowling Green State University

See Also: Age; Breast Cancer; Developing Countries; Disparities Within Nations (Elimination of Cancer); Egypt; France; Global Health Issues and Cancer; International Agency for Research on Cancer; Libya; Lung Cancer, Non–Small Cell; Lung Cancer, Small Cell; Morocco; Passive Smoking; Poverty; Smoking and Society; Tobacco-Related Exposures; Tobacco Smoking; Tunisia; Women’s Cancers; World Health Organization.

Further Readings
Boudinar Fatema, Zohra, and Abdelbaki Boukerche. “P-0070 Clinico-Epidemiological and Therapeutic Profile of Gastric Cancer: Experience of Oncology
Allergan (United States)

Allergan, Inc. is one of the major global pharmaceutical companies in the world, and though its involvement in direct cancer therapy is limited, it has played (and potentially will play again) a role in this arena. The precursor to what would become Allergan was founded in 1948, when Gavin Herbert developed its first antiallergy nose drop product; soon after, Gavin Herbert and his business partner Stanley Bly developed an eyedrop to treat allergic conjunctivitis. As a company, Allergan, Inc. was established in 1950 under the name of Allergan Pharmaceuticals. Beginning in 1957, the company was led first by Mr. Herbert’s son, Gavin Herbert, Jr., and more recently Allergan has been led by David Pyott, who served as president and chief executive officer (CEO) since 1998 and serves as chairman of the board and president as well. Allergan is headquartered in Irvine, California.

Allergan is a multibillion-dollar, global health care company with several lines of product in a variety of areas focused on ophthalmic pharmaceuticals, neurology, medical dermatology, urology, and medical aesthetics. The best-known pharmaceuticals offered by Allergan include Botox, Restasis, Lumigan, Botox Cosmetic, and the family of dermal fillers Juvederm. In addition to pharmaceuticals, Allergan’s products include breast implants, and until recently, the company produced the lap band and the Orbera system (an intragastric balloon designed to be inserted in the stomach and to assist in weight loss).

As part of the company’s focus on the urology therapeutic area, in 2008, Allergan and Spectrum Pharmaceuticals announced a collaborative agreement for the development of Apaziquone (EOquin), which was investigated for the treatment of non-muscle invasive bladder cancer (NIMBC), a form of cancer localized in the surface layers of the bladder and that has not spread to the deeper layers of the bladder muscles. However, at the beginning of 2013, Spectrum Pharmaceuticals reacquired all development and commercialization rights for Apaziquone. At least for the moment, Allergan is therefore not directly involved in cancer therapy, though this might change in the future.

Indirectly, some of Allergan’s products still affect the lives of cancer survivors. For example, Allergan is the producer of breast aesthetics products targeted at women who desire restoration of their breasts following a variety of events, including breast cancer.

Finally, it is worth mentioning that, in 2010, Allergan received the CEO Cancer Gold Standard accreditation, recognizing its commitment to concrete actions aimed to reduce the cancer risk of its employees and their families. This award is given yearly by the CEO Roundtable on Cancer, whose goal is to recognize the way in which companies can use screenings, early detection, and healthy changes in lifestyle as ways to reduce cancer risk.

Daniele C. Struppa
Chapman University

See Also: Bladder Cancer; Breast Cancer; Pharmaceutical Industry.

Further Readings


Hendricksen, K., et al. “Safety and Side Effects of Immediate Instillation of Apaziquone Following

**Alternative Therapy: Diet and Nutrition**

Good nutrition is significant during cancer treatment. It restores health and prevents malnutrition. Some cancer treatments rely more on diet and nutrition as natural alternatives to help patients recover from cancer rather than conventional medicine, such as radiation therapy. In most cases, the diets and therapies have not been well tested, and the government has not approved them. However, more research has been conducted, and new therapies are being introduced. A few of these therapies have entered the medical mainstream, and doctors and hospitals are adopting the techniques as a result of increasing requests from their patients.

Alternative therapies do not rely on surgery, radiation, and chemotherapy. Their origins extend far back to ancient times, when they were associated with religion and folklore. Some of the therapies have undergone scientific tests but were either found ineffective or unproven. The therapies analyze the pathological conditions that caused the cancer to take over the body and the conditions needed for the healing. The response to the illness includes spiritual, physical, mental, and emotional factors.

Some experts in the past have called the alternative therapy industry a fringe or quackery. They say it is based on theories; some therapies have not received thorough examination and may reduce the quality of life, and their use may delay treatments from medicines that have been proven to work. Researchers have conducted more studies that have improved the understanding of their benefits, hospitals have adopted some forms of alternative therapy due to requests from patients, and more therapies are being developed and presented to the public. Today, complementary medicine, which uses its approach with conventional medicine, and alternative medicine are generally associated with one another, and they are referred to as CAM. CAM has grown in popularity in the United States and throughout the world.

Experts use five categories to define CAM: mind-body medicines, manipulative and body-based practices, energy medicine, whole medical systems, and biologically based practices. Mind-body medicines imply that the mind can affect the body. Its activities include yoga, imagery, and meditation.

Manipulative and body-based practices involve working with one or more parts of the body, such as massage, chiropractic care, and reflexology. Energy medicine suggests the body has energy fields that can influence healing and wellness, such as tai chi, reiki, and therapeutic touch. Biologically based practices focus on dietary supplements and herbal products like vitamins, foods, herbs, and special diets.

Cancer cases are often explained by genetics and dietary factors. The food consumed and an individual’s nutritional status change a person’s risk of obtaining cancer, the types of cancer the person is at risk of getting, and the age when the cancer develops. Experts have indicated that diets high in fat increase cancer risk, while low-fat diets rich in fiber, fresh fruits, veggies, and whole grains ward off the disease. Diet and exercise increases the body’s defenses, helping slow or inhibit the cancer process.

Diet, nutrition, and medicine play significant roles in the quality of life of a cancer patient before, during, and after treatment. They build strength and energy, help maintain weight, and help accelerate the healing process during recovery.

Many cancer patients experience involuntary weight loss and malnutrition. Treatments like chemotherapy and radiotherapy may cause loss of appetite, problems with swallowing, or an upset stomach. The cancer and its treatments alter the way foods are consumed as well as which foods and nutrients the body tolerates. The nutritional needs of a cancer patient vary. The type of cancer, the treatment, and side effects need to be considered. Patients undergo nutritional screenings and assessments prior to treatment. The screening identifies
nutritional risks, and the assessment determines nutritional health. This also gauges how well the patient can handle the cancer treatment. The patient may have to change his or her diet to include food items that are not typically recommended.

A variety of foods can give the body the nutrients it needs to fight off cancer, and a significant number of patients have sought out alternative nutritional therapies as a result. These therapies have focused on changing the consumption of nutrients that could aid healing and detoxification from the cancer and the treatments.

**Asian Diet**

Many people living in Asian countries who follow the traditional diet have had lower rates of heart disease, obesity, cancer, and other chronic diseases. Most Asians live longer when compared to people in the United States. The diets in these countries are associated with religious practices and long-held customs.

Although the geographical base of the diet is broad and people in each country values their unique flavors and cooking styles, their most common food is rice. They also eat high amounts of plant-based foods, vegetables, fruits, beans, legumes, nuts, dairy, and fish.

Consumption of soy products and tea is very high throughout most parts of Asia. Both are considered food staples. Researchers found that hormone-dependent cancers are less prevalent in Asia. Their studies suggest bioactive components found in soybeans and tea have cancer-fighting properties.

Soybean proteins contain phytoestrogens, such as isoflavones which are found in abundance. Their chemical structure and function are similar to mammalian estrogens. Genistein is the major isoflavonoid present in soybeans. It has been shown in studies to inhibit the growth of cancer cells, depending on the dosage and when the soy is consumed. It has also been found to have antioxidant properties.

A growing number of studies show the cancer-preventive effects of teas. They suggest that tea not only slows down cancer progression, but it also changes the characteristics of the factors related to the cancer development. Most studies have focused on green teas. The components of the tea have been linked to stopping tumor growth at certain organ sites and during certain phases of growth. Other teas showing strong cancer-preventive effects include black, oolong, and white tea. Most of their cancer-fighting characteristics have been associated with the strong anti-oxidative activity of polyphenols, a large group of plant chemicals found in high amounts in green tea. Most of the polyphenols are catechins, which is a type of disease-fighting phytochemical compound.

Studies indicate the combination of the soy and tea have been effective at reducing the proliferation of tumors.

Fish and plant-based foods are consumed in high amounts. These foods are rich in phytochemicals and omega-3-fatty acids, which help to lower the risk of cancer. Phytochemicals are plant-based compounds that exhibit either antioxidant or hormone-like activity. They have been shown to block the action of carcinogens that attack organs and tissues, or they stop the development of the cancer. Omega-3 fatty acids have also been found to suppress the formation and growth of cancer.

The Asian diet also limits certain foods with a high glycemic index, like sugars and starches. The index estimates carbohydrate-containing foods’ effect on blood sugar. Recent research has associated a diet with a high glycemic load with an increased risk of cancer.

**Macrobiotic Diet**

The macrobiotic diet has been around for centuries, and it is believed to have originated in Japan. Macrobiotics started off as a cultural movement in the United States. The movement heightened when it was led by Michio Kushi, who founded the Kushi Institute in Boston. It promoted the macrobiotic way of life. The diet is rooted in spirituality. Its dietary principles include simplicity and avoiding toxins, which relates to some aspects of Buddhism. The concepts of yin and yang were woven into the philosophy. The diet’s association with cancer prevention arose when a popular book promoted the diet’s benefits for cancer treatment and prevention. Research has been limited, but the studies that have occurred show that the diet increases the survival rates for cancer patients and improves the quality of their lives. It also has lowered estrogen levels in women possibly because of its high phytoestrogen content.

The macrobiotic diet’s framework is tailored to the individual. Half of the diet consists of organically grown whole grains such as brown rice, barley, millet, oats, and wheat. Studies suggest the
cancer-preventive effects of whole grains come from estrogen metabolism, glucose and insulin metabolism, and oxidative processes. Local and organic fruits and vegetables make up a quarter of the diet, and the rest of the diet includes soups, seaweed, beans, and bean products particularly containing soy like tofu and legumes, such as chickpeas and lentils. The diet avoids meat, poultry, animal fats, potatoes, tomatoes, sugar, coffee, stimulants, aromatic herbs, and genetically modified foods. It also requires the use of specific cooking materials such as wood, glass, stainless steel, and ceramic. The diet should be properly managed to avoid nutritional deficiencies.

**Mediterranean Diet**

The Mediterranean diet derived from some of the cultures and traditional foods found along the Mediterranean basin. Scientists noticed how Mediterranean countries historically have had a lower incidence of all cancers when compared to northern European countries, the United Kingdom, and the United States. They found a connection with food people ate in those countries and began analyzing the food patterns. They found that it perhaps provides a protective role toward cancer in general.

Some scientists consider the Mediterranean diet as a low-fat diet. It consists of consuming high amounts of olive oil, fruits and nuts, potatoes, vegetables, legumes, seeds, cereals; moderate amounts of fish, seafood, and wine; and low amounts animal products like diaries, meat, and meat products. The diet is rich in antioxidants such as vitamin C, vitamin E, carotenoids, phenols, and flavonoids.

The olive oil is the principal source of fat, and the type of fat is monosaturated, which is a low-saturated fat. Researchers believe the monosaturated fat regulates the gene that has the potential to cause cancer. The consumption of red and white wine has shown that its polyphenolic substances like catechins and resveratrol provide an anti-oxidative effect.

Many of the foods associated with the diet have anticancer properties. Scientists have attributed the diet’s cancer-fighting effects to the integration and interaction of the foods. Some of the foods have undetectable health effects, but when working in combination with other foods, their effects become more pronounced.

The diet has also been associated with lowering heart disease and meets the nutritional requirements better when compared to the Western diet.

The diet also protects against heart disease, lowers bad cholesterol levels, and reduces the chances of getting Parkinson’s or Alzheimer’s diseases. Researchers found that people who followed the traditional Mediterranean diet closely had lower mortality rates.

**Vegetarian Diet**

Vegetarianism is the practice of eating a mainly plant-based diet. The plant sources include grains, nuts, fruits, and vegetables. The diet varies. Some common vegetarian diets strictly exclude animal products, such as a vegan diet, while others include some animal products, such as the ovo-vegetarian, lacto-vegetarian, and pesco-vegetarian diets. The vegetarian diet helps to lower the risk of several diseases, like heart disease, diabetes, high blood pressure, and certain types of cancer.

When compared to diets that contain meat, vegetarian diets offer more fiber, vitamins, minerals, antioxidants, and other plant chemicals. Studies show vegetarians have lower incidences of cancer compared to meat eaters; vegetarians receive more essential nutrients and absorb the nutrients more efficiently, and a vegan diet provides mild protection from all cancers, especially female cancers.

Vegetables are a major source of phytochemicals. Phytochemicals generally provide vegetables with their flavor and color. Studies have found phytochemicals may help to prevent the following activities: the formation of tumors, cellular mutations, and the growth of cancer cells. They have also been found to protect against the oxidation of lipids, which is considered a crucial step to the development of a disease, and they adjust immune and inflammatory responses.

Food processing has a major influence on the levels of phytochemicals in vegetables and vegetable products. Heat, washing, peeling, cutting, and drying can degrade phytochemicals, and many of them can be poorly absorbed; therefore, it is important to manage the diet properly to avoid protein and other nutritional deficiencies.

**Wheatgrass Therapy**

Wheatgrass was popularized for therapeutic purposes by Dr. Ann Wigmore. Most people consume wheatgrass as a dietary supplement, but it
Alternative Therapy: Diet and Nutrition

also has been used to treat common ailments like colds, coughs, and fevers. It is rooted in folk medicine, and not many clinical studies have occurred to help support its benefits. Wheatgrass has high amounts of chlorophyll, and supporters claim that the chlorophyll raises the body’s oxygen level, giving cancer patients energy. It also has an alkalizing effect. This and its antioxidant characteristics help it to fight free radicals in the body. Wheatgrass is rich in vitamins A, C, E, K, and B complex as well as minerals like calcium, iron, and magnesium. It is a great source of protein as it contains 17 amino acids, and eight of them are essential. It also has a high amount of enzymes. Supporters claim wheatgrass boosts the immune system, cleans the digestive system of bad bacteria, and detoxifies the body, causing the cancer to decrease. They suggest only a few ounces of the juice is needed on a regular basis to achieve some of its benefits. However, very little clinical data has been conducted to support its use.

Enzyme and Metabolism Therapies

Enzyme supplements are becoming a common form of alternative cancer treatment. Enzymes are natural proteins that activate and speed up biological reactions within the body. For instance, digestive enzymes break down food in the stomach, so nutrients are absorbed in the body, and metabolic enzymes build new cells and repair damaged cells. Some 10,000 enzymes of various types are produced by human cells to keep metabolism normal.

Enzyme supplements come from animal organs and some plants. They are consumed either by pills, capsules, or powders. Proponents claim the supplements strengthen the immune systems, improve circulation, aid weight loss, and relieve rheumatoid arthritis. They suggest the enzymes strip cancer cells of a protective layer, giving white blood cells the opportunity to identify and attack them.

The use of enzymes in mainstream medicine has occurred. They have shown up in chemotherapy drugs and treated digestive problems for patients who had their pancreas removed. Scientific research has yet to support the claims of the enzyme supplements’ effectiveness.

Metabolic therapies often incorporate enzyme therapy in combination with special diets and nutritional supplements. Research does not support this therapy as well, and some practices are considered harmful.

The metabolic therapy rids the body of toxic substances built up in the body from either food or the environment. Proponents believe the toxic substances create a chemical imbalance within the body.

The therapy uses special diets usually consisting of fresh fruits and vegetables, vitamins and mineral supplements, colonic irrigations with coffee or hydrogen peroxide enemas, visualization, and stress-reduction exercises.

The Gerson Therapy, Gonzalez treatment, Kelley’s Metabolic Treatment for Cancers, and the Issels's Whole Body Therapy are among the types of metabolic therapies.

Gerson Therapy

The Gerson Therapy originated from Dr. Max Gerson. When suffering from migraine headaches, he adopted a low-salt, vegetarian diet to help alleviate his pain. He used his diet to help with skin tuberculosis, which showed some success. The Gerson Therapy rids the body of toxins and boosts nutrition with an organic, plant-based diet that includes raw juices, coffee enemas, and natural supplements. It involves hourly consumption of raw juices, three plant-based meals, and fresh fruit for snacks. Between 15 and 20 pounds of nutrients from organically grown fruits and vegetables are delivered to the body each day. The diet stimulates the metabolism with thyroid, potassium, and other supplements. Coffee enemas help to rid the liver of toxins. The diet does not allow sodium, fats, or proteins. The intense detoxification removes waste from the body, reactivates the immune system, increases oxygen, and improves cell metabolism.

No scientific evidence has supported the claims of the therapy, and it has not been approved for use by the U.S. government. The therapy has been considered dangerous. The coffee enemas have been associated with infections and other health issues, and they even have been related to a few deaths.

Gonzalez Therapy

Gonzalez Therapy was derived from the analysis of early studies conducted by Dr. John Beard. Dr. Beard proposed that the early placenta behaved similar to a tumor, as pancreatic enzymes forcefully regulate their growth, and the development the very same enzymes could defend against cancer. Orthodontist William Kelley developed
Beard’s ideas. Dr. Nicholas Gonzalez began working closely with Dr. Kelley, and their combination of work developed Gonzalez’s regimen. The therapy acknowledges that tissue and organ efficiency are improved by diets, vitamins, minerals, and trace elements; however, pancreatic enzymes target and kill cancer cells.

The therapy involves the use of freeze-dried pancreatic enzymes from pigs, nutritional supplements, and special diets that range from vegetarian raw foods to the Atkins approach; coffee enemas are part of the detoxification routines. The therapy has been promoted to treat advanced pancreatic cancer, but it has not received approval from the government. Although Dr. Gonzalez’s program mimics Dr. Kelley’s, it has many differences. Dr. Gonzalez’s program does not employ the spirituality component, and it allows animal proteins in the initial stages of the program.

**Kelley’s Metabolic Treatment for Cancers**

Dr. William Kelley developed a nutritional program during the 1960s after he learned he had pancreatic cancer and only a couple of months to live. He self-administered doses of enzymes, vitamins, and minerals to treat it and recovered. The treatment comprises four components. Large amounts of pancreatic enzymes are administered daily for an antitumor effect. The diet and supplements support the body. The treatment includes carrot juice and a vegetarian diet. Detoxification occurs with coffee enemas. The program forbids animal proteins. The proteins it does allow include grains, glandulars, and eggs, which must be eaten when the body can metabolize them. The regimen was adopted by Nicholas Gonzalez, who began treating his patients with Kelley’s method. He then provided his patients with a variation of Kelley’s approach.

**Issels’s Whole Body Therapy**

The Issels’s Whole Body Therapy attempts to strengthen the entire body. Dr. John Issels, a surgeon, became convinced while treating cancer patients that a whole body approach was needed to treat the disease. Whole body therapies apply various approaches to cancer treatment and prevention, like combing diet and nutrition, herbs, immune enhancement, and detoxification. Dr. Issels perceived cancer as a general disease of the body and created a therapy intended to restore and regenerate the body’s natural defenses. The Issels’s Whole Body Therapy requires the removal of infected teeth to reduce toxic stress on the body. Tobacco, coffee, tea, and alcohol are among the harmful substances avoided.

Organic whole foods are consumed, and *Lactobacillus acidophilus* is taken for proper digestive support. Toxic emotions like stress and anger are released during an informal psychotherapy. Oxygen therapy is administered to sterilize and reanimate the blood for an aggressive immune response. It uses hyperthermia to reenergize the immune system and encourages a fever to increase white blood cells. Vaccines are deployed for different types of cancers.

Brigitte Yuille

*B. Y. Communications Worldwide*

**See Also:** Asian Diet; Diet and Nutrition; Western Diet.

**Further Readings**


Kállay, Enikő, et al. “Phytoestrogens Regulate Vitamin D Metabolism in the Mouse Colon: Relevance for


**Alternative Therapy: Herbs, Vitamins, and Minerals**

The popularity of dietary supplements has increased, driving more people to use the supplements to ward off disease. Recent research has indicated that some high-dose nutrient supplements can either protect against cancer or cause cancer. Dietary supplements include vitamins, herbs, enzymes, amino acids, antioxidants, and other substances. They are generally distributed as pills, powders, drinks, or energy bars.

Some people may need to take supplements to reach recommended nutrient amounts. These people may be on restrictive diets, or they may have an impaired ability to eat certain foods due to allergies or medical conditions.

Supplements are not drugs and do not need approval from the Food and Drug Administration because they neither treat, prevent, nor cure illnesses. If supplements are taken, use caution. In many cases, getting the adequate amount of essential vitamins and minerals is a balancing act. Getting too little leads to dietary deficiencies, while taking too much can become toxic and may lead to unintended consequences.

Some labels for supplemental products can be misleading. The combination of the supplement with certain prescribed medications or radiation or chemotherapy may interfere with the medications’ metabolism. For instance, some herbs may change the way a chemotherapy drug is absorbed, distributed in the body, metabolized, or eliminated; people taking high doses antioxidant supplements may not only protect healthy cells but tumor cells as well. Therefore, it is important to consult with a health care provider about possible side effects.

Experts recommend that people obtain their nutritional needs through diets rich in vegetables, fruits, and plant-based foods rather than through supplements. Meanwhile, researchers are conducting more clinical studies to determine whether the use of certain supplements cause more harm or provide great benefits when it comes to cancer treatment, survival, and quality of life.

**Herbs**

Herbal medicines have played significant roles in many different cultures. The use of herbs dates back to ancient times. Today, millions of adults throughout the United States have indicated that they use herbal products for health purposes.

Herbs are plants or plant parts that are used for their scent, flavor, or health-related properties. Some dietary supplements either contain only the herb, or the herb is combined with a mixture of other ingredients, but scientists are still learning how they may affect the body, so they can evaluate their safety and effectiveness.

Many health attributes of herbs have been linked to their antioxidant properties, but they can induce changes in a number of cellular processes linked to the risk of cancer or tumor behavior, such as cell division, cell death, and the ability for the body to produce an immune response. Herbs are considered natural health aids, but that does
not guarantee their safety. Sometimes the amount of the herbal supplement received may not agree with what is actually in the bottle. Some factors affect the contents, such as manufacturing and storage methods. Metal, unlabeled prescription drugs, microorganisms, and other substances have contaminated some herbal supplements in some instances.

Therefore, it is important to know how an herbal supplement may interact with prescription drugs and over-the-counter medicines and to receive guidance from a medical professional. It is also crucial that women who are pregnant and nursing take extra precautions.

Açaí. The açaí plant is a species of the palm tree found in Central and South America. The natives of the Amazon have used it for medicinal purposes. The plant produces berries, and studies have found that the berries have very high antioxidant activity. This helps ward off chronic disease. They have cited that the berries’ high concentrations of anthocyanins, which give the berries their deep purple color, exhibit anticancer properties. Also, their polysaccharide, a class of carbohydrates, stimulates white blood cells to help the body to ward off infections. Açaí helps support the immune system.

Allspice. In the 1600s the English thought the herb combined the flavors of cinnamon, nutmeg, and cloves. As a tropical plant, it evolved to protect and preserve its nutrients. It is thought to have antimicrobial, antioxidant, anti-inflammatory, and anticancer properties. It is believed to relieve pain, reduce fever, and offset the formation of tumors. Studies have shown that it can inhibit the growth of several cultured cancer cells. The anticancer properties have been associated with its ability to influence certain carcinogen conversions. However, scientists are concerned that excessive consumption of allspice oil can be toxic and promote inflammation, nausea, and vomiting.

Aloe. Aloe’s roots extend back 6,000 years to Egypt, where it was a common household plant. Aloe vera became a popular species of the plant. When used topically, it heals wounds from burns or abrasions. It is also used as a laxative when ingested. When used as an alternative treatment, its proponents believe that it boosts the immune system and acts directly on abnormal cells, either treating or preventing all types of cancers. Aloe vera is used as a remedy for diabetes, asthma, epilepsy, osteoarthritis, and psoriasis. Some concerns regarding its use include developing diarrhea, its glucose-lowering effects, and its potential danger or even lethality. Aloe products have not undergone a significant amount of review for the government to consider it safe and effective.

Basil. Basil comes from Iran, India, and tropical regions of Asia. Basil use includes treating anxiety, stings, headaches, cough, acne, warts, and kidney malfunction. Basil contains a compound called eugenol, which has been effective with breast cancers because it stops the development of tumors. Basil also has antioxidant, antiviral, and antibacterial properties. Studies have shown that it can lower oxidative damage in animal models.
Caraway. Caraway is used mostly in western Asia, Europe, and Africa. Its seeds have made it a medicinal plant to treat health problems like flatulence, colic pain, and bronchitis. It is known for helping with digestive problems such as relieving stomach spasm, upset stomach, ulcers, bloating, and gas. It also helps to regulate the menstrual cycle and increases breast milk production. An animal study has shown that caraway oils help to suppress the progression of colon cancer. Other studies have shown that thymoquinone, a natural component of the volatile oil of black caraway seeds, has caused some cancer cells to either stop growing or die.

Cardamom. Cardamom is commonly found in Indian cooking and various parts of Europe. The spice is added to sweets, baked goods, and coffee. The seed powder has been used to help with digestive problems like stomachaches, and it relieves vomiting and nausea. It acts as a painkiller and relieves muscle spasms. Its oil is believed to have antimicrobial and anti-inflammatory properties. Cardamom is reported to have antioxidant properties. Studies have evaluated some of its bioactive components and found that it can inhibit cancer development.

Chinese Herbal Medicines. Chinese herbal medicines focus on restoring balance and energy and maintaining spiritual health. The herbs have included astragalus, ginkgo, ginseng, green tea, and Siberian ginseng. Some herbs and extracts can aid in cancer prevention and treatment with mainstream treatment, but more research is needed to determine the effectiveness. Many Chinese herbalists believe that the herbs relieve some side effects from standard treatments like radiation therapy and chemotherapy. The herb can help improve the quality of life, boost the immune system, and stop and prevent tumors from spreading and growing.

Cinnamon. Cinnamon is a traditional Chinese medicine. It comes from the bark of trees that originate from China, India, and South East Asia. The components of cinnamon's extracts influence its antioxidant, antimicrobial, anti-inflammation, and antidiabetic activities as well as its anti-tumor activity. Studies have found that cinnamon inhibits tumor growth and suppresses the progression of certain cancers. However, more studies involving humans are needed. Some people may have allergic reactions to cinnamon, and it should not be consumed in large amounts.

Cranberry. Cranberries originated in North America, and these red berries help with a variety of problems such as wounds, urinary disorders, diarrhea, diabetes, and liver problems. They have high-quality antioxidants, such as flavonoids, and a large quantity of them. Their abundant flavonoid content and phenolic acids are believed to stop the oxidative process, and this may contribute to its antitumor activities. The phytochemicals, which are chemical compounds found in plants, have a strong effect on certain types of tumors. They either slow or inhibit tumor development, and they may also help decrease the risk of certain cancers. Take caution not to consume too much cranberry juice because it can cause an upset stomach or diarrhea. Cranberries should not be consumed with medications that affect the liver.

Garlic. Garlic has been used as a medicine for thousands of years. Eaten raw or cooked, this bulb from a plant has been used throughout the world to relieve a variety of ailments such as arthritis, asthma, toothaches, high cholesterol, heart disease, and high blood pressure. Clinically, garlic has been evaluated for a number of conditions including cancer. It is believed that the anticarcinogenic activity is associated with its organosulfur compounds, which contain amino acids, vitamins, and micronutrients. While garlic appears to be safe for most adults, it can thin blood like aspirin; therefore, it should be avoided during or after surgery or when receiving dental work.

Rosemary. Rosemary, commonly found in the Mediterranean, is a household plant in some parts of the world, and its purposes have included flavoring and cosmetic use. It has been used to relieve renal colic, which is stomach pain caused by kidney stones. It has also helped with stomach spasms, respiratory disorders, and the stimulation of hair growth. Rosemary contains compounds with high antioxidant effects. When rosemary is included with balsamic vinegar, it protects against oxidative stress in humans. It’s phenolic properties have provided protective effects from some cancers by inhibiting the growth of cancer cells as well
as related molecular conditions associated in their development.

**Turmeric.** Turmeric gives the cuisines of many Indian and tropical Asian regions their flavor and color. The root and rootstock contain curcumin. This antioxidant and active ingredient has exhibited anti-inflammatory properties and anticancer effects by slowing the growth and spread of some cancer cells. Studies show the active agent may provide benefits to other ailments like arthritis, Alzheimer’s disease, and stomach ulcers. It is also believed to lower bad cholesterol and improve the outcome of kidney transplants.

**Vitamins.** Vitamins are a group of organic compounds needed for the body to support an adequate diet. These natural chemicals aid biochemical and physiological processes, such as growth, development, and metabolic functions. They are needed to maintain overall health. Some vitamins dissolve in water, while others dissolve in fats and oils. An excess of water-soluble vitamins ends up in the urine, while an overabundance of fat-soluble vitamins gets stored in moderate amounts in the body’s fatty tissue.

Many cancer patients and survivors have opted to take vitamin supplements as a way to stave off side effects from cancer treatments and to avoid recurrence of the disease. Studies have not provided a firm conclusion regarding vitamin use, but doctors have raised concerns that the interaction of vitamins with treatments may lead to undesired consequences such as cancer progression.

Not enough proof has demonstrated that vitamins can prevent cancer, but the following have been studied recently.

**Vitamin B6.** Vitamin B6, a water-soluble vitamin, is found in abundance in foods such as whole grains, nuts, vegetables, and bananas, but the body only needs small of amounts of it to stay healthy. It helps to fight off infections, normalize blood sugar levels, and produce red blood cells. It makes sure enzymes function appropriately and keep skin and nerves healthy. Cancer patients often encounter decreased levels of the vitamin, and this deficiency can lead to mouth and tongue sores and a nervous disorder. Scientific observations suggest vitamin B6 metabolism influences cancer development and tumor progression. The vitamin has been studied in the prevention of hand–foot syndrome. The syndrome is provoked by certain anticancer drugs. The hands or feet either feel pain, swell, tingle, or become numb or red.

**Vitamin B12.** Small amounts of Vitamin B12, a water-soluble vitamin, are needed for bodily maintenance. This includes helping to make red blood cells, DNA, RNA energy, and tissues, and they support the health of nerve cells. Liver, meat, eggs, poultry, shellfish, milk, and milk products are good sources. A B12 deficiency can lead to certain types of anemia and neurologic disorders. Researchers have been studying the vitamin along with folate for the prevention of certain cancers. For instance, studies have suggested a deficiency of folate, a type of B vitamin, is related to cancer development. Folate helps to control the stability of DNA. B12 along with folate may be used to help improve the survival of those suffering from gastric cancer.

**Beta-Carotene.** Beta-carotene is a fat-soluble vitamin, and it is the most prominent carotenoid. A carotenoid is a colorful, natural plant pigment. The body makes vitamin A from beta-carotene. Beta-carotenes are found in yellow and orange fruits and dark green leafy vegetables. Studies have found that high dietary intake of fruits and vegetables with an abundance of beta-carotenes helps reduce the risk of several types of cancer. Beta-carotene is a type of antioxidant. Research has also shown that it influences the differentiation of cancer cells and suppresses their growth.

**Vitamin C.** Vitamin C is a water-soluble vitamin found in all fruits and vegetables. It helps to ward off infections and heal wounds. As an antioxidant, it prevents cell damage by free radicals. Studies determining its role of some types of cancer have demonstrated that large doses of vitamin C delivered intravenously help to reduce inflammation in cancer patients, and it supports chemotherapy drugs by increasing the drugs’ abilities to kill off cancers cells while leaving healthy cells intact.

**Vitamin D.** Vitamin D is a fat-soluble vitamin that helps in the creation of strong bones and teeth and is found in fatty fish, egg yolks, and dairy products.
Some experts indicate that vitamin D is a multifunctional prohormone rather than a vitamin. Skin exposure to sunlight also creates vitamin D in adequate amounts; however, many people throughout the world have become deficient because of concerns related to skin cancer, indoor occupations, and other reasons. A vitamin D deficiency can result in rickets, which is the softening or weakening of bones. Studies have suggested that a vitamin D deficiency not only increases the risk of developing cancer, but it can also worsen the disease.

**Vitamin E.** Vitamin E is fat soluble and it is found in seeds, nuts, leafy vegetables, and vegetable oils. It makes up the majority of food consumed in the Mediterranean diet. It helps to elevate the immune system and prevents the formation of blood clots and cell damage from free radicals that destroy cell membranes through lipid oxidation. Its antioxidant qualities have encouraged research in the prevention and treatment of some types of cancers.

**Folic Acid.** Folic acid is a water-soluble vitamin used to make and repair DNA, so it can create new cells. It also may help with turning some genes on or off. Folic acid is found in whole-grain breads and cereals, liver, green vegetables, orange juice, lentils, beans, and yeast. It is the man-made form of folate, and it is in most multivitamins and considered easier to absorb. Folate is found naturally in green vegetables, juices, and beans, and it has a significant role when it comes to cellular survival and proliferation and is needed for cells to divide. Low levels of folic acid are believed to change the chemicals affecting DNA, which may enable cancer growth.

**Minerals**

Minerals help change food to energy; they aid cellular activities and support a healthy immune system. Some minerals participate in the catalytic activity of enzymes. They fall into two categories: major or trace minerals depending on the amount needed in the diet. Food sources for minerals either come from plants or animals. However, the amount of the mineral found in plants depends on the soil and where the plant was found.

Minerals are an essential part of the diet. No food contains all these minerals, and without them, cellular damage, disease, or death can occur. Some of these elements have anticancer properties. Studies have shown that, when selenium, zinc, molybdenum, vanadium, and germanium are taken in the proper amounts, they can help cancer patients to prevent and improve their ability to achieve natural immunological remission of cancer.

The following minerals recently have undergone scientific review.

**Iron.** Iron supports cell replication, metabolism, and growth. It helps create red blood cells, and a deficiency of it results in anemia. Several studies have shown that elevated amounts of iron can lead to cancers. For example, a research team exposed human breast cancer cell cultures to large amounts of iron and discovered an increase in cell growth. Iron participates in free radical formation, which can contribute to both tumor initiation and tumor growth.

**Selenium.** Selenium is an essential trace element. Studies have focused on selenium’s antioxidant properties and its ability to inhibit experimental tumors, especially those in the gastrointestinal tract. Some researchers believe the mineral’s ability to counteract cell growth may be due to some of its activities, such as its effect on DNA stability, cell proliferation, and regulation of oxidative stress.

**Zinc.** Zinc supports the activities of certain enzymes. It is required for cell division and protein synthesis. Cancer patients generally are deficient in this mineral. Researchers have found that deficiencies can change patterns of gene expression, and when the mineral is replenished, it can induce cancer cell death. Its anticancer properties include inhibiting cancer development and improving immune response. Zinc supplements have been considered for the treatment and prevention of prostate cancer.

Brigitte Yuille
B. Y. Communications Worldwide

**See Also:** Beta-Carotene; Selenium; Vitamins.

**Further Readings**

Alternative Therapy: Manual Healing and Physical Touch

Alternative therapies are known by a number of names: unorthodox, unconventional, unproven, nontraditional, and so on. They have specific meanings in cancer therapy. They are remedies or cures that substitute for standard medical treatments. Nonetheless, most people who use alternative therapies also see physicians and follow standard treatments. This raises questions about physicians treating cancer patients who are also using alternative treatments. This entry discusses alternative cancer therapies and describes their current state and persistence despite the lack of scientific evidence of their effectiveness. Then the most frequently cited alternative therapies involving...
manual healing and physical touch are described and discussed.

**Background**

Medical therapies are a recent arrival; alternative therapies have long histories because they alleviate patients' anxieties concerning a disease that often is overt (openly visible), progressing destructively, and leading to death. The ancient dilemma of the healer is to distinguish a treatment that leads to a cure from the general palliative services provided by a healer. Palliative services are mainly psychological in offering hope in the face of chronic pain, incapacity, and death. But mind and body practices also include evoking a physical response that reduces stress, strengthens the immune system, and alleviates anxiety. This has been called a placebo effect, although it is also physical as the body produces endorphins with physiological effects from touch. This placebo effect can be significant and blurs the line between scientific treatments and other treatments that lack evidence of medical effectiveness.

While this entry focuses on physicians and their unorthodox counterparts, in standard cancer treatment, there are many occupational specialties involved. Their number and variety varies with the kind of cancer and often with the country in which the treatment is located. This entry focuses on the United States, which has a history of conflict between standard medicine and its competitors.

The physician faces a patient who desperately wants to hear more than is medically possible. In cancer, this demand is great, due to the course of the disease, as the patient continues on a downward path, often accompanied by acute suffering. How is this downward course toward eventual death to be managed? There is more to this question than a stark choice between standard and marginal types of treatment.

A third form of treatment appears: palliative care that treats the symptoms. In the competition between standard and alternative treatments, the latter's benefits are often opposed by the medical establishment (and promoted by those marginal to it) by considering only their effectiveness in treating the cancer. This is not the only way to assess their place in cancer care, but it is the way we have come to see the two, not as complementary but as competitors. Considering their potential benefit to the patient, they would be accepted widely if understood to be palliative care.

Competition between medically approved and alternative therapies continues. The former are more likely to prolong life and even effect a cure, while the latter bring hope for a cure through over-promising results.

From a medical point of view, alternative cancer therapies are worthless, and they can cause a patient to forego necessary treatment. Nonstandard treatments can have significant side effects that are harmful or can interfere with the effectiveness of standard treatments. However, there is another side to these therapies, often seen in traditional ones accepted in their native cultures for centuries. They increase the quality of the patient's remaining life by integrating the condition with the patient's culture through giving it meaning that the patient and family can accept.

Unwittingly, both physicians supporting standard cancer treatments and their nonstandard competitors have confused the basic question of how to help a patient in decline from cancer. The two competitors both lay claims to providing a cancer cure. When hope for a cure from standard treatments is small, the nonstandard types gain more traction. Their alternative treatments include those of physicians and others on the borderline between medicine and shamanism. These treatments vary from marginal experimental drugs and therapies to those based solely on wishful thinking that appeal to the desperate.

Open conflict erupted between conventional and alternative cancer treatments over Laetrile, which became the leading unorthodox cancer therapy in the United States during the 1960s and 1970s. Promoters of this unproven drug founded a patient organization, the International Association of Cancer Victims and Friends (IACVF) in 1963, which backed unconventional health approaches, including unproven cancer therapies. This organization founded book stores through their Cancer Book House and arranged transportation across the U.S. border to a Mexican clinic providing Laetrile. In this growing conflict, Laetrile and other nonstandard treatment supporters took to castigating the medical establishment for its opposition to their unproven treatments and characterized standard medicine as inhumane, blocking medical progress, and creating a monopoly.
The John Birch Society supported the Laetrile social movement through its book stores and chapters across the country. Together, they opposed the legal restrictions on unproven cancer treatments. The John Birch Society opposed the federal government in general and promoted opposition in local communities to the fluoridation of water as a communist plot to poison the American people. With support from the John Birch Society and other opponents of government regulation, Laetrile providers sponsored legislation that exempted Laetrile from the Federal Food and Drug Administration's (FDA's) control. Although strongly objected to by state medical societies, these local political movements often were successful in swaying the public and the legislatures of states. Eventually 27 states passed laws favoring unrestricted Laetrile use. However, the FDA remained in control as the federal government forbade the transport of Laetrile across state lines.

Despite efforts of medical practitioners to support education about medical treatment, alternative therapies continue to have public support. In a recent study by Yates and colleagues, 91 percent of cancer patients receiving radiation or chemotherapy admitted to their doctors use of alternative or complementary therapy. In cancer centers across the country, this combination is called integrative medicine. A cancer diagnosis continues to evoke a strong emotional response of fear, anxiety, and dread. Countering this reaction is integrative medicine, supplementing standard treatments with others that offer hope and, for manual methods and physical touch, the human touch.

The question remains of how many cancer patients use complementary and alternative practices. In some studies, patients are counted as using alternative treatments when they are merely using vitamin supplements or praying for good health. The number using specific alternative treatments appear to be rather small, although when the numbers include all forms of these alternative treatments, which are quite numerous, they can appear much larger.

In recent years, although they remain controversial, alternative therapies have been tolerated by many physicians. Their hope is that alternative treatments will supplement, not supplant, conventional cancer treatments. An alternative treatment can become complementary, save for the lingering conflict between standard medicine and supporters of nonstandard treatments who reject science, claim they have a new science that "doctors don't want you to know," or overpromise cures.

By remaining ethical and not offering false hope to needy people, physicians have opened the door to marginal therapies that mainly offer the hope that adept charlatans exploit. However, not all purveyors of alternative and complementary therapies are charlatans; many view themselves service providers or professionals in their craft. Each type of alternative therapy has its own social history and presentation to the client. It is a disservice to view such practitioners as charlatans or opponents of standard medicine. This is especially the case with manual healing and physical touch, which involve specialized occupations with considerable training and certification. They are found today in centers of integrative medicine and in a growing number of hospitals and clinics, alongside conventional medicine.

The unfortunate social history of nonstandard treatments in conflict politically with standard medicine has its echoes in the National Institutes of Health (NIH) today. The NIH has housed the National Center for Complementary and Alternative Medicine (NCCAM) since 1999. However, the center has been controversial within the NIH and medical establishment, especially as it offers grants for the study of certain of these alternatives. Nonetheless, the center has become a respected source of information about nonstandard treatments.

Summary of Manual Healing and Physical Touch

The picture of alternative cancer therapies is complex, filled with a large variety of nostrums and practices. The category of manual healing and physical touch alone includes 32 different therapies, according to the American Cancer Society. Each has its own characteristics of interest, and most will be included here. Unless noted otherwise, all have the following characteristics: (1) they do not have any proven benefit for the treatment of cancer, such as slowing or halting its progression; (2) they are sometimes helpful in providing palliative results in reducing stress, producing relaxation, and increasing tolerance for pain; (3) for some patients, they alleviate certain side effects of cancer treatments, such as nausea, and (4) their physical nature, which
may include forcible and vigorous manipulation of the patient’s body, carries risks. In all cases a cancer patient should consult with a physician before embarking on a course of alternative therapy.

**Acupressure and Shiatsu (Traditional Asian Bodywork)**

These therapies include varieties of traditional Chinese medicine (TCM). As such, they have a different social history from the alternative treatments that are a product of American culture. TCM has a history of being central to Chinese medical practice, while alternative treatments remain marginal in the United States. The benefits of TCM include the integration of the traditional patient and patient’s family into Western medical practice when TCM is used as a complement to standard medical treatments.

Asian bodywork is based on traditional theories of the body, including the pressure points along body axes that are more commonly known through their use in acupuncture. In bodywork, these pressure points are the focus of massage and finger pressure. The techniques include the following: acupressure, shiatsu, tui na, ohashiatsu, and watsu.

There are concerns that bodywork and massage in general can be harmful for cancer patients and should not be carried out in areas that may be affected by tumors. The concern is that cancer cells could be spread by vigorous massage, bones that are weakened by cancer and its attendant therapy could be fractured, and contraindications for specific types of Asian bodywork should be checked before undergoing those treatments for specific cancer conditions. In general, practitioners of Asian bodywork are usually trained and conversant with the limitations of their practice for cancer patients and should be open to discuss them with their clients. The American Cancer Society is a good source of information on all alternative cancer treatments.

**Acupuncture**

The best-known TCM, acupuncture, consists of inserting very thin needles through the skin along the pressure points visualized in TCM. It has the singular quality of being testable in double-blind experiments when the insertion of the needles through a mechanical device can be manipulated without the knowledge of either the patient or practitioner. That is, the needles can be inserted at the assumed proper depth or merely into the surface of the skin. The results show that the same degree of benefit is felt by the patient whether the needles are used traditionally or not. This finding supports the conclusion that these alternative medicine techniques are acting as placebos. Nonetheless, a placebo benefit can be useful and helpful, so it cannot be discounted completely.

Unlike more vigorous physical manipulation, acupuncture is considered safe when the needles are sterile and the acupuncturist is careful and well trained. However, certain health conditions (such as the use of blood thinners, which prolong bleeding) are contraindications for acupuncture. Acupuncture is not recommended for patients with implanted electrical devices such as pacemakers.

**Applied Kinesiology**

Not to be confused with the academic discipline of kinesiology (the study of human body movements), applied kinesiology is based on an archaic theory that organ function can be diagnosed through the pressure testing of an associated muscle. Evidence for these beliefs is absent. Practitioners can include medical professionals as well as trained applied kinesiologists. While mainly diagnostic, some claims of treatment and even cures of cancer have been made by practitioners. Other than the danger of postponing necessary cancer treatment, applied kinesiology is considered safe.

**Bodywork**

Various bodywork practices exist. They are active (through exercise and awareness activity) or passive (another person manipulates the body). In general, most practitioners claim benefits without claiming to prevent or cure cancer, although a few do in the absence of evidence to support such claims.

Bodywork includes Rolfing (a passive form with practitioners using deep pressure), the Feldenkrais Method (an active form following a sequence of movements under guidance), and the Alexander Technique and the Trager Approach (a combination of self-guided motions with practitioner touch).

As with Asian bodywork, cancer patients should avoid manipulation of areas where a tumor is or may be present along with vigorous movements and pressures on affected body areas. Practitioners
skilled in dealing with cancer patients will avoid risky activity.

**Chiropractic**
This alternative medical system has trained professionals who deal mainly with problems related to pain and stiffness in physical movement. The practice is based on a theory that alignment of the spinal vertebrae is the cause of various physical problems. The practice is also called spinal manipulation. A few practitioners also claim that diseases, including cancer, are caused by misalignment of the spine and promote chiropractic as a cure. There is no evidence to support such claims, but there is some that chiropractic alleviates some back pain and other bone and muscle problems. Chiropractic should be avoided in cases of advanced cancer or cancer of the bone. Cancer patients should consult their physicians before undergoing chiropractic.

**Craniosacral Therapy**
Also known as cranial balancing, cranial osteopathy, cranial sacral manipulation, and craniopathy, this is a massage treatment used on the head, back, and pelvic area. The treatment is said to normalize various body systems dependent (in theory) on the bones and fluids in the head, back, and pelvic area. In this theory, many different diseases and conditions are a product of obstructed flow among these areas. Cancer patients should consult their physicians before undertaking any such therapy involving manipulation of muscles and bones, as in acupressure.

**Cupping**
This is a form of TCM that is also found in other world cultures. It consists of inverting a cup or glass full of hot air over the patient's skin. As it cools, the air pressure inside reduces, causing the skin to be pulled into the container, along with what are believed to be poisons and, in some cultures, evil spirits. Sometimes the skin is punctured before cupping, causing blood to be sucked into the device as a kind of purge. While relatively safe, it has no known medical benefits and has been the cause of child abuse reports in the United States.

**Massage**
There are many forms of massage, using pressure, friction, and manipulation on the muscles of the patient's body. The manipulation can be with the hands, other parts of the therapist's body, and with tools. The objective is to enhance circulation and reduce muscle stiffness felt by the therapist and targeted as knots or trigger points. Massage may produce relaxation, reduce pain, and enhance range of movement.

Massage appears in various forms. The most popular in the United States is Swedish massage, or simply massage therapy. It consists of long, deep strokes and uses lotion and oils. Sports massage is designed for relaxing sore muscles and involves stretching as well as massage. Aroma therapy massage adds scented oils to vary the mood of the session. Hot stone massage involves heated stones placed on body areas for relaxation and gentle pressure, less than other massage techniques. Deep tissue massage is more forceful and uses friction techniques. Additional types focus on the target area (back massage), the type of client (pregnancy massage), and more (myotherapy, neuromuscular therapy, Thai massage, and trigger point therapy). Professional massage therapists are trained and certified. They are available in clinics, hospitals, and other venues. Massage has a long history in many cultures. It appears as alternative therapy but lacks evidence that it can treat or cure cancer. Massage has the contraindications of other forms of bodywork, but variations that use injections are more problematic.

**Moxibustion**
Also known as acumoxa or auricular mo, moxibustion consists of applying heat to a body's acupuncture points to stimulate the body's forces for self-healing. In TCM, a small pile of herbs (moxa) is burned on the skin, which may be painful and scarring. Today, the heat is applied through acupuncture needles. This technique is claimed to cure diseases but lacks evidence that it does, as in cupping.

**Myofascial Release**
The theory behind this therapy is that the body's connective tissue becomes rigid and needs stretching and manipulation to relieve pain and restore proper functioning. Practitioners include some chiropractors, massage therapists, osteopathic doctors, and others. The evidence supporting the theory and its resulting claims is lacking. The usual problems
with use for cancer patients are present, and cautions should be observed.

**Osteopathy**

Osteopathic medicine is an alternative medical practice with trained physicians (doctors of osteopathy [DOs]) who practice medicine. Osteopathy involves manually testing the patient’s bones and muscles. If not in balance, they can be brought into balance through physical manipulation. For many osteopathic physicians, their osteopathy practice is integrative medicine. But a few may place unwarranted faith in the efficacy of osteopathy itself to cure disease.

**Polarity Therapy**

A form of massage, polarity therapy (also called polarity balancing or energy balancing) uses a theory of bodily energy flow to direct the application of massage, combined with other forms of treatment. Polarity therapists are trained in this theory, with about 1,000 practitioners in the United States. They combine many alternative and complementary techniques, and no two patients are treated the exact same way. The benefits and cautions are the same as acupressure and massage.

**Psychic Surgery**

Practitioners claim that they can remove cancerous tumors, diseased organs, and toxic materials invisibly by using their fingers and hands pressing against the patient’s body, performing psychic surgery. This is a traditional form of healing practiced among Native Americans and notably in the Philippines. Close observation shows that the shaman produces blood, feathers, cotton, leaves, and other material from a place apart from the patient’s body. There is no evidence that this is effective against cancer or any other disease.

**Reflexology**

Similar to forms of massage and traditional healing, the cluster of therapies oriented to the hands and feet come from a belief in pressure points that affect energy flows through the body. Those points are targeted for massage in reflexology and zone therapy. The same results and cautions for acupressure and massage in general apply here.
Reiki
This is a traditional Japanese form of massage that channels the body’s natural, spiritual energy through the body. By removing obstacles to energy spread by massaging blockages, the body’s ability to heal itself is enhanced. Because only light touch is involved, Reiki is considered safe.

Rosen Method
This is a form of massage combined with counseling. Painful memories and thoughts are believed to be located in tense muscles that can be manipulated to free those negative thoughts for other therapy. As only light touch is involved, the Rosen Method is considered safe.

Rubenfeld Synergy Method
Very similar to the Rosen Method, the Rubenfeld Synergy Method (also called the Listening Hand) incorporates hypnosis and dream analysis with massage and talk. As in the Rosen Method, there is only light touch involved, and it is considered safe.

Therapeutic Touch
There is no actual touch involved in this technique, which is practiced mainly by registered nurses. Therapeutic touch is based on a nonstandard belief in a body’s energy fields; the touch therapist can feel, manipulate, and remove negative energy from the patient. Touch therapy has been tested, and therapists have been unable to distinguish the presence or absence of a human hand behind a screen.

Conclusion
Originating from many different cultures and theories of health and disease, manual healing and physical touch appear greatly varied. But as they move toward being complements to standard treatments and are incorporated into integrative medicine and normal hospitals, they become more similar to each other. They present a theory of the body being out of its natural order and use some kind of physical manipulation and talk to soothe the patient’s fears. They complement standard medicine by serving as a placebo, where standard medicine is constrained in what its practitioners can offer a suffering, even dying, patient.


Further Readings

The art and science of healing that involves mind, body, and spirit, variously called holistic medicine, unconventional medicine, complementary medicine, or integrative medicine, provides a viable system of medicine that focusses on empowering the individual for optimal health conditions. Although in existence for thousands of years, especially in India and China, healing and medical care have in recent years sought to include holistic medicine as providing an alternative care system alongside biomedicine.

More so, of late and also globally, alternative medicine has revealed a significant paradigm shift in the way human body, illness, and illness states have been observed, perceived, and interpreted. Being more akin to a revolutionary approach to dealing with health and disease conditions of the contemporary world, with focus on behavioral, psychosocial, and life-style interventions, alternative medicine understands the human being as a totality of mind, body, and spirit, which calls for understanding disease and health in accordance with the balance of three vital elements.

Needless to say, amid restoring the balance of the constituent elements, the patient occupies a central place in understanding his or her symptoms and eventually manages the treatment plan.
under the guidance of an alternative healer. In other words, owing to the indispensability of the patient’s contributions, empowering patients in a way that would contribute to producing his or her effective mental, physical, social and emotional well-being forms the basis of an individualized treatment philosophy in alternative medicine. It aims to resolve the physical, mental, emotional, spiritual, economic, and social elements of the patient. The ideal of integrated care, thus, entails, according to M. Nadeau and D. Moss, “that the full range of mind–body interventions are included from the first day of any patient’s health care, and remain a part of each successive episode of treatment.”

With a patient or individual-centered focus, a unique dynamic relationship between the physician and the patient becomes imperative. This dynamism builds up patient autonomy in the context of his or her social and physical environment, including the immediate family, peer groups, occupational links, and spiritual elements. Additionally, there develops a desire to know more about various alternative health options, philosophies, and therapies.

Understanding Alternative Medicine in History
In scholarly discussions on health care systems and alternative healing practices, an important issue that comes to the fore is the historical trajectory that has paved the way for the professionalization of contemporary elements of alternative healing practices.

The development of the medical profession has witnessed an interesting trajectory of medical practice and, concomitantly, the visions of medical practitioners. Physicians in the early part of the 19th century, while maintaining “allegiance to traditional drugs doing something active in place of waiting for nature, instilled confidence in patients that the doctor had power and confidence stimulated recovery,” according to James Whorton.

While the traditional knowledge systems have been in existence for almost 3,000 years, the framing of alternative medicine in some parts of the world, such as America, appear to have emerged in the early 1800s, but at the time, alternative medicine included practitioners of folk medicine herb doctors, the purveyors of native American medicine and other informally trained practitioners, who were not, as described by Whorton, “professionalized to any significant degree.”

Ironically, their practices were not termed alternative well until the late 1900s; prior to this, they were said to practice irregular medicine. Elsewhere and in the rest of the world, the early part of the 20th century was significant for the developing medical profession. The rise of the scientific discipline highlighted the professional unity among advocates of Western biomedicine against competition from nonconventional practitioners; besides, the rise of the pharmaceutical industry in the interwar years also added to this differentiation and distancing of Western biomedicine and nonconventional medicine. Although significant advances in the medical sciences were made in the late 19th century, they were regrouped only retrospectively at the turn of the 20th century. The development of the germ theory of disease alongside scientific advances in natural and biological sciences, and the founding of new institutions to study tropical medicine, strengthened the authority of Western biomedicine in the Western world. With these were heightened the nuances and differences between Western biomedicine and indigenous systems.

The global appeal of alternative medicine and its impact on health and wellness concepts have their roots in the early 20th century, when “natural” remedies and focus on physiological balance through diet and controlled personal life style took shape. In Wharton’s words, “‘The best antiseptic’ was not the chemical drugs but the ‘vital force.’” This force was largely responsible for the changes associated with various bodily processes such as metabolism, reproduction, and growth.

While there are several alternative practices of healing involved, Ayurveda exists as one of the oldest systems of medicine practiced in India since ancient times. Believed to have origins in the oldest repositories of Indian knowledge, the vedas, Ayurveda literally means knowledge of life or longevity (ayus = life and veda = knowledge) and was codified almost 3,000 years ago by sages. As an alternative and mind–body medicine, it was first introduced to Europe and North America in the late 1970s and 1980s. Vasant Lad’s Ayurveda: The Science of Healing (1984) was largely successful in bringing Ayurveda to the American audience. Similarly, Deepak Chopra’s reputed works reflect the success in appealing to a large audience through the language of biomedicine with a well-received focus on mind–body medicine; Deepak Chopra is also known for his tireless efforts
in translating the ancient 4,000-year-old healing knowledge into bringing emotional, physical, and spiritual balance in individuals’ lives across the globe; his signature program, Perfect Health, offers a unique blend of meditation, Ayurvedic healing, and yoga for optimizing good health and well-being.

Alongside Ayurveda, Chinese traditional medicine, has been equally successful in drawing a popular appeal for its ability to improve lifestyles and quality of life across the world. In effect, mind–body medicine is premised on the belief that the state of mind can affect bodily functions and symptoms. A healthy state of mind is achieved through meditation, relaxation and yoga, and qi gong. Qi gong refers to traditional Chinese medicine that aims to bring bodily functions into a balance through vital energy, or qi. Similarly, naturopathy guides the special energy that, in turn, guides other bodily functions. Both Ayurveda and traditional Chinese medicine have various specialties that strengthen their professional base and healing capacities. The unique combination of body doshas or bodily humors (vata, pitta, and kapha), which make up a unique mind and body constitution, is expressed through various blends of physical, mental, and emotional states of individuals.

Over the years, the appeal of alternative medicine has also been facilitated through the establishment of various institutions. For instance, the National Ayurvedic Medical Association was founded in the United State in 1998, while the Ayurvedic Practitioners Association was founded in 2005 in the United Kingdom; both have institutionalized alternative practices by providing leadership and a positive vision of a holistic approach to healthy living to promote and preserve the knowledge base of Ayurveda. Ideally, alternative or holistic medicine engages in the use of lifestyle changes aimed at treating the disease. While certain diseases may be easily dealt with, achieving mind–body–spirit balance in special life-threatening diseases can be particular helpful for patients suffering from cancer. Increasing stress owing to the uncertainty in a patient’s life heightens mental and physical stress. It is here that the significance of emotions, family, and social behavior becomes apparent. Finding self-help groups and survivors of cancer have an important role to play in decreasing the stress resulting from the dreadful affliction. Thus, according to Moshe Frenkel, “Where as evidence for the role of psychosocial factors in cancer initiation has been equivocal, support continues to grow for links between psychological factors such as stress, depression, and social isolation and progression of cancer.”

Premised on the crucial principles of innate healing powers and treatment directed toward understanding the cause of the disease rather than just treating it, holistic medicine addresses the nature of a person to enable self-healing and well-being with the eventual aim to enhance the quality of life and overall health. Thus, remark N. Cummings and J. Cummings, “The patient of the future will encounter an integrated system of behavioral and medical care, involving a partnership of behavioral practitioners, physicians and nurses, in ‘one house’ and ‘one system’.”

Poonam Bala
Cleveland State University; University of South Africa

See Also: Alternative Therapy: Diet and Nutrition; Alternative Therapy: Herbs, Vitamins, and Minerals; Alternative Therapy: Manual Healing and Physical Touch; Alternative Therapy: Pharmacological and Biological Treatment

Further Readings

Alternative Therapy: Pharmacological and Biological Treatment

Alternative therapy for cancer treatment encompasses those treatments not taught in conventional
Alternative Therapy: Pharmacological and Biological Treatment

medical schools and not generally offered at hospitals and cancer centers across North America. Some of these therapies have been used in the past, some use pharmaceutical substances, while some use variations on dietary interventions. It is impossible to review all alternative therapies, so the focus is on those that have been studied and have the most promise, listed here in alphabetical order.

**Alpha Lipoic Acid**

Alpha lipoic acid (ALA), also known as thiotic acid, is an organosulfur compound essential for aerobic metabolism. It is available as a dietary supplement and marketed as an antioxidant. ALA is a cofactor in the pyruvate dehydrogenase complex and at least four other enzyme systems including the production of acetyl-coenzyme A. ALA scavenges reactive oxygen species and reactive nitrogen species. Its therapeutic and antiaging effects may be due to modulation of signal transduction and gene transcription, which thus improve cell antioxidant status. This is likely through Phase II detoxification enzymes. Humans produce less ALA with aging.

ALA is found in foods such as kidney, heart, liver, spinach, broccoli, and various yeasts, but the quantities are extremely small; 10 tons of liver yields 30 milligrams. All ALA used as a supplement is chemically synthesized.

ALA helps cells undergo normal apoptosis, a process absent in cancer cells. ALA induces apoptosis in ovarian and lung cancer. This apoptosis occurs by up regulating the caspase-independent and caspase-dependent apoptotic pathway, which is mediated by intracellular calcium.

In three patients with pancreatic cancer, intra-venous ALA was instrumental in reversing their cancers and leading to survival of more than 78 months. One patient had a history of pancreatic cancer with metastases to his liver and retroperitoneal region as well as a history of B-cell lymphoma and prostate cancer. ALA in these patients reduced oxidative stress, stabilized NF-kappa-B, stimulated pro-oxidant apoptosis and discouraged malignant cell proliferation.

The main side effect of intravenous ALA is a hypoglycemic with nausea, fever, and chills that can develop several hours after treatment. This does not occur in all patients and may be dependent on the source of the synthesized ALA. ALA is sensitive to light, and so it is stored in the dark, and the IV bag is covered during the infusion. Clinical trials are required to confirm the successful case reports.

**Cancer Clinics Abroad**

There are many cancer clinics where patients go for treatment that operate outside of the United States and Canada. The number of clinics and types of therapies offered is too many to list and evaluate. There is no independent rating scheme or agency to evaluate the success of these clinics or the types of cancers they specialize in treating.

Mexico houses a number of these clinics. Some are small hospitals where patients can stay for several weeks; others are clinics where treatment is provided in nonhospital settings. Therapies include diet and fasting, vitamins, and chemotherapy cocktails.

Cuba has a large population of well-trained physicians who offer both conventional and alternative cancer treatments. Diet, fasting, surgery, chemotherapy, and vitamins are given as therapy. Patients from the United States cannot fly directly to Cuba because of embargo policies.

Europe offers numerous small clinics or small hospitals where patients can receive treatment. Diet, fasting, hydrotherapy, botanical medicines, homeopathy, chelation, vitamins, and chemotherapy are the principle treatments.

**Chelation Therapy**

Chelation is derived from the Greek word chele, which means claw, so named because a chelating compound binds with a metal and carries it out of the body in urine or stool. Various chelators have been developed to remove lead, mercury, arsenic, radioactive by-products of the nuclear industry, copper, iron, and other metals.

The first chelator used in a clinical setting was calcium-disodium ethylene diamine tetracetic acid (EDTA). It was infused in the 1950s into workers from a battery factory with high levels of serum lead. A side effect of this intravenous treatment was that several of the patients had improvement of their coronary heart symptoms and were able to walk farther with less pain. Subsequently, many physicians used EDTA as a treatment for coronary heart disease.

Controversy arose because there were no clinical trials, and EDTA had not been compared to the then standard coronary bypass surgery. A large trial
was recently undertaken, conducted in the United States, to assess the clinical effectiveness of EDTA for heart disease. It did not test the hypothesis that EDTA treated or prevented cancer. Anecdotal data published by several physicians noted that patients who had received multiple EDTA treatments had lower incidences of cancer or less-aggressive cancers than nonchelated patients.

Iron is an essential mineral, but iron overload can be a factor in the development and progression of cancer. Iron chelators have been tested for their antitumor effects in cell, animal, and human trials. Most studies use desferrioxamine (DFO), a drug approved for iron overload. DFO has a positive but modest effect on cancer. Newer compounds appear more promising. These compounds will require similar testing to determine their clinical potential.

Copper is an essential mineral but, at high levels, is a promoter of inflammation and tumor growth. Tetrathiomolybdate (TM) is a novel anticancer and antiangiogenic that chelates copper and causes NF-kapp-B inhibition. Cell line, animal, and Phase I and II human clinical trials have shown both efficacy and limited toxicity. Further study is needed to ascertain the place of TM in the treatment of cancer.

Coley Toxins
William Bradley Coley, M.D., was a bone surgeon at New York City Cancer Hospital, later part of Memorial Sloan–Kettering Cancer Center. When an early patient he operated on for sarcoma died, he sought answers. He found references to fevers and cancer going into remission back to the 1700s; the organism was likely Streptococcus pyogenes. Initially, he injected bacteria. The condition was difficult to control, and in 1893, he switched to dead bacteria: Streptococcus pyogens and Serratia marcescens. He injected more than 1,000 patients with at least 13 versions of what became known at Coley's Toxins. He published a case series showing about a 10 percent cure rate, with the greatest effect in ovarian cancer and postmenopausal breast cancer. In 1962 Coley's Toxins were assigned new drug status by the Food and Drug and Administration, meaning they could not be prescribed outside of a clinical trial. They are manufactured today in Canada, Europe, and China and used in Germany, Central America, and China. The bacterial formulae vary, and one company is studying the DNA of the bacteria as a treatment.

Research is limited despite wide clinical use. In a trial of follicular lymphoma, 85 percent had a complete response compared to 44 percent who received only chemotherapy. A study of advanced liver cancer found better results in those treated with Coley's Toxins than those who received liver resection. A retrospective study of surgery and Coley's Toxins to 1960 and conventional therapy in 1983 concluded that his patient survival rates were comparable. Factors at work with Coley's Toxins probably include IL-1, IL-6, GM-CSF, G-CSF, IL-12, interferons, TNF-alpha, and a shift from Th1 to Th2 cytokines.

Coley is known as the father of immunotherapy. His efforts led to the creation of immunology as it relates to medical conditions. In 1953, his daughter founded the Cancer Research Institute in New York to study how immunology can help diagnose and treat cancer. BCG therapy became possible because of the pioneering work of Dr. Coley.

Dichloroacetic Acid
Dichloroacetic acid (DCA) is an analogue of acetic acid (vinegar). DCA occurs in the seaweed Asparagopsis taxiformis, and it is produced in trace amounts by the chlorination of drinking water and by the metabolism of some chlorine-containing medications and chemicals. DCA can reduce the production of lactic acid and thus has been used in trials to treat lactic acidosis and topically to remove warts and skin growths.

Cancer cells express increased glycolysis because they rely on anaerobic respiration in the cytosol for energy. This is the Warburg effect, which occurs as a result of the hypoxia found in tumors and their malfunctioning mitochondria. A mouse study found that DCA restored mitochondrial function; this restored apoptosis and caused cancer cells to naturally self-destruct. Mitochondrial function is restored by inhibition of the enzyme mitochondrial pyruvate dehydrogenase kinase. This shifts metabolism from glycolysis to glucose oxidation, increases mitochondrial hydrogen peroxide, activates potassium channels, and thus activates normal cell death, or apoptosis. DCA induces these changes in cancer cells. Cell line studies found this reaction in glioblastoma multiforme brain tissue but not in healthy brain tissue. In the first trial of patients with glioblastoma who were considered
Alternative Therapy: Pharmacological and Biological Treatment

palliative, 80 percent survived for at least 15 months. Mean survival time at Stage IV without treatment is 3 months.

DCA is given to patients orally or intravenously. Intravenous treatments appear to be more effective, with resolution of glioblastoma multiforme and ovarian cancer in multiple clinical settings. DCA is often combined with intravenous vitamin C and intravenous alpha lipoic acid.

Side effects include reversible peripheral neuropathy, neurotoxicity, and gait disturbances that disappear one to two months after cessation of DCA. Patients are usually given a B-complex vitamin and benfotamine or thiamine orally or intravenously to prevent or reduce the neurologic side effects. The Environmental Protection Agency lists DCA as a cancer-causing agent and a cause of reproductive harm in men. In mice, 77 mg/kg/day for three or more years increases the risk of liver cancer. Downstream metabolites of DCA may cause increased liver cancer risks.

Homeopathy

Homeopathy is the use of minute doses of plant, animal, and mineral substances originally prepared according to the Organon of Samuel Hahnemann, M.D. Hahnemann conducted and published the first recorded blinded medical experiments, testing homeopathic medicines on himself and students. Today, homeopathic medicines are prepared according the Homeopathic Pharmacopeia United States and are regulated in the United States and Canada as drugs. They are also regulated as drugs and produced according to Pharmacopeias of the European Union and India.

The prescription of a homeopathic medicine is based on the patient's most unique mental and emotional symptoms: symptoms that set him or her apart from others with the same condition or diagnosis. Final selection of the medicine is based on repertorization of the patient's symptoms in combination with an understanding of the clinical actions of the medicine.

The first physician to use homeopathy extensively in the treatment of patients with cancer was James Tyler Kent, M.D., but his student Arthur Grimmer, M.D., treated many types of cancer. His best-known medicines include the cadmium salts, which he used especially for gastric cancers, severe abdominal pain, and bleeding.

Homeopathy is a significant part of the medical treatment of millions of people in India. Two clinics that have specialized in treatment of patients with cancer are the Banerji and Ramakrishnan. The Banerji Method is designed to treat thousands of people who cannot afford or access Western-style treatment. The clinic will typically see 1,000 patients a day of whom nearly 200 will be diagnosed with cancer. Patients are given two to three medicines that must be repeated one to three times per day. Some of the medicines are prepared homeopathically, and others are mother tinctures of medicinal plants extracted in a water-alcohol mixture based on the plant's chemical and botanical constituents. Selection of the medicines is based on the type of cancer the patient has. As the patient improves, a homeopathic medicine more closely aligned with the personality of the patient is added to the treatment protocol.

The Ramakrishnan Method uses two different medicines given during alternate weeks using a plussing method of delivery. Their method requires more time with the patient to get to know the patient's personality as well as the symptoms of the cancer. The first medicine will be selected based on the diagnosis of cancer, whether it is a solid tumor, and whether there is a family history of cancer. This medicine will be taken 8 to 10 times per day for one week. The second medicine that will be given based on the type of cancer and the unique symptoms associated with this cancer. This medicine also will be given daily, 8 to 10 times per day, during alternate weeks. Alternation of medicines continues for several months to a year and is changed only as the condition of the patient changes.

Clinical studies at major cancer research centers have shown that homeopathically prepared medicines have negative effects on cancer cells and cancer inoculated into animals. These include breast, prostate, colon, lung, and glioblastoma multiforme. A best-case series found that the Banerji Method improved the quality of life and patient survival in breast, lung, and esophageal cancers. Homeopathic medicines have not been shown to interfere with radiation and chemotherapy and in fact can reduce patient side effects from these treatments as well as the symptoms of menopause induced by conventional treatments. Side effects of homeopathy are limited and relatively minor.
No adverse events have been reported in the published studies.

**Insulin Potentiation Therapy**

Insulin potentiation therapy (IPT) was developed by Donato Perez Garcia, Sr., M.D., in 1930 for chronic disease and several types of cancer. Insulin became available in 1926. Treatment is based on the fact that tumor cells require glucose for metabolism, and insulin enhances the transmembrane transport of nutrients across the gut and blood–brain barrier into cells. The first case treated by Dr. Garcia was advanced tertiary syphilis. In 1947, he treated his first case of cancer with IPT. Insulin is secreted by several cancerous tumors including breast, lung, cervix, kidney, fibrosarcoma, and Hodgkin’s lymphoma. This helps supply the tumor with glucose for its metabolism.

Patients are given a slow, intravenous injection of insulin to decrease the plasma glucose level. A low point is maintained for a brief period and then a mixture of glucose and chemotherapeutic agents are given. Usually, the dose of the chemotherapy is less than that typically given. Both will be rapidly taken up by the tumor, leading to cell death and tumor lysis. Side effects are a profound hypoglycemic state of short duration during which the patient may become weak, sweaty, and disoriented. IPT awaits large clinical trials to determine its safety and the types of cancers that are most effectively treated by this therapy.

**Low Dose Naltrexone**

Low dose naltrexone (LDN) was initially shown to enhance a patient’s response to an infection by the human immunodeficiency virus (HIV). The dose was 3 milligrams. Naltrexone has been approved by the Food and Drug Administration since 1984 in 50 milligram doses for helping heroin and opium addicts by blocking both of these substances. Naltrexone blocks reception of opioid hormones that the brain and adrenal glands produce: beta-endorphin and metenkephalin. Many tissues have receptors for these endorphins and metenkephalins, including most of the body’s immune system. Cellular peptide opioid growth factor (met5-enkephalin)
and opioid growth factor receptor are important in both autoimmune diseases and cancer. If naltrexone is given at 50 milligrams, increased cell proliferation occurs, but if LDN is used, the effect is opposite: a decrease in cell proliferation. LDN is approximately 2 to 5 milligrams.

In the presence of LDN, cancer cells are prevented from proliferating rather than killed by apoptosis. LDN also decreases the tumor blood supply. Angiogenesis is critical to the growth and proliferation of solid tumors including ovarian, pancreatic, and lung cancers. LDN does not interfere with taxol and cisplatin and may actually enhance their effects. If LDN is combined with opioid pain therapy, such as morphine or codeine, its beneficial effects are blocked. LDN is most effective when taken at bedtime. The blocking effect is prominent between 2 and 4 a.m., producing higher levels of beta-endorphins the next day. The use of slow-release or timed-release LDNs prevents the essential therapeutic spike.

Side effects are uncommon. Some patients will have difficulty sleeping, but this rarely persists beyond one week. Patients taking thyroid replacement for Hashimoto thyroiditis hypothyroidism are advised to begin treatment at the lowest dose. Patients with an organ transplant and using immunosuppressant medication are advised not to use LDN.

There is currently a trial of LDN versus placebo in malignant glioma at Duke University. Results are not expected before late 2015.

Melatonin
Melatonin, chemically known as N-acetyl-5-methoxytryptamine, is a hormone found in animals, plants, and microbes. In animals, it plays a role in circadian rhythms, and it is an antioxidant. Melatonin is produced in the pineal gland, but 85 percent of its receptors are in the gut-associated lymph tissue (GALT). Blue light suppresses its nocturnal production. Campfires and incandescent lightbulbs have little effect on its production.

Melatonin is twice as active as vitamin E and scavenges radical oxygen and nitrogen species, including hydroxyls and nitrous oxides. Immunological effects are via the MT1 and MT2 receptors, and they have effects in viral and bacterial infections and cancer. Melatonin production decreases with age, and its production peaks earlier in the elderly, possibly explaining the sleep changes seen with aging.

Melatonin increases the cancer-killing activity of macrophages, monocytes, natural killer cells, T-helper cells, and eosinophils. It inhibits angiogenesis, and it reduces inflammation in the tissue around the tumor. Inflammation can help a cancer grow and spread in the body.

Low melatonin levels have been reported in patients with breast and prostate cancer. In women with breast cancer taking tamoxifen, the addition of melatonin caused tumors to shrink in over a quarter of the women. In another study, the use of melatonin before chemotherapy prevented reduction in platelet counts. Its use in prostate cancer leads to increased survival.

Melatonin’s use in patients with cancer starts at physiological doses and increases to supraphysiological doses over a period of several weeks to months. It has been given concomitantly with chemotherapy to lung cancer patients, yielding longer survival times compared to patients receiving only chemotherapy. Much of the melatonin research has been conducted in one research center. Duplication of clinical trials in various centers is required to confirm its clinical benefits.

Side effects of melatonin use may include increased memory of dreams and drowsiness during the day, but this disappears after a week or two. Melatonin can worsen depression in some individuals; its use should be closely monitored.

Mistletoe
Mistletoe extracts were developed by Rudolph Steiner, Ph.D., the founder of anthroposophy, Waldorf schools, biodynamic farming, and anthroposophical medicine. His system was based on intuitive thinking about the relationships between the human body and plants, minerals, and the cosmos.

Mistletoe is a parasitic plant that eventually kills its host: a parallel to cancer. This led Steiner to test and later use mistletoe in the treatment of patients with cancer. Extracts are prepared according to biodynamic principles and appropriately and serially diluted. They are injected in the abdomen subcutaneously, much like an insulin injection. Nearly 1,000 studies and trials have shown longer survival and better quality of life in patients who receive this therapy. There have been no large trials at major research or cancer centers to date. Mistletoe commonly is used in European cancer clinics and by
Extracts of mistletoe (*Viscum album*) contain alkaloids, lectins, and viscotoxins. Separately and together, these constituents have anticancer effects. Mistletoe found on different trees, both hardwoods and conifers, are selected for the treatment of different cancer types. In the case of breast cancer, whether the woman was pre- or postmenopause at the time of diagnosis will determine the type of mistletoe selected.

A common side effect of the injections is a superficial and subcutaneous inflammation. This is considered desirable as long as it is not too large. Occasionally, a fever will develop. Both of these usually resolve within a few days.

**714-X**

This is a camphor compound modified by the addition of a nitrogen atom. Chemically, it is trimethylbicyclonitramineoheptane chloride. Analysis has shown the presence of nitrogen, ammonium salts, sodium chloride, ethanol, and less than 0.01 percent camphor. 714-X was developed by Gaston Naessens, a Frenchmen who moved to Quebec, Canada, in the 1970s. This compound works by countering somatids, a life form that is neither bacterial or viral or fungal but distinct unto itself.

714-X is injected into the lymphatic system in the groin or may be inhaled by a nebulizer. It is manufactured in Canada and available under the Special Access Programme of Health Canada. 714-X is banned for sale and importation in the United States.

The few animal studies have shown no beneficial effect. There are no published studies on its safety or efficacy. The main side effects are pain in the groin after injection and the risk of infection if not administered using clean techniques.

**Conclusion**

There are a wide variety of alternative cancer treatments. Some have been studied more than others, some are widely used in certain settings or countries, and some have little data or theory to explain their use. Cancer patients may become desperate to find a cure, but they need to do extensive research before seeking alternative treatments.

Paul Richard Saunders  
*Canadian College of Naturopathic Medicine*

*See Also:* Alternative Therapy: Mind, Body, and Spirit; Diet and Nutrition; Vitamins.

*Further Readings*


---

**American Academy of Pediatrics, Section on Hematology/Oncology**

The belief that children have unique health and developmental needs was a new concept in 1930, the year the American Academy of Pediatrics (AAP) was founded by 35 pediatricians. The AAP’s mission is to care for infants, children, and adolescents to attain the best possible physical, mental, and social health. The general well-being of children is also a part of its mission. There are more than 62,000 primary care pediatricians, subspecialists, and surgical specialists currently in membership.

The AAP’s Section on Hematology/Oncology was first organized in 1975 to improve the care of children with cancer and blood disorders through an educational forum that discusses the problems and treatments related to pediatric hematology (dealing with blood and the organs that produce blood) and oncology (dealing with cancer and tumors). Not only does the Section on Hematology/Oncology aim to increase research in and the teaching of hematology and oncology in academia, it is a resource of knowledge for other medical professionals, the public, and governmental agencies.

There are two memberships granted in the Section on Hematology/Oncology. Section membership is granted to honorary international members, national affiliate members, postresidency training members, residents, emeritus fellows, candidate members, and corresponding fellows. Affiliate members must be under the direct supervision of
a certified pediatric hematologist or oncologist in a pediatric hematology or oncology department that has devoted at least 50 percent of their practice or work to addressing pediatric hematology or oncology. These members are licensed physicians, nurses, and clinical research associates.

The Section on Hematology/Oncology has provided guidelines that address the unique needs of pediatric hematology and oncology patients. Among these is a policy regarding long-term care for pediatric cancer survivors. This has become an increasingly pressing concern since 1970. Prior to 1970, almost all children with cancer died. Currently, almost 80 percent survive. Most of these children are followed by their primary care physicians, thus, the need for guidelines for long-term care.

Because chemotherapy, radiation, and surgery often have complications, long-term concerns can include problems with organs, growth, development, brain function, and academics. There is also the risk for additional cancer. There are also long-term psychosocial concerns that affect the family, peer, and financial domains.

Pediatric cancer survivors require ongoing long-term and comprehensive follow-up care to optimize long-term outcomes by successfully monitoring for and treating the late effects that may occur as a result of previous cancer therapies. The Section on Hematology/Oncology recommends that follow up is tailored based upon the unique age of the patient, type of cancer, type of treatment, and ongoing evaluations. They offer a report that addresses these and is available to pediatricians. They also facilitate working relationships between the pediatrician and pediatric oncology specialists. The Section of Hematology/Oncology believes that the family's pediatrician is in the position to address specific childhood disease and concerns, is family centered, is available in a timely manner, has a continuous relationship, and is comprehensive.

Pediatricians are also in the position to promote healthy lifestyles as survivors of childhood cancer have a high rate of chronic health conditions. Survivors coached to eat a well-balanced diet decrease their risk for obesity, cardiovascular disease, and osteoporosis. The pediatrician should accomplish coaching through appointments, written media, and Web-based material. The Section on Hematology/Oncology also offers these resources.

Further, transitioning from pediatrics to adult health services requires planning prior to the transition due to the additional challenges for survivors into adulthood. By the time survivors reach adulthood, they should be well-educated regarding their history and ongoing risks and concerns. Pediatricians and family members can coach survivors so that they have the knowledge and skills to maintain optimal health while being aware of their health risks and aware of new information as it becomes available.

The Section on Hematology/Oncology guidelines also include pediatric cancer centers. They recommend that care be provided by a board-certified physician whose subspecialty is in pediatric hematology and oncology by the American Board of Pediatrics. The pediatric team may consist of a number of individuals, including surgeons, urologists, pathologists, nurses, social workers, nutritionists, pharmacists, and other allied health professionals. All members should be board certified in their disciplines.

The facility should include a fully staffed, immediately accessible, on-site pediatric intensive care unit. Diagnostic imaging equipment should be state-of-the-art and include radiography, magnetic resonance imaging (MRI), ultrasonography, computed tomography, and other relevant technologies. Radiation equipment must be up-to-date. The laboratory must be capable of cell analysis, chemistry, and molecular diagnosis. Collection and storage of specimens must be easily accessible. The facility should also have a blood bank, a pharmacy, and access to stem cells.

The pediatric cancer center should offer educational and training programs, coordination of services, a multidisciplinary pediatric board that meets regularly, and protocols for follow-up care. They should also have memberships or affiliations with groups that offer information regarding clinical trials, new information, and treatment recommendations.

Programming for families and other health care providers involved with the child needs to be available as well as open communication regarding continuity of services. Parents and appropriate family members should also have access to educational information and supportive programs.

The American Academy of Pediatrics Section on Hematology/Oncology stresses that children
American Association for Cancer Education

The American Association for Cancer Education (AACE) is a multidisciplinary membership organization originally founded in 1947 under the name Coordinators of Cancer Teaching (CCT). Educators from various American medical and dental schools who gathered yearly to discuss common interests related to cancer research, methodology, and other pedagogical concerns for medical schools founded CCT. It was in 1967 that the CCT became the AACE. The AACE seeks to promote high standards for cancer education through evidence-based practices that result in high-level outcomes.

Educating patients, practitioners, politicians, and others is a key strategy to end the burden of cancer both nationally and internationally. As a membership organization, AACE provides an outlet and space for allied health care professionals and others concerned with improving the quality of cancer education at the undergraduate, graduate, continuing professional, and paraprofessional levels. Doctors, genetic counselors, nurses, occupational and physical therapists, patient advocates, patient educators, physicians assistants, radiologists, and social workers are a few of the professional and paraprofessional areas and disciplines represented by the membership who work collectively to exchange information and ideas to improve cancer education. Individuals and institutions interested in membership with AACE must first complete an application, pay the membership fee, and be approved for membership after completing the first two steps.

The AACE, along with the European Association for Cancer Education (EACE), offers two distinct forums for the dissemination of ideas, concepts, research, and pedagogical shifts related to cancer education: The Journal of Cancer Education (JCE), which serves as the official journal for both organizations, and the International Conference on Cancer Education. Both provided vetted participants an opportunity to share their ideas for best practices in cancer education research, pedagogy, and methodology.

JCE is an international, quarterly, peer-reviewed journal and features a varied editorial board made up of M.D.s and Ph.D.s working in the field who see the importance of disseminating information about improving cancer education worldwide. JCE serves as the ideal source to educate physicians, dentists, nurses, students, social workers, as well as other allied health care professionals, patients, and the general public in various aspects of cancer education techniques and contemporary issues. Articles featured include results of original educational research, discussion of current trends, problems, and techniques in cancer education. In addition, book and media reviews, announcements of educational programs, fellowships, and grants are also published.

JCE articles are abstracted and indexed and can be accessed via Academic OneFile, EMBASE, Science Citation Index Expanded (SciSearch), Journal Citation Reports/Science Edition, PubMed/
American Association for Cancer Education

Medline, SCOPUS, PsycINFO, Google Scholar, Cumulative Index to Nursing and Allied Health Literature (CINAHL), CSA Environmental Sciences, Current Contents/Clinical Medicine, Educational Research Abstracts Online (ERA), EMCare, Index to Scientific & Technical Proceedings, OCLC, Scimago, Studies on Women & Gender Abstracts, Summon by ProQuest, and Vocational Education and Training Abstracts.

The AACE and its longtime collaborator the EACE have broadened their cosponsorship of the International Cancer Education Conference to include the Cancer Patient Education Network (CPEN). The aim of the conference is to provide a platform for validated educational models, provide a multidisciplinary forum for the dissemination of cancer education research, facilitate interdisciplinary networking, and enhance the educational and evaluation skills of attendees. The goal of the conference organizers is to expand the cancer education community from which all can learn and share best practices in cancer education, making best use of its educational efforts.

Significant topics for both the journal and the conference include but are not limited to the following: interpersonal communication between doctors and patients; spirituality in cancer education; computer-assisted instruction in cancer education; teaching strategies and delivery methods for patients, practitioners, and students; palliative care; self-care; and oral cancer.

The AACE established two awards to honor excellence in cancer education: the Samuel C. Harvey Memorial Lecture award, established in 1951, and the Margaret Hay Edwards Achievement Medal, established in 1986. The Samuel C. Harvey Memorial Lecture award is named in honor of the CCT’s first chairperson, who also chaired Yale University School of Medicine’s Department of Surgery for 23 years. The first Harvey Lecture was delivered by Ward Darley, M.D., in 1951. Recent lecturers include: (2013) Mary Gospodarowicz M.D., Fellows of the Royal College of Physicians and Surgeons in Canada (FRCPSC), President of Union for International Cancer Control Princess Margaret Cancer Centre University of Toronto, Cancer Care Ontario—Cancer in the World: Addressing the Equity Gap; (2012) Rena J. Pasick, DrPH, Helen Diller Family Comprehensive Cancer Center at the University of California San Francisco—Persistent Cancer Disparities and Health Behavior Theory: Finding Our Way to the Real World; (2011) Katherine Oliveros, Susan G. Komen for the Cure—An Overview of the Susan G. Komen for the Cure: International Programs; and (2010) Betty Ferrell Ph.D., M.A., Fellow of American Academy of Nurses (FAAN), FPCN, Research Scientist and Professor, City of Hope—A Program of Research in Patient, Family and Professional Education.

The Margaret Hay Edwards Award, for whom the award was named, was a member of the National Cancer Institute and was instrumental in establishing peer-reviewed cancer education support mechanisms. The AACE Advisory Committee grants this award annually to individuals who have made noteworthy contributions to cancer education. Each recipient receives a medal and $1,000. Recent honorees include: Joe B. Harford, Ph.D. (2013), Virginia M. Krawiec, MPA (2012), Ajit K. Sachdeva, M.D., FRCPSC, Fellow of the American College of Surgeons (FACS) (2011), and Arthur M. Michalek, Ph.D. (2010). In addition to formal education programs for future allied health care professionals and continuing education or training for current allied health care professionals, AACE focuses on educational programs for those currently diagnosed with cancer, their families, the general public, and populations that are at high risk for cancer. The AACE Web site includes a variety of educational resources available to the general public.

Annette D. Madlock Gatison
Southern Connecticut State University

See Also: European Association for Cancer Research; National Cancer Institute; National Cancer Policy Board.

Further Readings
American Association for Cancer Research

The American Association for Cancer Research (AACR) is the world’s oldest and largest professional association related to cancer research. Located in Philadelphia, AACR focuses on basic, clinical, and translational research in etiology, prevention, diagnosis, and treatment of different cancers. It was founded in 1907 by 11 physicians and scientists; the institute now has more than 33,000 members in 97 countries.

Annual Meeting
The AACR annual meeting invites more than 18,000 participants from more than 70 countries and has been defined as the major forum to present and discuss cancer-related research. Attendees meet to discuss more than 5,000 abstracts and more than 300 presentations on substantial discoveries in basic, clinical, and translational cancer research. Scientific award lectures, grant-writing workshops, and educational sessions constitute this widespread program.

Publications
AACR publishes eight peer-reviewed journals: Cancer Discovery, Cancer Immunology Research, Cancer Research, Clinical Cancer Research, Molecular Cancer Therapeutics, Molecular Cancer Research, Cancer Prevention Research, and Cancer Epidemiology. In addition to its print publications, the AACR provides online access to the latest in cancer research, cancer prevention, and cancer reviews with online versions of each of its eight journals. The AACR also publishes Cancer Today, a magazine for cancer patients, survivors, and their families and friends.

AACR also offers monthly editors’ picks from highly-esteemed journal collections. They highlight one article from each issue that has been determined a must read by the editors. All of these research articles have been made freely available for a specific and limited amount of time.

Cancer Research is the most frequently cited cancer journal in the world. The journal publishes significant, original studies, reviews, and perspectives on all areas of basic, clinical, translational, epidemiological, and prevention research in cancer. Some of the topics include biochemistry; chemical, physical, and viral carcinogenesis and mutagenesis; clinical research including clinical trials; endocrinology; epidemiology and prevention; experimental therapeutics, molecular targets, and chemical biology; immunology and immunotherapy molecular biology, pathobiology, and genetics; radiobiology and radiation oncology; cell and tumor biology; tumor microenvironment; systems biology; nanotechnology; and other emerging biomedicine technologies.

The AACR Foundation for the Prevention and Cure of Cancer
The AACR foundation for the prevention and cure of cancer is a public charity that provides financial support for scientific research, education, and communication. The foundation funds programs considered by the AACR to be of the highest priority and effect.

Funding
The AACR foundation for the prevention and cure of cancer directly funds research that holds promise for a cure for cancer. The foundation’s mission to “speed up progress in the conquest of cancer by providing financial support for scientific research, education, and communication” is well-known by its support of scientists at all levels. The AACR offers support to cancer researchers at various steps in their careers, from fellowships to career development awards to key grants for independent investigators. In 1970, the AACR established the Cornelius P. Rhoads Memorial Award in honor of the prominent cancer researcher and administrator who directed Memorial–Sloan Kettering Cancer Center and had a long career in working to cure cancer. It is awarded annually to a promising young researcher. Due to revival in 2002 of a 1932 controversy, in which a racist letter by Rhoads was found and publicized, the AACR stripped his name from the award.

Since 1961, the AACR has presented about 500 prizes, awards, and lectureships to recognize the scientific accomplishments of scientists and physicians who cooperatively have made significant contributions to the understanding, diagnosis, prevention, and treatment of cancer. Details about the eligibility criteria and nomination process for each of these honors may be viewed on the AACR Web site.
Vibrant interactions and exciting science characterize all of the AACR's meetings, conferences, and educational workshops. The AACR annual meeting, the largest of its kind in the world for cancer researchers, attracts about 20,000 researchers from more than 50 countries each spring.

In addition to the annual meeting, the AACR holds several large conferences with 1,000 to 5,000 participants that focus on the latest breakthroughs in molecular targets and cancer therapeutics, frontiers in cancer prevention research, cancer health disparities, and frontiers in basic cancer research.

Several special conferences of 200 to 1,000 attendees are held each year that focus on demanding areas of cancer research and specific disease sites. The same conferences are also held overseas in collaboration with international cancer research organizations.

AACR’s educational workshops and special courses provide early-career investigators with opportunities to develop skills in clinical trial design, pathobiology, and related fields. Many programs enhance the educational aspects with mentoring, networking, and career development opportunities. Combined with a broad range of educational and career development sessions at the annual meeting and year-round Associate Member Council (AMC) programs and activities, younger researchers are prepared for the next critical steps in their careers.

Membership
New members join more than 34,000 investigators from around the world who depend on the association’s programs and activities for the exchange of appropriate scientific information. Moreover, members have the opportunity to take advantage of the many benefits of membership, including substantially reduced fees for meeting registrations and journal subscriptions as well as excellent opportunities to bolster important relationships and collaborations with cancer scientists internationally. These are just a few of the benefits that are offered to a member of AACR.

AACR offers seven categories of membership to support each aspect of members’ professional development and enhancement in cancer research.

Candidates applying for membership should be aware of the responsibilities of membership prior to submitting the membership application form.

AACR Membership Application

Applications for membership may be submitted at any time during the year. One may either submit the official AACR membership application online or download the application and submit it to the AACR office with the required documents. It takes 30 days for application review and approval notification.

Karim Daliri
Shiraz University of Medical Sciences

See Also: American Cancer Society; American Society of Clinical Oncology; Association of Cancer Online Resources; Association of Community Cancer Centers.

Further Readings

American Brain Tumor Association

The American Brain Tumor Association (ABTA) is a 501(3)(c) nonprofit organization headquartered in Chicago, Illinois. The organization is dedicated to advancing the understanding and treatment of brain tumors through education and information. Created in 1973 by two mothers—Susan Netchin Kramer and Linda Gene Goldstein—who both suffered the loss of a child due to a brain tumor, the ABTA’s mission is focused on not only improving the lives of patients suffering from a brain tumor diagnosis but also funding critical medical research that could lead to methods that would extend and save the lives of these patients.

As a result of their shared tragedy and with the help of medical professionals and experts in the field of brain tumor treatment and research, Kramer and Goldstein embarked on building the
first U.S. nonprofit organization dedicated solely to the research of brain tumors and potential treatments. Since 1973, the ABTA has built a comprehensive program focused on engaging with brain tumor patients and their caregivers, collaborating with other similar nonprofit organizations and medical professionals, and funding related research efforts.

In addition to the educational mission that provides information to patients on a variety of topics, including but not limited to symptoms, tumor types, treatments, and associated risks, the organization also funds major research initiatives out of its Brain Tumor Research Center. As of 2014, a majority of the center’s funding focused on research dealing with drug research—including development of new drugs and research into how existing drugs can be used in treatment of brain tumors. Other research efforts focus on improved diagnostics, vaccines, immunotherapies, and rehabilitative services for recovering brain tumor patients.

In addition to educational materials and funding of research, the following list outlines some of the other services provided by the ABTA:

- Phone and email-based supportive care provided by licensed health care professionals
- Online support community
- A free clinical trial matching service, TrialConnect
- An online caregiver support tool
- National and regional meetings for patients and caregivers

While the ABTA’s overall program and research can be applicable to both adults and children, the organization’s program for adolescent and pediatric patients is extensive and focuses on the complexities that can arise from dealing with young patients. As a result, the ABTA’s adolescent and pediatric program provides patients and their families with information and support services in the following areas: treatment methods, the long-term effects of treatment, impacts on families and caregivers, and tips on returning to school, to name a few.

While the ABTA does not conduct its own research, it provides a major source of funding for brain tumor research in the United States by providing grants to scientists and researchers working across the United States and Canada. ABTA’s program is highly competitive and is based on an application process. Funding decisions are based on ABTA’s research priorities that demonstrate the greatest potential for advancing the treatment and care of patients diagnosed with brain tumors. The funding decisions are carried out, in part, by the ABTA’s Scientific Advisory Council, which is made up of experts who volunteer their time and services to identify trends and new areas of research and make research funding recommendations to the organization’s board of directors. Researchers who are near the end of their research grant periods present their findings at ABTA’s annual Patients and Families Conference.

The three main research funding areas for the ABTA are: (1) career development initiatives, (2) exploration of innovative research, and (3) collaborative funding opportunities. The career development initiatives look to provide research opportunities for scientists and researchers at the early stages of their careers and are looking to begin research projects in the field of brain tumor research or are looking to remain in this field of research.

While the career development initiatives look to support young researchers, the exploration of innovative research areas focuses on research proposals that look at how brain tumors are diagnosed and treated and challenges the current processes with innovative improvements.

Last, the collaborative funding research projects provide a way for the ABTA to collaborate with other similar research institutions or nonprofit organizations in order to leverage the resources, expertise, and methods of multiple organizations for the good of a common goal. Programs that fall under ABTA’s research funding purview include the following:

- Basic research fellowships
- Translational grants
- Discovery grants
- Medical student summer fellowships
- Survivorship
- Brain Tumor Funders Collaborative
- ABTA/American Association of Neurological Surgeons (AANS)/Congress
of Neurological Surgeons (CNS) Young Investigator awards
- International Outreach Fellowship
- Brain Tumor Epidemiology Consortium (BTEC) Junior Investigator awards
- Central Brain Tumor Registry of the United States (CBTRUS) grant
- Spore Collaborative Funding Project

A majority of the research funded by ABTA focuses on glioblastoma and malignant gliomas, which are tumors that arise from the brain's supportive tissue, or glia, that helps keep the brain's neurons in place and functioning. These tumors are commonly found in the cerebral hemispheres of the brain but can also be found in other brain areas or the spinal cord. Additionally, the connective, supportive characteristics of the glia mean that tumors in this area of the brain are typically highly cancerous, with cancer cells rapidly reproducing due to access to the brain's large network of blood vessels found in the glia.

The ABTA also funds current research into pediatric brain stem tumors and studies focused on finding biomarkers or indicators of childhood brain tumors. Since its inception in 1973, the ABTA has become a driving force in brain tumor patient advocacy, education, and research and is currently the only U.S. nonprofit solely dedicated to advancing brain tumor treatments and research.

L. L. Lundin
Independent Scholar

See Also: Brain Tumor, Adult; Brain Tumor, Childhood; Childhood Brain Tumor Foundation; European Association for Cancer Research; National Cancer Institute.

Further Readings
Case Western Reserve University. "Brain Tumor Causes, Risk Factors Elude scientists." ScienceDaily (July 2014).

American Cancer Society

Founded in 1913, the American Cancer Society is a voluntary health advocacy group that is committed to eliminating cancer. Throughout its history, the American Cancer Society has lobbied for legislation that has served to increase research spending on cancer and to limit the availability of certain products believed to increase the public’s risk of contracting this disease.

The American Cancer Society is one of the best-funded charities in the United States, and it spends heavily on research initiatives, public awareness campaigns, and efforts to reduce risk-enhancing behaviors on the part of the public. Some have criticized the American Cancer Society for spending too much of the donations it receives on overhead and other expenditures, criticisms that have caused certain reforms within the organization.

Background
Originally named the American Society for the Control of Cancer, the organization that became known as the American Cancer Society has, since the beginning, sought to increase awareness of cancer, its causes, and possible treatment options. At the time of the American Cancer Society’s formation, few patients diagnosed with cancer discussed their condition with family or friends. Fear and denial meant the disease was not discussed, and this lack of knowledge contributed to an environment where those with cancer almost certainly died as a result.

To deal with this, the physicians and business leaders who founded the American Cancer Society wrote a variety of articles, published in both the popular press and professional journals, that raised public awareness of cancer and possible cures for the condition. The Sword of Hope symbol, frequently used in the American Cancer Society’s publications, was developed during the 1920s as the result of a poster contest submission.

During the 1930s, women volunteers created the Women’s Field Army, a group that wore uniforms, had rank and insignia, and went door to door to raise money for cancer research. Whereas there had been approximately 15,000 volunteers involved in cancer control in 1935, the year before the Women’s
Field Army’s birth, by 1938, this number exceeded 150,000. In the aftermath of World War II, Mary Lasker and other supporters of the American Cancer Society raised more than $5 million for the organization, with 25 percent of that targeted at funding a research initiative. In conjunction with efforts to educate the public about the signs of cancer, this research effort would be the focus of the organization for decades to come.

Research
From the beginning, researchers who received funding from the American Cancer Society made discoveries that assisted patients facing cancer. Sidney Farber, one of the first American Cancer Society grant recipients, administered aminopterin to a child with acute leukemia, achieving the first temporary cancer remission in a child. Other major breakthroughs also resulted from studies funded by the American Cancer Society. These included studies that established the link between cancer and smoking, confirmed the Pap test’s effectiveness, developed cancer-fighting drugs and biological response modifiers, noticeably increased childhood leukemia’s cure rate, and established mammography’s safety and effectiveness of mammography. To date, more than $4 billion has been provided to researchers by the American Cancer Society, and scientists who have received these grants have been awarded more than 45 Nobel Prizes for their efforts.

Leaders of the American Cancer Society used this research to advocate for legal and policy changes that aligned with these studies’ findings. For example, during the 1960s, the American Cancer Society supported the surgeon general’s report that established the link between smoking and cancer. This report was given added credibility with the public and press when early American Cancer Society-sponsored studies confirmed the connection between tobacco use and cancer. The surgeon general’s report laid the groundwork for changes in how tobacco is treated and controlled, changes that continue today.

The American Cancer Society supported the passage of the National Cancer Act in 1971, which changed the society’s role in cancer research. The National Cancer Act provided the government both the funds and authority to expand the National Cancer Institute (NCI). As such, the act radically changed the war on cancer, making research funding a consistent source of support for those scientists engaged in this activity. The NCI’s development also changed the role of the American Cancer Society with regard to such research by changing from providing primary funding for such studies to that of strategically funding those areas that fall outside of the federal government’s chief areas of focus. Since the establishment of the NCI, the American Cancer Society’s funding has focused chiefly upon cancer prevention and education. Recently, as National Institutes of Health funding for young investigators has decreased, the American Cancer Society has allocated more funds to that generation, maintaining its role in advancing cancer research.

Outreach
Raising approximately $1 billion each year to support its programs, the American Cancer Society is one of the largest charities in the United States. The American Cancer Society has more than 3,400 offices across the United States, and each year more than 2 million volunteers work in these. Because it views public health advertising
as important to its mission, the American Cancer Society sponsors a variety of events designed to promote public interest in cancer, its causes, and lifestyle changes that might decrease one's chance of getting cancer. These events include the Relay for Life, a multiday, outdoor public gathering held in multiple locations, and the Great American Smokeout, a day where those who smoke are encouraged to quit. The American Cancer Society also operates thrift stores that are used to generate income for its projects.

Criticized by some as spending too much on overhead and other expenses, the American Cancer Society has in recent years worked to ensure that as much money as possible is spent on research and direct services to cancer patients. Approximately 72 percent of the American Cancer Society's budget is spent on program services, which includes 28 percent on patient support, 16 percent on prevention, 16 percent on research, and 12 percent on detection and treatment. The remaining 28 percent of the American Cancer Society’s budget is spent on fund-raising (21 percent) and administration (7 percent). Although spending 7 percent on administration is in keeping with other large charities, the American Cancer Society has been criticized for the compensation provided its executive director, which has ranged from $850,000 to more than $2.5 million per year. Despite this controversy, the number of cancer patients surviving has increased dramatically over the lifespan of the American Cancer Society, as its efforts have been largely successful.

Stephen T. Schroth
Towson University

See Also: American Brain Tumor Association; American Lung Association; Childhood Cancers; National Cancer Institute; Tobacco in History.

Further Readings

American College of Gastroenterology

Founded in 1932, there are greater than 12,500 doctors, representing 86 countries, who are members of the American College of Gastroenterology. Members stay informed through a variety of measures, including meetings, postgraduate training, research, and the American Journal of Gastroenterology. They have 22 committees that gather and exchange information regarding the most effective care for patients.

Gastroenterology studies the diseases of the liver, bile ducts, pancreas, rectum, large intestine, small intestine, stomach, and esophagus. It is a detailed examination of normal function, disease, the movement of nutrients through the stomach and intestines, digestion and absorption of these nutrients, waste removal, and the function of the liver. Gastroenterologists are physicians who have dedicated training and experience in the management of the digestion system. Gastroenterologists study any number of these diseases: colon polyps, cancer, reflux, ulcers, colitis, irritable bowel syndrome, Crohn’s disease, pancreatitis, and nutritional absorption issues.

Gastroenterologists must first complete medical school. They then go on to three years in an internal medicine residency. Finally, there is a fellowship, which is an additional two to three years. The fellowship is a rigorous program that involves learning from nationally recognized experts to develop further skills in evaluating patients, caring for conditions, and providing recommendations for better health and to prevent disease. It is monitored by national groups that include the American Society for Gastrointestinal Endoscopy, the American Board of Internal Medicine, the American Gastroenterological Association, and the American College of Gastroenterology. Once training is complete, the fellows are board eligible. Once they have successfully passed the gastroenterology board certification test (administered by the American Board of Internal Medicine), they are board certified.

Endoscopy (upper endoscopy, sigmoidoscopy, and colonoscopy) is a diagnostic and treatment tool often used by gastroenterologists. It is a narrow, flexible, lighted tube with built-in video cameras. Training by expert instructors advises gastroenterologists
when and how to perform endoscopy, methods for safety and effectiveness, and use of sedation for comfort and safety for patients. A number of general procedures can be accomplished with the use of endoscopy, including removal of colon polyps, stretching of narrowed areas of the esophagus and intestines, stopping bleeding, and biopsy when cancer is suspected. Gastroenterologists learn to interpret the biopsy results and make recommendations regarding treatment. Some gastroenterologists take advantage of advanced training using endoscopes. Advanced procedures can include biliary examinations, removal of tumors, internal drainage tubes, and endoscopic ultrasound. These advanced procedures are not considered surgical but minimally invasive alternatives to surgery. Yet, the gastroenterologists can utilize them to remove stones in the bile ducts and evaluate and treat tumors.

The American College of Gastroenterology advocates a thoroughly comprehensive knowledge of the entire gastrointestinal tract as the best way to provide quality care in consulting and endoscopy services. Gastroenterologists should therefore be highly trained specialists with a unique skills set, broad medical knowledge, specific internal medicine training, and the best skills set in the utilization of endoscopy.

More than 250,000 people are diagnosed with gastrointestinal cancer in the United States every year. Gastrointestinal cancer consists of malignant cells that form in the digestive tract. Stomach cancer forms in the lining of the stomach. Of the 250,000 gastrointestinal cancers diagnosed each year, 21,000 are stomach cancer. There are a variety of risk factors, which include family history, H-pylori infection, long-term stomach inflammation, obesity, and poor diet. Small intestine cancer, which accounts for 7,000 new cases in the United States each year, has several common types: adenocarcinoma (cells that make and release mucus and other fluids); carcinoid (neuroendocrine cells); stromal tumor (wall of the intestine); lymphoma (lymph tissues); and sarcoma (connective supportive tissues). The risk factors for small intestine cancer include age, alcohol use, tobacco use, high-fat diet, family history, gender, and conditions where the small intestine is inflamed (celiac disease, Crohn's disease, etc.). Colorectal (colon or rectum) cancer accounts for 40,340 cancers diagnosed each year in the United States. Risk factors include age, family history, personal history of cancer, history of polyps in the colon, history of ulcers in the lining of the large intestine, and Crohn's disease. There are two types of esophageal cancer, squamous cell carcinoma (cancer in the flat cells lining the esophagus) and adenocarcinoma (cancer in the cells that make and release mucus and other fluids). There are more than 17,990 new cases diagnosed in the United States each year. Risk factors include age, gender, reflux disease, Barrett's esophagus, smoking, and obesity. Pancreatic cancer is diagnosed in the United States more than 46,420 times each year. The most common type is exocrine pancreatic cancer (cancer in the ducts that carry pancreatic fluids). Risk factors include diabetes, family history, obesity, inflammation of the pancreas, and smoking.

The American Journal of Gastroenterology is the official publication of the American College of Gastroenterology. It is published monthly and ranked first among clinical journals that cover gastroenterology. The journal provides both practical and professional support for gastroenterologists and most often covers common gastroenterological disorders. They organize their content by topics such as colon, small bowel, endoscopy, esophagus, inflammatory bowel disease, liver, pathology, stomach, and pediatrics. The American Journal of Gastroenterology includes a red section that summarizes important matters included in the journal, original research, editorials, clinical reviews, practice guidelines, and continuing educational opportunities. The journal is available online and in print.

The American College of Gastroenterology also sponsors an institute whose primary goal is to advance the field through education and research. They promote research, educate physicians and the general public, and provide resources for the further study of gastroenterology. It was founded in 1994 and is officially referred to as the ACG Institute for Clinical Research and Education. It serves as a major funder for patient care that falls within gastroenterology research.

Jessica Anne Hammer
Independent Scholar

See Also: American College of Radiation Oncology; Canadian Association of Medical Oncologists; Carcinoid Tumor, Gastrointestinal; Salivary Gland Cancer; Small Intestine Cancer.
Further Readings

American College of Radiation Oncology

The American College of Radiation Oncology (ACRO) is a nonprofit corporation whose goals include the advancement of radiation oncology science, improved patient care, improved education, and the study of the socioeconomic aspects of radiation oncology practice.

ACRO’s mission statement outlines its desire to provide high-quality care for patients receiving radiation therapy. They also wish to promote success for practitioners by integrating science and technology, responsible socioeconomic advocacy, and education. ACRO adopted its mission statement and vision statement in 2005, and essentially describes itself as the professional society for success in the practice of radiation oncology.

ACRO is managed by a board of chancellors who are volunteers. They are elected by the members and follow ACRO bylaws. The board has 17 elected members: chair, president; vice president; secretary–treasurer; the immediate past chair; four committee members; seven general members; two liaisons; and two nonvoting members. The entire board meets twice per year. However, the executive committee meets monthly through telephone conference. Elections are held annually. Each member serves a three-year term but not more than two terms. ACRO’s CEO is the president of ACRO, who automatically assumes the position of chair.

Committees in charge of programming are appointed by the board. Committee members rotate as per ACRO guidelines. A management company (PAI Management Corporation) assists the board with management direction, conference management, financial management, committee support, administrative services, publications, and membership administration. The board carefully appoints committees and supports participation of all members in educational activities.

There are four membership categories in ACRO. Initially, members are considered regular members. After 10 years of membership (continuous), regular members can apply for fellowship, which allows them to use the acronym FACRO. Regular members who also serve in the military or are in their first year of practice have reduced annual dues. Military members’ dues are $175 annually. First-year practitioners pay $275 annually. All others in this category pay $375 annually.

Associate members are practitioners engaged in radiation–oncology practice. These may be radiation therapists, radiology technologists, or administrators. Annual dues are $255. Associate members receive a number of publications as part of their membership: quarterly newsletters, the American Journal of Clinical Oncology, and the ACRO Practice Management Guide (at a discounted price). Associate members can be appointed to committees but cannot vote nor hold elective office. Any physician who has not been a member of ACRO but holds a residency position in radiation–oncology are resident members. They do not pay any dues. They also can be appointed to committees but cannot vote or hold elective office either.

Corresponding members are physicians who have been active members or associate members for greater than five years but are not employed more than 10 percent of their time in a field related to radiation–oncology. Practitioners who are not physicians but who have a major interest in ACRO and can prove involvement in the field or have worked to improve the field are also eligible to be corresponding members. As with associate members and resident members, they can be appointed to committees but cannot hold office or vote. Corresponding members’ dues are $100 annually.

ACRO developed an accreditation program in 1995. It is voluntary and consists of agreed-upon practice standards for quality practice. Audits are conducted to ensure these standards are followed. Since 1995, the accreditation program has been revised to include scientific advances. The most recent review, in 2010, included major changes to address online submission of cases, faster turnaround for applications for accreditation, and onsite visits (to include physics and administrative professionals).
ACRO has also created a code of ethics that aids in maintaining standards of service and ethical conduct. It is a set of standards radiation oncologists can utilize to monitor their own conduct in their relationships with colleagues, the public, patients, and other allied professionals. The ACRO code of ethics is divided into two primary categories: principle of ethics and rules of ethics. The principles of ethics are intended to be an exemplary code of conduct for all ACRO members. They are goals for all members. The principles of ethics are not subject to disciplinary action and are not enforceable. The primary objective is to provide medical care with a full respect for dignity. ACRO members should also continuously improve upon their knowledge and skills. ACRO members should protect the general public (and itself) from incompetence or physicians who do not hold a high moral character. All laws related to radiation oncology should be upheld, and violations of laws or ethics should be immediately exposed. ACRO members should focus not only on the health of their patients but also on the well-being of their communities. Patient confidentiality is upheld unless revealing information is required by law or to protect the public. Services should always be in the best interest of the patient, and the decision to accept or decline services is the patient’s.

The second part of ACRO’s code of ethics includes the rules of ethics. These are mandatory and specific regarding minimal standards of conduct. These are enforceable by disciplinary actions. ACRO members should offer only consultative opinions in settings where they participate in the quality of patient care, and utilization reviews are a matter of policy. ACRO members may not participate in misleading billing arrangements. ACRO members may never divide fees. Before practicing in hospital settings, ACRO members must apply and be accepted as a member of the hospital staff in the same way other medical staff have applied and been accepted.

When an ACRO member violates the code of ethics he or she may be disciplined, expelled, suspended, or censured. Complaints are filed with the president, who may initiate an investigation. If the complaint requires further attention, the president refers it on to the executive committee.

Jessica Anne Hammer
Independent Scholar

See Also: American Society for Radiation Oncology; Association of Freestanding Radiation Oncology Centers; European Society for Therapeutic Radiology and Oncology; Radiation, Gamma; Radiation, Ionizing.

Further Readings

American Joint Committee on Cancer

The American Joint Committee on Cancer (AJCC) created the guide for staging cancer, titled The Cancer Staging Manual. Physicians and the community rely on this manual as it is the most comprehensive guide available. Anatomic staging that is evidence based is one of the critical factors in understanding cancer and when treating patients. New science in oncology, radiology, pathology, and molecular science are routinely utilized to precisely define, assist with treatment planning, and offer prognosis during treatment. Cancer science is continually evolving, and the AJCC’s role continues to be crucial clinically in research and in patient advocacy communities.

The AJCC defines its mission to be providers of worldwide leadership in the classification and management of cancer through the development, maintenance, and promotion of evidence-based practices. The mission is multidisciplinary and dedicated to monitoring cancer and to improve care. The five key objectives include: a timely and rigorous, evidence-based, and biologically relevant system for classification and prognosis; proactive education of the oncology community (including program development and delivery to guide patient care); support of research and dissemination of predictive tools, prognosis factors, and other indicators that predict or classify cancer; collaboration and fostering relationships among
member organizations and organizations with similar objectives; and support and response to public or private efforts to predict outcomes or improve care.

Twenty member organizations comprise the AJCC. Member organizations have consistent or complimentary missions and goals to the AJCC. In general, the member organizations are involved in one (or more) of these areas: biostatistics, research, cancer epidemiology, cancer registration, patient care, cancer control, or professional education. Membership in the AJCC is derived from representatives from the member organizations. The executive committee makes decisions and sets the strategic direction of the organization.

The member organizations include: American Association of Pathologists’ Assistants; American Cancer Society; American College of Physicians; American College of Radiology; American College of Surgeons; American Head and Neck Society; American Society for Radiation Oncology; American Society of Clinical Oncology; American Society of Colon and Rectal Surgeons; American Urological Association; Canadian Partnership Against Cancer; Centers for Disease Control and Prevention; College of American Pathologists; National Cancer Institute; National Cancer Registrars Association; National Comprehensive Cancer Network; North American Association of Central Cancer Registries; Society of Gynecologic Oncology; Society of Surgical Oncology; and Society of Urologic Oncology.

The AJCC has four committees that individuals and member organizations can volunteer for. The Finance Committee monitors funds, reviews and advises on budgets, and identifies strategies for funding. The Membership and Bylaws Committee identifies new members who can add to the expertise that supports the mission and objectives of AJCC. These committee members also review the bylaws and make recommendations for any appropriate amendments. The Informatics Committee initiates dialogue with the National Cancer Institute to maintain AJCC’s Web site, explore vendor relationships, and develop electronic products. Short- and long-term goals to promote the staging system and related products, presentations, and journal articles are the responsibility of the Education and Promotions Committee.

Cancer staging, the primary function of the AJCC, describes how much cancer is present and where. Physicians use staging to develop treatment plans and offer prognoses. Understanding the cancer stage is also critical in determining if any clinical trials may be appropriate for patients. There are four types of staging: clinical staging (how much cancer based on exam, tests, or biopsies); pathologic staging (a combination of clinical staging and surgical interventions as with tumor extraction or biopsy); post-therapy staging (how much of the cancer remains after treatment); and restaging (extent of cancer if it reoccurs).

Staging is based on the knowledge of how cancer develops and spreads. Typically, there are four main factors: location of the original tumor, size and number of tumors, whether the cancer has spread to lymph nodes, and whether the cancer has spread to a distant site in the body (not adjacent to the original tumor). The T category, which describes the primary (original) tumor, has three classifications: TX (tumor can’t be evaluated), T0 (no evidence of primary tumor), and Tis (cancer is early and has not spread to surrounding tissues). The T1 through T4 ratings describe the size of the primary tumor. The N category describes whether the cancer has reached lymph nodes that are nearby: NX (cannot be evaluated), N0 (no involvement), and N1 through N3 (number and extent of lymph nodes involved). The M category describes the spread of the cancer: M0 (no spread) and M1 (cancer has spread).

Some forms of cancer (i.e., breast and prostate) further subdivide. On the other hand, some cancers do not follow the above system at all, though this is uncommon. Spinal cord and brain cancers, for example, are described by their grade and cell type. Certain bone marrow and blood cancers also use other staging systems.

There are a variety of tests that assist physicians with staging. Physical examination may be utilized to locate and size a tumor and whether lymph nodes or other organs are involved. Imaging, magnetic resonance imaging (MRI), computed tomography (CT), and X-rays can identify the location and size of the tumor and whether it has spread. Laboratory tests provide information on fluids, in particular blood and urine, which may have indicators of type and severity of the cancer. Pathology reports are often used to confirm diagnosis and type of the cancer and determine size, if invasion of other tissues has occurred, and the grade of the tumor. Surgical reports (tumor removal or biopsy)
can indicate the size and appearance of the tumor and offer additional information about other tissue or lymph node involvement.

Jessica Anne Hammer
Independent Scholar

See Also: American Society of Clinical Oncology; American Society of Hematology; National Cancer Registrars Association; Society of Gynecologic Oncology; Society of Surgical Oncology.

Further Readings

American Lung Association

With more than a 100-year history, the American Lung Association (ALA) is the oldest health-related organization of its type in the United States. The association, originally named the National Association for the Study and Prevention of Tuberculosis (NASPT), began in 1904 and was dedicated to the fight against tuberculosis, the most feared and deadly disease at that time. In 1918, continuing its central thrust on tuberculosis, its name changed to the National Tuberculosis Association (NTA). As tuberculosis declined and was controlled across the United States and other serious lung diseases commanded attention, the focus of the organization grew. Expanding its mission to improve the health of lungs and to prevent diseases of the lungs, the organization was renamed the American Lung Association in the early 1970s. Today, it continues work on this expanded mission, and its efforts center in three main areas: (1) ending consumption of tobacco products and thus eradicating lung disease linked to tobacco use, (2) improving air quality overall to ensure that it does not harm the lungs, and (3) assisting patients and families affected by lung disease. Along with its community, state, and regional affiliates, the ALA, headquartered in the national's capitol, Washington, D.C., is at the forefront of ensuring the health of our lungs and the quality of the air that we breathe.

The ALA engages in a three-pronged effort—research, education, and advocacy—to achieve these goals. Endeavors address a variety of respiratory issues, including lung cancer, emphysema, asthma, chronic conditions (bronchitis, sinusitis, and hay fever), respiratory distress, sudden infant death syndromes (RDS and SIDS), influenza (flu), and pneumonia. Research efforts address topics ranging from asthma to lung cancer and seek to prevent or slow illness development, alleviate patient suffering, and discover new treatments or cures. Educational efforts include assisting patients in better managing illness as well as well-respected smoking cessation programs. The ALA also works to educate the public on the dangers of using tobacco products, with a goal of preventing tobacco use by nonusers as well as on the environmental and workplace dangers of air pollution. Advocacy efforts include lobbying for legislation to ensure clean air. Recently, the ALA was instrumental in securing passage of a bill allowing the Food and Drug Administration to oversee the manufacturing, marketing, and selling of tobacco products. The organization also produces a number of reports, such as the yearly State of the Air report and the State of Tobacco Control report, that are useful to policy makers, researchers, educators, and citizens.

Given the heavy toll of lung disease on the U.S. population, the ALA is advancing important health initiatives. Lung cancer is the most frequent cancer across the globe, and it kills more people (both men and women) in the United States each year than any other cancer. Further, lung disease ranks as the third-highest cause of death in the U.S. population, and millions of additional people suffer from the effects of chronic lung conditions. The ALA has played a leading role in addressing the negative health effects caused by using tobacco products and working to eliminate these preventable risks as well as focusing attention on the role of air pollution in lung disease.

Much information and many resources are chronicled on the organization's Web site. Users
American Lung Association

can easily access information on topics such as lung function and health, air quality, research, and smoking cessation as well as discover ways to get involved in the association’s efforts or to donate to the cause. The Web site also houses publications and reports, features news stories and a link to register for the electronic newsletter, and facilitates connections with activities in one’s community.

Christmas Seals

Perhaps the most widely recognized effort of the ALA is its Christmas Seal Campaign. This initiative began in 1907 and continues today as an illustration of the key role that volunteers play. Emily Bissell created Christmas Seals to generate funds for tuberculosis care and subsequently headed the popular fund-raising initiative for several years. Commemorating her pioneering health efforts, Bissell was recognized with a U.S. postal stamp in 1980. Since its inception, the Christmas Seal campaign has raised millions of dollars.

Building on an idea employed in Denmark for fund-raising for tuberculosis, Bissell borrowed money to print the first Christmas Seals and began selling them for 1 cent apiece. To combat slow sales, she enlisted the help of a popular newspaper, which ran a Stamp Out Tuberculosis campaign. With the newspaper support and an endorsement from President Roosevelt, Bissell raised 10 times her initial fund-raising target. In 1908, the Christmas Seal campaign became a national effort in partnership with the American Red Cross. By 1920, the National Tuberculosis Association, which later became the ALA, began managing the fund-raiser on its own, and its symbol, the double-barred cross, began appearing on Christmas Seals. This double-barred cross, or modified Lorraine Cross, had long been the symbol for antituberculosis efforts. The organization had been using this cross since shortly after it was founded and, in 1920, registered the cross as its official trademark.

Over the years, several celebrities have acted as chair of the annual Christmas Seal Campaign, and the seals, especially early ones, have become popular items for stamp collectors. Each year the fund-raiser significantly contributes to ALA initiatives.
and raises awareness of the importance of clean air and the prevention and cure of lung disease.

Joy L. Hart
University of Louisville

See Also: Lung Cancer, Non–Small Cell; Lung Cancer, Small Cell; Pollution, Air; Smoking and Society; Tobacco Smoking.

Further Readings

American Psychosocial Oncology Society

The American Psychosocial Oncology Society (APOS) represents the only organization primarily devoted to the psychosocial aspects of cancer. The society offers a strong, two-prong approach by providing both professionals and nonprofessionals a forum for the psychological, social, behavioral, and spiritual characteristics of cancer.

The mission of APOS encompasses elevating awareness about the psychosocial realms of care for patients with cancer. The organization develops and implements education programs for professionals and nonprofessionals. By developing a research agenda, the organization helps guide scientific priorities in the psychosocial aspects of cancer and cancer care for the nation.

The APOS core values comprise five statements aimed at the care of individuals with cancer. The significance of the values is paraphrased as follows:

Psychosocial care improves quality of life and lowers the stress of cancer. The distinct profession of psychosocial oncology is integral to the science of caring for cancer patients by using evidence-based knowledge. Interdisciplinary research, education, and networking teach the science and practice of psychosocial oncology. Integrity, honesty, and accountability to professional ethics and standards of care provide the backbone to APOS. Because a diversity of experiences transpire in individuals with cancer, APOS maintains intense respect for the rights of the individual to choose their desired courses of action in state-of-the-art treatment.

Members benefit from an online subscription to the journal Psycho-Oncology. APOS provides subscriptions to three other professional journals at reduced rates. Palliative and Supportive Care, Journal of Cancer Survivorship, and the Journal of Psychosocial Oncology comprise the three journals offered to members. APOS hosts special-interest groups to join, including Bereavement, Genetics, Health Disparities, Pediatrics, Sexual and Reproductive Health, Spirituality, and Survivorship. Belonging to these special groups provides a venue for networking and opportunities to build bridges to complementary organizations and other professions. The society maintains a list of care providers for online referrals though a toll-free number. This directory of sorts gives professionals the unique ability to contact specialists in difficult or unusual cancer cases.

APOS maintains a store of products. A “Quick Reference for Oncology Clinicians” and a “Quick Reference for Pediatric Oncology Clinicians” refer to pocket-size handbooks on essential information about the psychosocial needs of oncology patients, available in the online store. The store sells DVDs like the History of Psychosocial Oncology. This DVD commemorates interviews with past presidents of the APOS and tells stories of previous challenges present in APOS. Many webinars can be purchased online with titles such as “Acceptance and Commitment Therapy,” “Bright IDEAS Problem-Solving Skills,” and “Evidence-Based Psychosocial Interventions.”

APOS represents an extremely active organization at the forefront of implementing programs to assist both oncology professionals and cancer patients. In 2014, at the APOS annual conference, APOS announced funding by the National Cancer
Institute (NCI) and initiation of a Screening for Psychosocial Distress Program as a joint venture between APOS and the Yale University School of Nursing. The NCI is providing funding for this five-year initiative beginning in 2014.

The Psychosocial Distress Program initiative financially supports cancer care professionals’ attendance at a one-day workshop at the beginning of each year, followed by webinars every three months for two years. The program aims to educate select professionals to attend the program, learn about a comprehensive distress-screening instrument, acquire knowledge about cancer patients’ distress or depression and assist cancer patients’ movement to appropriate psychosocial health care services. A total of 39 oncology professionals represent cancer care organizations nationwide. Two people from a facility representing the disciplines of oncologists, nurses, chaplains, psychiatrists, psychologists, and social workers attend the program.

The APOS held their 11th Annual Conference on February 13 to 15, 2014, in Tampa, Florida. The focus of the conference centered on executing quality-of-care standards for psychosocial oncology and compassionate care of cancer patients. The conference aimed to raise awareness about the Commission on Cancer’s Cancer Program Standards 2012 to Ensure Patient Centered Care and to identify gaps in psychosocial cancer care through research or policy analysis. The conference program emphasized all age groups by highlighting pediatric, adolescent, young adult, and adult populations in psychosocial oncology during the education sessions.

APOS supports many links via social media to other organization sharing similar goals to improve access for cancer patients to useful information. APOS shared a link via Facebook to the Center for Advancing Health for an app developed for patients receiving negative health news (e.g., diagnosis of cancer, failure of treatment, and side effects of medications).

Publications in the professional literature represent another area that APOS endorses to diffuse information to the variety of health care professions caring for cancer patients. Researchers provided up-to-date information on significant cancer standards and reviewed the distinctive role of the APOS Referral Helpline to help oncology staff and patients find appropriate psychosocial care for cancer patients.

In conclusion, APOS arose to fill a gap in cancer care regarding the psychosocial aspects of cancer patients. The APOS actively pursues issues related to psychosocial issues and engages a variety of existing agencies to achieve its mission.

Sharon A. Takiguchi  
Nurse Consultant

See Also: Education; Health Advocacy; Survivors of Cancer.

Further Readings

American Society for Radiation Oncology

The American Society for Radiation Oncology (ASTRO) is a professional association of doctors, scientists, and researchers who utilize various radiation therapies to treat cancer.

The society presently has more than 10,000 members worldwide and is headquartered in Fairfax, Virginia. ASTRO’s internationally recognized facility accreditation program, APEx, offers an
international standard for radiation oncology care team, policies, and procedures.

The organization's annual meeting is attended by thousands of health care professionals from various countries and is the premier radiation oncology-based scientific event in the world.

History
ASTRO was founded in Chicago, Illinois, in November 1958 under its original name, the American Club of Therapeutic Radiologists. The society sprung from three other major radiological organizations functioning at that time, namely the American College of Radiology (ACR), the Radiological Society of North American (RSNA), and the American Roentgen Ray Society (ARSS).

In 1966, the society officially changed its name to American Society for Therapeutic Radiologists. ASTRO's first officially sponsored scientific journal, the *International Journal of Radiation Oncology, Biology, Physics* (IJROBP), also referred to as the Red Journal, was published in 1976.

ASTRO was pivotal in the fostering of new technological breakthroughs in radiation oncological care throughout the 1970s and 1980s, centered on the emergences of its annual meeting as one of the world's premier stages for the introduction and popularization of new technologies related to treating cancer with radiation treatments.

Throughout the 1990s, ASTRO's membership nearly doubled as the organization continued efforts to establish itself as an international organization and one that would become instrumental in legislative and regulatory arenas related to radiation oncology care.

ASTRO's administrative team moved to its new headquarters in Fairfax, Virginia, in 1998. The society's latest initiatives, member profiles, and available course work are published in its quarterly magazine *ASTRONews*.

ASTRO's administrative affairs and governance are operated under the direction of a 15-member board of directors. Elections for chair of the board, treasurer, and vice chair of Clinical Affairs and Quality Control are held annually.

Clinical Efforts
Among ASTRO's major initiatives is its frequent publication of evaluations of emerging trends in the field of radiation oncology as well as the construction and adaptation of recommended patient guidelines for use by member and nonmember physicians and oncologists. In addition to its ongoing list of active treatment guidelines, ASTRO also invited members to suggest topics and offer treatment guideline endorsements.

ASTRO's office of Clinical Affairs and Quality Control oversees the organization's treatment guidelines under the oversight of the group's Guidelines Subcommittee. ASTRO guidelines are outlined for varying radiation treatments for a wide variety of cancer types, including genitourinary cancers, brain tumors, and thoracic malignancies.

Grants and Funding
ASTRO operates an evolving database of funding options for member clinicians and researchers to apply for aid from varying organizations and government agencies. ASTRO also offers a variety of annual research awards to foster new clinical trials and research initiatives surrounding radiation treatments and their effects on cancer biology. Annual grants include the ASTRO Junior Faculty Career Research Training Award, a two-year grant award to new students involved in radiation oncology, and the ASTRO/ROI Comparative Effectiveness Research Award, a two-year grant granted to established researchers conducting experiments exploring developments in the effectiveness of radiation oncology.

The organization also offers several grants each year to members to defray travel costs related to attendance to the annual meeting as well as a series of travel grants for member students to attend specialty meetings related to their specific disciplines within radiation oncology.

Accreditation Programs
ASTRO's newly implemented accreditation program, known as APEx, debuted in 2014 and was created to assess the radiation oncology policies and procedures at cancer treatment facilities worldwide. The accreditation system's five-phase application process evaluates facilities in all phases of patient care. In addition to an evaluation care processes, APEx evaluators also review each facility’s radiation oncology team, safety practices, quality control management, and quality of patient-centered care. The APEx accreditation is
one of the most advanced accreditation programs of excellence ever offered to radiation oncology treatment centers.

**Member Education Resources**

ASTRO is the world’s leading provider of professional and educational development for physicians and nonmedical professionals working in the radiation oncology community. In addition to hosting a rotating schedule of webinars, virtual meetings, and certification maintenance seminars, ASTRO members are also granted access to a variety of self-assessment models where they can evaluate treatment techniques and learn of new developments in radiation oncology care.

The organization also offers a series of online seminars dedicated to ethical and professional issues, which educate member physicians and physicists about the nonmedical and policy nuances related to the practice of diagnostic radiology and radiation oncology.

**Publications**

ASTRO’s official peer-edited scientific journal is published 15 times a year and is considered the premier source for research related to radiation oncology treatments and research developments.

The journal publishes both laboratory and clinical investigations related to radiation oncology in addition to works related to health policy relevant to radiation care. Articles covered in the journal include: prospective clinical trials, outcomes research, and evaluations of large statistical databases on cancer treatment statistics. Emerging technical advances related to radiation treatment are also frequently featured in addition to ongoing investigations related to tumor physiology and molecular biology and their effects on cancer’s response to radiation treatments.

ASTRO also publishes the *Journal of Practical Radiation Oncology*, which is comprised of studies and evaluations related to specific radiation treatment techniques, and is published six times per year.

In addition to its annual meeting, ASTRO also operates an annual symposium dedicated to the discussion, evaluation, and dissemination of information related specifically to emerging technologies in radiation treatment. The State of the Art Radiation Therapy Symposium includes seminars on the latest developments in practical treatment, biology, and imaging techniques that utilize radiation technology.

---

**See Also:** American College of Radiation Oncology; Association of Freestanding Radiation Oncology Centers; Radiation Therapy.

**Further Readings**


---

**American Society of Clinical Oncology**

The American Society of Clinical Oncology (ASCO) is a professional organization for oncologists of all specialties. Founded in 1964 by doctors Fred Ansfield, Harry Bisel, Herman Freckman, Arnoldus Gouldsmit, Robert Talley, William Wilson, and Jane Wright, it is headquartered in Alexandria, Virginia, with a membership of about 35,000. The ASCO founders are widely credited with the organization and development of the modern clinical oncology field. Bisel, the Mayo Clinic’s first oncologist and founder of its Section of Medical Oncology, served as the first president of ASCO as well as consulted with the National Cancer Institute; he also founded the American Society of Preventive Oncology and the American Association for Cancer Education. ASCO
cofounder Jane Wright was one of the first African American female oncologists and the granddaughter of William Fletcher Penn, the first African American graduate of Yale’s medical school; she was a pioneer in chemotherapy, the first to identify methotrexate's usefulness in destroying cancer cells and to develop tested and proven chemotherapy regimens that minimized side effects while maximizing efficacy.

ASCO publishes the peer-reviewed journals *Journal of Clinical Oncology* (JCO) and the *Journal of Oncology Practice* (JOP) as well as a number of newsletters, books, smaller journals, and educational curricula for oncology. JCO was founded in 1983 and is published three times a month, with open access to online articles provided with a one-year delay. ASCO’s first official journal, JCO was proposed by Emil Frei III, former director and physician in chief of the Dana-Farber Cancer Institute. Recent articles have included an ASCO statement on obesity and cancer, a special series of articles on radiation oncology, and a study of the effect of vitamin D deficiency on rituximab patients. JOP was founded in 2005, with a slightly different focus, covering day-to-day issues of oncology practice. Its premier issue, for instance, covered the effects of recent Medicare changes on oncology; recent issues similarly covered the effects of the Affordable Care Act and related state laws.

The Quality Oncology Practice Initiative was launched by ASCO in 2003 to 2006. In response to the Institute of Medicine’s National Cancer Policy Board’s 1999 report on the state of cancer care in the United States, ASCO launched a five-year study, the National Initiative on Cancer Care Quality (NICCQ). Among its goals were not only assessing the quality of care (specifically of breast and colorectal cancer patients, in five specific geographical areas, for the purposes of the study) but a methodology of quality monitoring in order to investigate the feasibility of ongoing accurate and useful national quality monitoring of cancer care. Pediatric oncologist Joseph Simone proposed a quality assessment program with a national infrastructure provided by ASCO but local implementation by the medical oncology community. At the time, most nationwide reporting programs collected information from hospitals and medical centers, pertaining to brief episodes of care, specifically surgeries and other interventions and their short-term (30-day or less) outcomes. What Simone called for would focus on a broader array of practice settings and would thus survey the bulk of cancer care settings and scenarios. He presented a pilot plan for this initiative—Quality Oncology Practice Initiative (QOPI)—while the NICCQ was still ongoing, in 2002, and meetings began in 2003 to formulate QOPI’s methodology. Pilot programs were operated until 2006, when QOPI was officially opened nationwide to the oncology community. The waiting list of practices waiting to join was nearly 100 names long.

Under QOPI, practices collect patient-level data, which is reported to the national leadership at six-month intervals and returned at the following interval with an anonymous comparison of the practice’s performance compared to other practices. Participation is both voluntary and free: In return for its practice-level data and the work required to collect it, each practice receives access to nationwide data and recommendations of cancer-specific measures. Simone guided the initiative as the senior-most oncologist associated at the national level. Face-to-face meetings were limited to the annual ASCO meeting, and ASCO provided staff resources at the national level. Other meetings were held by telephone, designed to be efficient and make the best use of time.

By 2014, when ASCO celebrated its 50th anniversary, QOPI included 450 participating practices and about 4,000 oncologists. In 2010, QOPI launched its certification program in response to requests by participants as a way of demonstrating a certified practice’s commitment to quality assessment, safety standards, and QOPI measures.

ASCO operates Cancer.Net, a patient information Web site. It includes information ranging from types of cancer and coping with cancer to survivorship, 120 guides to different diseases, and tips for finding a cancer clinical trial. A mobile app has been developed for both English and Spanish speakers.

ASCO University is ASCO’s educational program, providing an e-learning center for oncology professionals. Topic-specific courses are offered as well as oncology training programs, maintenance of certification (MOC) courses, and both a printed and e-book version of ASCO-SEP, a self-assessment continuing medical education (CME) program.
The Conquer Cancer Foundation is ASCO’s 501(c)(3) registered charity, funding initiatives in clinical research, patient education, and patient advocacy. Since 1984, it has awarded 800 research grants as well as a number of specific research awards like the Merit Award, the Cancer Development Award, and the Young Investigator Award.

Bill Kte’pi
Independent Scholar

See Also: American Cancer Society; American Society for Radiation Oncology; American Society of Pediatric Hematology/Oncology.

Further Readings

American Society of Hematology

The American Society of Hematology (ASH) is a global professional society of hematologists, researchers, and clinicians headquartered in Washington, D.C., founded in April of 1958, when it held its first official meeting in Atlantic City, New Jersey. Since that first meeting, the ASH has been a critical organization in helping develop hematology as a specialized discipline and advancing the understanding and treatment of blood diseases.

Currently, the ASH focuses its efforts and resources on three main areas of interest in the area of hematology: research, education, and advocacy. Under the umbrella of these three focus areas, the organization aims to help the global community of hematologists become poised to better develop research efforts focusing on various blood diseases in order to provide effective treatments and cures.

Hematology is the study of the physiology of the blood and the diseases that can affect its health, and hematologists are a specialized group of doctors, researchers, scientists, and clinicians focused on treating patients afflicted with these conditions and finding cures for the world’s population. Blood diseases most commonly under the ASH's hematologists’ purview include various blood conditions and blood cancers, such as anemia, sickle-cell anemia, hemophilia, blood clots, leukemia, lymphoma, and myeloma.

ASH reports that the organization has more than 14,000 members spanning almost 100 countries. This membership count places ASH as one of the largest professional societies committed to helping researchers, scientists, and clinicians who specialize in hematology focus on researching and curing blood diseases on a global scale.

Governance and Structure
The governance of ASH is carried out by a member-elected executive committee, which is made up of 13 representatives. The committee’s membership includes a president, a president elect, a vice president, secretary, treasurer, and eight councilors. In addition to the executive committee, ASH has 14 standing committees and 18 scientific committees. The standing committees are charged with carrying out the overall operations of the society and recommending policies, programs, and actions to the executive committee, and the scientific committees are charged with developing the agendas and topics for ASH’s annual meeting as well as identifying new areas of research and advising the organization on scientific policy priorities.

ASH's standing committees include the following: ASH Foundation and Development Committee, the Awards Committee, the Committee on Communications, Committee on Educational Affairs, Committee on Government Affairs, International Members Committee, Committee on Investment & Audit, Nominating Committee, Committee on Practice, Committee on Promoting Diversity, Publications Committee, Committee on Quality, Committee on Scientific Affairs, and Committee on Training, which also includes a subcommittee called the Trainee Council.

In addition to focusing on their specific scientific areas, the ASH’s scientific committees routinely collaborate and work with ASH's standing committees
in order to carry out their functions and are active participants in the organization’s advocacy mission. The ASH’s 18 scientific committees include the following:

- Ad Hoc Scientific Committee on Epigenetics and Genomics
- Scientific Committee on Blood Disorders in Childhood
- Scientific Committee on Bone Marrow Failure
- Scientific Committee on Hematopathology and Clinical Laboratory Hematology
- Scientific Committee on Hematopoiesis
- Scientific Committee on Hemostasis
- Scientific Committee on Immunology and Host Defense
- Scientific Committee on Iron and Heme
- Scientific Committee on Lymphoid Neoplasia
- Scientific Committee on Myeloid Biology
- Scientific Committee on Myeloid Neoplasia
- Scientific Committee on Plasma Cell Neoplasia
- Scientific Committee on Platelets
- Scientific Committee on Red Cell Biology
- Scientific Committee on Stem Cells and Regenerative Medicine
- Scientific Committee on Thrombosis & Vascular Biology
- Scientific Committee on Transfusion Medicine
- Scientific Committee on Transplantation Biology and Cellular Therapies

**Current Research**

ASH’s research agenda is focused on areas that will produce the greatest impact on critical need areas. To carry out that agenda, ASH lobbies and advises federal agencies to develop funding methods that focus funding on hematology research on efforts that would produce the greatest impact in those critical need areas while leveraging and coordinating with other funding resources. ASH’s research is outlined in a three-year strategic plan titled the “ASH Agenda for Hematology Research.” The 2012 to 2014 edition of the plan, which is collaboratively developed by ASH’s scientific committees, represents the third instantiation of ASH’s strategy. The ASH Agenda for Hematology Research 2012–2014 plan not only outlines significant contributions of international hematologists and related research fields but also prioritizes the top hematology areas ASH believes should be funding in the near and long term.

**Membership in the ASH**

Membership in the ASH consists of the following types: (1) active membership, which is available to persons residing in the United States, Canada, or Mexico who hold a doctoral degree or an equivalent degree and work in a field or discipline directly involved in or related to hematology; (2) international membership, which is available to persons fitting the same professional description as active members but who reside outside of the United States, Canada, or Mexico; (3) associate membership, which is reserved for individuals who are either classified as postdoctoral fellows with a medical degree or equivalent, who reside in the United States, Canada, and Mexico, and who are enrolled in an approved hematology or oncology-related training program, or those trainees who have earned their degrees from programs in the United States, Canada, or Mexico and are in a postdoctoral position or training program in a hematology- or oncology-related field; (4) resident members include persons who reside in the United States, Canada, or Mexico and are enrolled in an
accredited hematology-related residency program; and
(5) graduate and medical student memberships, which are granted to graduate or medical students in the United States, Canada, or Mexico who are enrolled in either a postdoctoral or doctoral North American biomedical program or enrolled in an accredited medical school and working toward a medical degree or equivalent doctoral degree.

Publications
As part of its overall education efforts, the ASH produces four main publications that include clinical and scientific research and education on current efforts in the field of hematology. These publications include

Blood—ASH’s official scientific journal dedicated to publishing peer-reviewed articles on hematology research and clinical treatment efforts;

Hematology, ASH Education Program—providing in-depth overviews of the scientific sessions that take place during the ASH annual meeting;

ASH Self-Assessment Program (ASH-SAP)—an educational product that provides current information on the field of hematology with a target audience of internists, hematologists, pediatricians, and fellows in the hematology or oncology fields of study;

The Hematologist: ASH News and Reports—serves as the organization’s newsletter for its members; and

How I Treat—A Compendium for the Practicing Hematologist—which takes 33 “How I Treat” articles from the editions of ASH’s magazine Blood and republishes the article along with updates that might have occurred since the initial publication date.

L. L. Lundin
Independent Scholar

See Also: Leukemia, Acute Lymphoblastic, Adult; Leukemia, Acute Lymphoblastic, Childhood; Leukemia, Acute Myeloid, Adult; Leukemia, Acute Myeloid, Childhood; Leukemia, Chronic Lymphocytic; Leukemia, Chronic Myelogenous; Lymphoma, AIDS-Related; Lymphoma, Burkitt’s; Lymphoma, Hodgkin’s, Adult; Lymphoma, Hodgkin’s, Childhood; Lymphoma, Hodgkin’s During Pregnancy; Lymphoma, Non-Hodgkin’s, Adult; Lymphoma, Non-Hodgkin’s, Childhood; Lymphoma, Non-Hodgkin’s During Pregnancy; Lymphoma, Primary Central Nervous System.

Further Readings

American Society of Pediatric Hematology/Oncology

The American Society of Pediatric Hematology/Oncology (ASPHO) is a multidisciplinary organization dedicated to the best care of children and adolescents with blood disorders and cancer. Creating premier education opportunities for hematology/oncology fellows and continuing education for pediatric oncologists is also a central goal of the organization. ASPHO was initiated in 1974 by pediatricians who had a commitment to pediatric cancer and who approached the American Society of Pediatrics and the Society of Pediatric Research for sponsorship. In large part creating a new specialty, their early meetings took place at the Blood Club, held in conjunction with the annual meetings of the American Society of Pediatrics/Society for Pediatric Research. At the Blood Club meeting in 1977, Carl Pochelly first proposed a society for pediatric hematologists and oncologists. Bill Krivit was also a leader in the Blood Club and, with others, began to plan the incorporation of a separate society devoted to pediatric hematology and cancer.

ASPHO was incorporated in Illinois in April 1981. In 1987, Carl Pochelly advocated for a freestanding meeting of ASPHO, and that first meeting was held in Chicago in 1988.
The new society was publicized through the *American Journal of Pediatric Hematology/Oncology,* first published in 1979. Although closely identified with ASPHO, the journal predated it by two years. After ASPHO's incorporation, the journal's front cover identified it as “The Official Journal of the American Society of Pediatric Hematology/Oncology.” The name of the journal was changed in 1995 to the *Journal of Pediatric Hematology/Oncology* to reflect the increasingly international nature of the contributors and subscribers. Today, *Pediatric Blood and Cancer* is the official publication of ASPHO.

The core purpose of the society is to serve the membership in their goal to improve the health and well-being of children with blood disorders and cancers. Its values are compassion for patients and their families, dedication to the health and well-being of children and adolescents with cancer and blood disorders, commitment to excellent service to members, promotion of high standards of quality and safety, the practice of absolute integrity, fostering of innovation, dedication to professional development, an fostering of collegiality and cooperation. The society wishes to be the premier organization for pediatric hematology and oncology worldwide. A key focus of ASPHO is the educational opportunities for its members, particularly fellows. The annual meeting is the center of these opportunities as well as the annual review course, workshops, and webinars. Certification for the pediatric hematology and oncology specialty is provided in these courses.

In recent years, ASPHO has created the ASPHO Advocacy Alliance With the American Academy of Pediatrics (AAP). The purpose of this alliance is to create a subspecialty-specific advocacy agendas for the pediatric hematology and oncology community as well as unite and combine to promote better outcomes for children. The ASPHO Advocacy Committee works closely with the AAP Department of Federal Affairs, leading advocacy efforts on behalf of children with cancer and blood disorders. Advocacy activities include educating ASPHO members about policy issues in frequent communications, encouraging members to contact their legislators when important issues arise, planning advocacy programming at the annual meeting, and bringing ASPHO representatives to Washington, D.C., to meet directly with policy makers.

The Advocacy Committee has several priorities and important issues that it shares with pediatric hematology and oncology physicians. These are the current goals and objectives: (1) guaranteeing a sufficient supply of existing drugs for children with hematologic or oncology disease and decreasing or ending the number of drug shortages in the United States; (2) making sure every child with sickle cell disease has a medical home with access to primary and subspecialty care; (3) educating policy makers about coordinated care, delivery system reform, and payment barriers; (4) ensuring needed access to subspecialists for children with cancer and improving Medicaid payments; (5) increasing the number of pediatricians going into the hematology and oncology fields to guarantee a sufficient number of these physicians in the future.

Robin L. Rohrer
Seton Hill University

**See Also:** American Society of Clinical Oncology; Bone Marrow Transplants; Brain Tumors, Childhood; Childhood Cancers; International Society of Paediatric Oncology; Leukemia, Acute Lymphoblastic, Childhood; Leukemia, Acute Myeloid, Childhood; Lymphoma, Non-Hodgkin's, Childhood.

**Further Readings**

---

**Amgen (United States)**

Amgen, Inc. is considered to be one of the first biotech pharmaceutical companies and is currently the largest independent biotechnology organization in the world. In 2013, Amgen reported revenues of $18.7 billion, with total product sales of $18.2 billion and a research and development budget of $5.2 million. This represents an increase of product sales of $16.8 billion in 2012 and $16.3 in 2011 and in research and development budgets of $3.4 billion in 2012 and $3.2 billion in 2011. Further, seven of
Amgen’s pharmaceutical products are on the list of the top 100 drugs in the United States.

Pharmaceutical products manufactured and marketed by Amgen focus on the therapeutic areas of hematology, oncology, inflammation, bone health, nephrology, cardiovascular, and general medicine. Names of the products and marketing agreements with other countries (e.g., Pfizer markets Embrel outside of the United States and Canada) vary across countries, but in the United States, their primary products are as follows:

- **Aranesp**, generic name: darbepoetin alpha; indications/marketed for: treatment of anemia associated with chronic kidney disease (CKD) and the treatment of anemia due to concomitant myelosuppressive chemotherapy in patients with nonmyeloid malignancies (indicated for patients both on dialysis and not on dialysis)
- **Enbrel**, generic name: etanercept; indications/marketed for: moderate to severe rheumatoid arthritis, chronic moderate to severe plaque psoriasis, and active psoriatic arthritis
- **Epogen**, generic name: epoetin alpha; indications/marketed for: treatment of anemia associated with CKD for patients on dialysis
- **Neopogen**, generic name: filgrastim; indications/marketed for: reducing incidence of infection associated with febrile neutropenia in patients with nonmyeloid malignancies who are undergoing myelosuppressive chemotherapy
- **Neulasta**, generic name: pegfilgrastim; indications/marketed for: to decrease incidence of infection associated with chemotherapy-induced febrile neutropenia in cancer patients with nonmyeloid malignancies
- **Sensipar/Mimpara**, generic name (note: marketed in the United States as Sensipar): cinacalcet; indications/marketed for: treatment of secondary hyperparathyroidism in CKD patients on dialysis
- **Xgeva/Prolia**, generic name (note: same product, different indications for different names of product): denosumab; indications/marketed for: Xgeva is indicated for the prevention of skeletal-related events in adults with bone metastases from solid tumors, and Prolia has four indications all related to the treatment of osteoporosis

As previously indicated, Amgen, Inc. invests a significant amount of its revenue in research and development, resulting in up to 10 innovative molecules of which, according to the letter to shareholders in their 2013 annual report, six have the potential to be introduced and marketed beginning in 2017. Products in the Phase 3 clinical trials include a human monoclonal antibody to be used in the treatment of dyslipidemia; a product for the treatment of unresected stage IIIB, IIIC, or IV melanoma; and a drug for the treatment of ovarian cancer. Other products under development focus treatment of heart failure and angina.

Thus far, this description of Amgen depicts a large organization, one with a presence in more than 75 countries, yet it was an organization with a meager start and many years of profit losses. The company, originally called Applied Molecular Genetics, was founded in 1980 by William Bowes, who came from Centus Corporation, one of the first biotechnology companies. Bowes established Amgen in Thousand Oaks, California, within reach of three research universities and hired Winston Salser, a scientist from the University of California, Los Angeles (UCLA), and George Rathmann, the former chief of Abbot Laboratories’ diagnostics division. Rathmann was hired as CEO, and his original office was in a trailer so that the scientists whom were hired would have enough lab space.

Amgen was far from an immediate success as, for the first five years, they suffered losses and did not break even until 1986. In 1986, research grants from other pharmaceutical companies were a crucial source of income. The company was also in fierce competition and legal disputes regarding alleged patent infringements with another biotechnology organization, Genetics Institute (GI). Amgen also underwent a long legal conflict with Johnson and Johnson’s Ortho Pharmaceutical Division regarding sales of EPO in the United States and other countries.

The product involved in the lawsuits was EPO, a synthetically produced hormone that stimulates the production of red blood cells. The small target
market for EPO was patients on dialysis as dialysis lowers the kidneys’ capacity to produce natural EPO. EPO was not approved for use by either GI or Amgen until 1987, when an article on the use of EPO on 25 dialysis patients was published in the *New England Journal of Medicine*. In the article, Eschbach and colleagues reported encouraging results with the use of Amgen’s EPO in that it demonstrated reduction of transfusions and increased hematocrit levels to normal in these high-risk patients. The Food and Drug Administration (FDA) then granted orphan drug status to Amgen’s EPO because the market for the drug was small, yet soon, EPO was found to be a product that could be used for anemia that was related to cancer, arthritis, and other treatments.

Amgen applied for new drug status in 1987 for its EPO, Epogen. Epogen was the first FDA-approved EPO, and when it was approved on June 1, 1989, Amgen shipped out the first batch the next day. At the end of the first month of sales, Epogen had brought in close to $17 million. The company followed with Neopogen and other products previously listed. Amgen also established successful partnerships with companies like Kirin Brewery, which could help in the manufacture of its products.

The company continues to demonstrate a focus on research and development but also currently has focused efforts on sustainability. In particular, it reports that, in 2013, they recycled 74 percent of wastewater generated at its largest manufacturing plant. Further, since 2008, it states that the company has also reduced energy costs by $20 million due to conservation projects that were put in place.

Finally, Amgen has demonstrated a commitment to philanthropy. The company provides research grants that help in promoting patient care and science as well as science-related (e.g., lab equipment) donations to assist public schools and nonprofit organizations. They also provide Embrel and other medications free to patients based on need and provide health care and nonhealth care donations that are related to education or have literary or scientific purposes.

Anne Hubbell  
*New Mexico State University*

**Further Readings**

“Amgen—A Biotechnology Success Story: From Drug Development to the Mass Market.” MaRS.  


Amgen, Inc. “Amgen’s 2013 Revenues Increased 8 Percent to $18.7 Billion and Adjusted Earnings per Share (EPS) Increased 17 Percent to $7.60.”  


Eschbach, Joseph W., Joan C. Egrie, Michael, R. Downing, Jeffrey K. Browne, and John W. Adamson.  
“Correction of the Anemia of End-Stage Renal Disease With Recombinant Human Erythropoietin.”  


---

**Anal Cancer**

The term *anal cancer* refers to any form of cancer associated with the anus. There are many types of malignant and benign cancers as well as precancerous conditions that can be found in the anal canal (a canal approximately an inch and a half long, connected to the rectum).

Some of the earliest signs of anal cancer include bleeding from the anus or rectum, pain around the anus, itching or discharge from the anus, and a lump near the rectum. Currently, there are no national screening guidelines for anal cancer.

Tests that may indicate the presence of anal cancer include a physical examination, a digital rectal examination, an anoscopy or proctoscopy, an ultrasound procedure in the anus or rectum, and a biopsy.

Many benign tumors occur in the anus. Some of these include polyps, warts, fibroid tumors (leiomyomas), granular cell myoblastoma (large cells filled
with fine granules), hemangiomas (extra blood vessels in the skin that look like strawberry-colored birthmarks), lipomas (growths of fat under the skin), and schwannomas (tumors originating in the peripheral nerve fibers). Sometimes, benign tumors in the anus can turn malignant. These tumors are known as precancerous conditions, and those associated with anal cancer are specifically called anal intraepithelial neoplasia. Some anal warts are examples of anal intraepithelial neoplasia.

The prognosis for anal cancer depends on a number of factors, including the size and location of the tumor and whether it has spread to the lymph nodes.

In terms of malignant (or cancerous) tumors, the most common type of anal cancer is squamous cell carcinoma, which can be found in the tissues that line the anal canal and the anal margin. When these carcinomas have not spread from the original cancerous site, they are called carcinoma in situ. Another type of cancer occurs in the cloaca, which is located between the rectum and the anal canal. A specific type of scaly, cancerous tumor can occur there, known as cloacogenic carcinoma. Adenocarcinomas are another form of anal cancer involving tumors that grow in the glands under the anal epithelium and discharge cancerous secretions into the anal canal. Those forms of cancer that form under the rectum are called rectal carcinomas. Basal cell carcinomas are another form of cancer that can develop in the skin outside the anus.

Anal cancer is usually curable, and there are many treatment options. Treatment options for people with anal cancer include surgery (which may completely remove the cancerous site), radiation therapy, chemotherapy, or a combination of all of these treatments. However, treatment options depend on a number of factors, including the stage of the cancer, its location, whether this is a recurrence of cancer, and whether the person has the human immunodeficiency virus (HIV). People who have primary tumors that are less than 2 centimeters in size have better prognoses.

For Stage 0 anal cancer (carcinoma in situ), the primary treatment for lesions of the perianal area, not involving the anal sphincter, is surgical resection. For Stages I, II, and IIIA anal cancers, small tumors of the perianal skin or anal margin are usually excised, and chemoradiation is often necessary for cancers of the anal canal. Follow ups, including rectal examination every three months for the first two years are important, and doctors may also perform endoscopy with biopsies or endorectal or endoanal ultrasound in certain cases.

Patients with Stage IIIA cancer receive the same treatment as those with Stage I and II, including radiation plus chemotherapy, but they may also receive a radial resection.

For those with Stage IIIB cancer, treatment includes radiation therapy plus chemotherapy as well as surgery and inguinal node dissection for residual or recurrent tumor. Cure of this stage of the disease is still possible. However, the presence of inguinal nodes associated with metastatic disease is a poor prognostic sign. As a result, patients should be included in clinical trials whenever possible. For patients with Stage IV anal cancer, palliative care is vital. Such palliative care might include surgery, radiation therapy, combined chemotherapy and radiation therapy, and the inclusion of the patient in clinical trials.

Overall, the incidence of anal cancer is increasing in the United States. According to the National Cancer Institute, there were 7,210 new cases of anal cancer in the United States in 2014, and 950 deaths were expected. Approximately 0.2 percent of the U.S. population will be diagnosed with anal cancer at some point. The five-year survival rate for anal cancer is 65 percent, according to the National Cancer Institute.

Anal cancer is one of the most common forms of cancer for people in high-risk sexual categories, such as those who have HIV and men who have sex with men (MSM). It affects people with HIV at a much higher rate than people who do not have HIV.

Some of the risk factors for anal cancer include having HIV, age (it is more prevalent among people over 50), being infected with human papilloma virus (HPV), smoking (smokers have a higher rate of anal cancer), having many sexual partners, and having receptive anal sex. Organ transplant recipients and people with chronic immunosuppressive states are at much higher risk of getting anal cancer.

Anal cancer affects men and women differently. Men tend to get anal cancer outside the anus, whereas women tend to get anal cancer inside the anus. Although most forms of anal cancer can be cured, women experience a mortality rate from anal cancer that is approximately twice the rate experienced by men. Women who have a history of cervical, vaginal, and vulvar cancer are at higher risk of developing anal cancer.

One preventive intervention, the quadrivalent HPV vaccine, has been approved for use by the Food and Drug Administration (FDA) since 2010.
for the prevention of anal cancer. The Centers for Disease Control and Prevention (CDC) recommends routine vaccination of males ages 11 and 12 and vaccination of those 13 to 21 who have not been vaccinated previously.

Mark D. Sherry
University of Toledo

See Also: Clinical Trials; Colorectal Cancer, Childhood; Rectal Cancer.

Further Readings

Angola

Angola is situated in Southern Africa. The People’s Republic of Angola, as it was formally called, is bordered on the north by the Democratic Republic of the Congo, on the east by Zambia, south by Namibia, and west by the Atlantic Ocean. It is the seventh-largest country by area in Africa and 31st-largest globally. It is the 15th-most populous country in Africa and 59th in the world, with a population of more than 18 million. There are many different ethnic groups in Angola, each of which has its own cultural traditions, including traditional medicine and ethnopharmacological practices. Although Portuguese is the official national language, there are 38 other indigenous languages still spoken by respective ethnic groups in Angola; the most widely used languages include Cokwe, Kikongo, Kimbundu, Oshiwambo, and Umbundu.

There are many traditional medicinal preparations used in the Angola. Most of these traditional medicines incorporate use of myriad local plant materials, many of which have been shown to have medicinal properties in laboratory studies. For example, extracts of *Euphorbia tirucalli* and *Vernonia ambigua*, both of which are used for traditional healing, demonstrated antitumor activities. Research also suggests that use of certain plants may help protect against cancer by reducing oxidative stress and stimulating enzymes and other processes that help the body fight carcinogens. For example, an extract from *Cochlospermum angolensis*, locally referred to as *borututu*, demonstrated substantial antioxidant potential, as did an extract from *Nymphaea lotus*, referred to as *mbandu* in Kimbundu.

Medicinal plants are used in Angola to treat many health problems commonly associated with cancers. For example, the powdered bark of *Canarium schweinfurthii*, which the Chokwe call *mubafo* or *mupaxi*, is eaten with millet to treat coughs. A bark infusion of *Cochlospermum angolensis*, locally referred to as *borututu*, demonstrated substantial antioxidant potential, as did an extract from *Nymphaea lotus*, referred to as *mbandu* in Kimbundu.

The average number of cancer cases annually in Angola are 95.7 per 100,000 population. Cancers account for a substantial amount of disability and suffering among impacted populations. According to the World Health Organization’s “Disease and Injury Country Estimates,” the age-standardized disability adjusted life-year estimates for 2004, the 10 most prevalent cancers in Angola were led by stomach cancer at 289 per 100,000 population; cervical and uterine cancers at 226 per 100,000 population; breast cancer at 218 per 100,000 population; lymphomas at 178 per 100,000 population; mouth and oropharynx cancers at 172 per 100,000 population; trachea, bronchial, and lung cancers at 134 per 100,000 population; liver cancer at 118 per 100,000 population; esophageal cancer at 89 per 100,000 population; colon and rectal cancers at 71 per 100,000 population; prostate cancer at 70 per 100,000 population.

There are serious deficiencies of modern pharmaceutical supplies, as opposed to traditional preparations, and in modern medical services for cancer and similar conditions. Angola, for instance, is among the countries with the lowest morphine consumption rates in the world; it is ranked 152nd of all nations at 0.0005 milligrams per capita. In 2010, the annual prevalence of use of all opiates as a percentage of the population age 15 to 64 years in Angola was 0.25 percent, which ranks it as the 61st-highest country. These factors make access to appropriate palliative care highly problematic. A 2012 report by Lopes and colleagues found that the National Oncology Center in Luanda provided chemotherapy for cancer treatment, and
also had radiotherapy equipment supplied by Varian, but that the latter was not yet in operation.

Ten cancers are among the 50 leading causes of death in Angola. Breast cancer is the 23rd leading cause of death; the age-standardized death rate for breast cancer in Angola is 13.04 per 100,000 population, which ranks Angola as the 139th-highest country in the world for breast cancer deaths. Cervical cancer is the 24th-leading cause of death; the age-standardized death rate for cervical cancer in Angola is 12.52 per 100,000 population, which ranks it 28th in the world. Liver cancer is the 27th-leading cause of death; the age-standardized death rate for liver cancer in Angola is 9.57 per 100,000 population, which ranks it 56th globally. Prostate cancer is the 31st-leading cause of death; the age-standardized death rate for prostate cancer in Angola is 8.55 per 100,000 population, which ranks it 54th. Lymphomas are the 41st-leading cause of death; the age-standardized death rate for lymphomas in Angola is 4.68 per 100,000 population, which ranks it 112th.

Stomach cancer is the 42nd-leading cause of death; the age-standardized death rate for stomach cancer in Angola is 4.50 per 100,000 population, which ranks it 136th. Esophageal cancer is the 44th-leading cause of death; the age-standardized death rate in Angola is 3.98 per 100,000 population, which ranks it 65th. Oral cancer is the 46th-leading cause of death; the age-standardized death rate is 3.56 per 100,000 population, which ranks it 73rd. Colon and rectal cancers are the 47th-leading cause of death; the age-standardized death rate is 3.51 per 100,000 population, which ranks it 168th. Lung cancer is the 50th-leading cause of death; the age-standardized death rate for lung cancer in Angola is 2.33 per 100,000 population, which ranks it 168th in the world.

Furthermore, according to the World Health Organization’s “Global Health Observatory Data Repository,” in 2008, the age-standardized estimates of deaths from all cancers was 88 per 100,000 population for males and 83 per 100,000 population for females in Angola. As a consequence, life expectancy as of 2011 for males is 50.0 years and that for females is 52.9 years, which gives an average life expectancy of 51.5 years, ranking Angola as the 168th highest globally. There is a clear and urgent need for improved cancer awareness, early detection programs, and health services infrastructure in Angola.

Victor B. Stolberg
Essex County College

See Also: Congo, Democratic Republic of; Developing Countries; Tanzania; Zambia.

Further Readings


Bossard, Eric. La Medecine Traditionnelle au Centre et a l’Ouest de l’Angola. Lisbon, Portugal: Instituto de Investigacao Cientifica Tropical.


Antibiotics

Antibiotics (also called antimicrobials) are a category of medications (living organisms and synthetic antimicrobials) that target, terminate, or inhibit the multiplication of microorganisms. Originally, antibiotics were used to describe antibacterials but have been broadened to include fungi, viruses, and parasites. Antibiotics are classified by the microorganism...
they target, such as antibacterials (bacteria), antifungals (fungi), antivirals (viruses), and antiparasitic (parasites). Antiseptics can terminate microorganisms that live on the skin or in the mucous membranes and also aid in reducing infection associated with surgical operations. There are also a number of mostly nonmedical disinfectants that terminate or reduce microorganisms from medical instruments, work surfaces, and so on, and prevent the spread of bacteria, fungi, viruses, and parasites.

Antibiotics are considered one of the most significant advances in medicine in combating microbes to date. Yet, the modern medical community struggle continues as the microbe evolves and the medical community seeks to gain the upper hand.

**History of Antibiotics**

Throughout history, the healers as well as the modern medical community have been in a constant struggle to develop treatments that inhibit and terminate microbes. The early use of antimicrobials dates back at least 2,000 years to early Egyptian, Chinese, and Greek civilizations as well as indigenous groups of Central America. The ancient civilizations were known to use molds, soils, and plant extracts for the treatment and management of infections. For example, ancient civilizations used mold from bread and other molds to prevent infections from serious cuts. Other groups used molds to treat rashes. Infections and other diseases were thought at the time to be the product of evil spirits and the molds, soils, and plant extracts expelled the evil spirit from the body.

In 1877, Louis Pasteur (1822–95) demonstrated that microorganisms were causative agents of diseases (e.g., the germ theory of disease). Pasteur also verified that anthrax (a bacterial disease) could be rendered innocuous by injecting the animal with bacteria from soil. His work on chicken cholera (also called avian pasteurellosis) discovered that introducing weakened bacteria (similar to the treatment of smallpox) to the chickens resulted in them becoming ill and subsequently becoming immune to the disease. In 1888, building on the germ theory, E. de Freudenreich by chance discovered the blue pigment from *Bacillus pyocyaneus* could inhibit bacterium from growing in cell cultures.

In 1899, Rudolf Emmerich and Oscar Low conducted an experiment where they took germs from infected bandages and grew them in cultures. The bacteria (i.e., *Bacillus pyocyaneus*) that caused green infections in open wounds was isolated and placed into test tubes with other bacteria, such as cholera, typhoid, diphtheria, and anthrax. Their experiment demonstrated that germs that cause one disease were a possible cure for others. From this experiment, the first antibiotic drug, called pyocyanase, was created. However, pyocyanase was potentially toxic to humans, and its effectiveness in patients was inconsistent and thus was considered clinically unusable. In 1910, Paul Ehrlich was investigating possible agents that would kill specific microorganisms, or a “magic bullet.” He discovered the first modern chemotherapeutic agent, known as arsphenamine (e.g., compound 606 or Salvarsan). Arsphenamine was the first effective treatment for syphilis and valuable in treating the parasitic disease trypanosomiasis.

In 1928, Alexander Fleming (1881–1955) discovered (apparently by chance) a natural antimicrobial fungus that could treat *Streptococcus aureus* (which earlier and little-known work by Andre Gratia and Sara Dath had done). Fleming’s discovery was known as *penicillium*. Harold Raistrick grew Fleming’s *penicillium* in cultures but was not able to isolate the mold producing penicillin. Charles Thom helped Raistrick correctly identify the responsible organism as *Penicillium notatum*.

In 1930, Cecil George Paine used *penicillium* to cure several infants with a gonococcal infection. Building on the work of others, Ernst Boris Chain and Howard Florey made it possible for mass production of antibiotics. Florey, Chain, and Fleming won the Nobel Prize in Physiology or Medicine in 1945. *Penicillium* was renamed penicillin in 1942, and it proved successful in treating a host of infectious diseases, in particular gram-positive bacteria, such as genera bacillus, clostridium, streptococcus, and staphylococcus. Penicillin is used to treat conditions such as gangrene, leptospirosis, Lyme disease, pneumonia, sexually transmitted infections (e.g., chlamydia, gonorrhea, and syphilis), strep throat, and typhoid fever.

**Antimicrobial Treatments for Bacteria, Viruses, Fungi, and Parasites**

Antimicrobial treatments are categorized broadly into two types: microbiostatic or microbicidal. Microbiostatic antimicrobials operate by hindering or inhibiting the replication of the pathogen,
Antibiotics are a category of medications that target, terminate, or inhibit the multiplication of microorganisms. Although microbes have acquired or developed resistance to antimicrobials in antibiotics, the drugs are still considered one of the most significant advances in medicine in combating microbes to date. (Flickr/Angela Doss)
schizont of the malaria parasite include combinations of chloroquine, quinine sulfate, and artemisinin. Treatments to reduce symptoms are a combination therapy of blood schizonticidal medications (e.g., attack and kill the schizonts) such as chloroquine, quinine sulfate, and artemisinin. To prevent relapses of \textit{P. vivax} and \textit{P. ovale}, a schizonticidal medication called primaquine is used to kill parasites residing in the liver. Gametocytocidal medications are used to prevent spread by killing the gametocysts include primaquine (for \textit{P. falciparum}) and chloroquine for all other parasite species.

\textbf{Antibiotic Resistance}

Antimicrobial resistance is a natural phenomenon because microbes have always exchanged genetic material rapidly and mutated often. Although antibiotics are still effective, over the years, microbes have acquired or developed resistance to antimicrobials, and their ability to evolve rapidly is aided by the misuse and overuse antimicrobials. Antibiotic resistance is the microbe itself rather than humans becoming resistant to the antimicrobial medicines. For example, in the late 1940s and throughout the 1950s, penicillin was the standard medical treatment for \textit{Staphylococcus aureus}.

Staph infections were primarily viewed as a manageable nuisance; however, during this time, staph began to show signs of being penicillin resistant. The main problem with antibiotic resistance is that, once a microbe becomes antibiotic resistant, humans can become infected with the evolved, antibiotic-resistant microbe and transmit it to others. The new infectious disease strains make it more expensive and require more advanced treatments as well as those infected experiencing longer illnesses, disability, and higher mortality. Antibiotic resistance is more common in bacteria than in fungi, viruses, and parasites. Other infections that have become antibiotic resistant include: \textit{Mycobacterium tuberculosis} (TB), HIV/acquired immune deficiency syndrome (AIDS), \textit{Enterococci}, \textit{plasmodium parasite} (malaria), and various gram-negative bacteria, such as \textit{E. coli}, \textit{Acinetobacter baumanii}, \textit{Pseudomonas aeruginosa}, \textit{Klebsiella pneumonia}, and \textit{Neisseria gonorrhoeae}.

Some significant public health examples of antibiotic resistance conditions are: methicillin-resistant \textit{Staphylococcus aureus} (MRSA), TB, and malaria. After staph infections started showing penicillin resistance, the medical community developed a semisynthetic penicillin called methicillin. Methicillin became a standard medical treatment for \textit{staphylococcus aureus} until the early 1960s. In 1961, scientists in Britain documented the first MRSA. There are drug-resistant TB strains, and if infected with one, it can still be treated with up to two years of chemotherapy in combination the second-line anti-TB drugs. If left untreated, active TB can result in the infection spreading to other body parts via the bloodstream, such as the bones (spinal pain, rib and joint destruction), inflammation of the brain (meningitis), liver or kidneys failure (inability to detox blood), and heart (pericardial tamponade), or be lethal. Treatment for these conditions requires extensive medical treatment and intervention. In certain areas, such as select areas of Africa, the plasmodium species have become resistant to antimalarial drugs. Globally, three of the five malaria species known to affect humans—\textit{P. falciparum}, \textit{P. vivax}, and \textit{P. malariae}—are resistant to treatments. The emergence of artemisinin-resistant \textit{P. falciparum} is of considerable concern to global public health efforts to eradicate malaria. As a result, antibiotic resistance is no longer simply a manageable nuisance, but is a growing global public health concern. Another emerging issue is the superinfection, which is when new bacteria, virus, fungal, or parasite infection occurs, or a coinfection develops during antimicrobial treatment.

Andrew Jon Hund

\textit{United Arab Emirates University}

\textbf{See Also:} Disinfectants and Antiseptics; Infection; \textit{Mycosis Fungoides}.

\textbf{Further Readings}


Anticancer Drugs

Anticancer drugs are those used to treat or target cancerous cells or growths detected in living tissue and have been used frequently to treat cancer patients since the late 1940s. Medical knowledge and research over the past 50 years has significantly advanced the therapies and treatments—the most common being chemo- and radiation therapies—used by doctors and oncologists to treat their patients. As such, chemotherapy and radiation treatments have benefitted patients’ life expectancies by significantly increasing the overall survival rates for many types of cancers. However, secondary carcinogenicity, which is when anticancer drugs cause secondary cancer, is a serious medical issue for cancer patients undergoing long-term chemotherapy or radiation as part of their treatment regimens.

A carcinogen is defined as any substance that causes cancer in living tissues, and the process of cancer developing in living tissues is referred to as carcinogenesis, oncogenesis, or tumorigenesis. Basically, this process is when a living, normal cell is transformed into a cancerous cell that then divides in an uncontrollable manner and forms a malignant mass, or neoplasm. Researchers and medical professionals typically classify carcinogens by their structure or chemical as a way to differentiate among known carcinogens and the ways they behave; however, all chemical carcinogens have the ability to directly or indirectly change the DNA structure of a living tissue. This effect is caused by the fact that many anticancer drugs used in treatments today are themselves classified as carcinogens. Many researchers, doctors, and cancer patients have reported acute, toxic side effects that occurred after patients underwent prolonged treatment. These treatments then unduly caused additional damage or cancers to occur in a patient’s vital organs and tissues. Additionally, the use of anticancer drugs that are classified as carcinogens have been seen to cause neoplasm, or the growth of tumors in living tissue. Neoplasms are classified into four categories: benign neoplasms, in situ neoplasms, malignant neoplasms, and unknown or uncertain neoplasms. The malignant neoplasm is classified as cancer.

This cell division is a physiological process that can occur for a variety of reasons. However, carcinogenesis mutates the normal cells and throws off the cells’ natural balance, resulting in uncontrolled and rapid cell division. This can lead to the benign tumors that are not typically a threat to a patient as they most often do not invade other tissues or to malignant tumors that do spread to other areas of a patient’s body and are life threatening.

In general, anticancer drugs target cancerous cells that are identified by their ability to multiply rapidly. In chemotherapy regimens, a patient’s normal cells also can be damaged as a direct result of the drug’s ability to cause or induce mutations. A few other anticancer drugs are also proven to generate free radicals that harm the DNA of a patient’s normal cells.

Despite the fact that studies of second carcinogenicity have been ongoing since the late 1940s, today’s researchers better understand how and why anticancer drugs may contribute to second cancers in patients. As such, the medical and research community recently has started spending a significant amount of time researching preventative measures that would lessen the carcinogenic effects of common anticancer drugs used in treatment therapies and programs.

Today’s chemotherapy and radiation treatments have progressed significantly since first being developed, with studies focusing on various types of new anticancer drugs or combinations of drugs that reduce the carcinogenic effects of common products used in treatments, including the addition of various compounds or molecules that would negate the carcinogenicity of the main drug used to treat the cancer. This includes recent success demonstrated with a compound called metallothionein that works as a suppressant of the cancer-inducing properties found in carcinogenic anticancer drugs. Additionally, researchers and medical professionals have published studies that show a standard, minimum dose of anticancer drugs given to patients can reduce the risk of patients being diagnosed with a second cancer due to treatment. However, researchers agree that second cancers can occur in
patients randomly without any indication that anticancer drugs played a role in the cause.

Research shows that anticancer drugs that work through binding to the DNA, or alkylation, are carcinogenic in humans and are shown to cause long-term damage to a patient, to include damage to bone marrow and, although rare, acute leukemia. This risk has been shown to be dose dependent, so researchers advocate for as minimal a dose as possible to avoid the carcinogenic effects of the drug or treatment being used. In many cases, patients who experience secondary carcinogenicity do so several years—possibly five to ten years or two to three decades later—after receiving treatment for their initial diagnoses. Furthermore, research has shown that some patients may be more susceptible to secondary carcinogenicity than others. These factors can include age and genetic predisposition. This indicates that children may be more susceptible to the carcinogenic effects of treatment therapies verses adults. Regardless, cancer patients who have survived their initial prognoses and treatment regimens are closely followed throughout the remainder of their natural lives.

Those anticancer drugs used in chemotherapy that are alkylating agents are believed to increase the risk secondary cancers, especially leukemia, in patients who have been diagnosed with Hodgkin's disease, non-Hodgkin's lymphoma, ovarian cancer, lung cancer, or breast cancers. All in all, 37 anticancer drugs have been determined to be carcinogenic. However, several of these drugs have links to causing leukemia in cancer patients and survivors years after their initial treatments end. These drugs include, but are not limited to, the following:

- Mechlorethamine
- Chlorambucil
- Cyclophosphamide (Cytoxan)
- Melphalan
- Semustine
- Lomustine (CCNU)
- Carmustine (BCNU)
- Prednimustine
- Busulfan
- Dihydroxybusulfan

Additionally, researchers do not yet have data that indicates the possibility of anticancer drugs causing carcinogenic effects to those that handle these products in occupational settings, especially those working in hospital environments, although this topic is a research area of interest to many in the medical community. The limited research data available suggests that there might be a link between anticancer drugs and a slight increase in the risk of abnormalities in pregnancy, to include miscarriages, malformations in children, and difficulty in getting pregnant in women who work closely with anticancer drugs in hospital environments.

Overall, researchers, medical professionals, and oncologists do not believe the potential risk of secondary cancers caused by some anticancer drugs and agents should not dissuade cancer patients from seeking chemotherapy and radiation therapies as treatment options to their current diagnoses. While the risks are evident, today's researchers and medical professionals' awareness of the potential risks have led to numerous studies to proactively mitigate any risk factors in their patients. In short, patients are more likely to experience more short-term negative side effects as a result of their treatment options than experiencing the risk of secondary cancer caused by these treatments.

L. L. Lundin
Independent Scholar

See Also: Breast Cancer; Cervical Cancer; Chemotherapy; Colon Cancer; Lung Cancer, Small Cell; Lymphoma, Hodgkin's, Adult Melanoma; Plasma Cell Neoplasm/Multiple Myeloma; Ovarian Epithelial Cancer; Pancreatic Cancer; Prostate Cancer; Skin Cancer, Melanoma.

Further Readings
“Chemotherapy Principles: An In-Depth Discussion of the Techniques and Its Role in Cancer Treatment.” American Cancer Society (February 2013).
Lavie, O., O. Barnett-Griness, S. Narod, and G. Rennert. “The Risk of Developing Uterine Sarcoma...
Argentina

Argentina is a Latin American country located in the southern cone of South America with a current population of approximately 42 million people. Cancer is a leading cause of death in this region of the world. Between 2012 and 2030, cancer deaths in the Americas will increase from 1.3 million to 2.1 million.

Argentina has an incidence rate of 206 per 100,000 inhabitants and a mortality rate of 148 in men and 97 in women. The most common cause of cancer mortality is breast cancer in women and prostate and lung cancer in men. Common risk factors include: alcohol consumption, tobacco use, low level of physical activity, and obesity. Leukemia is the most common type of cancer in children. The incidence rate in children and adolescents under 15 years of age is 128.5 per million, while the mortality rate is 43.8 per million. These rates are similar to those in other Latin American countries, with the exception of leukemia, where mortality rates are lower.

Several programs for cancer prevention and early detection have been created for breast, colorectal, and cervical cancer, as well as the control of tobacco use. These programs have resulted in the training of provincial medical teams, the dissemination of information to the general population about the lifestyle risk factors related to cancer, and the introduction of cancer prevention and control in the political agenda. In 2011, the Plan Nacional de Tumores Familiares y Hereditarios (National Plan of Hereditary and Family Tumors) was created to improve early detection and treatment in high-risk groups. February 15 has been established as the Day Against Childhood Cancers to increase awareness of the early signs of cancer in children and promote prompt diagnoses. There are also future plans to develop a national program for the coordination of palliative care.

Argentina spends 8.1 percent of its gross domestic product (GDP) on health. The country has a complex health care system that is divided into three main sectors: a public health system based on a universal care model, different private insurance companies, and a system of social security linked to employment and managed by unions. It is estimated that 37 percent of the population rely on public coverage, 51 percent on social security, and 12 percent on private insurers. The Programa Médico Obligatorio (Obligatory Medical Program) guarantees all of the population free access to medical attention, regardless of residency status or nationality. There are specific health policies that guarantee equal access to medical treatment for cancer.

Argentina has a national cancer registry at the hospital level and 13 population-based registries. Cancer cases in patients under 15 years of age are recorded under the Registro Oncopediátrico Hospitalario Argentino (Argentinian Oncopediaiatric Hospital Registry).

The Instituto Nacional de Cáncer (National Cancer Institute) was created in 2010 to coordinate national strategies aimed at preventing and controlling cancer. Its main responsibilities include: the development of prevention campaigns, the establishment of early detection and screening programs, the training of health professionals, the design of guidelines for patient care, the identification of risk factors, the reduction of cancer incidence and mortality, epidemiological surveillance, and the promotion and funding of research.
Cancer research is funded and directed by the Consejo Nacional de Investigaciones Científicas y Técnicas (National Council of Scientific and Technical Research). There are also private institutions, such as the Instituto Leloir, with extensive experience in applied research and clinical trials. Four of the main hospitals leading cancer research in the country are: Instituto de Oncología Angel H. Roffo, Universidad Católica de Cordoba, Hospital Eva Peron, and Hospital Municipal de Oncología Marie Curie.

Despite policies establishing the provision of medical services to all diagnosed cancer patients, the Argentine health care system currently is dealing with inappropriate screening and diagnosis processes, the interruption or suspension of treatment protocols, and inadequate follow-up care. Oncology services are concentrated in major cities, leaving large areas of the country, usually rural, without trained personnel and equipped facilities. This leads to delays in the diagnosis of cancer and the treatment of the disease in advanced stages, a factor that is linked to higher rates of mortality. Furthermore, this centralized distribution of services forces patients to travel long distances to access care or relocate to distant cities. The need to leave the place of origin to access medical treatment puts pressure on the families of patients as they must find ways to deal with travel costs and the effects of family separation.

There is a national shortage of medical equipment required for screening, diagnosis, and treatment such as magnetic resonance imagings (MRIs), computerized tomography (CT) scans, positron emission tomography (PET) scans, and radiotherapy units. Furthermore, despite the establishment of national and regional oncology drug banks, there have been documented shortages of anticancer medicines.

Nongovernmental organizations are currently working with state institutions to improve oncology services across the country. These organizations provide assistance in the form of improving the training of medical professionals, preparing campaigns on cancer prevention, carrying out research on the design of new medical protocols, and delivering medical and support services to patients and their families (medication, psychosocial support, and housing and travel allowances).

See Also: Breast Cancer; Childhood Cancers; Future of Cancer; Government; Lung Cancer, Small Cell; Prostate Cancer; World Health Organization.

Further Readings


Asbestos

Asbestos is a set of six naturally occurring silicate minerals used primarily for its insulation properties. While many countries have banned the use of this material in most applications, it is still mined, manufactured, and used around the world today.
Asbestos despite the known carcinogenic hazards. Human exposure increased as demand increased in the 20th century, which included both occupational and public exposure. Due to the unique size ratio of asbestos, this long but very thin material may penetrate into the deep lung tissues, causing permanent health problems. Those exposed to asbestos most commonly see repercussions later in life through the form of lung cancer, asbestosis, or mesothelioma among other irreversible diseases.

**Type of Asbestos and Uses**
Each of the six types of asbestos comes from different types of rock, depending on the location of the mine. The mining of asbestos has been taking place for thousands of years and continues to be mined today. The small crystalline fibers that can be extracted from asbestos mines have many practical uses, and its popularity exploded in the mid-20th century. The six types of asbestos include actinolite, tremolite, crocidolite, anthophyllite, amosite, and chrysotile (most commonly used); they are further categorized by their fiber characteristics as serpentine (long, flexible fibers) and amphibole (brittle, straight fibers). The only type of asbestos categorized under serpentine is the commonly used chrysotile asbestos, while the remaining five are classified under amphibole. These fibers were and are still today valued and utilized for their specific qualities in many applications, such as insulation products, roofing and flooring materials, fire-resistant clothing, car parts, piping, cement, and countless other products. Asbestos can be used across an extremely wide array of products, and this, along with its relative abundance, efficacy, and low cost, has proliferated its usage even further.

Most uses of asbestos are banned in the United States and many other countries, although there are still products in which it is not banned, such as cement piping, vinyl floor tile, and disk brake pads, among other applications, where the asbestos is suspended in a solid matrix like plastic or cement with little to no chance of fibers becoming airborne. Since the discovery of asbestos’ carcinogenic nature, government regulations have been set up to phase out and remove applications that pose a risk to public health. Exposure occurrences range from residential homes to shipyards and can lead to seriously harmful long-term health effects.

**Types of Exposures**
Exposure to asbestos can occur by inhalation and subsequent lodging of the material in the delicate lung tissues, or alveoli, used for exchange of oxygen to red blood cells. Once these fibers are lodged in the tissues, they are stuck there permanently, causing the lung tissue to scar over, thus reducing the number of alveoli and making it harder to breathe. Also, once the fibers are lodged, it can migrate or cause the cells that it comes in contact with to mutate, leading to cancer and other asbestos-related diseases later in life.

Occupational exposure has been one of most clear links in determining the carcinogenicity of asbestos. Asbestos fibers are released into the environment from the use and deterioration of more than 5,000 asbestos products, including roofing and electrical insulation, cement pipe and sheet, flooring, plastics, and textile and paper products. Workers in asbestos insulation, brake maintenance and repair, and building demolition jobs are exposed to high levels of asbestos. The fibers can subsequently stick to the clothing and other personal items of the workers, who may then carry them home to contaminate their families. After the links were made between lung disease and asbestos fibers, it was already too late for many exposed individuals who would go on to develop asbestosis, mesothelioma, or lung cancer later in life. Because of the clear link and tens of thousands of people who have died from occupational asbestos-exposure-related diseases, there was no denial in the carcinogenicity of this substance, and it remains today as one of the most notorious, causative cancer agents, even though its exact cancer-causing mechanism is not wholly understood.

Although occupational exposure has had a devastating toll, the public was also being exposed to smaller, but still concerning, amounts of asbestos from the countless products and buildings in which asbestos products were used. After new legislation concerning asbestos, removal projects started around the country, and the business of asbestos removal now presented the public and workers with possibly more hazardous exposures. Most of the asbestos used in insulation or other products was sealed and presented little risk of inhalation hazards, although once the removal process started, it was easily made airborne. Places like schools, homes, and other public buildings began to remove
and replace their asbestos insulation, and this process is still going on today with great precautions.

**Types of Cancer and Asbestos-Related Diseases**

Asbestos has been classified as a known human carcinogen by the U.S. Department of Health and Human Services, the Environmental Protection Agency (EPA), and the International Agency for Research on Cancer. Increased rates of mesothelioma and cancer of the lung have been consistently observed in a variety of occupations involving asbestos exposure. Mesothelioma is an incurable tumor that develops inside the abdominal cavity on the pleural tissue leading to trouble breathing, chest pains, and death. This disease has a relatively long delay period from initial exposure and onset, about 20 to 40 years. In addition to lung cancer and mesothelioma, asbestos exposure has been linked with gastrointestinal and colorectal cancers as well as an elevated risk for cancers of the throat, kidney, esophagus, and gallbladder; however, evidence is inconclusive.

Asbestos exposure may also lead to asbestosis, which is an inflammatory condition that causes shortness of breath, coughing, permanent lung damage, and pleural (tissue surrounding the lungs) disorders, specifically pleural plaques. Pleural disorders can induce changes in the pleural, or tissue membrane, surrounding the lungs, causing the tissue to collect fluid abnormally between its thin layers. Although pleural plaques are not precursors to lung cancer, evidence suggests that people with pleural disease caused by exposure to asbestos may be at increased risk for lung cancer. Through unknown mechanisms, asbestos is able to migrate out of the lung tissue and into the pleural tissue surrounding the lungs, which can lead to pleural plaques and mesothelioma.

Asbestos exposures account for the largest percent of occupational cancer, with the greatest risks among workers who smoke. The entire population may have been exposed to some degree because asbestos has been so widely used in the past. Exposure to the general population has decreased due to restricted use in the United States. Nonetheless, workers employed in construction trades, as electricians and carpenters, can still experience high levels of asbestos exposures through renovations, repairs, and demolitions. Several factors are useful to determine how asbestos exposure can and will affect the health of an individual, including size, shape, chemical composition of the asbestos fibers, dose (how much asbestos exposure an individual incurred), duration (how long an individual was exposed), and individual risk factors (e.g., smoking and preexisting lung disease). Although the exact mechanism as to how asbestos causes cancer is not certain, there are a few theories. The simplest is direct mutagenic contact between asbestos fibers and host cells; other theories suggest that the immune system response to asbestos causes a reactive oxygen species (molecule) to be formed, which is in turn carcinogenic to lung cells, while others link inflammation mechanisms as a cause of the carcinogenic effects. However the mechanism works, asbestos is a known carcinogen and mutagen that affects cells on a molecular level to change and erase DNA, which can lead to malignant tumors, cancer, and respiratory illnesses.

**U.S. Legislation**

Government action on asbestos is still ongoing, and although asbestos products are not completely banned, most products that pose a serious threat of airborne fibers are banned. Under authority granted by various laws, governmental agencies, like the EPA and Occupational Health and Safety Administration (OSHA), issue and enforce different regulations, which include: the Clean Air Act (CAA), Toxic Substance Control Act (TSCA) and the Consumer Product Safety Act (CSPA). The TSCA, enforced by the EPA, has banned the manufacture, importation, and distribution of certain materials like asbestos corrugated paper, roll board, and flooring felt due to its affinity to release airborne fibers. The CAA has enabled the banning of certain uses of asbestos for uses such as piping insulation and as a spray-applied surface coating. The CSPA has prohibited asbestos products from being used in household fireplaces for insulation purposes. These regulations are designed to protect the public and industrial workers, phase out the use of hazardous asbestos, and encourage awareness about the dangers associated with certain asbestos materials.

**Conclusion**

Asbestos is a well-known and well-documented carcinogen, and even though certain uses of the
product have stopped in the United States, there is still risk of exposure in older buildings and removal situations. Exposure occurs by inhaling small, crystalline asbestos fibers, which get lodged permanently in the delicate lung tissues, causing serious health effects and even death. Government regulations have excluded many uses of the product and continue to support removal and the cleanup of sites like schools and other public buildings. Even though many people have been affected by the deadly diseases caused by asbestos, it is still mined and used today. The mechanism by which asbestos causes cancer is not completely understood, although it is a known mutagen and carcinogen that affects the lung and pleural cells, with possible links to other cancers. Although asbestos is a natural, abundant, and useful product under certain conditions, its carcinogenicity makes it a notoriously deadly substance.

Hueiwang Anna Jeng
Zachary Hargis
Old Dominion University

See Also: Lung Cancer, Small Cell; Mesothelioma, Adult Malignant; Nasopharyngeal Cancer.

Further Readings

Asian Diet

Unlike the traditional Western diet that is high in fats, Asian diets consist mainly of healthier foods including fish, rice, noodles, soy, fruits, vegetables, and tea. The Asian diet contains greater amounts of fiber, antioxidants, vitamins and minerals, protein, iron, and calcium than does the typical Western diet, which is heavily reliant on foods of animal origin, such as dairy products and meat, especially red meat. Asian diets are viewed by many as a way to reduce the risk of cancer as the cancer incidence of those who choose such a diet over the traditional Western one is much lower.

Background

Asia is the largest continent, and the diets consumed by its various peoples vary widely. In addition to Chinese and Indian cuisine, the major categories include East Asian, southeast Asian, south Asian, as well as central Asian and Middle Eastern cuisine. East Asian cuisine includes that of Japan and Korea and is heavily influenced by the Chinese cooking tradition. Southeast Asian encompasses Brunei, Cambodia, Indonesia, Laos, Malaysia, the Philippines, Singapore, and Vietnam. South Asian cuisine includes Bangladesh, Burma, Pakistan, and Sri Lanka and has been inspired by Indian cooking. Central Asian and Middle Eastern cuisines usually are not included when referring to the Asian diet. A cuisine that constitutes the Asian diet has greater amounts of healthy elements than Western diets. Asian diets typically include approximately five times the amount of cruciferous vegetables as the diet most Americans consume. This difference has been suggested as leading to the health benefits, including reduced cancer rates, of the individuals who consume it.

The most common cruciferous vegetables are those that come from the cabbage family. These include broccoli, Brussels sprouts, cabbage, cauliflower, Chinese cabbage, kale, and watercress. In addition to these, however, some root vegetables such as kohlrabi, parsnips, radishes, rutabaga, and turnips are also included in this category. Cruciferous vegetables make a valuable contribution to good health, insofar that they contain natural substances called glucosinolates. Glucosinolates break down in the body to form indoles and other compounds that are believed to fight the incidence of the development of cancer in a variety of different ways.

Indoles and other anticancer compounds that are derived from cruciferous vegetables slow down enzymes that can activate carcinogenic substances. Indoles and these other anticancer compounds are
also believed to accelerate other enzymes that serve to detoxify carcinogens in the body. These compounds are seen as beneficial to reducing the risk of cancer because they increase the self-destruction of cancer cells and stop or slow down the growth of cells that might become cancerous. Certain studies that have investigated cruciferous vegetables suggest that the protective compounds they contain may also alter how the body metabolizes estrogen, which might decrease the risk of hormone-related cancers.

Most of the studies that have examined the effectiveness of the Asian diet have been population studies. Population studies show the link between the increased consumption of certain foods, such as cruciferous vegetables, and a decreased risk for a variety of cancers for those who consume this diet. Breast cancer is one form of the disease that has shown a decreased incidence of the condition when an Asian diet is followed, although recent studies suggest that the benefits of eating cruciferous vegetables are greater for premenopausal women than they are for older females. Other cancers have also shown a decreased incidence when an Asian diet is followed. These cancers include that of the colon, lung, and ovaries. While some studies have indicated that consumption of an Asian diet results in no reduction in prostate cancer risk, others suggest that consumption of cruciferous vegetables exhibits a protective influence on patients during the early stages of prostate cancer development.

As an Asian diet also tends to be higher in foods derived from soy beans, many are also interested in the effects of soy consumption on humans, especially as it relates to cancer. Soy-based foods include edamame, miso, tempeh, tofu, and many products derived from soy flour, such as veggie burgers. These soy-derived foods contain isoflavones, which are chemically similar to estrogens.
Two major types of isoflavones, genistein and daidzein, can emulate estrogen in the body, although this occurs at a very small fraction of the potency of circulating free estrogen in women. These effects of this can be good or bad. While certain animal studies suggested a link between soy and breast cancer, epidemiological studies that have followed large populations of healthy women, who reported details about their diets for many years, have either shown no association between soy and breast cancer or suggested that soy has a protective association, meaning that women who ate more soy-based products had lower incidences of breast cancer.

Studies regarding the effects of soy in the diet have shown contradictory results, with those focusing on Asian women finding women who eat more soy having a lower risk of breast cancer, while those concentrating on women in the United States have not found a relation between the amount of soy consumed and the risk of breast cancer. A meta-analysis of 14 epidemiologic studies found that, in Asian countries, women who consumed more soy isoflavones had a 24 percent lower risk of developing breast cancer than women who consumed the link, while there was no statistically significant difference between the two groups in Western nations. A major difference between the two cultures, however, includes the great difference in the amount of soy consumed, with Asian women typically consuming up to four servings of soy isoflavones daily, while those in the United States consuming less than half a serving.

Embracing the Asian Diet
Those seeking to enjoy the benefits associated with the Asian diet often look to increase their consumption of vegetables and soy-based foods. For those doing so, it is important to cook vegetables only until tender. This is because this is how Asians consume vegetables, and also, overcooking them tends to produce bitterness. While many in the United States traditionally have boiled vegetables in lots of water, this method should be avoided because this leaches essential vitamins from the cooked vegetables. By contrast, briefly steaming or stir-frying vegetables produces a cooked product that has much better flavor and texture. Some vegetables, such as parsnips and Brussels sprouts, are excellent when roasted in the oven.

During the winter months, fewer vegetables are available in many parts of the United States. At times like these, when salad vegetables are more scarce, using more raw broccoli, cabbage, and cauliflower can assist those striving to maintain an Asian diet. The assertive taste of these vegetables are too strong for many, but this can be countered by the use of equally assertive flavorings, such as extra virgin olive oil or soy sauce, which smooth out the flavor of the vegetables. A variety of groups, such as the American Cancer Society and the American Institute for Cancer Research, provide a variety of recipes that utilize cruciferous recipes through a variety of cookbooks on their Web sites and via CD-ROMs and other databases. Using these sources can provide those interested in following an Asian diet with a variety of suggestions and tips.

Soy-based products can also be used by those seeking to reduce their risk of certain cancers. Recently, three studies examined women's soy consumption. The inclusion of soy was examined in the diets of more than 9,000 breast cancer survivors. The studies examined three groups of women, all of whom were breast cancer survivors, and examined these women's eating habits and other lifestyle decisions after breast cancer. Two of the groups studied were from the United States, and the other was from China. Women from both the United States and China who consumed 10 milligrams per day or more of soy-based foods were found to have a 25 percent lower risk of breast cancer recurrence than those women who did not. Those interested in achieving these results might include more edamame, miso, tempeh, tofu, and other soy-based foods in their diets.

Soy is an especially rich source of protein. While many do not care for meat-substitute soy-based products, there are many more options than these. Soy is found in a variety of foods, such as tofu, that can be used in many ways to prepare meals. Rich in protein but low in fat, soy offers a better choice than many animal-based proteins. Soy milk has become more popular in recent years, especially among the lactose intolerant, but can be used as a substitute for many milk products. Soybeans themselves are becoming more popular, and their use will likely increase.

Stephen T. Schroth
Towson University
Aspirin

Evidence from clinical studies continues to show that aspirin serves as a possible agent in the prevention and treatment of cancer. The natural form of aspirin has been used since antiquity. Scientists created a tablet form that's easier to digest, and it has been used for more than 100 years. Aspirin's two main actions in the body are to function as an antiprostaglandin and an antiplatelet agent. These actions result from aspirin's effect on an enzyme in the body. However, scientists discovered more benefits of its use during the last few decades. Research has found that the same daily dose of aspirin used to prevent heart disease may also help prevent some cancers. Public health organizations, like the American Cancer Society, need more evidence demonstrating that daily aspirin can work as a cancer preventive agent and that its benefits outweigh the side effects before they can make a recommendation to the public.

What Is Aspirin?
Acetylsalicylic acid is aspirin's active ingredient. It is a man-made derivative of the compound salicin. Salicin is naturally found in willow trees. Extracts from the willow tree's bark were boiled to make an early form of aspirin, and it has been around for thousands of years. For example, the Egyptians used willow bark and myrtle to reduce pain and fever; the Greek physician Hippocrates in 400 B.C.E. suggested willow to be brewed to relieve labor pains; and, Greek and Roman physicians in 30 C.E. used willow leaf to treat inflammation.

Scientific observations of the natural form of aspirin occurred in the 18th century by an English clergyman known as Reverend Edward Stone. Stone noticed that the bitter taste was similar to chin-chona bark that was used to treat malaria at that time. He pulverized the willow bark, dried it, and administered it to his parishioners suffering from malarial symptoms. He noticed that his patients soon found relief.

The initial attempt to change salicin to salicylic acid was not well received. It tasted bitter and awful, it was hard to swallow, it irritated the lining of the mouth and stomach, and it led to upset stomachs and vomiting.

Scientist Charles Fredric Gerhardt attempted to prepare acetyl salicylic acid in 1853. He tried to prepare it by adding an acetyl chemical to natural salicylic acid, but he chose not to market it.

During the fall of 1897, chemist Felix Hoffman of the German dye manufacturer Fredrich Bayer & Co. in Elberfeld concentrated on developing a process that synthesized the acetylsalicylic acid. His efforts worked. His attempt was personal. Hoffman was trying to help his rheumatic father, who had taken the salicylic acid for his arthritis, but he could no longer take it because it made him vomit. The chemical process he used produced a more chemically pure, stable, and palatable aspirin. It received its trademark under the Imperial Office of Berlin in 1899, and it was marketed.

For centuries, no one really understood how aspirin worked. It was not until the 1970s that British scientist Sir John Vane determined that aspirin blocks an enzyme called prostaglandins. This enzyme is a natural hormone that participates in several processes in the body. Vane later received a Nobel Prize in 1982 for his work.

The derivation of aspirin's name acknowledges its origins. The a is associated with the use of acetyl in its preparation, the spir relates to the plant Spiraea ulmaria, from which salicylic acid was extracted, and the in is the suffix.

How Aspirin Works
Today, aspirin is widely used. Billions of tablets are swallowed throughout the world each year. It generally is purchased over the counter, and it usually contains about 325 milligrams per tablet.
In the world of chemistry, aspirin goes by the name of acetylsalicylic. Acetylation, a chemical reaction, transforms salicylic acid into the compound with the help of acetic anhydride, which is a colorless liquid with a sharp odor.

Acetylsalicylic acid inhibits the production of prostaglandins in the human body by inhibiting the enzyme that produces it, and this provides relief from pain, fever, and inflammation. Prostaglandins are found in the body and increase the perception of pain, fever, and redness and inflammation that occurs with injuries that result from issues, such as excessive stress, poor posture, or force. They send strong pain signals through nerves to the brain. They also cause the area where the pain is perceived to swell or inflame. Inflammation is part of the healing process, and it occurs with the help of enzymes. The enzyme known as cyclooxygenase 2 is a protein that takes chemicals floating around in bodily tissues and converts them into prostaglandins. When aspirin is consumed, it dissolves in the stomach or small intestine and travels throughout the body by way of the bloodstream. It latches onto cyclooxygenase-2, making it difficult for the enzyme to do its job. Ultimately, the aspirin does not stop the problem causing the pain; it lowers the intensity of the signals.

For nearly half a century, scientists have discovered how aspirin can play a much larger role within the human body. For instance, doctors’ observations in the 1940s noticed how some children given aspirin-laced chewing gum to relieve pain after a tonsillectomy bled more than those who did not receive the gum. This led the doctors to question and analyze aspirin’s role at preventing blood clots and heart attacks. Some studies were done, but they did not receive too much attention due to how they were published. Later, the 1970s controlled trials demonstrated aspirin’s helpful effects in preventing blood clots.

When blood clots occur, certain prostaglandins cause platelets to stick together to form the clots, such as those that clog the blood vessels that transport oxygen to the heart. The heart pumps blood throughout the body, and these types of clots can lead to heart attacks. Taking aspirin can slow the process of clot production. Researchers began suggesting that an aspirin a day may help prevent heart disease. In addition, scientists have discovered that aspirin can also help with cataracts, gum disease, dementia, and high blood pressure during pregnancy and cancer. Some side effects can occur from taking aspirin. This can include upper abdominal pain from gastric irritation and gastrointestinal bleeding. The risks of these side effects are influenced by dosage. Also, prostaglandins are produced in the lining of the stomach. They exist there to protect against the acid. Aspirin has the potential of depleting the protective barrier, and this can cause stomach ulcers.

The Chemopreventive Effects of Aspirin
Researchers have analyzed the use of aspirin as a prevention agent since a large number of studies conducted over recent years that demonstrated definitive evidence that taking aspirin daily may reduce the risk of cancer and prevent it from spreading. Regular aspirin has been shown to help to prevent colorectal, esophageal, stomach, prostate, ovarian, breast, and certain skin cancers. In addition, it has helped keep cancer from spreading once it has been diagnosed. Studies have found the following benefits:

- **Breast cancer**: Women who swallowed aspirin or ibuprofen at least biweekly for five years or more had reduced their chance of getting breast cancer.
- **Colorectal cancer**: Regular aspirin intake can reduce the risk of polyps and colon cancer.
- **Esophageal cancer**: People with the most aggressive forms of Barrett’s esophageal cancer have benefited from aspirin, ibuprofen, and other nonsteroidal anti-inflammatory drugs.
- **Ovarian cancer**: Daily intake of aspirin reduces risk by 20 percent.
- **Prostate cancer**: Longtime use of aspirin has helped lower risk of developing prostate cancer by about 30 percent.
- **Stomach cancer**: Gastric cancer risk dropped with the increasing frequency of aspirin use.
- **Skin cancer**: Women between 50 and 79 years old who consumed aspirin on a regular basis reduced their risk of melanoma by 21 percent.

While other methods have been proposed, most studies have suggested that the direct inhibition
Aspirin is proposed to stop the development of certain cancers. Despite these findings, scientists want to help health professionals and patients make well-informed decisions about aspirin use. Currently, the evidence is not clear enough to fully confirm the potential benefits; therefore, public health organizations have not recommended aspirin as a sole cancer prevention agent. The results for many clinical studies have been mixed for reasons that include different study strategies, uneven use of aspirin and the long periods of time and large patient numbers needed to collect statistically significant results.

Researchers have expressed another concern. The evidence is not strong enough to prevail over harmful side effects like internal bleeding and hemorrhagic stroke, which is caused by the rupture of a blood vessel in the brain. Another issue is how soon the benefits of aspirin begin. For instance, researchers suggest a delay of several years occurs between when a person starts an aspirin regimen and when the risk of developing colorectal cancer is reduced.

The American Cancer Society learned different types of studies that can help clarify the confusion and provide the evidence showing aspirin benefits as a cancer-preventive agent. Ongoing studies like randomized trials designed to study the effects of aspirin on heart disease and high-quality observational studies that track large numbers of people for decades requesting detailed information from time to time are considered effective. An ideal study is a randomized trial involving tens of thousands of people. The participants would be assigned randomly to take an aspirin or a placebo pill daily for at least 10 years. In the meantime, researchers continue to collect evidence about the preventative effects of aspirin to determine what other types of cancers it prevents. Consult with a health care professional before starting an aspirin regimen to account for the effects the aspirin will have regarding your medical history and the other medications that are taken.

**How Aspirin Differs From Some Other Nonsteroidal, Anti-Inflammatory Drugs**

Aspirin is an NSAID. NSAIDs are considered safer than steroids like cortisone. Steroids were liberally prescribed for all sorts of conditions during the 1950s, but over a period of time, a number of serious side effects occurred, such as cataracts and osteoporosis. NSAIDs became more popular as a result. The health issues, which were ulcers and heartburn, were not frequent. Aspirin and other NSAIDs aim for the same molecular targets. The difference is how aspirin stops cyclooxygenase isozymes. Isozymes are enzymes that have a different sequence of amino acids but activate a chemical reaction the same way. For instance, cycloxgenase-1 appears in most tissues. Its main role is platelet aggregation and gastric cytoprotection.

This isozyme is found in mature platelets. It is a source for a major metabolite, a substance produced during metabolism. The metabolite supports the activation and aggregation of platelets, vasoconstriction, and the proliferation of vascular smooth muscle cells. Cycloxygenase-2 is found in vascular endothelium, kidney, and brain tissues as well as others. It occurs in other tissues during inflammation, healing of a wound, and the formation of tumors. It is the main source of prostacyclin, a prostaglandin found in the vascular endothelium. Both cyclooxygenases 1 and 2 are irreversibly inactivated in the presence of aspirin.
Assisted Suicide

See Also: American Cancer Society; Breast Cancer; Chemoprevention; Colon Cancer; Esophageal Cancer; Pain and Pain Management; Prostate Cancer; Stomach (Gastric) Cancer.

Further Readings


Assisted Suicide

Assisted suicide or physician-assisted suicide refers to the ending of life, usually for terminally ill patients, through voluntary self-administration of lethal medications expressly prescribed by a physician for that purpose. This is seen as morally distinct from euthanasia because the physician does not cause the patient’s death but offers the patient the choice of the time and circumstances of his or her own death.

The ethical basis for assisted suicide is derived from the doctrine of double effect, which states that, if the conduct of a morally good act (here, relief of pain) has a morally bad side effect (namely, death), it is ethically permissible provided the bad side effect was not intended. The check for the intention is based on the Sulmasy test, where physicians are supposed to ponder whether they would feel a sense of failure if the patient were not to die after the prescription.

Terminologies Used
Euthanasia, from the Greek eu (good) and thanatos (death), is the intentional premature termination of another person’s life either by direct intervention (active euthanasia) or by withholding life-prolonging measures and resources (passive euthanasia), either at the express or implied consent of that person (voluntary euthanasia) or in the absence of such approval (nonvoluntary euthanasia). Physician-assisted suicide is where doctors provide a prescription for a terminally ill patient to hasten his or her death. This term has been replaced with physician-assisted dying in the state of Oregon to describe the action of its Death With Dignity Act. This act legalizes physician-assisted suicide but prohibits euthanasia.

Assisted suicide should not be confused with death after treatment is stopped on the instructions of the patient, either directly or through a do
not resuscitate (DNR) order. The latter is a written order based on an advance directive from a person, or from someone entitled to make decisions on his or her behalf, that resuscitation should not be attempted if the person suffers cardiac or respiratory arrest. Enforcing a DNR order is not considered legally assisted suicide or suicide of any kind. However, in any cases of doubt, emergency medical technicians, paramedics, and other medical workers are required to function as if a DNR order does not exist.

Regional and National Legislations
As of 2009, places that legally permit active assistance in dying of patients include the following:

1. The U.S. states of Oregon, Vermont, Washington, and Montana (physician-assisted suicide only)
2. Switzerland (physician and nonphysician-assisted suicide only)
3. Belgium (permits euthanasia but does not define method)
4. Netherlands (voluntary euthanasia and physician-assisted suicide)
5. Luxembourg (permits euthanasia for the terminally ill)

Two doctors must be involved in most cases, plus a psychologist if there are doubts on the patient’s competency. This is not stipulated in Switzerland, although at least one doctor is usually necessary as right-to-die societies insist on medical certification of a terminal condition before giving lethal drugs. United States and Switzerland prohibit death by injection. Switzerland alone does not bar foreigners, but careful watch is kept to ascertain that the reasons for assisting are altruistic.

Since 1980, right-to-die groups have tried to change the laws in Washington, California, Michigan, Maine, Hawaii, and Vermont, so far without success. In Australia’s Northern Territory, euthanasia was legalized by the Rights of the Terminally Ill Act (1995). Soon after, the law was voided by an amendment by the Commonwealth to the Northern Territory (Self-Government) Act 1978. However, before this amendment was made, three people had already been legally euthanized.

The Netherlands passed the Termination of Life on Request and Assisted Suicide (Review Procedures) Act on April 1, 2002, that permits assisted suicide when all of the following conditions are met:

1. The patient’s suffering is unbearable with no prospect of improvement
2. The patient’s request for euthanasia is voluntary, given in a state of mental competence, and persists over time
3. The patient is fully aware of his or her condition, prospects, and options
4. Consultation with at least one other independent doctor is obtained who confirms the conditions mentioned above
5. The death is carried out in a medically appropriate fashion
6. The patient is at least 12 years old (patients between 12 and 16 years of age require parental consent)

Death is usually effected by intravenous administration of the sedative sodium thiopental to induce a coma. Once ascertained that the patient is in a deep coma, typically after some minutes, a muscle relaxant is administered to stop the breathing and cause death. An alternative method is the oral administration of a strong barbiturate potion. By far, most reported cases in the Netherlands concerned cancer patients.

Oregon Ballot Measure 16 in 1994 established Oregon’s Death with Dignity Act (DWDA), which legalized physician-assisted suicide for capable adult Oregon residents who were diagnosed with a terminal illness. Under the law, a patient can request a physician for a prescription for a lethal dose of medication for the purpose of ending his or her life. The request must be confirmed by two witnesses, one of whom cannot be related to the patient, be entitled to any portion of the patient’s estate, be the patient’s physician, or be an employee of a health care facility caring for the patient.

Once the request is made, another physician must confirm the patient’s initial diagnosis. If the request is authorized, the patient must wait at least 15 days to make a second oral request before the prescription is given. The patient has a right to rescind the request at any time. The 2005 Death with Dignity Act Annual Report notes that assisted-suicide participants were more likely to have malignant neoplasms, be younger, and have more formal education compared to all Oregon decedents.
In 2013, 121 individuals received prescriptions under the DWDA, and 73 died from ingesting prescription drugs received under the DWDA; in 2014, 155 received prescriptions and 105 died.

Public Perceptions
According to a 2013 Gallup Poll, 70 percent of Americans were in favor of allowing doctors to hasten a terminally ill patient’s death when the matter was described as allowing doctors to “end the patient’s life by some painless means.” However, only 51 percent supported it when the process was described as doctors helping a patient “commit suicide.” In the United States, significant differences in perceptions toward assisted suicide are also encountered between religious and ethnic groups. Among Christians, conservative Protestants are usually more opposed to euthanasia than nonaffiliates and the other religious groups. Moderate Protestants and Catholics show mixed views concerning end-of-life decisions in general, while liberal Protestants are the most supportive of the groups. In general, Buddhists view termination of life, no matter under what circumstances, as amounting to destruction of human life. In Jewish law, nearly every other consideration is put second to saving a life. The premature ending of a person’s life is against this perspective, and thus, suicide and euthanasia are unequivocally rejected in modern Judaism. Conversely, Hinduism refers to death as the ultimate truth and as one of the stages in human life. While Hinduism does not explicitly disapprove of euthanasia, an alternate perspective philosophizes that euthanasia interrupts the timing of the cycle of rebirth and both the physician and patient will take on bad karma as a result.

Opinions also have varied between various ethnic groups on this issue. Recent studies have shown that European Americans are more accepting than African Americans regarding euthanasia. They are also more likely to have advance directives and to use other end-of-life measures. Among African Americans, those without a four-year degree were twice as likely to oppose euthanasia as those with at least that much education.

Ethical Concerns
Advocates of voluntary euthanasia contend that, if a person is terminally ill; is unlikely to benefit from the discovery of a cure for the illness during what remains of his or her life expectancy; is as a direct result of the illness suffering intolerable pain or only has available a life that is unacceptably burdensome because the treatment entails the person being unacceptably dependent on others or on technological means of life support; has an enduring, voluntary, and competent wish to die (or has, prior to losing the competence to do so, expressed a wish to die in the event that the first three conditions are satisfied); and is unable without assistance to commit suicide, then there should be legal and medical provisions to enable him or her to be allowed to die or assisted to die.

However, despite the growing support for right-to-die activist groups, there is still strong opposition to assisted suicide. Objections commonly stem from the increased availability of palliative and hospice care and the fear that one never can have adequate evidence of the genuineness and competence of a dying person’s request. Most importantly, people fear that a society that legally permits voluntary euthanasia will have set off on a slippery slope that will lead to supporting other forms of euthanasia, including nonvoluntary euthanasia.

Modern society will continue to debate on legalization of euthanasia, but physician-assisted suicide is now legal in some parts of the world with increasing popularity elsewhere, although opposition for it is also based on genuinely grave concerns.

Anirban P. Mitra
University of Southern California

See Also: Belgium; Hospice Care; Netherlands; Religion; Switzerland.

Further Readings

Association for the Cure of Cancer of the Prostate

The Association for the Cure of Cancer of the Prostate (CaP CURE) or the Prostate Cancer Foundation (PCF) started with a personal crusade that aimed to find cures for prostate cancer by raising public awareness, providing funding for breakthrough research, accelerating the pace of discovery, and broadening the knowledge of the disease. Today, PCF is the leading philanthropic organization committed to curing prostate cancer in the United States and worldwide.

Prostate Cancer

Prostate cancer is the most common cancer among men. According to Centers for Disease Control and Prevention, the three most common cancers among men from 1999 to 2010 were prostate cancer, lung cancer, and colorectal cancer (ranked by rate of incidence from high to low). Prostate cancer was first among men of all races and Hispanic origin populations. In cancer-related deaths, prostate cancer was the second-leading cause among white, black, American Indian and Alaska Native, and Hispanic men and fourth among Asian and Pacific Islander men. Among the ethnic groups, African American men are at high risk of being affected by prostate cancer and are more likely to die of the disease. Their incidence rate is two-thirds higher than whites, and the mortality rate is at least twice higher than men of other racial and ethnic groups (note: Hispanic origin is not mutually exclusive from races).

The National Cancer Institute estimates that, in 2014, 233,000 men will be diagnosed with prostate cancer, and 29,480 will die of it in the United States. Compared with the 2010 estimate that 217,730 were diagnosed with the disease and 32,050 die of it, it is safe to infer that cases of prostate cancer have increased (due to population growth), while the number of deaths has decreased. Between 2004 and 2010, the five-year survival rate of prostate cancer survivors was 98.9 percent.

Prostate cancer is nicknamed the silent killer because it develops slowly and shows few, if any, signs in its early stage. In the late 1980s, the prostate-specific antigen (PSA) test for screening prostate cancer was introduced and used widely. It caused a rapid increase of incidence rates in the United States. In the subsequent decade, both the incidence and mortality rates were declining. The trend continues to this date. In a sense, the decline represents a personal crusade as well as collective efforts in advancing prostate cancer research and treatment.

Mission and Commitment

When CaP CURE was first established in 1993, prostate cancer was the second-leading cause of cancer deaths among men, yet there was little knowledge about the disease. In fact, the common belief was prostate cancer was a disease of elderly men. In addition to the age factor, prostate cancer was a sexual symbolic taboo to men just like breast cancer to women.

CaP CURE’s founder, Michael Milken was diagnosed with advanced prostate cancer at the age of 46 (in 1993); his case broke the myth that men would not get prostate cancer until older. Because of the progressive condition of his cancer, at one time, he was informed of 12 to 18 months’ life expectancy and advised to do arrangements. During his search for all possible treatment and wellness approaches (including diet, yoga, and meditation), Milken found critical gaps particularly in prostate cancer treatment and research with very limited government funding to fill the gap. He founded CaP CURE, later renamed as the PCF, with a specific mission—“Firmly committed to curing prostate cancer.”

At its establishment, PCF originated a groundbreaking awards process that limits applications to no more than five pages in length, selection is made in 60 days, and grants are disbursed within 90 days (from application) to awardees. The length of funding is for one year; however, prostate cancer researchers can apply multiple times to continue their promising research projects. This process is drastically different from seeking government funding that involves much paperwork. It allows prostate cancer researchers to focus their valuable time on innovative research leading to better diagnostics
or treatments. As Milken reaffirmed, it was for “cutting red tape and encouraging collaboration to speed breakthroughs.” The awards PCF offers include Recognition Awards, Young Investigator Awards, the Creativity Award, Challenge Awards, and other programs (including the clinical scholar A. David Mazzone Awards Program Funding Opportunities, Team Science Partnership Award, translational cancer research, and so on) with a purpose of encouraging and supporting innovative scientific research, translational research, and new drugs for effective treatments for stomach cancer (institutional overhead or other indirect costs are not covered in the awards).

Achievements
PCF has been engaged actively in raising public awareness and education, financially supporting research, advocating for increased federal funding specifically for prostate cancer research, conducting fund-raising to benefit prostate cancer research, building support networks for cancer survivors and their families, and sharing resources. It is worth mentioning that funds raised by PCF are strictly used for research purposes; PCF’s administrative expenses are covered by an annual grant from the Milken Family Foundation independent from PCF (the Milken Family Foundation was cofounded by Michael Milken and his brother in 1982).

Conclusion
For two decades (1993–2013), PCF raised more than $575 million and provided funding to more than 1,600 research projects at nearly 200 institutions in 15 countries in the world. In 2001, the Safeway Foundation has paired with PCF, participating in the annual Safeway campaign that raised a total of $81 million for PCF between 2001 and 2013 ($6.2 million in 2013). Also, the amount of federal funding for prostate cancer research was ranked third in 2012. These are significant achievements of PCF since its establishment in 1993, when Milken was diagnosed with advanced prostate cancer under the age of 50. It was a time when prostate cancer was deadly, yet there was little funding support for breakthrough research, clinical programs, and effective treatments of the disease.

Paige Mayleen True
California State University, Monterey Bay

See Also: Anticancer Drugs; Experimental Cancer Drugs; Prostate Cancer; Surgery; Survivors of Cancer; Survivors of Cancer, Families of.

Further Readings
Waldo, M. “CaP CURE: Association for the Cure of Cancer of the Prostate.” Neoplasia (July 2002).

Association of Cancer Online Resources

The Association of Cancer Online Resources (ACOR.org) is an organization providing support and information to patients and friends and family of patients who are fighting cancer. It is a 501(c)(3) organization founded in 1995 and is run by volunteers whose lives have been touched by cancer.

It is one of the first social networks dedicated to health and to bringing together individuals and
organizations with information on more than 142 types of cancer, including rare forms.

The mission of ACOR.org is to provide support and information through Internet mailing lists and Web sites. ACOR.org is dedicated to improving communication among those diagnosed with cancer and health care professionals. Advocacy through providing information and support, according to ACOR.org, is key to survival of patients.

ACOR.org maintains a Web site with links to more than 142 online cancer communities as well as mailing lists where patients and their families and friends can connect to others struggling with cancer to learn about research and experimental or Phase III clinical trials of medications and receive support and encouragement from others. The online communities focus on forms of cancer—some rare, some more common. As information is crucial to understanding treatment options, the ACOR.org Web site serves as a means of providing information through connection between individuals struggling with cancer.

Several of the sites are maintained by ACOR, and these include the following: Cancer-pain, Oncochat.org, Steve Dunn's CancerGuide, Patty Feists' Ped Onc site, Leiomyosarcoma Is a Rare Cancer, GrannBarb & Art Flatau's Leukemia Links, the CMPD Foundation Information Web site, Doug Bank's Testicular Cancer Resource Center, Colon Cancer Alliance, The CLL Foundation, and the Association of Oncology Social Work. Each of these sites provides information on cancer as well as advice on areas that may be of concern for families, friends, and patients. ACOR.org maintains these sites through volunteers, which include patients, caregivers, and family and friends of those afflicted with cancer. All information provided through ACOR.org is free to the public.

An example of one of the sponsored Web sites is Steve Dunn's CancerGuide. The Web site was started by Steve Dunn, who passed away in 2005, and is still maintained. He started the Web site when he found that it was difficult to get information he needed on the Stage IV kidney cancer with which he was diagnosed. The site he created includes a wealth of information that could be used for those struggling with any cancer as it focuses on cancer basics, the mind and attitude, experimental treatments, financial issues, and other practical and supportive information. ACOR.org also provides links to other Web sites that are maintained by other respected organizations and foundations. Examples of other Web sites include the following: The Sarcoma Alliance, the Cutaneous Lymphoma Foundation, and the Carcinoid Foundation. Similar to the ACOR.org supported sites, these too are free.

Another of the sponsored Web sites is the Association for Oncology Social Work. This professional association's Web site includes information on addressing health disparities, joining the organization, and a guide to shopping for insurance. The site, like the others discussed here, is updated regularly, but the focus of the Web site is on supporting those affected by cancer as well as individuals looking at becoming an oncology social worker.

Not just any site is accepted and promoted by ACOR.org; it has to be supported by a reputable individual or organization and has to provide privacy and protection to those who use the Web site, mailing list, or chatroom. For example, on one of the ACOR.org-sponsored sites, Oncochat.org, it discourages using online discussions for research purposes, and religious conversations are also discouraged as religion is a sensitive topic for those who may be facing the end of their lives. Researchers and lurkers are also discouraged from entering Oncochat.org.

It is important to note that the Web sites and mailing lists with which one can connect to through ACOR.org do not promote any form of treatment. Instead, they encourage communication among patients, their caregivers, and health care professionals. Information on multiple treatment options, pain management, and other individuals’ experiences can be found through searching sites specific to common and even rare forms of cancer.

When searching for information on diseases online, it is crucial that patients, family members, and friends be able to access reliable and factual information. Yet, there are many sites that will promote products or treatments. Those searching for information and support should look for Web sites that are sponsored by nonprofit organizations, information provided by universities, or U.S.-supported government organizations. Those looking for health information should consider who is sponsoring a Web site to be sure information is credible. ACOR.org is considered to be one of the top-rated resources with regard to cancer as it is a nonprofit run by volunteers without a focus on promoting products or treatments. It is particularly useful for
individuals with rare forms of cancer who find it difficult to find the information and support they need.

Anne Hubbell

New Mexico State University

**See Also:** Association of Oncology Social Work; Experimental Cancer Drugs; Insurance; Pain and Pain Management; Religion; Survivors of Cancer; Survivors of Cancer, Families of; Technology, New Therapies.

**Further Readings**


---

**Association of Community Cancer Centers**

The Association of Community Cancer Centers (ACCC) was formed in 1974 by a group of community cancer physicians. The group focuses on clinical protocols and standards of care, funding community care, treatment innovation, and information and lobbying and advocacy. The ACCC advocates for affordable patient care, access to clinical trials, and the advancement of cancer care standards. ACCC's membership currently includes medical and radiation oncologists, oncology nurses and pharmacists, administrators, medical directors, radiation therapists, social workers, and others employed in various settings. Given the diverse membership, interdisciplinary collaboration is important as are educational programs and publications. The organization's 40th anniversary occurred in 2014.

ACCC was formed in 1974 by a group of community cancer physicians but has since grown into a national organization that advocates for the entire cancer oncology team. In the early years, ACCC was active in lobbying the U.S. government on issues related to community-based cancer care. Subsequently, the National Cancer Act, passed by Congress in 1978, was amended to emphasize community care and community representation on the National Cancer Advisory Board (NCAB). ACCC's membership quadrupled by 1991 as community-based oncology programs increased in popularity.

The mission of the ACCC is to be the leading education and advocacy organization for the multidisciplinary cancer team while adhering to its set of core values (i.e., integrity, collaboration, stewardship, knowledge, service, innovation, excellence, and compassion). At the heart of this mission, the organization seeks to serve the community-based oncology team by leveling the playing field between community-based oncology, which can have fewer resources and less support compared to their colleagues at medical research universities. This is despite the fact that community-based care is estimated to care for up to 60 percent of cancer patients. ACCC, as of 2014, seeks to fulfill its three- to five-year goals, including meeting financial objectives, developing collaborations and partnerships, expanding its influence and advocacy, examining its leadership and structure, and using its resources for knowledge exchange, education, and networking.

The rising cost of cancer care has led the ACCC to advocate for the cancer patient's financial well-being. The ACCC recommends that community oncology teams employ a financial counselor to advise patients on financial issues. The ACCC provides support on how to judge the cancer benefits provided by your insurance and navigating insurance rules, for instance, helping Medicare recipients get coverage for oral anticancer drugs. ACCC has been critical of changes to Medicare in 2006 that changed the drug reimbursement guidelines for hospitals because of the potential impact to patient care. ACCC has also taken an active role in other financial issues related to cancer care, such as getting Food and Drug Administration (FDA)
approval for and insurance to pay for clinical trials and experimental cancer drugs and treatments including off-label uses of drugs. Off-labels use is when a drug was developed to treat one disease while evidence suggests that the drug might have cancer-fighting properties. For instance, the drug Clodronate (clodronic acid) was approved by the FDA to fight osteoporosis and is marketed under brand names like Bonefos, but it is also believed to be effective in fighting breast cancer.

As a knowledge exchange and educator, ACCC created its Standards for Cancer Programs (now called Cancer Program Guidelines) in 1988, which they continue to revise and update. The Cancer Program Guidelines inform the standards of community cancer care across the United States through ACCC’s member programs. ACCC additionally has collaborated with publications such as Physician’s Weekly (PW) to produce two special issues for oncologists and cancer care professionals focusing on legislative changes, care costs, and clinical approaches. PW is estimated to reach 1,500 leading hospitals and academic centers. Online communication is an interest of the ACCC to the extent that it can serve as a platform for building electronic information exchanges for the use of oncology team members, patients, their families, advocates, and others.

The ACCC’s governing structure includes the House of Delegates or the policy body with representatives of each member program, the Board of Trustees, the governing body (i.e., finance and administration) with 15 elected members (e.g., president, president elect, immediate past president, secretary, treasurer, and 10 trustees). The organization is headed by an executive director, currently Christian G. Downs, M.H.A. (health administration), J.D. (regulatory and administrative law), who previously worked for the American Society of Clinical Oncology (ASCO), the Education and Health Committee of the Virginia State Senate. Downs is affiliated with Centers for Medicare & Medicaid Services (CMS), Patient Advocate Foundation, and C–Change.

ACCC sponsors several awards, including the Innovator Award for members who innovate to improve the access, quality, and cost-effectiveness of cancer care. Award winners present their innovation at the ACCC’s annual National Oncology Conference. ACCC’s Annual Achievement Award recognizes an individual with outstanding contributions to community cancer care and cancer patients. The organization’s Clinical Research Award recognizes an individual or individuals producing cancer research with a significant and positive impact. Finally, ACCC’s David King Community Clinical Scientist Award recognizes individuals who have demonstrated leadership in the development, participation, and evaluation of clinical studies or are active in the development of new screening, risk assessment, treatment, or supportive care programs for cancer patients.

Many ACCC functions are managed by committees, and the organization also has liaisons to other national organizations. Several national U.S. cancer organizations exist to serve various exigencies. The ACCC exists alongside cancer organizations such as the National Cancer Institute, American Cancer Society, and the American Association for Cancer Education. The ACCC has more than 700 member cancer programs.

Gordon Alley-Young
Kingsborough Community College

See Also: American Association for Cancer Education; American Cancer Society; Breast Cancer; Experimental Cancer Drugs; National Cancer Institute.

Further Readings
Association of Community Cancer Centers (ACCC).

Association of Freestanding Radiation Oncology Centers

The Association of Freestanding Radiation Oncology Centers (AFROC) is an oncology organization

See Also: American Association for Cancer Education; American Cancer Society; Breast Cancer; Experimental Cancer Drugs; National Cancer Institute.

Further Readings
Association of Community Cancer Centers (ACCC).
that was founded in 1987 and is based in the United States. AFROC aims to bring advancements in cancer treatment closer to individuals who need care but has faced difficulties in recent years due to changes to the Medicare and Medicaid payment system and other bills that resulted in significant losses.

Michael J. Katin, MD, and president of AFROC, stated that AFROC represents a fraction of oncology professionals. Oncology itself is a fraction of the greater medical community, so it has been difficult for them to lobby for changes to these bills. Still, Katin issues a message of hope while recognizing the struggles AFROC’s members are facing. Prominent on the official Web site of AFROC is the president’s message with themes of educating members and promises to continue lobbying for this profession.

The Centers for Medicare & Medicaid Services (CMS) released a 2014 Hospital Outpatient Prospective Payment System (HOPPS) that sets the rates at which Medicare and Medicaid will make payments. As of 2014, hospitals will charge for all clinical visits at a flat rate. Formerly, patients’ visits were labeled between levels one and five, where one was lowest and five was highest. For oncology programs, usually patients are on the higher end of the spectrum. The 2014 HOPPS rates were actually higher than the 2013 payment rates.

The changes that concern oncologists most are changes to the relative value units (RVU). RVUs are a breakdown of charges by service and are made from a formula of payment that includes the doctor’s labor, practice expense, and malpractice expense. It is these formulas for specific services that have been cut, sometimes by more than 50 percent. This means that freestanding radiation oncology centers will suffer as they will now have to accept much lower reimbursement from Medicare.

Freestanding radiation oncology centers are able to keep patient costs down because their overhead is a fraction of that for an entire hospital. The reimbursement changes that the government is making will significantly lower imaging revenue for independent radiologists. On the opposite side, it increases the reimbursements that hospitals will receive. Private practice radiologists already charge less per service than hospitals do.

Radiation is a tool physicians use to treat many different types of cancer. Radiation therapy uses doses of high-energy radiation to shrink tumors and eradicate cancerous cells in the body. There are three main specialties in cancer treatment: surgical, medical, and radiation. Radiation can be used alone or in tandem with other techniques. In radiation treatment, the cancer cells are destroyed by damaging their DNA with high-energy radiation. Treatment has to be very careful, though, as radiation will damage healthy cells as well.

Radiation may come from a machine outside of the body, or radioactive material can be placed in the body near cancerous cells. It also can be injected into the patient’s bloodstream. Radiation is not used only with a curative intent, however. Radiation also can be used to relieve a patient’s suffering. If an inoperable tumor is causing pain, for example, radiation may be used in hopes that it can shrink the growth and ease the discomfort of the individual.

The radiation oncologist begins by planning the treatment. Computed tomography (CT) scans are generally used in order to plan the therapy. The oncologist has to make sure the patient will be able to lie completely still in order to target the cancer, even to the point of using body molds or other tools to prevent the patient from moving. The tool used to keep the patient still differs depending on the body part being treated and sometimes includes masks or other restraints.

All of these services are expensive, which means that the lower revenues for freestanding imaging centers are going to cause many of these centers to join into partnership with a hospital. The workers will likely have to become employees of a hospital, and some of these centers will simply have to close their doors.

AFROC is attempting to reverse the bills that will cause so much harm to freestanding radiation centers. They represent and lobby on behalf of many independent radiation oncology centers. With the recent Medicare- and Medicaid-related changes to the fee and reimbursement schedules, the group AFROC represents is facing an alarming future for many of its members. Its Web site, afroc.org, states their mission as the following:

The Association of Freestanding Radiation Oncology Centers have helped to support the needs of people who offer cancer care solutions to patients in many parts around the United States. These physicians, physicists, professional support personnel, and administrators are the key to the current and ideal system that allows most cancer patients
to be treated with advanced techniques within a reasonable distance from their homes. Now more than ever, this is being threatened by policy makers who do not recognize the potential results of their actions. Help AFROC continue to monitor and intervene to maximize our standing before irreversible changes occur.

Only time will tell whether this organization will be able to reverse the decisions that are currently harming their professionals. They will certainly continue to try on behalf of their members.

Michael Fox
Independent Scholar

See Also: Breast Cancer; Liver Cancer, Adult (Primary); Lung Cancer, Non–Small Cell; Radiation Therapy; Stomach (Gastric) Cancer.

Further Readings

Association of Oncology Social Work

While researchers have made gains in the early detection of and treatment of cancer, it continues to be the second-leading cause of death in the United States. The psychosocial factors associated with cancer and the impacts on those affected and their families are vast. Social workers in oncological social work provide care to those at risk, affected by, and diagnosed with cancer. The Association of Oncology Social Work (AOSW) is a nonprofit professional organization of social workers headquartered in Deerfield, Illinois. It was founded in 1984 by a group of oncological social workers. The organization’s mission is the enhancement of psychosocial services to those affected by cancer and their families. Members do this through networking, education, research, resource development, and advocacy.

Oncology social workers provide counseling, support, education, and resources to persons dealing with cancer and their families. They provide care in many settings including hospitals, hospices, outpatient clinics, and community-based programs. They promote the field of oncological social work through publishing position papers and providing grants, scholarships, and awards to those practicing in the field. The AOSW news blog is another way the organization communicates with others to promote their efforts.

AOSW members network by participating in various online and face-to-face networking groups and special issues groups. AOSW provides many opportunities to expand members’ knowledge bases and gather new information on practice and research. Research is a core part of AOSW’s commitment to excellence in oncology. The organization supports research that informs practice and policy. Research often addresses clinical, policy, and theoretical approaches that benefit AOSW members and the public at large. AOSW believes knowledge is power, therefore, it provide links, contacts, and information on resources for practitioners working with and families dealing with cancer. Advocacy is at the center of oncological social workers.

AOSW envisions a global vision of cancer care that meets the needs of the whole person and his or her family. The goals of the AOSW are widespread, including to increase awareness of the psychosocial effects of cancer; advance the practice of psychosocial interventions that enhance quality of life and recovery of persons with cancer and their families; foster communication and support among psychosocial oncology caregivers; further the study
The psychosocial factors associated with cancer and the impacts on those affected and their families are vast. Social workers in oncological social work provide care to those at risk, affected by, and diagnosed with cancer. The Association of Oncology Social Work’s mission is the enhancement of psychosocial services to those affected by cancer and their families. (Photos.com)

of psychological and social effects of cancer through research and continuing education; advocate for programs and policies to meet the psychological needs of oncological patients and their families; promote liaison activities with psychosocial oncology groups and professional oncology organizations; and promote the highest professional standards and ethics in the practice of oncology social work.

AOSW partners with corporate affiliates to provide professional development through various outlets including the AOSW annual conference, research publication, oncology social work certificate, and development of standards of practice. The conference is an opportunity for oncology professionals to network, educate, and present the latest research in their respective areas of cancer research and treatment. AOSW promotes the field of oncological social work through its publications The Journal of Psychosocial Oncology and the Social Work Toolbox.

To further their mission, AOSW supports special projects such as clinical trials, special events, and research that furthers our knowledge about cancer prevention and treatment. The AOSW is a voluntary membership organization of oncology social workers. Members receive benefits that include access to member-only resources, voting privileges, and opportunities to serve on the board of directors and committees. The board of directors includes the president, the president elect, and treasurer. The organization has recently restructured and reduced the number of U.S. regions from five to two. Currently, there are three regions.

Lisa Hines
Wichita State University

See Also: American Society for Radiation Oncology; International Psycho-Oncology Society.
Further Readings


Association of Pediatric Hematology/Oncology Nurses

The Association of Pediatric Hematology/Oncology Nurses (APHON) is an organization for nurses and other health care professionals who specialize in pediatric hematology and oncology. APHON promotes and provides expert practice to its members and the public. Members are dedicated to the best nursing care for young adults, adolescents, and children who have cancer or blood disorders. APHON defines and promotes the best standards of practice.

In 1973, four pediatric oncology nurses recognized the need to share information, successes, and concerns that are unique to pediatric nurses. At that time, pediatric cancer was just beginning to be recognized as a specialty. The original four planned a special interest session at the Association for Care of Children’s Health (ACCH) conference in 1974. Forty nurses attended and concluded they needed a professional organization. On November 3, 1974, the Association of Pediatric Oncology Nurses (APON) was created. They incorporated in 1976. The association grew quickly, began an annual conference, and began to develop educational materials. The primary members were registered nurses, although a few allied health care practitioners (social workers, child life specialists, and pastoral care providers) with similar career interests and experience were also members. In 2006, the association recognized that most of their members also cared for hematology patients, and the association voted to change its name to the Association of Pediatric Hematology/Oncology Nurses. The association has grown to 3,100 members in the United States, Canada, and around the world.

APHON is run by a board of directors who are elected by the association members: president, vice president, secretary, treasurer, and six other association members. All serve three-year terms. Six committees are appointed by the board: Nominating Committee, Education Provider Unit, Steering Council, Local Chapter Committee, Chemotherapy/Biotherapy Provider Program, and the Journal of the Association of Pediatric Hematology/Oncology Nursing (JOPON) Continuing Education Committee.

APHON developed the Pediatric Chemotherapy/Biotherapy Provider Program. It is a two-day course that teaches theoretical knowledge and the key principles to consistently, competently, and safely administer biotherapy and chemotherapy. Successful completion earns certification as a Pediatric Chemotherapy and Biotherapy Provider. Renewal is required every two years.

JOPON is the official journal of APHON. It is published six times per year. It consists of peer-reviewed original research and definitive reviews on the entire spectrum of nursing care of childhood cancers. JOPON encompasses the entire disease process from diagnosis to end-of-life care and is distributed to APHON members free of charge. *APHON Counts* is a quarterly newsletter shared with members that features new trends in treatment and best practices as well as in-depth, personal accounts regarding pediatric hematology or oncology. *APHON Counts* is only available to members. Other benefits to membership include discounts on products and educational conferences, grants, awards, and networking opportunities.

APHON’s core purpose is to support and advance nurses and their practices to optimize the care and outcomes for pediatric patients with cancer or blood disorders and their families. Core values include: pride in the profession, commitment to professional and organizational excellence, collaboration as an effective strategy, visionary leadership embracing innovation, continuous professional development.
Astellas Pharma (Japan)

Astellas Pharma is a Japanese pharmaceutical corporation with 17,649 employees worldwide, including subsidiaries as of early 2014. Astellas Pharma came out as number two in Japan and as number 18 on a global basis in the Almanac 2013 Medical Care & the Pharmaceutical Industry 2013 overview of pharmaceutical corporations’ 2011 sales. Astellas Pharma considers itself to be a global category leader (GCL) within urology and has in extension a focus on kidney diseases as well as diabetes complications, immunology and infectious diseases, oncology, and neuroscience. The top-selling urology-related products Vesicare and Mirabegron sold globally for approximately ¥100 billion (about US $1.21 billion) in fiscal year (FY) 2011 (April 2011–March 2012) and ¥117 billion in FY 2012 (April 2012–March 2013).

Astellas Pharma is aiming at establishing itself as a GCL when it comes to oncology related to urology and transplantation. Thus, new products through lifelong learning, absolute integrity and high ethical standards, and gratifying experience through involvement. APHON’s primary vision is to be recognized as the leader in hematology and oncology nursing in pediatrics.

APHON and the Pediatric Nursing Certification Board (PNCB) recognize five issues as important to pediatric health care and where pediatric nurses could make contributions: schools used as points of access for health care; a focus on lifelong learning; coordination of care, including in the home; an advocacy presence whenever children’s groups meet; and quality, evidence-based, safe practice.

Membership in APHON includes the following: active membership (registered nurses who are practicing or interested in pediatric hematology or oncology); associate membership (nonregistered nurses who practice pediatric hematology or oncology and are interested in APHON’s mission); graduate nursing student membership (enrolled full time in a graduate nursing program); and National Student Nurses’ Association (NSNA) membership.

There are 40 local chapters in APHON throughout the United States and Canada. Each chapter engages in community outreach that has included: grocery store gift cards to family members of patients, food donations to homeless shelters, food and toiletry donations to the Ronald McDonald House, diaper and clothing drives, and collection of school supplies. Community outreach occurs most often during the holidays, but chapters are highly encouraged to participate year-round. Community outreach offers an opportunity to network and make a difference in local communities.

APHON has a mentoring program that links members who are interested in the following areas: clinical and project development, teaching and education, research, higher education pursuit, leadership, role integration, and professional and career development. The program matches mentors and mentees with the goal of the mentees’ growth in their careers and to support leadership development in the mentors. The relationships officially last two years and can continue after on an informal basis. Learning materials and manuals are provided, and progress is reviewed every six months through self-report.

APHON also offers its members an enhanced career center. Members can post a résumé or job announcement, browse and search available jobs, and create a personal search agent that e-mails matches according to criteria set by the member. Through the career center, members also can access the National Healthcare Career Network, which consists of more than 200 associations and organizations, tens of thousands of résumés, and more than 1,500 job postings.

Jessica Anne Hammer
Independent Scholar

See Also: American Academy of Pediatric Hematology/Oncology; International Society for Preventive Oncology; International Society of Paediatric Oncology; Society of Gynecologic Oncology; Society of Surgical Oncology.

Further Readings

Astellas Pharma (Japan)
from 2012 such as Xtandi and Gonax are used in connection with the treatment of prostate cancer. Xtandi (enzalutamide) is marketed for prostate cancer worldwide and is considered as the corporation’s driving force within oncology. It is as of 2013 also in Phase 2 clinical trials for breast cancer in Europe and in the United States. Gonax (degarelix) is also for prostate cancer and is marketed in Japan. The oncology portfolio includes still another prostate cancer-related product, Eligard, and some treatments of other types, including Tarceva, used under some specific conditions such as first-line treatment of people with metastatic non-small cell lung cancer. The oncology segment sold combined for ¥46.4 and ¥47.5 billion in FY2011 and FY2012.

History of Astellas Pharma
Astellas Pharma was formed from the 2005 merger between Yamanouchi Pharmaceutical Co., Ltd. and Fujisawa Pharmaceutical Co., Ltd. These two corporations had before the merger some shared research areas, such as diabetes, urology, and the central nervous system. Yamanouchi had, however, cardiovascular, gastrointestinal, and locomotorium areas of specialization, in contrast to Fujisawa’s immunology, inflammation, and infectious diseases. Fujisawa had been noted for a focus on patented prescription drugs, whereas Yamanouchi had been more comprehensive. The Yamanouchi part was founded in Osaka in 1923, whereas the Fujisawa part had been founded in Osaka already in 1894. The two former corporations had somewhat separate profiles as for strengths overseas, with Fujisawa being focused on North America and Yamanouchi on Europe. Fujisawa acquired Lyphomed Inc. based in Illinois in 1990 and established a research and development (R&D) center there. Yamanouchi acquired the Royal Gist Brocades’ pharmaceutical division in the Netherlands in 1991, and a European R&D location was thereafter developed there.

In addition to these premerger acquisitions, Astellas Pharma acquired the U.S. firms Agensys (2007), a California-based firm specializing in antibodies, and OSI Pharmaceuticals (2011), a biopharmaceutical firm specializing in oncology based in Long Island, New York. Another U.S. acquisition was attempted in 2009, the biotechnology firm CV Therapeutics Inc., but it was acquired by Gilead Sciences instead. On the other hand, Perseid Therapeutics was founded in California in September 2009 as a joint venture with Maxygen, Inc. In 2006, a subsidiary focusing on over-the-counter drugs, and so on, Zepharma, was sold to Daichi Sankyo.

Corporate Philosophy and Recent Strategy
The name of the corporation, Astellas, is based on Latin astella (star) and Greek aster (forward), and the meaning is hence a forward-moving star. The corporation also wants to reflect this momentum in its slogan “Changing Tomorrow.” R&D expenditures as relative to sales were 18.1 percent in FY 2012, a decline from 22.8 percent in 2011 and 19.6 percent in 2010. Astellas Pharma has in recent years undergone reforms of its R&D structure. A Disease Frontier Research Laboratory was established in April 2012, aimed at exploring new potential activity areas. One aim was stated as embarking onto full-scale research into cell therapies. Then, in May 2013 Astellas Pharma announced plans regarding a more comprehensive reshaping of its R&D framework, including new initiatives aiming at, first, utilizing external capabilities and resources to a greater extent; second, initiatives toward new therapeutic areas and innovative technologies such as regenerative medicine and vaccines; third, acceleration of the development speed when it comes to its preclinical pipeline; and fourth, ensuring that there is sufficient investment in its late-stage pipeline. At the same time, Astellas announced the establishment of Astellas Innovation Management in order to strengthen innovation during the preclinical development stage. Overall Astellas has reorganized toward a sequential pattern when it comes to its research functions and structures. As a part of the reorganization, the corporation also announced the closure of OSI Pharmaceuticals and Perseid Therapeutics subsidiaries as well as a scaled-back Astellas Research Institute of America in the United States, abandonment of in-house fermentation research, and a transfer of functions between research sites in Japan. Also in May 2013, Astellas entered into a strategic alliance with Amgen, Inc., concerning co-development and co-commercialization in Japan of five Amgen pipeline medicines, including three treatments for cancer and the establishment of a joint venture, Amgen Astellas BioPharma, for the purpose of developing these five drug candidates. In April 2014, Astellas Pharma and Daiichi Sankyo announced that they planned to form a joint compound library-sharing partnership for approximately 400,000
selected compounds. Such a collaboration would enable them to promote their R&D efforts. This was the first occasion of such a collaboration between Japanese pharmaceutical corporations.

Astellas Pharma has implemented a corporate social responsibility (CSR) program and strives to conduct CSR-based management consisting of five fields: society, environment, employees, economy, and compliance. Societal activities include, for example, the Changing Tomorrow Day, where Astellas Pharma employees may volunteer activities as contributions to the local communities where they work.

Terje Grønning  
University of Oslo

See Also: Daiichi Sankyo (Japan); Eisai (Japan); Ono Pharmaceutical (Japan); Takeda Pharmaceutical (Japan).

Further Readings

AstraZeneca (United Kingdom)

Headquartered in London, the multinational company AstraZeneca is the seventh-largest pharmaceutical company in the world by prescription drug sales. The sixth-largest company with a primary listing on the London Stock Exchange, it has a secondary listing on the New York Stock Exchange and is part of the Financial Times Stock Exchange (FTSE) 100 Index. The company was formed in 1999 through the merger of the Zeneca Group, a UK company spun off in 1993 from Imperial Chemical Industries, and the Swedish pharmaceutical company Astra AB. While Astra, the largest Swedish pharmaceutical company at the time, was focused mainly on pain control and medications for gastrointestinal, cardiovascular, and respiratory disorders, the largest part of Zeneca’s portfolio was devoted to oncology. Recent corporate acquisitions have included Cambridge Antibody Technology, makers of Humira; antiviral company Arrow Therapeutics; Spirogen, a biotech oncology firm; and MedImmune, makers of FluMist. MedImmune and CAT have been combined into the wholly owned subsidiary MedImmune LLC. AstraZeneca’s American headquarters is in North Wilmington, Delaware. In 2014, amid speculation of an attempted takeover by Pfizer, AstraZeneca expanded its commitment to varied cancer treatments.

AstraZeneca’s product portfolio has been reorganized to focus on three major areas: respiratory, inflammation, and autoimmunity; cardiovascular and metabolic disease; and oncology. Among the Zeneca portfolio the company began with are the cancer drugs Casodex, Nolvadex, and Zoladex. Casodex is bicalutamide, a nonsteroidal antiandrogen used in combination with castration to treat advanced prostate cancer and clinically trialed for ovarian cancer. Zoladex is the trade name for Goserelin acetate, a luteinizing, hormone-releasing hormone agonist that supresses sex hormones (testosterone and estrogen) as part of the treatment of breast or prostate cancer. In prostate cancer treatment, this can lead to a temporary increase of symptoms, particularly bone pain, in the first weeks of treatment, a phenomenon known as the tumor flare effect, preceding the desensitization of hormone receptors.

Nolvadex is the original trade name of tamoxifen, one of the most important breast cancer drugs and listed by the World Health Organization (WHO) as one of the medications constituting a basic health system. Tamoxifen was originally developed by Zeneca when it was part of Imperial Chemical Industries and targets the estrogen receptors in breast tissue. In premenopausal women whose cancer is hormone-receptor positive, tamoxifen is one of the standard
and most successful treatments (and is common for postmenopausal women as well). Because these cancers require estrogen to grow, tamoxifen prevents growth by binding to estrogen receptors without activating them. Tamoxifen is also approved for the prevention of breast cancer in high-risk women and is the most common hormone treatment for men with breast cancer. It can also be used to treat some causes of infertility and gynecomastia, premature puberty as a result of McCune–Albright syndrome, and manic episodes in bipolar patients. Despite initial fears that tamoxifen would contribute to osteoporosis, it actually has had the opposite effect, preventing the development of osteoporosis by inhibiting osteoclasts. It has been linked to an increased risk of endometrial cancer and uterine cancer and so is listed as a carcinogen by the American Cancer Society. It also causes some unpleasant side effects, notably reduced cognition, memory, and libido.

In addition to the above drugs, today, AstraZeneca manufactures Arimidex, Faslodex, Iressa, Tomudex, and Caprelsa. Arimidex is the trade name for anastrozole, an aromatase-inhibiting breast cancer treatment used postsurgery or to treat metastasis. Faslodex is the trade name for fulvestrant, a metastatic breast cancer treatment for postmenopausal women designed to follow antiestrogen therapy, administered through monthly injections. Though AstraZeneca's patent on Faslodex has expired, there is no generic available, perhaps in part because it has been less successful than the also off-patent anastrozole. Iressa is the trade name for gefitinib, an epidermal growth factor receptor (EGFR) inhibitor used to block the growth of certain cancers with overactive EGFR, usually breast or lung cancers. Tomudex is the trade name for the antimetabolite raltitrexed, used as part of chemotherapy regimens for colorectal cancer or mesothelioma. Calpresa is the trade name for vandetanib, used in the treatment of some thyroid cancers.

It is also developing cediranib, currently under the trade name Recentin, a vascular endothelial growth factor inhibitor that began clinical trials for non-small cell lung cancer, kidney cancer, and colorectal cancer in adults, and central nervous system tumors in children, in 2007. Trials for non-small cell lung cancer and metastatic colorectal cancer failed, but development continues in other areas.

AstraZeneca's MEDI-4736, the working name for a drug designed to help the immune system fight cancer, entered phase II clinical trials for colorectal cancer, head and neck cancer, and lung cancer in 2014, with phase III trials fast-tracked later in the year. MEDI-4736 is a human monoclonal antibody and shows potential for treating some of the deadliest cancers. It was this and other experimental cancer drugs that provided part of the motivation for Pfizer's attempted, but ultimately unsuccessful, takeover bid of AstraZeneca in the same year.

AstraZeneca's wholly owned subsidiary MedImmune LLC includes the portfolio and assets of the former Cambridge Antibody Technology, which developed a number of human monoclonal antibodies or mabs, a category of biological treatment that is sometimes used in cancer treatments. MedImmune is also developing CAT-5001, acquired from Enzon Pharmaceuticals, an immunotoxin that targets mesothelin in the treatment of some mesotheliomas as well as ovarian and pancreatic cancer.

Bill Kte'pi
Independent Scholar

See Also: Breast Cancer; GlaxoSmithKline (United Kingdom); Shire UK.

Further Readings

Australia

Cancer control is one of Australia's nine National Health Priority Areas (NHPA). Initially driven by the World Health Organization's Global Strategy for Health for All by the Year 2000, the purpose of the NHPA is to support collaborative action between all levels of government, policy makers, clinicians, and health professionals. Cancer control is a priority due to the significant contribution of cancer to Australia's burden of illness. By 2032, Australian
health care costs of cancer are projected to increase from $AU3.8 billion dollars to more than $AU10 billion dollars per annum. However, it is estimated that one-third of Australia’s current cancer cases could be prevented through lifestyle change, with a resultant major reduction in health care costs.

As Australia’s largest disease burden, cancer accounts for approximately 16 percent of the total burden of disease. Of a total Australian population of 22.68 million, estimates indicate that 128,290 Australians will be diagnosed with cancer in 2014, with approximately 57 percent of the total attributed to males. In 2012, the most commonly diagnosed cancers in Australia were prostate cancer (18,560 people), bowel cancer (15,840 people), breast cancer (14,680 people), melanoma of the skin (12,510 people), and lung cancer (11,280 people).

Australia has the highest rate of melanoma in the world, accounting for approximately 10 percent of all cancers. While melanoma only accounts for 2.3 percent of all skin cancers, it is responsible for 75 percent of skin cancer deaths. Among young Australians age 20 to 34, melanoma accounts for more cancer deaths than any other single cancer. Given Australia’s geography and climate, national campaigns focusing on reduced exposure to direct sunlight, protective clothing, sunscreen, wide-brimmed hats, and sunglasses are addressed as reductions in melanoma incidence. These programs are particularly prevalent in schools as an attempt to reduce the incidence of melanoma among young people.

Age-standardized rates indicate the incidence of cancer is higher for those living in areas of lower socioeconomic status and in inner regional Australia. The incidence among Aboriginal and Torres Strait Islander Australians is 461 per 100,000 compared to 434 per 100,000 for the nonindigenous population.

Cancer diagnosis in Australia is expected to rise, with cancer diagnosis rates rising significantly between 1982 and 2010. In 1982, 47,388 Australians were diagnosed; by 2010, the figure was 116,850. Projections indicate that, by 2020, 149,990 Australians will receive a cancer diagnosis. In 2009, the average age of diagnosis was 65.4 years, with the risk of developing cancer before 85 being one in two for men and one in three for women. Cancer rates rise sharply across the age gradient, with new cases most common in men age 60 years and over.

In 2012, it was estimated that cancer accounted for 551,300 disability adjusted life years (DALYs), with 457,400 DALYs lost through premature death. In 2011, there were 43,221 Australian deaths attributed to cancer. When standardized for age, male deaths per 100,000 males were 219.1 compared to 136.7 deaths per 100,000 women.

On a landmass of 7.692 million square kilometers, approximately 84 percent of Australia’s population resides in the most densely populated 1 percent of the country, largely around the coastal perimeter. Approximately 32 percent of Australia’s population resides in rural and regional areas. Delays in diagnosis of cancer in rural areas can result in more advanced disease than urban counterparts, with resultant poorer survival rates. The ramifications of a geographically dispersed population, geographic isolation, large distances to urban centers, lack of access to services, lack of access to health professionals, and the impact of relocation for treatment have major impacts on rural people with cancer.

While rates of cancer diagnosis are rising, five-year survival rates for all cancers in Australia rose between the period of 2006 to 2010. Over a 20-year period, these rates have increased from 46.9 percent to 66.1 percent across combined cancer groups. These figures have created significant numbers of people who enter the cancer survivor phase. Initiatives such as the Olivia Newton John Cancer and Wellness Centers are integrating research, cancer treatment, and evidence-based wellness programs to support people across the cancer trajectory.

Australia’s National Cancer Prevention Policy focuses on recommendations for action by government and nongovernment organizations. The policy includes primary prevention, screening and immunization. Chapters of the policy on preventable risk factors include tobacco, being overweight or obese, physical inactivity and nutrition, ultraviolet radiation, alcohol, and occupation. Action on screening is directed at melanoma, colorectal, cervical, breast, and prostate cancer. In 2007, Australia introduced a national human papillomavirus (HPV) vaccination program. The incidences of cervical cancer and mortality rates have fallen by approximately 50 percent since the introduction of a national cervical screening program in 1991. It is expected that the combination of HPV vaccination, HPV testing for secondary prevention, and cervical screening will have major impacts on the incidence of cervical cancer into the future.

The Cancer Council Australia has played a leading role in the development of clinical practice guidelines
to support the delivery of optimal care. Using a wiki platform, the aim is to improve consistency and standards of clinical practice with the Web-based approach enabling constant updates and to incorporate new scientific evidence and changes to evidence that influence contemporary clinical practice.

Amanda Kenny
La Trobe University Rural Health School

See Also: Sun Exposure (Australia).

Further Readings

Austria

Cancer statistics in Austria (population 8.46 million) mirror those of other high-income nations. Cancer in Austria is thus a costly and serious public health issue. Austria faces various hurdles to cancer care and prevention due to unhealthy lifestyle factors. The Austrian Ministry of Health (MOH) has brought forth new initiatives to promote the prevention and early detection of various forms of cancer. Although these initiatives are still in their early stages, they have only had limited participation. Moreover, initiatives in cancer control must also contend with persistent stigmatization and the taboo nature of cancer in Austrian society.

Epidemiology of Cancer in Austria
In 2012, prevalence for all cancers (404.4 per 100,000) was slightly lower than the average among other high-income nations, while the age-standardized mortality rate (157.8 per 100,000) is equivalent. Cancer accounts for 27 percent of all deaths, which is superseded only by mortality from heart disease. Five-year cancer survival rates have increased since the mid-1990s in part due to improvements in treatment.

Both cancer prevalence and mortality are higher among men. The most commonly diagnosed cancers among women are breast, lung, and colon cancer. For men, prostate, lung, and colon cancer are the most common. While rates of lung cancer for men have flattened out, rates among women are on the rise, which is in part due to the later onset and persistent popularity of smoking among women.

Differences in the quality and methods of provincial cancer registries limits comparisons across Austria’s nine provinces, but data from 2009 to 2011 suggest that the urban province of Vienna has the highest cancer mortality rates, and the Alpine province of Carinthia has the highest incidence rates.

Primary and Secondary Cancer Prevention
Health policy scholars have suggested that preventive health measures are not a high priority for Austrians, thereby making cancer prevention a challenging task. Primary cancer prevention in Austria is hindered by the high rates of tobacco and alcohol use. The World Health Organization (WHO) estimates that around 40 percent of Austrians currently use tobacco. Smoking rates of women continue to increase, whereas smoking rates for men have decreased throughout the 1970s and since leveled off. Considering that tobacco-free legislation in Austria is virtually nonexistent and smoking is not a social taboo, tobacco use is likely to remain high. At more than 13.5 liters per capita per year, consumption of alcohol is fairly high, and drinking is considered a cultural norm.

Being overweight or obese is also implicated in cancer risk. The prevalence of both factors is rising, with just over half of adult men and over 40 percent
of adult women classified as overweight or obese. Incidence rates are also increasing among children. As is the case with other high-income nations, those in lower socioeconomic groups have a higher risk of being of overweight and obese.

Given the difficulty of primary prevention strategies, the MOH in conjunction with the Austrian Cancer Society (ACS) has focused its efforts in cancer control on secondary cancer prevention. One exception is the recent introduction of the human papilloma virus (HPV) vaccine free of charge for all children nine years of age. Another is the availability of genetic testing for breast cancer (BRCA) mutations, followed by optional mastectomy and reconstruction. In regard to secondary prevention, the MOH restructured Vorsorge Neu, a program to promote various cancer screening tests including Pap smears, colonoscopy and fecal-occult tests, mammography, and the prostate-specific antigen (PSA) test in 2005. Despite universal access, participation in screening programs is low, and is even more reduced in lower socioeconomic groups and among those with an immigrant background. In January 2014, the MOH enacted a breast cancer screening program whereby women between 45 and 69 are invited to receive a mammogram by a program-certified radiologist every two years, and women between 40 and 44 and 70 and 74 can opt in. Due to very low participation and political pressure, in summer 2014, an invitation is no longer required, and women over 75 can continue to attend screening.

Cancer Therapy and Additional Services

Biomedical cancer care in Austria is excellent, although access is not equally distributed. Austria has a two-tiered health care system, consisting of mandatory government health insurance and the option to enroll in privatized health insurance at an increased cost. Those with private health insurance have shorter wait times for therapy and more time with medical practitioners. There are no cancer-specific hospitals and only four university hospitals with cancer centers. Patients can participate in clinical studies sponsored by groups such as the Austrian Breast and Colorectal Cancer Study Group. In an effort to increase overall access to care for those in rural regions, cancer patients can obtain a free taxi service to attend treatment. Patients have a right to psychological therapy, a stay in a health resort (Kur), oncologic rehabilitation, a wig, prostheses, and certain forms of complementary medicine.

The ACS, subdivided into the nine Austrian provinces, offers informational materials and events, consultation, and psychological therapy. The ACS recently unveiled a computer application to help organize a patient’s individual therapy. Psychosocial support is available through regional cancer self-help groups, but patients do not readily utilize them. The ACS also sponsors Pink Ribbon Austria as part of international breast cancer awareness. The Europa Donna Coalition for breast cancer advocacy is also active in Austria. In addition, there are multiple state and privately sponsored cancer informational events in urban regions.

Cultural Perceptions of Cancer

Despite well-established efforts in cancer care, cancer still remains a stigmatized condition. Qualitative research demonstrates that many with cancer do not readily speak openly about their disease. One reason for this may be the cultural belief that a cancer diagnosis should be accepted as one’s fate, which can lead to an attitude of resignation and a feeling of hopelessness. Since the early 2000s, this stigma has gradually been lifted in part due to better treatment options, the presence of cancer in the media, and celebrities and politicians speaking out about their personal diagnoses. It is clear that the MOH will have to work together with medical practitioners and community leaders in order to mobilize cancer control and remove the stigmatization of cancer.

Kathryn Bouskill
Emory University
Margret Jaeger
UMIT University for Health Sciences, Medical Informatics and Technology

See Also: Europa Donna, the European Breast Cancer Coalition; Obesity; Screening; Smoking and Society.

Further Readings


Automobiles

Automobiles are responsible for a number of carcinogens, made more serious by the prevalence of these vehicles in American life and their necessity to most Americans. Though automobile exhaust and the exhaust of factories manufacturing automobiles are the most obvious sources of carcinogens, they are not the only ones.

The clearest link between automobiles and cancer is the contribution of traffic-related air pollution from muffler exhaust to cancer risks. A University of California, Los Angeles (UCLA) study in 2013 found a link between traffic-related air pollution and several rare childhood cancers, for instance: retinoblastoma (eye cancer), acute lymphoblastic leukemia, and germ-cell tumors. About 4,000 California children diagnosed with cancer were studied, with their pollution exposure during their mother’s pregnancy and their own first year of life examined based on traffic volume, weather, vehicle emission rates, and roadway geometry. Pollution exposure turned out to be highly correlated to cancer risk, especially these particular cancers.

Diesel emissions specifically have been positively correlated with lung cancer, according to studies by the National Cancer Institute and National Institute for Occupational Safety. Though the highest risk is faced by miners and others who are exposed to diesel exhaust in poorly ventilated conditions—a group that faces a lung cancer risk five times higher than Americans who are not exposed to diesel exhaust in the course of their work—many Americans are regularly exposed to diesel exhaust fumes from commercial trucks and public transportation vehicles. In general—though local weather conditions have considerable impact on how quickly exhaust is dispersed—more densely populated, urban areas see greater exposure to exhaust fumes. This is true not only as a result of population density—more people means a greater number of goods to transport to them—but because the largest cities tend also to be transportation and freight hubs, through which a disproportionately high number of commercial trucks, freight and passenger trains, and passenger buses will pass.

Although diesel is generally considered more polluting than the gasoline mixtures used in passenger cars, a National Oceanic and Atmospheric Administration Earth System Research Laboratory study of the Los Angeles area found that diesel traffic did not contribute as great a share of secondary organic aerosols (SOAs)—carcinogenic particles formed in the air as pollutants and precursors oxidize into them—as was expected, and that as much as 80 percent of the SOAs in the air were contributed by gasoline engines.

Automobile exhaust, which contains carbon monoxide, nitrogen dioxide, sulfur dioxide, polycyclic hydrocarbons, benzene, formaldehyde, and a vast array of particulate matter and compounds created through combustion, has long been known to be carcinogenic, especially posing a risk of lung and bladder cancer. A 2010 Canadian study found a positive link between automobile exhaust and breast cancer.

Lung cancer risk analyses have been difficult because of the number of different exposures faced by the same population and contributing similar risk—even apart from smoking and occupational exposure, it is difficult to sort out the different factors contributing to air pollution (traffic exhaust, air traffic, factory exhaust, wood and leaf burning, and other minor factors) and to divide cancer risks among them. That automobile exhaust contributes to cancer risk is certain; exactly how much is less clear. A 2014 study hinted at just how much there is left to learn. Oregon State University (OSU) toxicology professor Staci Simonich’s team published an environmental science and technology report on the mutagenicity of various compounds that result from automobile exhaust and other forms of combustion. Almost every form of combustion generates polycyclic aromatic hydrocarbons (PAH); in the air, these PAHs, many of which are already carcinogenic, become nitrated as they interact with nitrogen, which can increase their mutagenicity by a factor from six to 467, according to the OSU study. These estimates imply that the toxicity of exhaust has actually been understated in the past. An earlier 2008 report published in Science News found that carcinogens’ interactions with nanoparticles could result in their lingering far longer than had previously been realized, making them as harmful as cigarette smoke.
Benzene is a known carcinogen and is strongly linked to leukemia and other cancers of blood cells, with possible links to multiple myeloma and non-Hodgkin’s lymphoma. Claims are made periodically by consumer safety and public health advocates—especially in less-formal and discerning settings like daytime talk shows—that dangerous levels of benzene are released from the plastic surfaces of automobile interiors, which can build up on warm days when the windows are closed in a parked car. The American Cancer Society’s investigation of these claims found that, although drivers and passengers of some moving cars may be exposed to benzene levels that exceed the chronic exposure recommendations for workplaces, this is the result of a poorly maintained car rather than the default condition of every automobile. Most benzene exposure, other than by factory workers, actually comes from cigarette smoke, whether first- or secondhand.

However, some automobile-related activities do involve benzene exposure—gasoline, for instance, contains benzene (as does automobile exhaust), and pumping gas at a gas station without vapor recovery systems to limit fume exposure will expose the customer to some amount of benzene. Modern gasoline pumps and intakes are fairly efficient at limiting drips and fumes.

Many automobile parts, including the brakes, hood liners, gaskets, clutches, and heat seals are used to contain asbestos due to their heat-insulating abilities. While less common today, asbestos linings are still used in some models and in aftermarket parts. Ordinarily the asbestos exposure to the passenger as a result is negligible; mechanics, on the other hand, and those in repair shops may well be exposed to considerable asbestos dust, especially as a result of cleaning out brake surfaces. Automobile repair shops tend to be poorly ventilated, and asbestos particles can accumulate over time. One study by the Seattle Post-Intelligencer in 10 cities has found that one in 10 mechanics is at risk for developing asbestos-related cancer, that many repair shops contain dust that exceeds by as much as 60 times the level of asbestos at which the Environmental Protection Agency (EPA) recommends the use of respirators, and that two-thirds of brake jobs involve dangerous asbestos exposure for the mechanic.

In 2005, an asbestos compensation fund was proposed by a bipartisan group of senators, in part for automobile workers and mechanics who had developed mesothelioma as a result of asbestos exposure. It was endorsed by the United Auto Workers, but the relevant bills died in committee.

Hybrid vehicles offer many advantages, including reduced emissions of carcinogens resulting from the burning of fossil fuels. However, they also have raised new health concerns, most of which are equally applicable to fully electric cars. For instance, the flow of electrical current to the motor produces magnetic fields. While the link is not clearly established, some studies suggest prolonged exposure to magnetic fields—such as over the course of a commute or a road trip as opposed to the brief exposure from using a hair dryer or electric razor—is linked to several health concerns, including a heightened leukemia risk for children. Because of the construction of the car, in which the batteries and power cables are close to both the driver and the passengers, this risk is faced whether one is driving the car or not. Both the National Institutes of Health and the National Cancer Institute have expressed concerns about magnetic field exposure in the past, notably in multiple studies of the cancer risks associated with living near high-voltage power lines and the use of electric blankets. Unlike chemical exposure, however, there is no federal or industry standard defining acceptable exposure levels.

Bill Kte’pi
Independent Scholar

See Also: Daily Life; Electronics; Pollution, Air.

Further Readings

Azerbaijan

The Republic of Azerbaijan is located in the Caucasus region, which is situated at the crossroads
of western Asia and eastern Europe. The country has an ancient and historic cultural heritage and is known to be one of the first Muslim-majority countries to host theaters. Until October 1991, when the country proclaimed its independence, Azerbaijan was a part of the Soviet Union.

Though Azerbaijan claimed its independence at this time, its health care system still bears many of the same key elements as the Soviet model, the Semashiko system. Some reforms have been put in place, but changes have been slow and incremental.

Unfortunately, the government of Azerbaijan does not invest much capital in its health care system, and in 2007, out-of-pocket payments accounted for more than 60 percent of total health expenditures. This leads to financial barriers and burdens for many of the country's citizens. The private health care system is growing in the country, and parallel services provided by other state enterprises and ministries continue to count for a large portion of health care in Azerbaijan.

Recently, due to a boom in the oil industry, the government has invested in projects such as the building of new hospitals with the latest technologies and equipment. Future plans for health care in the country include introducing mandatory health insurance and strengthening primary care.

The number of cancer cases increased by 6 percent from 2009 to 2010, as reported by the cabinet of ministers, revealing a frightening trend that shows an increase of the disease over the next several years. In 2010, more than 8,000 tumors were discovered in the population of Azerbaijan. Cancer deaths were around 5,000 the same year. According to the U.S. National Cancer Institute, in 2012 an estimated 42.7 percent of patients with newly diagnosed cancer in Azerbaijan required surgery (5,609 patients), 71.1 percent required chemotherapy (9,333 patients), and 56.0 percent required radiation therapy (7,346 patients).

**Cancer Incidence and Mortality**

According to the International Agency for Research on Cancer, a specialized agency of the World Health Organization, the age-adjusted standardized incidence rate of all cancers except non-melanoma skin cancer in Azerbaijan in 2012 was estimated at 141.9 per 100,000 population, with a mortality rate of 93.2 per 100,000. The five most common types of cancer in Azerbaijan are breast cancer (incidence of 25.4 per 100,000, mortality of 8.6 per 100,000), stomach cancer (incidence of 13.0 per 100,000, mortality of 11.2 per 100,000), lung cancer (incidence of 11.5 per 100,000, mortality of 10.5 per 100,000), cervix uteri cancer (incidence of 9.8 per 100,000, mortality of 3.9 per 100,000), and prostate cancer (incidence of 8.5 per 100,000, mortality of 4.5 per 100,000). However, incidence and mortality, as well as the most common types of cancer, differed between men and women.

For men, overall cancer incidence (excluding non-melanoma skin cancer) was 165.8 per 100,000 population, and mortality was 118.7 per 100,000. The most common type of cancer was lung cancer (incidence of 20.2 per 100,000, mortality of 18.6 per 100,000), followed by stomach cancer (incidence of 18.2 per 100,000, mortality of 16.0 per 100,000), prostate cancer (incidence of 8.5 per 100,000, mortality of 4.5 per 100,000), brain and nervous system cancer (incidence of 7.8 per 100,000, mortality of 5.0 per 100,000), and colorectum cancer (incidence of 7.1 per 100,000, mortality of 4.3 per 100,000). A man had a 13.6 percent risk of dying from cancer before age 75.

For women, overall cancer incidence (excluding non-melanoma skin cancer) was 124.0 per 100,000 population, and mortality was 73.3 per 100,000. Breast cancer was the most common type, with an age-adjusted standardized incidence rate of 25.4 per 100,000, and a mortality rate of 8.6 per 100,000. Second most common was cervix uteri cancer (incidence of 9.8 per 100,000, mortality of 3.9 per 100,000), followed by stomach cancer (incidence of 8.8 per 100,000, mortality of 7.5 per 100,000), colorectum cancer (incidence of 6.4 per 100,000, mortality of 4.0 per 100,000), and lung cancer (incidence of 4.3 per 100,000, mortality of 3.9 per 100,000). A woman had an 8.1 percent risk of dying of cancer before age 75.

Epidermoid cancer is the most common histological type of skin cancer in all regions of Azerbaijan. The highest rate of epidermoid cancer, with 230 individuals (55.56 percent) was revealed in industrial regions and industrial cities such as Baku and Sumgait. The lowest rate of lung cancer was found in the country's mountain region, with 12 individuals (3.76 percent). Skin cancer was also most common in regions with more sunny days. Smoking and drinking alcohol increases the risk of epidermoid cancer, and almost half of the patients with lung cancer in the country use these substances. The highest morbidity (13.55 per 100,000 population)
and mortality (0.11) rates from lung cancer have been observed in the country’s industrial regions. Other endogenous and exogenous factors are also associated with the disease.

Environmental Effects
A recent environmental study done for the years 1980 to 2000 in Azerbaijan shows that residents in its industrial city of Sumgayit have an increased likelihood of developing cancer due to intense environmental and occupational pollution from industry.

Poisson regression analysis of age- and sex-specific data from these years shows an increased risk for selected cancers in Sumgayit when compared to the rest of the country, as measured by adjusted rate ratios (aRR [95 percent confidence interval, or CI]): lung 1.67 (1.44, 1.92), larynx 1.39 (1.04, 1.85), bladder 2.49 (1.93, 3.22), and all sites 1.51 (1.43, 1.58).

Sumgayit appears to suffer from an increased cancer burden, suspected underreporting, and poor data quality. These prevent accurate estimates of incidence or mortality rates, and estimates indicate that pollution may have an even larger impact on the population than statistics indicate.

Cancer Care
In 2012, the International Agency for Research on Cancer estimated that there were 13,916 new cases of cancer in Azerbaijan, and 8,947 cancer deaths. Both measures were higher for men (7,154 new cases, 4,983 deaths) than for women (6,762 new cases, 3,964 deaths). These estimates are much higher than those reported by official government statistics. For instance, in 2011, the Cabinet of Ministers of Azerbaijan reported that malignant tumors were covered in 8,119 people.

Cancer care for Azerbaijan patients starts with a visit to the oncological outpatient clinics in their hometowns. For an official diagnosis, a patient first applies to the District Oncology Dispensary, where he or she is examined and treated by specialists. Treatment and diagnoses are also available in the department of Onco-Hematology of Azerbaijan Medical University and at the country’s Scientific Oncology Center.

About half of cancer patients in the country consult their doctors for the first time when they are at Stage III or IV in the disease. Radical treatments for these patients often prove ineffective, and there is a distinct need for early diagnosis and prevention campaigns across the country.

Conclusion
Azerbaijan still has much work to do in terms of cancer care. Though some governmental programs have been put in place, there is a need for greater education and awareness surrounding cancer screenings and prevention. Because of the way that the country’s health care system is set up, these changes must be perpetuated by the government, and the country must take pains to branch out from its old Soviet model to address changing trends in cancer and the lifestyle factors that are associated with it. A formal cancer/cancer control plan must be established to ensure that quality of life is preserved for all citizens.

Katie Moss
Independent Scholar

See Also: Breast Cancer; Lung Cancer, Non–Small Cell; Lung Cancer, Small Cell.

Further Readings


Bangladesh

Bangladesh, officially named the People’s Republic of Bangladesh, is a country located in south Asia. It is bordered by India and Burma and faces the Bay of Bengal to the south. Bangladesh is the eighth-most populous country in the world, with more than 160 million people.

Education and health levels remain relatively low across the country, though poverty levels have decreased slightly over the last few years. Most Bangladesh residents live on subsistence farming in rural villages, and village doctors with very little formal training compose 62 percent of the country’s health care practitioners. Formally trained providers are occupying a mere 4 percent of the total health workforce in the country. About 70 percent of residents consult only village doctors for their health care needs. This leads to an abundance of health problems, including issues from infectious diseases and water contamination. Common diseases include dengue, leptospirosis, tuberculosis, and malaria.

Bangladesh’s poor health conditions stem from the lack of professional medical training and services provision by the government. In 2009, the government spent only 3.35 percent of its gross domestic product (GDP) on health care, according to a World Bank report. There are reportedly four hospital beds per 10,000 citizens, and a large majority of citizens pay their health care bills as out-of-pocket expenditures. This problem is further exacerbated by the fact that 26 percent of Bangladesh’s dense population of 150 million people lives below the national poverty line of US $2 per day.

Cancer in Bangladesh

Cancer is an increasingly important cause of morbidity and death in Bangladesh. In 2012, there were 122,700 new cancer cases diagnosed in Bangladesh. According to the Bangladesh Bureau of Statistics, cancer is the sixth-leading cause of death. The International Agency for Research on Cancer has estimated cancer-related death rates in Bangladesh to be 7.5 percent in 2005. This number is expected to almost double to 13 percent in 2030. In Bangladesh, there are 17 radiotherapy centers in public and private sectors, only one of which is in a rural area. There are only 15 linear accelerators installed across the country, along with 12 cobalt-60 machines and 12 brachytherapy machines.

The two leading types of cancer in Bangladeshi males are oral and lung cancer, and the leading cancers for women and cervical and breast cancer. Currently, Bangladesh is in severe shortage of hospital beds, trained oncologists, radiation therapy machines, physicists and technologists.

Many Bangladeshi are affected by cancers caused by smoking and smokeless tobacco use. The human papillomavirus (HPV) infection is also a concern, as are hepatitis B and C infections, arsenic-contaminated
waters, chemical carcinogens in fruit, *H. pylori* infections, and chromium contamination.

**Antitobacco Campaigns**
According to the World Health Organization, the annual cost of illnesses in Bangladesh attributable to tobacco usage is $500 million, and the total annual benefit from the tobacco sector is $305 million as tax revenue. The National Institute of Cancer Research and Hospital (NICRH) and Bangabandhu Sheikh Mujib Medical University (BSMMU) cancer registry data revealed that 60 percent of the cancers in males and 5 percent of the cancers in females in Bangladesh are tobacco related and hence entirely avoidable. Because tobacco is major contributor to several types of cancer, Bangladesh has developed a National Cancer Control Strategy and Action Plan with the aim of delivering a universal, timely, and quality-based service. The campaign focuses on cancer prevention through tobacco control, promoting health and vaccination programs, and early breast, cervix, and oral cancer detection. Some efforts are being made to develop more cancer research throughout the country as well as create additional cancer detection and diagnostic facilities.

**Age-Related Cancer Statistics**
According to the BSMMU and NICRH, more than 66 percent of the cancers in Bangladesh occur in the age group of 30 to 65 years. About 20 to 25 percent of cancers in the country are diagnosed in a localized stage. Two-thirds of cases are diagnosed when the disease is regional. Disease with distant metastasis at the time of diagnosis is greater than 15 percent.

Childhood cancers in the country make up only 1 percent of the overall incidences, and cancer treatment for children has been considered successful over the past several years. Seventy percent of childhood cancers are curable, with the top five kinds of childhood cancer in the country being soft tissue sarcomas and renal tumors, lymphomas, leukemia, and central nervous tumors.

**National Institute of Cancer Research and Hospital**
The NICRH in Bangladesh is the only tertiary-level center of the country that works within multidisciplinary cancer patient management. The hospital was created in 1982 and moved to its present location in 1986. The hospital is currently composed of 300 hospital beds and is the most comprehensive cancer center in the country.

**Improving Cancer Care**
Currently, in Bangladesh, researchers are striving to build a model program to improve the care of women who have breast cancer and do not have the funds to care for themselves or their families. Researchers across Bangladesh have collaborated with *Amader Gram* (Our Village), a rural information technology organization to build four breast cancer clinics, one specialty treatment, and outpatient diagnostic center.

Radiation therapy is standard for many instances of breast cancer, and the organization’s next step is to create a radiation therapy center that will also provide education for patients and training for new oncologists. No facilities for this kind of treatment currently exist anywhere in the Khulna region of Bangladesh, and right now, there are 18 operational radiation therapy facilities throughout the country. Approximately 300 of these centers are needed.

The current proposal estimates for the next new center include a plan to offer radiation treatments for $125, compared with thousands of dollars in the United States. The total start-up costs for the center would be approximately $1.3 million.

In addition to financial issues, researchers are facing challenges in recruiting women for clinical trials. Many women in Bangladesh believe that they cannot act on their inclinations to seek help with their cancer because of their place in the family. Researchers are attempting to develop a team of social scientists to investigate the complex issues that may explain this behavior and to find solutions to address them. For now, the country’s first free walk-in breast care clinic has been developed. Women are attended by all female doctors, and serious issues are referred to doctors at Khulna Medical College.

**Conclusion**
The cancer burden in Bangladesh is worrisome, but there are some solutions being developed to treat additional patients in the country. To effectively treat this burden, the government must invest in cancer care; private institutions cannot address all of the health care issues in the country alone.

Katie Moss
Independent Scholar
Barbara Ann Karmanos Cancer Institute

Detroit, Michigan, is a city that has endured many vicissitudes in recent years. Between the 2000 and 2010 census, the city suffered a 25 percent population decline and had declined 60 percent since the 1950 census. Between 2000 and 2010, the city’s ranking among the largest municipalities in the United States declined from 10th to 18th. The associated decline in economic status resulted in the city filing the largest municipal bankruptcy case in U.S. history in 2013.

The resultant judgment cited Detroit’s $18.5 billion debt and declared that negotiations with its thousands of creditors were unfeasible. The city has suffered from the blight of urban decay, with thousands of abandoned homes, apartment buildings, and commercial structures. Certain areas have become so sparsely populated that municipal services are sporadic or entirely unavailable. Rampant unemployment and high crime rates in many parts of the city have exacerbated the problems faced by this municipality. Yet with all of the troubles, bright spots remain. Three of these are located in midtown: Wayne State University, the Detroit Medical Center, and the Barbara Ann Karmanos Cancer Institute.

Located in Detroit's Midtown Cultural Center Historic District, Wayne State University (WSU) occupies 203 acres and more than 100 education and research buildings. Wayne State was founded in 1868 as the Detroit Medical College, now the School of Medicine. The university now provides more than 370 academic programs through 13 schools and colleges to approximately 28,000 students. Among the student body are more than 1,600 international students from 70 countries. WSU's comprehensive academic offerings are divided among their schools and colleges: the School of Business Administration; the College of Education; the College of Engineering; the College of Fine, Performing, and Communication Arts; the Graduate School; the Law School; the College of Liberal Arts and Sciences; the College of Library and Information Science; the School of Medicine; the College of Nursing; the Eugene Applebaum College of Pharmacy and Health Sciences; the Irvin D. Reid Honors College; and the School of Social Work. The institution is a leading contributor to the cultural life of Detroit.

The WSU School of Medicine is the nation's largest single campus medical school. The school enrolls more than 1,000 medical students in undergraduate medical education, master’s degrees, Ph.D.s, and M.D.–Ph.D. programs. Fourteen areas of basic science are taught along with graduate programs, including their M.D.–Ph.D. and 10 doctor of philosophy programs, eight master of science programs, and three certification programs. WSU School of Medicine is the academic affiliate of the Barbara Ann Karmanos Cancer Institute. The physicians at Karmanos are appointed as faculty members of the School of Medicine.

The Detroit Medical Center was established in 1985 as a union among several hospitals: Harper University Hospital, Grace Hospital, Hutzel Women's Hospital, and Children's Hospital of Michigan. It is a hospital with more than 2,000 beds, 3,000 affiliated physicians, and more than 12,000 employees. As such, it is the largest single employer in Detroit. The center is affiliated with the medical schools of WSU and Michigan State University. The center operates eight general and specialty hospitals in southeast Michigan. The Barbara Ann Karmanos Cancer Institute is closely affiliated with the Detroit Medical Center but operates as a separate not-for-profit entity.

The Karmanos Institute began in 1943 as the Detroit Institute for Cancer Research. Later, it became the Michigan Cancer Foundation, which included the Meyer L. Prentis Comprehensive Cancer Center of Metropolitan Detroit and the
cancer programs of the Detroit Medical Center and WSU. In 1995, the institute was named after Barbara Ann Karmanos, the late wife of Peter Karmanos Jr., chairman and chief executive officer of Compuware Corporation. Barbara Ann Karmanos died of breast cancer at the age of 46, after an eight-year battle with that malignancy. The institute is one of 41 National Cancer Institute-designated comprehensive cancer centers in the United States with 1,200 staff members, including 300 physicians. Approximately 12,000 patients are treated each year. In addition, 700 cancer-related scientific investigations and clinical trials are conducted each year.

The lofty stated mission of the Karmanos Cancer Institute is the ultimate prevention and cure of cancer. To this end, its programs are directed toward the prevention, early detection, or treatment of malignancy. The institute primarily is based upon laboratory, clinical, and population research. This research is centered upon five programs:

The Breast Cancer Biology Program is dedicated to the study of breast cancer progression, mechanisms of tumor growth and control, the genetic aberrations of the disease, possible dietary prevention, and the improvement of therapy. The Developmental Therapeutics Program focuses on a better understanding of drug pathways and finding ways to improve the prediction of response, including a strong medical imaging initiative. The Molecular Biology and Genetics Program concentrates on mechanisms of genomic instability, encompassing studies of chromatin structure, cell cycle checkpoint control, transcriptional regulation of signal transduction, and posttranslational control mechanisms.

The Proteases and Cancer Program is directed toward determining the functions of proteolytic enzymes in malignant cancer progression. The Population Studies and Prevention Research Program has as a goal to increase the understanding of the causes of cancer in the diverse population of metropolitan Detroit. This is an effort to decrease racial and ethnic disparities. Key features of this program include measurement of cancer incidence, morbidity, survival, and mortality in this population. Measurements also include assessment of genetic predisposition, environmental and behavioral risk factors, screening practices, and quality of care. The center’s Metropolitan Detroit Cancer Surveillance System was a founding participant in the NCI’s national Surveillance, Epidemiology and End Results (SEER) program. This system facilitates investigations into race-related disparities in cancer incidence and survival.

While an important objective of the Karmanos Institute is clinical programs with community outreach activities to local populations in Detroit, the center is directed toward not only patient care but research. More than 300 clinical trials of modalities to improve cancer treatment and cure are ongoing, including one of the country’s leading phase I trial programs of new treatments for the scourge of malignancy. Research as always is the foundation upon which the future of cancer treatment is based.

Walter Landers
Independent Scholar

See Also: Cancer Communication; Clinical Trials; Experimental Cancer Drugs; Future of Cancer; National Cancer Institute.

Further Readings

Battery Acid

Battery acid, commonly known by its scientific name sulfuric acid, poses little if any risk of cancer to people who use batteries in their cars and appliances. In other words, people can buy, install, and change batteries, including car batteries, in relative safety. The risk of cancer is greater for people who work in production facilities where battery acid is used and may form mists that can be inhaled. Intensive and long-term exposure to such mists has been linked to lung cancer and gastric cancer but
more conclusively to laryngeal cancer. Those at risk include workers in the production of lead acid batteries; metals, especially steel; soap; and phosphate fertilizers. Studies in small mammals suggest a correlation between cancer and sulfuric acid exposure; however, studies in humans are less conclusive because of the difficulty in screening for lifestyle behaviors that also result in cancer. Sulfuric acid can also contaminate water.

Battery acid is not a recent discovery. It was referred to by the ancients as *vitriol*. A Sumerian text dating back to 600 B.C.E. refers to a substance that is likely to be battery acid and categorizes the substance by color. Dioscorides, a Greek medical doctor of the 1st century C.E., referred to vitriol production in Cyprus in the neighborhood of copper ore deposits.

Battery acid is a highly corrosive liquid mineral. It is an active ingredient not only in batteries but also in drain cleaners and other cleaning agents. It is the active ingredient in Debacterol, an ointment used to treat mouth sores or cankers. This acid is also used in the production of illegal narcotics and psychotropic drugs.

As a consequence, it is listed in Table II of the United Nation's Convention Against Illicit Traffic in Narcotic Drugs and Psychotropic Substances. In the United States, the Drug Enforcement Administration controls the sale, import, export, and transportation of battery acid.

Battery acid is generally colorless or a very pale yellow. Like any acid, it can quickly destroy many substances with which it comes in direct contact. The greatest health and safety hazard associated with battery acid occurs when it comes in direct contact with the skin, in which case it can lead to severe burns. If direct contact occurs with the eyes, blindness is the worst possible outcome. There is no known correlation, however, between such burns and the development of cancer.

Battery acid can become airborne in industries where it is used. It poses the greatest risk of cancer when it forms a mist that can remain suspended in air for varying amounts of time. In the present day, the people most often exposed to dangerous quantities of battery acid usually work in the lead acid battery production industry, though people are also exposed to sulfuric acid if they work in phosphate fertilizer production, metal pickling, glue production, explosives production, petroleum purification, printing, photography, production of other acids, and soap manufacture. Sulfuric acid has been linked to lung and gastric cancer, but the greatest risk from exposure to battery acid is the development of laryngeal cancer, that is, cancer of the voice box. Treatment for such cancer, if it is detected early, is usually successful. However, the overall outlook for patients with this type of cancer is a 62 percent chance of survival over 10 years.

Several studies of workers in lead acid battery production plants have been conducted with mixed results. A higher-than-average mortality was found in the workers, but causes of death included hypertension (high blood pressure) and nephritis (kidney disease). Deaths associated with lung and gastric cancer among the battery plant workers was 5 percent higher than normal in one study, but the same study concluded that such increased risk was not statistically significant. Studies of battery plant workers have been flawed because the studies could not factor out other causes of cancer such as smoking, diet, and alcohol consumption. Five studies conducted in the late 1980s among deceased steel workers exposed to battery acid more conclusively point to an increased risk of laryngeal cancer. These studies screened for smoking and alcohol consumption and found that the incidence of laryngeal cancer in the studied workers was higher than that in the larger population. One study in particular observed that the occurrence of laryngeal cancer in a group of 879 U.S. steelworkers was more than two times higher than expected. It is worth noting that the use of battery acid in the three plants in the study was phased out by 1980.

A similar study was conducted among workers in a large chemical plant and refinery in Baton Rouge, Louisiana. Fifty workers who contracted upper respiratory cancer were the subject of study. Thirty-four of them had cancer of the larynx. They were compared to three control groups who were like the first group in age, gender, and race. The study suggests that the chemical plant and refinery workers were four times more likely to contract upper respiratory cancer.

On the basis of these studies, the International Agency for Research on Cancer (IARC) determined that battery acid (sulfuric acid) is a known human carcinogen. The World Health Organization, too, has pronounced that there is sufficient evidence that prolonged exposure to sulfuric acid is carcinogenic.
However, in the United Kingdom, the Industrial Injuries Advisory Council concluded that the cancer risks associated with exposure to battery acid would not make people eligible for the Industrial Injuries Disablement Benefit. The council made this decision after looking at several studies of cancer risks among workers exposed to battery acid.

The U.S. Environmental Protection Agency limits the amount of sulfuric acid that can be legally released into the air. The Occupational Safety and Health Administration and the National Institute of Occupational Safety and Health have limited the amount of battery acid that can be released legally within the workplace to one milligram per cubic meter of air. Individual states in the United States have the authority to enact further protections for people who live near facilities using battery acid. For example, in California, the Toxic Hot Spots Program (AB2588) mandates that businesses that produce toxic air pollutants perform assessments to measure health risks. If the calculated risk of cancer is 10 in 1 million or more, the business must inform the community of the risk. The link between battery acid and lung cancer is more tenuous than the link to laryngeal cancer. One study, published in 1987, looked at 1,165 workers in the metal picking industry. As in the aforementioned studies, the workers were exposed to aerosolized chemicals including battery acid. The study concluded that these workers were approximately a third more likely to develop lung cancer than people not working in metals. However, the same study found other acid mists, especially hydrochloric acid, to represent a greater cancer risk than battery acid. Another study found a significant increase in death among pensioners who were former employees of four lead acid battery factories from 1925 to 1976. But the most of those deaths were found to be caused by cerebrovascular accidents, not from cancer. The risk of developing cancer caused by battery acid for people not working in industries that employ it is minimal, though battery (sulfuric) acid can be released into the atmosphere by burning coal, oil, or gas. Children may be at an elevated risk because of their smaller airways and the fact that they inhale more air per body kilogram than adults.
How airborne battery acid causes cancer is unknown. It may irritate epithelial cells—the cells found in glands and skin—or it may lower the body’s pH, that is, the body’s natural acids, causing acidosis and leading to gene mutation and chromosome aberration. Currently, no medical test exists to discover whether someone has been exposed to battery acid. Inhalation of battery acid mist can be extremely toxic. Someone who has inhaled a substantial quantity of such mist should be removed from the environment where the threat is posed and exposed to fresh air. If the patient’s breathing is difficult, he or she should be given oxygen.

A poison center should be consulted, and the patient should go to a hospital. To minimize the cancer risks and other health risks of people working with batteries, the work environment should be well ventilated with a corrosion-resistant exhaust ventilation system. Process enclosure should be implemented to prevent escape of acid mists into the workplace. Those workers who work directly with the acid should wear chemical safety goggles and face shields as well as protective clothing made from butyl rubber. Depending on the level of their exposure, they may need to use air-purifying respirators. Battery acid in the workplace has to be carefully stored in a container that will not deteriorate over time from contact with the acid. Glass, for instance, is nonreactive with battery acid and makes a suitable storage container.

People who use batteries domestically should exercise common sense in handling them. If a battery’s seal is breached, the acid can leak out, in which case the battery should be handled with gloves and immediately discarded. Dead batteries should be deposited at an appropriate recycling facility, not placed in landfills. Improperly discarded batteries can contaminate the soil, though such contamination results more from the release of lead into the soil than from the release of acid. Improperly discarded batteries can also leak acid into waterways. This happens most frequently when batteries are disposed of improperly in landfills. If the landfill is unlined or if the lining has ruptured, the acid from a battery can find its way directly into the groundwater and endanger the quality of drinking water.

Battery acid is commonly referred to by its scientific name, sulfuric acid. Historically, it was called oil of vitriol. It also goes by the names vitriol brown oil, mattling acid, dipping acid, electrolyte acid, dihydrogen sulfate, and hydrogen sulfate.

Lynn Marie Hamilton
Independent Scholar

See Also: Laryngeal Cancer; Lead; Lung Cancer, Small Cell.

Further Readings

Belarus
The Republic of Belarus is a landlocked country in eastern Europe that is bordered by Poland, Russia, the Ukraine, Lithuania, and Latvia. Since the country’s independence in 1991, the organizational structure of Belarus has remained relatively the same. Regulated by the state, the health care system is primarily public, with about 7 percent of medical services being provided by the private health sector. The government strives to create conditions so that everyone has a right to health on the basis of state guarantees.

Of special consideration to the government are maternity and childhood protection services. Free medical care is offered during and after childbirth, and observation of newborns is guaranteed to all pregnant women. In Belarus, 100 percent of births are attended by skilled health professionals. This has led to a large decrease in the country’s infant mortality rate and an increase in life expectancy at birth.
In relation to cancer, programs to develop early detection of precancer diseases for the female reproductive system in patients with hormone-dependent neoplasms have been developed. Treatment methods of patients with cancer of the liver have been developed. These involve chemoembolization of the hepatic artery. Treatment for patients with superficial cancer of the urinary bladder and patients with mesothelioma of pleura of I through IIIA stage without remote metastases and local cervical carcinoma have also been developed.

**The Chernobyl Catastrophe**

The Chernobyl disaster, or Chernobyl accident, was a catastrophic nuclear accident that occurred in April of 1986 at the Chernobyl Nuclear Power Plant in Ukraine, under the authority of the Soviet Union. Deemed the worst nuclear power plant disaster in history, the explosion and fire released huge quantities of radioactive particles into the air, spreading all over the western Union of Soviet Socialist Republics and Europe.

Unfortunately, all of this radioactive matter led to a large increase in cancer incidences—about a 40 percent increase in all cancers across the country overall. Increases in cancer are apparent in all regions, with the highest concentration being apparent in the Minsk (49 percent increase) and Gomel (52 percent increase) regions. The 40 percent estimate shows this increase between the years in 1990 and 2000, with findings by the *Swiss Medical Weekly*. Today, it is expected that those rates are even higher.

Some governmental agencies (such as a United Nations committee in the year 2000) have stated that there is no evidence of a major public health impact related to the Chernobyl catastrophe, apart from the increase in thyroid cancers for children following exposure. This comment predominately focused on the disease leukemia and nonmalignant disorders, along with the statement saying that these radiation levels would be comparable or a few times higher than the country’s natural background levels. These results have been proven inaccurate in the years since.

**Thyroid Cancer**

Thyroid cancer is one cancer type that has been well researched by various groups and studies. One such study invested age-adjusted thyroid cancer incidence rates (adjusted to the World Health Organization [WHO] 2000 world population) and showed that they have increased between 1970 and 2001 from 0.4 per 100,000 to 3.5 per 100,000 among males and from 0.8 per 100,000 to 16.2 per 100,000 among females in the country. These estimates mark an increase of more than 700 percent and 1900 percent, respectively. High exposure areas showed an increase of 1,020 in males and 3,286 in females, quite a large difference between increases in lower-exposure areas of Belarus, with a 571 percent increase in males and 250 percent increase in females in these areas. Increases in thyroid cancer are noted among both females and males in all age groups. The highest ratios are shown among those from higher exposure areas age 0 to 14 at the time of diagnosis. The greatest increases have been shown among children across the board. This suggests that a high prevalence of preexisting iodine deficiency in combination with unique susceptibility among younger people might have contributed to potential carcinogenic exposures to the thyroid.

In comparison to areas of Ukraine and other regions of the Russian Federation, there have been many more incidences of childhood thyroid cancers in Belarus. At the time of the accident, many children were heavily contaminated by iodine isotopes. This peaked in the year 1996, while the peak of incidence in the Russian Federation Region was highest in 1998, at 12.6 cases per 100,000 residents.

In sum, on the whole, observations in the Chernobyl childhood thyroid cancer series show that the majority of patients live proximally to the Chernobyl power plant. The highest risk for thyroid cancer has been found in patients 0 to 4 years old at the time of exposure. Papillary thyroid carcinoma was the prevalent pathological type (94 to 98 percent), and most patients have an advanced stage of disease when their conditions are discovered.

**Kidney Cancer**

Kidney cancer is the 12th-most common cancer in the world and the 11th-most common cancer in Belarus. The most common type of kidney cancer is renal parenchyma cancer, which makes up 80 to 90 percent of cases. Smoking is a major cause for kidney cancer, as is dialysis, which occurs through the development of acquired renal cystic disease. Body fat and alcohol can also be factors for kidney
cancer. Many of these cases could be prevented with prevention campaigns throughout Belarus.

Belarus Cancer Treatment
Despite its own cancer troubles, Belarus is known for providing health care services to foreigners due to its excellent resources and the number of specialists. The following treatment methods are available in the country: transplantation of hematopoietic stem cells, photodynamic therapy of patients with cervical dysplasia, and thermo-chemotherapy for patients with advanced lung cancer.

The Children's Oncology and Hematology National Center has an excellent reputation for treating malignant tumors: The efficiency of treatment of lymphoblastic leukemia is 75 percent, and of Hodgkin's lymphoma is more than 90 percent. Medical tourism is becoming increasingly popular in Belarus. Foreign tourists can combine recreational travel with excellent health care. Further adding to its appeal, Belarus is centrally located in Europe and has a well-developed mass transit system. Its mild climate also promotes faster rehabilitation. In 2012, 130,000 foreigners received cancer treatment in Belarus.

Katie Moss
Independent Scholar

See Also: Kidney (Renal Cell) Cancer; Radiation; Thyroid Cancer.

Further Readings


Belgium
Belgium, or the Kingdom of Belgium, officially, is a federal monarchy in western Europe that plays host to the European Union. Belgium has a population of about 11 million people. Health care in Belgium is provided by a mixture of nonprofit and public hospitals.

Seventeen percent of the Belgian population is 65 or older, and about 5 percent is 80 or older. Life expectancy continues to increase, meaning the elderly population is expected to increase threefold by the year 2060.

Cancer in Belgium: The Stats
In terms of cancer, in 2008, 59,043 new invasive tumors were discovered in Belgians, with 54 percent of these found in males and 46 percent in females. The mean age at diagnosis was 67 and 65, respectively. In 2008, 26,647 Belgians died from cancer, composed of more males (57 percent) than females (43 percent). Five-year relative survival for all tumors diagnosed between 2004 and 2008 shows a poorer outcome in males than in females (59.5 percent vs. 67.8 percent). This female survival advantage reflects the fact that, for most cancers, females have a better prognosis than males, and males tend to be afflicted by cancers with worse prognoses.

In both genders, survival rate is largely rated to the age at diagnosis, with a younger diagnosis improving the chances of survival. In males, five-year relative survival is 67.6 percent for patients age 15 to 29 and 57.4 percent for patients 65 years and older. In females, the numbers are even more pronounced, with five-year relative survival rates at 84.4 percent for females age 15 to 49 and only 57.3 percent for those who are 65 and older. The almost equal prognosis for both sexes in seniors suggests that female survival benefits disappear at older ages, possibly due to the fact that sex-hormone patterns have a role in women's superior ability to cope with cancer.
Belgium

The Belgian Cancer Registry Foundation
Many of the statistics in this piece can be attributed to the Belgian Cancer Registry Foundation, which collects data on all new cancer diagnoses in the country and how they are followed up to accurately represent the burden of cancer in the country. The most recent data are to be found in Cancer Incidence in Belgium 2008. In addition, the Belgian Cancer Registry also collects all anatomic pathological test results for the purposes of early detection of particular cancers (colon, cervical, and breast).

To aid in the prevention and treatment of cervical cancer, a central cytohistopathological registry for cervical samples (CERVIBASE) is currently being created on the organization’s Web site. This registry collects patients’ comprehensive data to enable the compilation of records.

Colorectal Cancer
In Belgium, colorectal cancer is the third-most frequent cancer in males and the second-most frequent in females. The disease also ranks as the second-most frequent cause of death by cancer in males and the third in females in Belgium.

Colorectal cancer predominately affects males and occurs most commonly in patients age 65 and older. Given the aging of the population, colorectal cancer is expected to remain an important health issue for Belgium in the coming years. This fact is reinforced by the increasing incidence rates of colorectal cancer for both males and females over the last 10 years in the Flemish region. When diagnosed early, colorectal cancers have a high survival rate (above 90 percent when diagnosed during stage I), so education surrounding this cancer is a necessity for Belgium.

Corpus Uteri Cancer
Corpus uteri cancer is the fourth-most frequent tumor in females and the most frequent gynecological cancer across Belgium, with a mean diagnosis age at 68 years old. It is also the gynecological cancer with the best prognosis, with a one-year relative survival rate above 92 percent and the five-year relative survival rate at 79.6 percent. Relative survival rates are marginally better in the Flemish and the Walloon regions (five-year survival rate: 80.1 percent and 79.5 percent, respectively) than in the capital of Brussels.

Breast Cancer
In Belgium, breast cancer is the most frequent cancer in females (around 35 percent of all cancer cases), and it occurs at a mean age of 62 years. Breast cancer also causes the most cancer death in Belgium females, at more than 20 percent. Males have a very low chance of having breast cancer in Belgium—around 0.2 percent—and death is very uncommon.

Breast cancer has a relatively good prognosis, with five-year relative survival rates of 88.0 percent in females and 78.2 percent in Belgian males, according to studies done between 2004 and 2008. Due to late relapses and their related deaths, 10-year survival decreases by about 10 points for both males and females.

Five-year relative survival rates for breast cancer in females show no difference among the three Belgian regions. There is a markedly poorer survival rate for those age 70 and older.

In 2004, breast cancer incidences for Belgium amounted to 110 per 100,000 person-years for all ages and 172, 390, and 345 per 100,000 person-years for those age 35 to 49, 50 to 69, and 70 and over, respectively. Mortality rates for breast cancer increased until the late 1980s and afterward decreased in all Belgian regions for those less than 70 years old.

The burden of breast cancer in Belgium is very high. In 2004, Belgium women ranked first in Europe for all ages combined and in the 35 to 49 and 50 to 69 age groups; however, survival rates are favorable. Mammogram screenings should continue to be encouraged across the country.

Lung Cancer
Around 1.6 million new cases of lung cancer were diagnosed across the world in the year 2008, making it the most common type of cancer in the world. Due to its high mortality rate, it is also the most frequent cause of death by cancer.

Tobacco smoking is well-known as the most important cause of lung cancer, and though the incidence rate for this type of cancer is decreasing in males in Belgium and across the world, it is rising steeply in females.

In Belgium, this cancer is the second-most frequent type of cancer in males and the third-most frequent in females. It is also the leading cause of cancer deaths in males and second in females.
More than half of lung cancer patients die within the first year.

Katie Moss
Independent Scholar

See Also: Breast Cancer; Colorectal Cancer, Childhood; Lung Cancer, Small Cell.

Further Readings

Benin

The Republic of Benin (shortened to Benin) is a country in west Africa that is bordered by Togo to the west, Burkina Faso and Niger to the north, and Nigeria to the east. A large portion of the Benin population lives on its small southern coastline on the Bight of Benin.

In Benin, most serious epidemic diseases have been brought under control through the spread of mobile health units, but there are still many major health issues facing the country. The government of Benin has set goals of upgrading the quality of referrals, expanding its health care system overall, improving care in the public sector and promoting private sector care.

The five most common cancers in Benin are gynecological (including cervix uteri, ovary, and corpus uteri), breast, liver, urological (including bladder, testis, prostate, and kidney), and hematological malignancies (including Hodgkin’s lymphoma, leukemia, non-Hodgkin’s lymphoma, and multiple myeloma).

Breast Cancer
Breast cancer is one of the leading causes of death for women around the world and the principal cause of deaths from cancer. African women, in particular, in comparison with their low incidence of cancer, bear a disproportionately high cancer mortality rate.

It has been estimated that, by the year 2020, approximately 70 percent of new cancer cases will occur among individuals in developing countries and among groups that have previously experienced only low incidences of the disease, with a large fraction of these incidences being breast cancer related.

According to the latest World Health Organization (WHO) data published in April 2011, breast cancer deaths in Benin reached 449 individuals this year, or 0.55 percent of total deaths for the country. The age-adjusted death rate for Benin women with breast cancer is 18.41 per 100,000 individuals, ranking it number 71 in the world in terms of breast cancer. However, as this does not seem like a large percentage, it is a real problem because of the previously mentioned high mortality rate.

Late breast cancer diagnosis is a real problem for African women, with about 70 to 90 percent of cases being diagnosed in late stages and often leading to death that could have been prevented had the disease been recognized sooner.

Breast cancer awareness and attitude are common denominators to several factors determining the stage at which patients with breast cancer arrive at the hospital for treatment. Many of these factors are related to women’s knowledge and beliefs about breast cancer and how to treat the disease. One important strategy in reducing breast cancer mortality in Benin and other parts of Africa is encouraging mammogram screening to achieve earlier detection of cancer. Early diagnosis leads to a greater survival rate and better management of the disease.

Prostate Cancer
According to the GLOBOCAN 2002 database, there are about 255 new cases of prostate cancer diagnosed in men in Benin each year. Though this number may not seem high, death rates from the disease are quite elevated. The estimated age-standardized rate of new cases per year is 19.3 per 100,000 in the country, and the number of deaths
each year is 210, making the estimated age-standardized number of deaths each year 16.0 per 100,000. Estimated one-year prevalence for the disease in Benin is 203, and the estimated five-year prevalence is 677.

Interestingly enough, there seems to be a decrease in incidences of prostate cancer for Benin men. In 2002, the estimated age-standardized incidence was 77 per 100,000, and the estimated age-standardized death rate in 2005 was 60 per 100,000. These increases may be due to greater education surrounding risk factors and early detection of the disease.

Challenges to Cancer Care in Benin
In addition to a lack of funds, Benin faces a number of issues in terms of cancer care. In Benin, cancer treatment capacity cannot meet demand. The same situation is true of many developing countries, and hundreds and thousands of cancer sufferers face a lack of accessibility for care.

For patients in Benin, the cancer treatment capacity cannot meet demand—a tragic reality that is repeated throughout the developing world where cancer has reached epidemic proportions. Hundreds of thousands of cancer sufferers in developing countries face an uncertain fate.

To help find a solution, the Beninese Health Ministry recently requested the International Atomic Energy Agency’s (IAEA’s) Program of Action for Cancer Therapy (PACT) conduct an imPACT review mission. This mission would review all current cancer information, including care, diagnosis, and early detection. The imPACT mission learned that, currently, Benin does not have specialized cancer treatment services or oncology doctors, meaning that many patients must be shipped abroad to receive proper treatment.

With approximately 8.66 million Benin residents and an estimated cancer incident rate of about 5,300 new cases in the year 2008, it is imperative that Benin get the cancer support it needs. Newly diagnosed cancer patients are in need of radiation, chemotherapy, and pathology.

In 2008, it was estimated that Benin is in need of at least seven surgical oncologists, 31 radiation oncologists, 13 pathologists, and several other specialists, amounting to about 45 cancer specialists needed for the country. For developing countries, the IAEA recommends training radiation and clinical oncologists who can prescribe both radiation and chemotherapy for common solid cancers instead of separate specialists for each segment.

To aid in the prevention, diagnosis, and treatment of cancer, Benin (along with other African countries) must put a reliable cancer registration system in place. Many countries do not have this, and the fear is that cancer incidences may be higher in Africa than is actually reported. There is a distinct need to assess accurately the total burden of cancer in each country and to correctly document mortality rates.

Conclusion
Like many other countries in Africa, Benin deals with a lack of funding, education, treatment centers, and prevention tactics surrounding cancer. Breast cancer, for example, can be identified in its early stages, greatly increasing the likelihood that the patient will survive the disease. However, because African women have little access to medical attention and screenings, they are often diagnosed in the late stages of the diseases, leading to high mortality rates. The same is true of several other types of cancer in the country not mentioned here, including lung cancer. The African government must take the threat of cancer seriously, or as studies have proved, incidences of the disease will continue to rise.

Katie Moss
Independent Scholar

See Also: Breast Cancer; Developing Countries; Prostate Cancer.

Further Readings


Bereavement Issues

The American Cancer Society estimated that 585,720 Americans were expected to die of cancer in 2014, almost 1,600 people per day. Cancer is the second-most common cause of death in the United States exceeded only by heart disease. For each person who dies of cancer, there are primary and secondary survivors—caregivers, family members, and friends who have felt a caring bond with the dying person. All survivors will experience a grief and bereavement experience that in many respects is unique based on the characteristics of the illness and treatments used to care for cancer patients.

Cancer Illness Trajectory

Cancer is characterized by uncontrolled cell growth and is usually classified according to the body organ or body system in which it occurs. Upon detection and depending on staging and other factors, treatments include surgery, radiation, and chemotherapy or some combination of these approaches. Alternative and experimental treatments abound, and many patients will opt for these approaches as well.

The impact of the cancer diagnosis is far-reaching and touches the patient’s functional life (the ability to work, be an active participant in family life, etc.) and emotional and spiritual life. Initially, in the midst of making serious decisions regarding treatment, the patient and those close to him or her are dealing with reactions and fears as they try to chart the best course of care. Once the needed medical decisions are made and a course of treatment decided, ongoing care for the patient must be addressed.

The physical side effects of treatment define the cancer experience and carry a strong emotional impact. Hair loss, extreme fatigue, and weight loss are common, especially with many of the chemotherapies. These symptoms often impact family, social, and work roles. It is not uncommon for issues of self-esteem and control to surface as the debilitating impact of treatment ensues.

The emotional swings of treatment must be noted as factors in the bereavement experience. Upon diagnosis, most patients and those close to him or her will experience both shock and hope, assuming the medical prognosis is favorable; that is, the cancer has been diagnosed at a stage that is responsive to intervention. Assuming treatment is successful, the patient and those close to him or her will ultimately move on and are able to put the illness experience in perspective although never without anguish about the potential for recurrence. For those less fortunate, for those for whom the treatment is not successful, the dashing of the initial optimism about the success of treatment is crushing.

The emotional distress can be intense if more surgery is needed or if more chemotherapy or radiation is required. This often can be an emotional turning point as initial optimism about cure or a return to normal life is dispelled. As treatments extend and the patient becomes more debilitated, optimism fades, and the patient may become more emotionally and physically compromised; all involved may have to accept the prospects of death and loss. It has been noted that families undergo a very stressful time when a family member is diagnosed as they must stand by during the period of the illness and intrusive and often harsh treatments followed by a period of terminal illness and death. Factors in a Cancer Death

At various junctures during the illness trajectory, family members may question the care of the patient as they question themselves and their role in the care—did they act quickly enough to get medical treatment for the patient, should they have gotten varied opinions regarding treatment, did they take the patient to the best cancer care centers or hospitals, were they loving enough as the patient’s condition worsened, could they have done more or done it better, were they patient and loving as the struggles mounted?

To complicate some situations, certain types of cancers, especially lung cancer, are often related to behaviors and their link to a cancer diagnosis. Many people believe that there is a cause-and-effect connection between behavior and cancer, that is,
smoking and lung cancer and diet and stomach cancers. This results in bereavement issues that can surely linger and provoke self-blame and anger toward the deceased in the bereaved person.

Cancer is often associated with mutilation of the body, such as that which occurs with mastectomy. Was the adaptation to the surgery handled lovingly, accepted by the caregiver in a way that eased the patient?

In addition, the unknown etiology of cancer has given rise to speculation about the causes of cancer with no clear-cut research that helps explain its cause. This ambiguity can extend bereavement as existential questions about life and how it should be lived abound.

Initially, people with cancer and their families hope for cure or as much quality time as possible; as the disease progresses and becomes terminal, hope is transformed into a statement about dying with dignity and without pain. Suffering due to pain can be one of the pivots complicating the bereavement experience. Was the patient in great pain, were surgeries especially debilitating, was there emotional turmoil and suffering beyond what one should have to endure? These questions may haunt the bereaved person for some time.

In sum, the unique aspects of cancer diagnosis and treatment create difficult and often protracted bereavement issues. In some cases, bereavement can be made even more complex depending on the precancer relationship between the griever and the deceased. In all cases, the demands of care for the cancer patient, the fluctuations of hope and periods of despair when treatment has not succeeded, and the potential for pain and mutilation of the body all combine to make the bereavement due to cancer death a complex experience. Loss of a loved one is never easy. In cancer deaths, bearing witness to extended decline and suffering can create a bereavement of deep anguish and questioning.

Joan Beder
Yeshiva University

See Also: Hospice Care; Pain and Pain Management; Survivors of Cancer, Families of.

Further Readings

Beta-Carotene

Beta-carotene is a pigment that occurs naturally in many photosynthetic plants and organisms and is one of the most abundant carotenoids found in human blood. The richest dietary sources of beta-carotene are yellow, orange, and leafy green fruits and vegetables, such as carrots, spinach, sweet potatoes, and cantaloupe.

There are several mechanisms by which beta-carotene may be able to offer protection against cancer. Beta-carotene acts as a fat-soluble antioxidant to protect plants and animals against free radical-induced oxidative damage to DNA, lipids, and other molecules. Beta-carotene also serves as a precursor to vitamin A and represents the major dietary source of vitamin A for much of the world's population. Through vitamin A action, beta-carotene can exert effects on cellular proliferation and differentiation, immune function, and cell-to-cell communication. Epidemiological studies suggest that a higher dietary intake of carotenoids, including beta-carotene, may offer protection against the development of certain cancers (e.g., lung, prostate, cervix, bladder, gastrointestinal tract, and breast) as well as other health conditions linked to oxidative damage (e.g., heart disease, macular degeneration, and cataracts). However, two large, double-blind clinical trials have shown that supplementation with high doses of beta-carotene do not reduce the risk of lung cancer and may even increase that risk in smokers. These findings have led to an increased effort over the last decade to better understand the mechanisms behind the conversion of beta-carotene to vitamin A and the role of beta-carotene and its metabolites in the process of carcinogenesis.

Beta-Carotene and Cancer

Observational studies have consistently shown that high intakes of fruits and vegetables rich in carotenoids, including beta-carotene, are associated with a decreased risk of cancer at several sites.
A meta-analysis of case-control and prospective studies reported a significant inverse correlation between an increase in fruit intake of 100 grams per day and the risk of lung, bladder, stomach, colorectal, and head and neck cancers, with estimated odds ratios ranging from 0.53 for mouth and pharynx cancers to 0.93 for colon and rectum cancers. There is also a significant inverse correlation between an increase in vegetable intake of 100 grams per day and the risk of cancers of the breast, lung, stomach, colon and rectum, and esophagus. Estimated ratios range from 0.78 for stomach cancer to 0.89 for esophageal cancer. It appears that diets high in fruits and vegetables may offer significant protection against a variety of cancers, and these diets are known to be high in beta-carotene, lycopene, lutein, and other carotenoids. However, it is still unclear whether these carotenoids are conferring this protection or whether they simply are markers for consumption of fruits and vegetables that may contain other chemopreventive agents. Prospective studies provide weaker evidence for chemopreventive effects than do case-control studies, and results from clinical supplementation trials studying the effects of isolated carotenoids on the prevention of primary or secondary tumors have been much less convincing.

Dietary intakes of total vitamin A and beta-carotene, as well as circulating concentrations of beta-carotene, have been strongly and inversely associated with the risk of lung cancer. These relationships were the rationale behind the large, placebo-controlled clinical trials testing the effects of beta-carotene supplementation on lung cancer incidence in high-risk populations. In the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study (ATBC), 29,133 Finnish male smokers age 50 to 69 were randomized into four groups who received either 20 milligrams beta-carotene per day, 50 milligrams alpha-tocopherol per day, a combination of 20 milligrams beta-carotene plus 50 milligrams alpha-tocopherol per day, or a placebo. After five to eight years of follow-up, groups receiving beta-carotene had an 18 percent higher incidence of lung cancer and an 8 percent higher rate of total mortality, while alpha-tocopherol supplementation had no effect on lung cancer. Beta-carotene had little or no effect on the incidence of cancer other than lung cancer. These unexpected results were substantiated when the results from the Beta-Carotene and Retinol Efficacy Trial (CARET) were reported.

In this study, 18,314 male and female smokers, former smokers, and asbestos-exposed workers were randomized to receive either 30 milligrams beta-carotene plus 25,000 international units (IU) retinol per day or a placebo. After four years of follow-up, the trial was stopped early when researchers reported the incidence of lung cancer in the treatment group was 28 percent higher, lung cancer mortality 46 percent higher, and total mortality 17 percent higher than the control group. While these studies did confirm an inverse relationship between baseline dietary and serum beta-carotene and the risk of lung cancer, they also reported a small but significant increase in the incidence of lung cancer in response to beta-carotene supplementation, with this adverse effect more likely to occur in smokers and in those reporting higher alcohol consumption.

A third large study, the Physician’s Health Study (PHS), examined supplementation of 22,071 U.S. male physicians age 40 to 84 with 50 milligrams
beta-carotene every other day. After approximately 12 years duration, this study reported no overall effect of beta-carotene supplementation on total cancer, overall mortality, lung cancer, or lung cancer mortality. Finally, the Women's Health Study (WHS) investigated supplementation with this same 50 milligram dose of beta-carotene on alternate days in 39,876 U.S. female health professionals age 45 and older. After two years of follow-up, there were no significant differences between treatment and placebo groups in overall incidence of cancer, site-specific cancer incidence, or total mortality.

**Study Contrasts**

Two clear differences between the PHS and WHS studies and the earlier ATBC and CARET trials were the serum beta-carotene levels reached in the treatment groups and the environmental exposures of the populations examined. Serum beta-carotene levels in the treatment groups of the ATBC and CARET studies reached 210 to 300 μg/dL, while serum levels in the PHS and WHS treatment groups averaged 120 μg/dL. For comparison, serum beta-carotene levels in the U.S. population generally range from 5 to 50 μg/dL. Second, ATBC researchers studied beta-carotene supplementation in smokers, and CARET researchers studied current and former smokers and asbestos-exposed workers, while the U.S. physicians in the PHS study consisted of only 11 percent current smokers and 39 percent former smokers, and the WHS population consisted of only 13 percent current smokers. Based on these results, beta-carotene supplementation is currently not recommended for the general population, and smokers are especially cautioned to avoid high-dose beta-carotene supplements. Rather, increasing consumption of food sources of beta-carotene and other carotenoids is recommended for reducing the risk of lung cancer in populations. On the other hand, the Linxian (Chinese) Cancer Prevention Study found that supplementation with beta-carotene, vitamin E, and selenium led to a 13 percent reduction in cancer incidence (particularly stomach cancer) and a 9 percent decrease in total mortality. This suggests that correction of preexisting nutrient deficiencies may be important in cancer prevention and that the right combinations of beta-carotene and other antioxidants, through a healthy diet or nutrient repletion efforts, may provide protection against cancer. In addition, recent studies have shown that carotenoids other than beta-carotene (beta-cryptoxanthin and lycopene) can contribute to protection against cancer.

Results from epidemiological studies investigating the intake of beta-carotene on breast cancer outcomes have been inconsistent, with some evidence suggesting that beta-carotene intake and serum beta-carotene may have a protective effect against the development of primary breast cancer and a positive effect on overall survival rate after a breast cancer diagnosis.

With relation to prostate cancer, a beneficial effect of beta-carotene supplementation was observed in a large clinical trial; however, observational epidemiological studies report everything from protection to null effects to a positive association between carotenoid intake and prostate cancer risk. Continued efforts attempt to determine the effectiveness of beta-carotene supplementation against prostate cancer and whether effects are dependent on the dose of beta-carotene administered. Carotenoid intake and serum carotenoid concentrations have been shown to be associated with a lower risk of colorectal cancer in many studies.

However, this effect did not reach statistical significance in two large studies, including a prospective study on fruit and vegetable intake and incidence of colorectal cancer and a case-control study of carotenoid intake and colon cancer risk, where lutein was the only carotenoid studied that was statistically associated with reduced risk of colon cancer. Studies specifically investigating beta-carotene supplementation on risk of adenomatous polyps and other biomarkers of colon cancer showed no significant beneficial effect of supplementation. Therefore, supplementation with beta-carotene is not currently recommended as a strategy to prevent primary or secondary colorectal cancer. Whether intake of other carotenoids or total fruit and vegetable intake can influence colon and rectum cancer risk remains to be seen.

Observational epidemiological studies have also shown inverse relationships between dietary carotenoids, dietary vegetables, and fruits and serum beta-carotene and incidence of cancers of the head and neck, esophagus, stomach, and skin. However, placebo-controlled studies have failed to show consistent protective effects of beta-carotene supplementation against these cancers. Epidemiological
studies suggest a beneficial role for consumption of diets high in carotenoids on the risk and progression of cervical cancer; however, supplemental beta-carotene has failed to show any effects on regression of cervical dysplasia. Results are mixed for studies investigating the role of carotenoids in ovarian cancer. Case-control studies suggest an association between dietary carotenoid intake and reduced risk of this cancer, with alpha-carotene, beta-carotene, and lycopene specifically implicated in these protective effects. While prospective studies have failed to show a significant relationship between dietary or serum carotenoids and risk of ovarian cancer, there is some evidence to suggest that carotenoid intake might be protective in certain subgroups, including adolescents and smokers. Supplementation with beta-carotene or other carotenoids has not yet been studied with relation to risk and progression of ovarian cancer.

**Beta-Carotene Metabolism**

Beta-carotene (C\textsubscript{40}H\textsubscript{56}) has a chemical structure characterized by a large carbon chain with alternating double and single bonds, terminated at each end by a ring structure. In addition to conferring antioxidant properties, these alternating double bonds, called conjugated double bonds, are susceptible to oxidative cleavage and isomerization from trans to cis forms. Cleavage of these double bonds in beta-carotene can result in the formation of potentially bioactive metabolites, including retinoids (vitamin A and its derivatives). While beta-carotene is probably the most well-known of the provitamin A carotenoids and results in the highest beta-carotene yield per molecule, other carotenoids with similar chemical structures can also give rise to vitamin A (e.g., alpha-carotene and beta-cryptoxanthin). In addition to the many functions of vitamin A in vision, reproduction, growth, and immune function, an active form of vitamin A called retinoic acid can serve as a ligand for nuclear retinoid receptors (retinoic acid receptors and retinoid X receptors), ligand-dependent transcription factors that are involved in control of gene expression and cellular differentiation. The molecular mode of action of beta-carotene against cancer can be explained, in part, by the transcriptional activation of genes with distinct antiproliferative activity and by induction of apoptosis by retinoic acid, eliminating cells with unreparable alterations in the genome or killing neoplastic cells.

Two pathways exist for conversion of provitamin A carotenoids to vitamin A, and they are known as the central cleavage pathway and the eccentric cleavage pathway. Central cleavage, or symmetric cleavage, is a major pathway leading to vitamin A formation. In this pathway, the enzyme carotene 15,15'-oxygenase cleaves carotenoids at their central 15,15'-double bond. An alternative pathway for carotenoid metabolism into vitamin A in mammals is the eccentric cleavage pathway, characterized by asymmetric cleavage of beta-carotene at a position outside its central double bond. Recent identification and biochemical characterization of carotene 9,10'-oxygenase demonstrates that this enzyme can catalyze the eccentric cleavage of both provitamin A carotenoids (beta-carotene) and non-provitamin A carotenoids (lycopene). Understanding the actions of carotenoid oxidative metabolites may yield insights into both physiological and pathophysiological processes in human health and disease, particularly the potential for beneficial effects of small quantities of beta-carotene and harmful effects of large quantities of beta-carotene metabolites.

The dosages of beta-carotene used in the ATBC and CARET studies were 20 to 30 milligrams per day for two to eight years, over tenfold higher than the average intake of beta-carotene in the typical American diet (2 to 5 milligrams per day). This pharmacological dose of beta-carotene in humans is believed to result in the accumulation of relatively high levels of beta-carotene and its oxidative eccentric cleavage metabolites in lung tissue, especially after long periods of supplementation. Studies in animal models of lung cancer suggest that beta-carotene is unstable in the free radical-rich environment of lungs exposed to cigarette smoke and that such an environment alters beta-carotene metabolism, increasing eccentric cleavage and producing undesirable eccentric cleavage metabolites. These metabolites have been shown to facilitate a number of changes associated with the carcinogenic process, including induction of carcinogen-activating enzymes, binding of carcinogen metabolites to DNA, interference with vitamin A metabolism, down-regulation of tumor-suppressor genes, upregulation of oncogenes, induction of oxidative stress, and enhanced induction of cell transformation by carcinogens. To better understand the beneficial and detrimental potential for
Beta-carotene in cancer prevention, research is now being conducted to elucidate the mechanistic basis for the bioactivity of carotenoid metabolites. Studies are examining dose effects and the combination of carotenoids with other antioxidants to determine what combinations provide optimal protection against cancer without increasing the formation of undesirable metabolic by-products in smokers and chronic alcohol consumers.

**Tobacco and Alcohol Consumption**

The observation in clinical trials that heavy smokers and drinkers were at an increased risk for lung cancer in response to high doses and high tissue concentrations of beta-carotene has led to an increased effort to understand the mechanisms underlying the relationship between carotenoids and cancer. Studies in animal models of lung cancer, particularly in the smoke-exposed ferret model, have confirmed detrimental effects of pharmacological (supplemental) doses and beneficial effects of physiological (dietary) levels of beta-carotene. Cigarette smoking is associated with substantially decreased plasma levels of beta-carotene despite only slightly lower dietary intakes of carotenoids in smokers compared to nonsmokers.

This suggests that lower levels of β-carotene among smokers may not be due to dietary differences alone. Studies have found that smoke exposure results in decreased cellular antioxidants (e.g., vitamin C and vitamin E) that normally serve to stabilize the reduced form of beta-carotene. The metabolites produced by excessive oxidative cleavage of the beta-carotene in the smoke-exposed lung can interfere with normal vitamin A action and regulation of cellular growth and proliferation. High-dose beta-carotene supplementation, while increasing tissue levels of beta-carotene, has been shown to result in lower levels of lung retinoic acid due to the induction of degradative enzymes (e.g., certain cytochrome P450 enzymes) in animal studies. Furthermore, animals receiving high-dose beta-carotene also show detrimental effects in biomarkers related to cellular proliferation and apoptosis, and these effects are accompanied by precancerous lung lesions when high-dose beta-carotene is combined with exposure to cigarette smoke. On the other hand, animals receiving low-dose beta-carotene, equivalent to the amount contained in five to nine servings of fruits and vegetables, had no evidence of precancerous lung lesions and no changes in molecular biomarkers associated with carcinogenesis, and this level of supplementation was associated with protection against smoke-induced changes in lung retinoic acid levels.

Alcohol also can have a detrimental effect on beta-carotene metabolism and vitamin A action. Interference with vitamin A nutritional status and metabolism is one of the major alterations caused by chronic alcohol intake, and daily consumption of alcohol is related to reduced beta-carotene levels independent of smoking status. Alcohol and vitamin A metabolism involve a similar two-step oxidation process, and these compounds share some of the same metabolic enzymes. Alcohol can interfere with vitamin A metabolism by competing for specific dehydrogenase enzymes, and the hepatotoxicity of alcohol consumption can be exacerbated by high beta-carotene intake.

Chronic and excessive alcohol consumption, especially when coupled with carotenoid oxidative metabolites, can induce the expression of cytochrome P enzymes. These enzymes activate procarcinogens present in alcoholic beverages, tobacco smoke, and diet, leading to increased formation of carcinogen-DNA adducts. The covalent modification of DNA bases by chemicals can alter the structure and biological processing of the DNA by cellular proteins governing replication, transcription, and repair. If not repaired or repaired incorrectly, these modifications may eventually lead to mutations and ultimately cancer, especially if the adduct is located in an oncogene or tumor suppressor gene. In addition, cytochrome P enzymes can break down vitamin A and lead to significantly decreased liver vitamin A stores.

**Antioxidant and Pro-Oxidant Activity**

Beta-carotene has been shown to be an effective antioxidant in vitro, and evidence suggests that this may be one mechanism behind its chemopreventive effects in vivo. Oxidative damage to DNA by free radical species is thought to be a major factor in the initiation and propagation of cancer, and beta-carotene has been shown to reduce DNA damage in vitro, often in combination with vitamins E and C or other carotenoids. However, the antioxidant role of beta-carotene in vivo is more difficult to characterize. Attempts to study this have been complicated by the methodological issues involved in designing
Beta-Carotene

a system to evaluate antioxidant efficiency in living systems. Therefore, while carotenoids have been shown to demonstrate antioxidant activity in certain animal models, beta-carotene from diet and food sources has yet to be clearly shown to act as in vivo antioxidant in human studies.

There exists some evidence that carotenoids might behave as pro-oxidants under certain circumstances. At very high oxygen tension, high concentrations of beta-carotene can have decreased antioxidant activity or possibly even pro-oxidant effects. Based on the evidence presented earlier from the large clinical trials of beta-carotene supplementation in people at increased risk of developing lung cancer, it appears that beta-carotene may act as a protective antioxidant against cancer at physiological levels but may lose its effectiveness or even exert pro-oxidant effects at pharmacological levels, especially in highly oxidative body compartments (e.g., the lungs of a smoker or the liver of a chronic alcohol drinker).

Epidemiological evidence suggests associations between high levels of dietary and circulating beta-carotene and a reduced risk of cancer at multiple sites. However, clinical trials have returned null findings or even evidence of harmful effects of beta-carotene supplementation in certain populations. Studies in animal models of lung cancer have provided possible mechanistic explanations for this discordance. Disruption in vitamin A metabolism and signaling may play a key role in the process of carcinogenesis, and the restoration of vitamin A homeostasis by treatment with beta-carotene could help to maintain normal cell proliferation and apoptosis and may be useful in the prevention and treatment of neoplastic transformations. However, there appear to be detrimental interactions among beta-carotene, cigarette smoke, and alcohol, and the molecular mechanisms that underlie these interactions need to be understood before beta-carotene can be further pursued in the prevention of carcinogenesis in humans.

Recent observations highlight the emerging role of beta-carotene and carotenoid cleavage in vertebrate metabolism and health. The almost ubiquitous expression of carotenoid cleavage enzymes indicates that many tissues may contribute to their own vitamin A homeostasis by endogenous retinoid formation. It appears that, while small quantities of beta-carotene can offer protection against certain cancers and chronic diseases related to free radical oxidation, larger amounts of beta-carotene metabolites may actually be harmful, especially when coupled with a highly oxidative environment, such as the lungs of a cigarette smoker or liver of an excessive alcohol drinker. Oxidative destruction of beta-carotene results in the formation of metabolites that may facilitate the carcinogenic process. Strong interactions among beta-carotene, vitamin E, and vitamin C, and the capability of these compounds to recycle each other, acting as an antioxidant network to regenerate efficient antioxidants from their radical cations, have led researchers to speculate about the potential utility of combined antioxidant therapy in vivo. It is possible that this additional protection against oxidative degradation may increase the utility of nutritional interventions targeting lung cancer in smoke-exposed models, surpassing effects seen in single-agent intervention studies.

The mechanisms behind the chemopreventive effects of carotenoids are not completely known. In addition to antioxidant activity, beta-carotene and other carotenoids may exert biological activity through stimulation of gap junction intercellular communication, induction of detoxifying enzymes, interaction with hormonal growth factors, and inhibition of cellular proliferation. As we await better scientific understanding of carotenoid metabolism and mechanisms of action, a prudent strategy to reduce the risk of cancer incidence and mortality would include increased consumption of vegetables and fruits as part of a healthy, balanced diet. Experts recommend eating between five to nine servings of fruits and vegetables every day.

Given that beta-carotene found in the diet is around six times less bioavailable than supplemental beta-carotene, there is currently no evidence of any dangers associated with high levels of dietary beta-carotene from natural food sources, aside from the occasional appearance of carotenodermia, an accumulation of beta-carotene in the skin that gives it a yellow or orange tint. At this time, supplemental doses of beta-carotene beyond the recommended dietary intake to meet vitamin A needs (700–900 μg retinol activity equivalents per day) are not advisable for the general population. Beta-carotene supplements seem to offer no protection against cancer, heart disease, or mortality in healthy populations of nonsmokers. Smokers and other populations with exposure to high levels of environmental oxidants, as well as those who drink more than one
alcoholic drink per day, are especially encouraged to avoid high doses of supplemental beta-carotene.

Heather Mernitz  
Xiang-Dong Wang  
*Tufts University*

**See Also:** Alcohol; Diet and Nutrition; Tobacco  
Smoking; Vitamins.

**Further Readings**

Krinsky, Norman I. and Elizabeth J. Johnson.  

---

**Bicycles**

In its simplest form, a bicycle is a lightweight frame with two wheels designed to be propelled by pedaling. Credit for the invention is generally given to Baron von Drais, who invented a walking machine in 1817. The user straddled the wooden frame and rolled forward by pushing off with alternating feet against the ground. Obviously, several iterations were required before the modern bicycle assumed its final form.

Some have described the bicycle as the most efficient form of transportation ever devised. It is particularly well adapted to commuting short distances, and in many parts of the world, substantial numbers of people use bicycles as their primary means of everyday transportation. It is particularly when people choose to bicycle rather than to drive that the benefits of this alternative means of transportation become apparent from the medical standpoint.

**Potential Adverse Effects and Benefits**

There are, unfortunately, some potential adverse effects as well. One researcher mapped the distribution of ultraviolet exposure on various anatomic sites of cyclists during a seven-day bicycle ride in Australia. Substantial exposure of even vertically oriented areas such as the lower leg were documented. Thus cyclists, as any other participants in outdoor activities, may be at increased risk of developing skin cancers unless adequate precautions are taken. Another research team documented that individuals who cycled in traffic were exposed to increased levels of carbon monoxide, nitrous oxide, nitrogen dioxide, and ultrafine particles, all of which may have an adverse effect on health. And, the cyclist must observe safe cycling behavior to avoid accidental injury. However, the preponderance of evidence suggests that increased use of bicycles as alternative means of transportation (as opposed to motor vehicles) provides several advantages. First, the bicycle commuter automatically gets a certain amount of outdoor exercise every day that he or she chooses the bike over the automobile. Second, when large segments of the population choose alternative means of transportation, including bicycles, the levels of airborne pollutants may decrease, with attendant health benefits to the population. Similar benefits occur when individuals choose to walk or jog rather than use motor vehicles; however, because the bicycle is a more efficient means of covering moderate distances, most of the effort has concentrated on bicycling as an alternative.

**Benefits to the Cyclist and Community**

The most direct evidence for potential benefit to the individual comes from epidemiologic studies that demonstrate that increased physical activity and decreased obesity (both characteristic of the use of alternative transportation such as bicycling) are associated with decreased incidence of carcinoma. For example, a rapid increase in colon cancer incidence has been noted in Shanghai, China, over recent decades. Researchers examined the effects of physical activity (primarily commuting by alternative transportation) in a case-control study and noted that colon cancer risk was significantly reduced among subjects with high commuting
physical activity. In San Francisco, breast cancer risk was noted to be decreased in women with high lifetime levels of physical activities (including bicycling). Similar results were noted in studies from Finland and Norway.

The decreased risk of obesity associated with increased physical activity may account for some of these observations, and there is clear evidence for a link between obesity and increased risk of some malignancies. For example, the Nurses’ Health Study Research Group documented an association with increased metabolic equivalent (MET)-hours per week of physical activity and decreased risk of colon cancer and supported the concept that obesity was detrimental. Similar effects have been noted with non-Hodgkin’s lymphoma and breast cancer.

Recently, data have emerged suggesting that vitamin D may help to protect against cancer development. It is tempting to speculate that daily outdoor exercise (avoiding excessive sun exposure as already noted) might provide additional vitamin D; however, data to support this hypothesis are at present lacking.

When large percentages of a population use alternative means of transportation, congestion on roads is decreased, and airborne pollutants diminished. In 1999, the city of Vancouver did a study and found that individuals who chose to commute to work or school by bicycle did so on a daily basis.

A similar study in California found that the potential length of a commute did not appear to adversely affect the likelihood of opting to bicycle rather than drive. Other studies have shown that bicycle commuters in areas where networks of trails are available may travel as much as an average of seven miles in their commutes; clearly, this is a greater distance than most people would be willing to walk or jog, but it is a bikeable distance.

Communities can encourage the use of alternative means of transportation by developing networks of trails and providing information such as trail maps. Employers can provide bicycle racks and areas where employees can change clothes if necessary. Other strategies include urban planning, which clusters housing, employment, and stores within bikeable or walkable distances. Communities can also encourage cycling by providing bike-sharing programs. In recognition of the importance of these activities, May 18 has been designated Bike to Work Day.

The use of alternative means of transportation such as bicycles provides individuals with an easy way to obtain daily exercise. In addition, by decreasing reliance on internal combustion engines (cars), urban pollution and congestion may be decreased.

Carol Scott-Conner
University of Iowa
Bile Duct Cancer, Extrahepatic

Extrahepatic bile duct cancer is considered a rare form of cancer that creates malignant cells that settle in the ducts that are located outside the liver. However, there are more than 22,000 cases of cancer involving the liver and bile ducts reported every year. There are two different parts of the bile duct that are associated with the extrahepatic bile duct:

- Common hepatic duct, which is also referred to as the perihilar part of the extrahepatic duct
- Common bile duct, which is also referred to as the distal part of the extrahepatic duct

The common bile duct and the common hepatic duct are part of the major connections in the gastrointestinal tract, which include the liver, gallbladder, and small intestine. Part of the digestive process in the body, the liver is the reservoir for the bile. Bile is the liquid that is responsible for destructing fats during the digestive process. Bile moves through the extrahepatic duct to the gallbladder that houses the bile.

Risk Factors
Because the extrahepatic duct has a major involvement in the digestion process of the gastrointestinal tract, there are several risks that could predispose an individual to the possible development of extrahepatic bile duct cancer:

- History of colitis that affects the movement of bile through the ducts
- Primary sclerosing cholangitis, which involves the scarring of the bile ducts that can lead to the formation of cancer cells in the bile ducts
- Development of chronic ulcerative colitis, which causes a disturbance in the gastrointestinal tract that can weaken the bile ducts
- Formation of choledochal cysts, which are congenital deficiencies within the bile ducts that can cause the development of cysts to block the ducts
- Development of an infection that involves contracting a Chinese liver fluke parasite

Symptoms of Extrahepatic Bile Duct Cancer
Some of the symptoms or characteristics of extrahepatic bile duct cancer can mimic those that are associated with other diseases and conditions that affect the gastrointestinal tract. Because of these similarities with the symptoms, individuals should report these symptoms to medical professionals to ensure proper treatment is given. Possible symptoms of extrahepatic bile duct cancer include the following:

- Yellowing of the skin, also known as jaundice
- Chronic abdominal pain
- Fever
- Urticaria or intense itching of the skin—hives will appear on the skin with the intensity of the itching

Staging of Extrahepatic Bile Duct Cancer
Like with any type of cancer, extrahepatic bile duct cancer is classified in various stages. There are five different stages of extrahepatic cancer that deal with the early stages of the conditions to the hardest stage, where the cancer has spread to other parts of the body and requires more invasive treatment. In addition to the stages, there are different
subcategories that break further down how to stage extrahepatic bile duct cancer.

**Tests or Diagnostic Tools for Extrahepatic Bile Duct Cancer**

There are several tests or diagnostic tools that medical professionals use to diagnose and treat extrahepatic bile duct cancer. Most of the testing that is done for extrahepatic bile duct cancer is also used to test and treat for diseases and conditions that affect the liver and the rest of the gastrointestinal system. One examination includes getting a detailed history that pertains to the individual’s symptoms or characteristics of problems with the gastrointestinal process.

An ultrasound employs the use of intense energy waves that surround the organs and tissues to detect any abnormalities—once the test is completed, a sonogram is printed out to review for any problems or abnormalities. A medical professional may order a computed tomography (CT) scan or magnetic resonance imaging (MRI) that is able to highlight and identify any areas that could be affected by any diseases or conditions. A more detailed test such as a positron emission tomography (PET) scan is used widely to identify cancerous cells in the body; this test involves using glucose that can be picked up in the tissues in the body—more glucose will be absorbed in the areas where the cancerous cells are found.

A biopsy may be performed to extract suspect cells from the body through a fine needle aspiration (FNA)—diseased tissues and cells can be taken out during this procedure. A doctor may order endoscopic retrograde cholangiopancreatography (ERCP) to take film of the ducts that transport bile from the liver to the gallbladder and from the gallbladder to the small intestine to detect any abnormalities with the ducts; there is a chance that extrahepatic bile duct cancer can develop when a narrowing of the bile duct occurs, causing a slow movement of bile, which in turn causes jaundice—this test involves using an endoscope and catheter to view the pancreas and smaller ducts; during the procedure, tissue samples can be obtained as well as the stones in the bile duct possible being removed. A specialized test, percutaneous transhepatic cholangiography (PTC), is ordered to take film of the liver and bile ducts—a thin tube injected with dye can detect abnormalities with the liver and bile ducts.

Tests that include monitoring liver function can aid in detecting problems with the liver, gallbladder, and gastrointestinal tract.

A tumor marker test can be performed to detect two antigens that identify extrahepatic bile duct cancer—these two antigens, carcinoembryonic antigen (CEA) and CA 19-9, become increased in the body to alert medical professionals to rule out extrahepatic bile duct cancer—this test involves samples from urine, blood, and tissue that are monitored to assess the presence of cancer cells in the body, including the gastrointestinal tract.

**Treatments for Extrahepatic Bile Duct Cancer**

With respect to the staging of extrahepatic bile duct cancer, this helps medical professionals develop treatments to help individuals with their battles with cancer. There are several treatment options for extrahepatic bile duct cancer:

- Surgical treatment that includes removing the malignant cells from the bile ducts—this is the first treatment option
that is explored if the cancer is in the early stages or when the cancer is not that advanced
• Therapy that involves radiation
• Chemotherapy that also can be combined with radiation
• Palliative therapy—this includes alternative therapy to handle and help manage the effects the disease has on the patient and caregivers both physically and mentally—this treatment is aimed at approving the quality of life for everyone involved in taking care of the person who is dealing with the aftermath of treatment for cancer.

Cindy Ferraino
Independent Scholar

See Also: Chemotherapy; Hepatocellular (Liver) Cancer, Adult (Primary); Hepatocellular (Liver) Cancer, Childhood (Primary); Liver Cancer, Adult (Primary); Liver Cancer, Childhood (Primary); Unusual Cancers of Childhood.

Further Readings

Biologic Therapy

Biological or biologic therapy is the use of living organisms, the substances derived from them, or laboratory-produced synthetic formulations of those substances in order to treat illness, including cancer. Common biological therapy strategies are using such therapeutic substances either to attack cancer cells or to assist the body’s immune system in doing so. Types of biological therapies include cell-based therapies like vaccines, monoclonal antibody therapies, cytokine therapies, and experimental approaches like gene therapy.

There are numerous Food and Drug Administration (FDA)-approved biological therapies and more in the development stage sometimes available to cancer patients as part of clinical trials. Related terms are immunotherapy or biological response modifier therapy—therapies that stimulate the immune system—and targeted therapies, those therapies that target and eliminate cancer cells. Biological therapies may also treat the side effects of other cancer treatments, such as chemotherapy. Increasingly, the term *biologic* (as a noun, as in “Ask your doctor about taking a biologic”) is used to refer to biological therapy products.

The immune system’s ability to fight infection and disease is predicated on its ability to distinguish between foreign and host (self) tissue, which is precisely why cancer is difficult for it: Tumor cells are the patient’s own cells, not a foreign infection. However, tumor cells also display antigens that would normally not be found in that environment or that cell type, which makes it possible to target them, such as through monoclonal antibodies, the first technique developed in immunotherapy.

One of the earliest biological treatments for cancer was Coley’s toxins or Coley’s vaccine—a mixture of dead *Streptococcus pyogenes* (responsible for many strep infections) and *Serratia marcescens* (responsible for many hospital-acquired infections) bacteria, with the intention of provoking an immune response that would work against tumor cells.

It is named for its developer, William Bradley Coley, who first prepared it in 1893. Radiation therapy overtook Coley’s toxins as the preferred treatment, and from 1923 until 1962, the preparation was available only from Parke-Davis. The new FDA regime following the passage of the Kefauver Harris amendment of 1962 (in response to the thalidomide disaster) effectively took Coley’s toxins off the market by classifying them as a new drug requiring clinical trials. Today, they are part of cancer research and clinical trials conducted by Pfizer and Sanofi-Aventis and are available as a treatment from specialists in Germany.
Monoclonal Antibodies

Monoclonal antibodies are a type of monospecific antibody, antibodies with the affinity for the same antigen (any substance that provokes a response from the immune system, which in the case of cancers is usually but not always a protein), produced by cloning a parent immune cell. The generic name of monoclonal antibody therapies ends in -mab by convention, and doctors sometimes refer to them collectively as “mabs.” (Other naming conventions include -tumu- for fully human mabs like panitumumab; -tumo-, -govo-, -pro-, or -colo- for those derived from mice; -tuxi- for chimeric mabs; and -tuzu- for humanized mabs.) Monoclonal antibody therapies were first proposed in the early 20th century by Paul Ehrlich’s description of a “magic bullet” treatment; this work led to the first treatment for syphilis and the beginning of chemotherapy. The first real mab treatments for cancer were developed in the 1970s by Georges Kohler, Cesar Milstein, and Niels Kaj Jerne, who shared the 1984 Nobel Prize in Medicine for their work. Initially cloned from the cells of nonhuman animals, these therapies could result in side effects even after processes were pioneered in the 1980s to humanize the antibodies. A number of commercial technologies have been developed using transgenic mice to produce fully human antibodies.

Monoclonal antibodies used as cancer treatments include mabs designed to induce an immunological response against the cancer cell or to deliver a substance to attack the cancer. Mabs are given intravenously, usually every two weeks; a typical course of treatment can cost around $30,000. Mabs may also be designed as bispecific monoclonal antibodies, which combine fragments of multiple mabs in order to bind to multiple antigens. This is an approach almost entirely unique to cancer treatments. Bispecific mabs have a higher cytotoxicity; that is, they are deadlier to the cells they target.

Bevacizumab is a humanized mab derived from mice, used to treat colorectal, lung, breast (until revoked for this use in 2011), renal, and brain cancer by slowing angiogenesis (the growth of new blood vessels). It was the first angiogenesis inhibitor approved in the United States and was used first in combination with chemotherapy for metastatic colon cancer in 2004. Side effects include hypertension and a possible worsening of artery diseases.

Cetuximab is an epidermal growth factor receptor inhibitor, a chimeric (mouse and human) mab used to treat some colorectal, lung, and head and neck cancers. In the United States, it is marketed under the trade name Erbitux (manufactured by Eli Lilly). Side effects can include a pimple-like rash, fevers, chills, rigo, dizziness, photosensitivity, and respiratory difficulties. In 2013, it was one of the 10 top-selling cancer drugs.

Panitumumab is a newer fully human mab, an epidermal growth factor receptor inhibitor used in the treatment of colorectal cancer. Because it is fully human (developed from the XenoMouse transgenic mice platform), it inflicts fewer side effects than cetuximab while operating with a similar mechanism of action.

Trastuzumab is a humanized mab used mainly to treat breast cancers by interfering with HER2/neu receptors. It has been shown to increase survival in metastatic breast cancer by several months and to reduce the risk of cancer recurring after surgery in early-stage breast cancer by almost 10 percent. Side effects include flu-like symptoms and, in less than 8 percent of cases, cardiac dysfunction that prevents it from being taken by patients with preexisting heart problems.

Ipilimumab, marketed as Yervoy, is a mab developed by Bristol-Myers Squibb to treat melanoma. It is also undergoing trials as a treatment for non-small cell lung carcinoma, small cell lung cancer, bladder cancer, and metastatic hormone-refractory prostate cancer. It is expensive even by mab standards, costing about $120,000 for a course of treatment.

Ofatumumab is a fully human mab sold under the trade name Arzerra to treat chronic lymphocytic leukemia, follicular non-Hodgkin’s lymphoma, diffuse large B cell lymphoma, and rheumatoid arthritis.

Ibritumomab tiuxetan, sold under the trade name Zevalin, is a mab radioimmunotherapy treatment that utilizes ibritumomab in conjunction with a radioactive isotope in order to treat non-Hodgkin’s lymphoma. Non-Hodgkin’s lymphoma can also be treated with tositumomab (trade name Bexxar), though tositumomab was discontinued in 2014 due to a decline in prescriptions being written for it.

Hodgkin’s lymphoma and systemic anaplastic large-cell lymphoma can be treated with Adcetris,
Biologic Therapy

the trade name for brentuximab vedotin, which was approved by the FDA in 2011. Though clinical trials were largely promising, it has been linked with two cases of progressive multifocal leukoencephalopathy, a fatal viral disease causing progressive damage of the brain's white matter, seen almost exclusively in patients receiving certain kinds of chemotherapy or mabs and in acquired immune deficiency syndrome (AIDS) patients.

Acute myelogenous leukemia was once treated with gemtuzumab ozogamicin, a humanized antibody marketed as Mylotarg from 2000 to 2010, but it was removed from the market after a clinical trial showed that there was no benefit over conventional therapies and that patient death actually increased. Several leukemias, as well as transplant rejection and many lymphomas, can be treated with the chimeric mab rituximab, marketed as Rituxan, MabThera, and Zytux. Rituximab was developed in 1998, and the patent will expire in 2015, making it one of the few mabs available as a generic. Chronic lymphocytic leukemia, cutaneous T-cell lymphoma, and T-cell lymphoma can be treated with alemtuzumab under the trade names Campath, MabCampath, and Campath-1H. It also is sometimes used in kidney or bone marrow transplants and for treatment of steroid-resistant, graft-versus-host disease after bone marrow transplant. Its most significant side effect is the increased risk of opportunistic infections, with other side effects including flu-like symptoms, rash, arrhythmia, and respiratory arrest.

Humanizing with respect to mabs means that, after antibodies have been harvested from mice, genetic engineering is used to replace as many mouse portions of the antibody with human portions as possible. Without this process, the antibody itself can provoke an immune response. Fully human mabs are still derived from mice, but transgenic—that is, genetically modified—mice that can carry human tissue, much like the mice on which human ears are grown for transplant purposes. Human immunoglobulin genes are transferred to these mice, which are then vaccinated against the antigen in order to stimulate production of mabs.

Recent work has focused on developing immunoliposomes, liposomes that can carry drugs and are conjugated with mabs in order to target cancer cells. Tissue-specific tests have been successful with brain and breast cancer tissue, and clinical trials are presumed to lie in the near future.

Monoclonal antibodies also are used to treat autoimmune diseases like Crohn’s disease, asthma, and viral infections to prevent coagulation during angioplasty and in kidney transplant patients.

Cancer Vaccines

A number of vaccines have been developed to treat existing cancer; none has yet been shown to function as a general immunization against cancer, though cancers caused by viruses can be prevented by the administration of vaccines like the human papillomavirus (HPV) vaccine and hepatitis B vaccine. The HPV vaccine prevents infection by human papillomavirus, the most common sexually transmitted disease in the world, which is responsible for the development of 70 percent of cervical cancers, 80 percent of anal cancers, 60 percent of vaginal cancers, and 40 percent of vulvar cancers. The World Health Organization recommends universal HPV vaccination for young women, specifically to prevent cancer. Men are at risk principally if they have sex with men, but vaccination helps protect their partners. The hepatitis B vaccine, which has been routinely recommended for infants since 1991, also prevents liver cancer because it had been demonstrated for years that liver cancer is caused by hepatitis B. Despite this, liver cancer remains one of the most common cancers in the world, principally in China and Africa.

Bacillus Calmette-Guerin (BCG) vaccine is a tuberculosis (TB) vaccine that is one of the most basic medications in modern medicine. In addition to its use as a vaccine in parts of the world where TB is endemic, it is used for leprosy, for type 1 diabetes, and as a cancer treatment. Injecting BCG into the bladder, for instance, is an effective immunotherapy for bladder cancer, though the mechanism is not well understood. It has since been used for colorectal and lung cancers as well as melanoma.

BCG is the only cancer vaccine approved worldwide for clinical use, but there are more than two dozen in various stages of development, including GlaxoSmithKline’s melanoma vaccine and Merck’s vaccine for breast cancer. Merck’s vaccine, Tecomotide, formerly known as Stimuvax, was developed in collaboration with Canadian biotech company Biomira. A study of tecemotide as a treatment for non–small lung cancer ended in 2014.
after no improvement was shown, but trials continue as a breast cancer therapy.

In the United States, Supluecel-T, marketed by Dendreon under the trade name Provenge, is an FDA-approved, cell-based therapy for prostate cancer, costing about $100,000 per patient. An autologous cancer vaccine treatment, it uses the patient’s own white blood cells, which are treated and incubated with a prostate cancer antigen and granulocyte-macrophage colony-stimulating factor before being reinjected into the patient. Clinical trials, which began in 2001, showed consistent survival benefits. Side effects include flu-like symptoms. Dendreon is also developing Neuvenge, a modification of Provenge for treating bladder and breast cancers.

In Cuba, the first lung cancer vaccine was released in 2011. CimaVax-EGF was developed at Cuba’s Center of Molecular Immunology.

In Brazil, HybriCell was released, a cancer vaccine for the treatment of late-stage melanoma or kidney cancer. It uses autologous leukocytes to attack the tumor cells and showed an improvement rate of 80 percent in clinical trials.

Cytokines

Cytokines are a group of proteins that are released by cells for cell signaling purposes and influence the behavior of other cells. They are important parts of the immune system, helping to regulate immune responses as well as responses to inflammation, trauma, infection, and cancer. Genetically engineered cytokines have been used as therapies for various conditions, including hepatitis, multiple sclerosis, anemia, and both cancer and side effects of cancer or cancer treatments. Interleukins, for instance, are cytokines released by white blood cells (leukocytes). Interleukin 2, which is key in the body’s ability to discriminate between host and foreign tissue, has been adapted for the treatment of renal cell cancer and malignant melanoma under the trade name Proleukin. Proleukin has also been used in conjunction with the Gp100:209-217(210M) cancer vaccine, using amino acid residues of melanoma antigen. Interleukin 11, derived from marrow stromal cells, is marketed as oprelvekin to treat thrombocytopenia (the decrease in blood platelets) in cancer patients. Granulocyte-macrophage, colony-stimulating factor and granulocyte-colony stimulating factor are cytokines used to treat chemotherapy patients to help stimulate the production of white blood cells.

Adoptive Cell Transfer

Adoptive cell transfer is the transfer of immune system cells—usually autologous, that is, the patient’s own cells—back into the patient in order to promote immune system function. For instance, this can help combat graft-versus-host disease in bone marrow transplants. The adoptive transfer of tumor-infiltrating lymphocytes has also been used to treat advanced tumors like melanoma and colorectal carcinoma.

Oncolytic Viruses

An oncolytic virus is one that infects and kills cancer cells, which then release new virus particles that move on to destroy more cancer cells. They may also help stimulate immune responses in the
host. Oncolytic viruses as a cancer therapy was conceived of in the early 20th century after observations that some cancer regressions seemed linked to infection by viruses, and attempts to treat cancer through deliberate viral infection began in the middle of the century. Early research focused on poliovirus and other existing viruses in the search for a naturally occurring oncolytic virus, absent the technology to tailor a virus to order. Controlling the infection proved difficult, though at the other end of the spectrum, it was also difficult to prevent the immune system from destroying the virus before it could attack the cancer.

Many of the viruses explored as cancer killers are adenoviruses, a family of nonenveloped viruses originally derived from human adenoids. Adenoviruses are also used as vectors in gene therapy (particularly in treating cystic fibrosis), due to their ability to accommodate large transgenes and affect both replicating and nonreplicating cells.

In the 1990s, clinical trials were conducted using modified herpes simplex viruses to selectively attack cancer cells. Herpes was selected due to its relative harmlessness in the event of infection and the ease with which the virus can be manipulated. Clinical trials on patients with glioblastoma multiforme brain tumors showed no evidence of toxicity or serious side effects and may have assisted in long-term survival. Subsequent trials have targeted melanoma, squamous-cell carcinoma of the head and neck, and other cancers. The first positive phase 3 study for an oncolytic virus in the West ended in 2013, with Amgen's T-VEC (originally developed under the name OncoVEX GM-CSF), a herpes-based virus treatment for advanced melanoma. China had previously approved Shanhai Sunway Biotech's H101, a genetically modified adenovirus targeting head and neck cancer.

**Gene Therapy**

Gene therapy delivers therapeutic DNA to a patient's cells, usually in order to replace a mutated gene with functional DNA. The package with which therapeutic DNA is delivered (usually a virus) is called a vector. Gene therapy has been developed since 1972 and was used first on humans in 1990 in an immunodeficiency treatment. The field saw numerous clinical failures in the 20th century, but the 21st century has seen an upswing in gene therapy successes, and research investments have increased substantially since 2006. One of the dangers of gene therapy is the possibility of inducing a tumor if the therapeutic DNA is mis-integrated in the genome; this has occurred in clinical trials, resulting in several patients developing leukemia, one of whom subsequently died.

Gene therapy remains experimental: Cancer patients who are treated with it are participants in clinical trials for products that eventually may or may not be approved for the market. The only gene therapy treatment approved for the market in either the United States or Europe is Glybera, used in treating lipoprotein lipase deficiency and introduced commercially in 2014. However, it is widely suspected that gene therapy is on the cusp of a commercial breakthrough and that several cancer treatments under development will be available in the coming years—at least to some. Glybera, for instance, costs roughly $1.6 million per patient.

**Trophoblast Glycoprotein**

Trophoblast glycoprotein (TPBG) is not a biological therapy, but its discovery has been important to the development of such therapies. A human protein encoded by a TPBG gene, it is an antigen released by many different carcinomas. It was first discovered in fetal trophoblast and so is sometimes called oncofetal antigen. Its expression by the cancer cells of colorectal, ovarian, and gastric cancers is used as a prognostic measure, and it has been targeted by two different biologic therapies: a monoclonal antibody immunological therapy called mab5T4 (5T4 is another name for TPBG) and the cancer vaccine TroVax.

Bill Kte’pi

Independent Scholar

**See Also:** Clinical Trials; Gene Therapy; Vaccines.

**Further Readings**


Bladder Cancer

Cancer of the urinary bladder represents the ninthmost common type of malignancy worldwide. More than 386,000 cases of bladder cancer are diagnosed annually worldwide, and more than 150,000 patients die of the disease each year. The hollow bladder is designed to store urine and has a specialized epithelial lining—transitional cell epithelium or urothelium—that is capable of stretching. Bladder cancers generally arise from alterations in cells within this epithelial layer, although they may also include other rare tumors of nonepithelial origin. It is primarily a cancer of adults, with men being more commonly affected. Prognosis depends on the stage of the tumor, and treatment may involve multimodal therapies including surgery, immunotherapy, chemotherapy, and radiation.

In developed countries, tobacco smoking is considered the most important risk factor for bladder cancer. There is a linear relationship between smoking and risk, and quitting smoking has been shown to reduce this risk. In addition, exposure to aromatic amines (e.g., in occupations that involve dyestuff and rubber manufacturing, leather processing, aluminum smelting, painting, hairdressing, and truck driving), arsenic, and chemotherapeutic agents such as cyclophosphamide have been suggested to increase the risk. Infection with *Schistosoma haematobium*, a bladder fluke commonly found in Africa and the Middle East, has been associated with the development of squamous cell carcinoma, a particularly aggressive type of bladder cancer in that region. Bladder cancer development and progression is also associated with mutations in HRAS, FGFR3, and P53 genes in some cases.

The most common presenting symptom is the presence of blood in the urine, which may be visible to the naked eye or may only be detected by a microscope or specialized dipsticks. Other possible symptoms include pain during urination, frequent urination, or feeling the urge to urinate without being able to do so, although these may not be specific for the presence of cancer. Nevertheless, patients with these complaints need to be evaluated thoroughly to determine the cause of their urinary symptoms. Patients are often initially referred to a urologist to undergo a cystoscopy, a procedure where a flexible tube with a camera is introduced into the bladder through the urethra. More recently, cystoscopy may be also performed under Cysview/Hexvix guidance (blue light cystoscopy), which can reveal lesions that may not be visible with standard white light. Suspicious lesions within the bladder are biopsied and sent for pathologic analysis. Urine cytology may also be used as an adjunct diagnostic test, although it is not very sensitive. Urine-based marker assays have also been used recently for diagnosis and detection of recurrence, including nuclear matrix protein 22 (NMP22) and UroVysion.

Treatment and eventual prognosis of bladder cancer generally is dependent on the stage of the primary tumor, the presence of any metastases to lymph nodes or other organs, and the degree of tumor cell differentiation. Superficial tumors that do not invade the muscle layer of the bladder wall are generally resected transurethrally under cystoscopic view. These tumors have a high tendency to recur following initial resection. Patients with such tumors may therefore also be offered immunotherapy by intravesical delivery of bacillus calmette-guérin (BCG) to prevent tumor recurrence. BCG is a vaccine against tuberculosis that is prepared using attenuated live *Mycobacterium bovis*, a bovine tuberculosis bacillus.

While the exact mechanism by which BCG prevents recurrence is unknown, it is suggested that the presence of bacteria in the bladder triggers a localized immune response that clears residual cancer cells. Intravesical chemotherapy instillations may also be used to treat BCG-refractory disease when cystectomy is not an option. While patients undergoing such bladder-preserving procedures generally retain their voiding function, they need to be monitored closely at regular intervals to determine whether the cancer has recurred or progressed to a higher stage.

Patients whose tumors recur after treatment with BCG and those who present with muscle-invasive disease are generally advised to undergo cystectomy. This is a more radical surgery where the bladder is partially or completely removed, and adjoining lymph nodes may also be dissected. This usually also includes removal of the prostate in males, and ovaries, uterus, and parts of the vagina in females. The urinary stream is diverted into an isolated loop of bowel (called an ileal conduit). In some cases, a substitute bladder (called a neobladder) may be
reconstructed from a segment of intestinal tissue, but this may depend on patient preference, age, renal function, and extent of disease. Micrometastatic disease is a major issue in muscle-invasive cancer, which refers to the possibility of few cancer cells being disseminated to distant organs that can subsequently give rise to metastases. This has implications on long-term survival, and patients with muscle-invasive tumors are often administered neoadjuvant chemotherapy to address this problem. This involves administration of anticancer drugs such as gemcitabine and cisplatin prior to cystectomy to reduce the size of the tumor and kill any potential micrometastatic tumor cells. Following radical cystectomy, and depending on patient performance and tumor stage, adjuvant chemotherapy may also be administered. In this setting, the role of chemotherapeutic drugs is to kill any small foci of tumor cells that may not have been resected at the time of surgery. A combination of radiation and chemotherapy may also be used as an alternative to radical surgery to treat invasive disease. The comparative effectiveness of this form of treatment to radical cystectomy has not yet been fully determined.

Tumor recurrence following radical cystectomy unfortunately heralds a grave prognosis. Most recurrences following cystectomy usually occur within the first two to three years, and if a patient does recur, the survival following recurrence is generally less than two years. However, few patients have a more prolonged survival following recurrence, especially if the tumor recurs in the upper urinary tract or urethra. In such cases, patients may undergo surgical resection of the recurred tumor. Metastatic disease at other organ sites, however, may not be amenable to surgery. Such patients are often administered salvage chemotherapy to limit the disease progression.

Bladder cancer is a major malignancy with debilitating consequences that can impact long-term survival and quality of life. Current treatment options include a gamut of modalities that are dependent of extent of the tumor, patient performance, and patient preference. While early aggressive management is generally successful, the nature of the disease requires lifelong follow-up to monitor for cancer recurrence.

Anirban P. Mitra
University of Southern California

See Also: Bladder Cancer, Childhood; Chemotherapy; Radiation Therapy; Surgery.

Further Readings

Bladder Cancer, Childhood

The National Cancer Institute lists carcinomas of the urinary bladder as an unusual cancer of childhood, referring to its extreme rarity. Bladder cancers are more common in men than in women and in the age group of 50 to 70 years. In contrast, less than 1 percent of bladder cancers are detected in patients within the first two decades of life. The rarity of this tumor is reflected in the fact that only small series have been described in the literature. In fact, only more than 100 cases of transitional cell carcinoma of the bladder in children have been reported since 1950. In contrast to adults, most bladder carcinomas in children are low grade and superficial and have a good outcome following surgical resection.

The urinary bladder is normally lined by a layer of specialized epithelium called transitional epithelium (or urothelium). This layer is designed to withstand constant stretching when the bladder distends to store urine. Bladder cancer usually originates from this layer and is referred to as transitional cell carcinoma. This also represents the most common type of bladder cancer in childhood. Advanced tumors may infiltrate the underlying muscle layers before involving the entire bladder wall and metastasizing. More aggressive tumors such as squamous cell carcinomas have also been reported to involve the urinary bladder. In this scenario, the overlying
urothelium transforms into an abnormal flat layer of epithelium similar to the skin that is incapable of stretching. This may occur due to genetic alterations or may be seen with chronic infections with bladder flukes (*Schistosoma haematobium*). Bladder cancer in adolescents may also develop as a consequence of alkylating agent chemotherapy given for other childhood tumors or leukemia. The association between the chemotherapeutic agent cyclophosphamide and bladder cancer is the only major established relationship between a specific anticancer drug and a solid tumor. Another rare group of bladder tumors arising from the underlying muscular wall of the organ is called rhabdomyosarcoma. Originating from cells that have primitive features of muscle cells, these generally tend to occur in boys and respond favorably to treatment. It should also be noted here that exposure to secondhand smoke among children increases their risk of acquiring bladder cancer during adulthood by nearly 40 percent.

As in adults, bladder cancer in childhood is relatively more common in males than in females. Children generally present with the painless passing of blood in urine (referred to as hematuria). This may or may not be accompanied by increased frequency of urination and pain during urination. Blood in the urine, however, is not a definitive sign for bladder cancer, and a thorough workup of the patient is essential before a diagnosis is reached. Most bladder tumors in children are generally of low stage and have a low grade of malignancy, with little tendency to recur following surgical resection. A preliminary diagnosis may be made on the basis of examining cells shed in the urine (i.e., cytology) in conjunction with imaging tests such as CT scans, MRI, and ultrasonography.

Urinary cytology alone may not be sufficient to definitively diagnose all cases of childhood bladder cancer as its sensitivity may be limited especially if the tumor is low grade. A diagnosis is usually established based on cystoscopic evaluation wherein the surgeon places a small, hollow viewing tube through the urethra to visualize the bladder. Any abnormal tissue is usually biopsied and sent for pathologic evaluation. Definitive treatment in children is generally surgery, which often involves removal of the tumor tissue by cystoscopy while preserving the healthy part of the bladder. This is generally performed under sedation or anesthesia, and patient recovery after the procedure is generally rapid. Depending on the stage of the tumor, administration of chemotherapy or radiotherapy also may be considered as treatment options. Instillation of bacillus calmette-guérin, a vaccine usually administered to confer immunity against tuberculosis, in the bladder to stimulate the body’s immune response to fight the cancer is also an option for early-stage tumors.

Urachal carcinoma is another rare cancer that sometimes can involve the bladder. This malignancy does not arise from the urothelium but rather from the epithelium in the urachus, which is an embryonic structure located between dome of the bladder and the umbilicus. The most common locations for urachal cancer are the umbilicus and dome of the bladder. While the malignancy commonly presents later in adult life, it is believed to exist for several years without any symptoms. The initial diagnosis can be difficult as there are often no specific symptoms.

As with bladder cancer, the diagnosis of urachal carcinoma generally is confirmed by cystoscopy and endoscopic biopsy. Surgery is the mainstay of treatment for clinically localized disease, and the entire urachal remnant and bladder dome are often resected en bloc. It is unclear whether removal of adjacent lymph nodes, radiation, or conventional chemotherapy is of any benefit to patients with urachal carcinoma. In fact, the cancer does not seem to respond to the usual chemotherapeutics for bladder cancer, but chemotherapy regimens used for bowel cancer may have more success. The overall five-year cancer-specific survival rate is approximately 50 percent. However, the prognosis for patients with metastatic or recurrent disease is poor, with median survivals reported in the range of one to two years.

Bladder tumors in children generally have low malignant potential, and their tendency to relapse after surgical removal is relatively lower than in adults. Nevertheless, patients are monitored closely with regular follow-up visits to detect any early signs of tumor recurrence. During the past three decades, multimodality therapy for childhood bladder cancer has resulted in markedly improved survival. The therapy responsible for this survival, however, can also produce adverse long-term health-related outcomes that manifest months to years after completion of cancer
treatment. These include organ dysfunction and second malignant neoplasms. Physicians and families also need to realize the adverse psychosocial sequelae that may accompany the treatment of children with bladder cancer. Thankfully, however, this yet remains a rare cancer among the pediatric age group.

Anirban P. Mitra
University of Southern California

See Also: Bladder Cancer; Childhood Cancers; Unusual Cancers of Childhood.

Further Readings

Bolivia

Bolivia is a large, landlocked country in South America. It is varied in topology with different cultural as well as topographical areas. It is mineral rich, supporting extractive industries. Many workers are miners and are exposed to heavy metals as an occupational hazard. The high altitudes where much of the population lives causes them to be at risk from cosmic radiation and ultraviolet solar rays. The national habit of chewing coca leaves with lime presents a risk of irritation to the mouth, lips, esophagus, and stomach. It is too early to assess these cancer risks as the people suffer from other more immediate problems of poverty, malnutrition, and limited access to doctors and health facilities. In recent decades, the country has made significant progress in development, although it remains one of the poorest countries of Latin America.

A nation’s experience with cancer is directly related to its demographic profile and to the country’s level of social and economic development. A young population will be relatively cancer free, while an aging population will have cancer as one of the most frequent causes of mortality. Bolivia has a young population due to its high fertility rate of about three children per family. Forms of cancer found mainly among the elderly are less frequent in the Bolivian population due, in part, to the low percentage of the population age 65 and above (4.8 percent). In addition, the lack of access to medical facilities, especially in rural areas, may prevent the diagnosis of occult forms of cancer. These characteristics of Bolivian society are shared with many of the world’s countries at lower stages of economic and social development. Historically cancer characterizes Western, industrial countries, often attributed to a rich diet, sedentary life style, and other unhealthy practices. While many social critics focus on these negative sides of modernization, the worldwide rise in cancer is recognized as a product of longer life spans in all countries.

More recently, cancer is seen as a worldwide cause of death and as a rapidly growing threat to less-wealthy countries that are not well prepared for treatment, palliative, and terminal care. According to the World Health Organization (WHO), cancer rates will be rising rapidly among countries least prepared to respond, such as Bolivia. This is a foreseeable health crisis as a third of cancers are preventable and others can be treated successfully if diagnosed early. This health crisis will affect Bolivia greatly as it is at the low end of public health facilities and resources, according to the Pan American Health Organization (PAHO). Bolivia’s demographic profile is of a young population of 10,088,000 with a median age of 24 years. The country is nearly the lowest or is the lowest in many measures of health and development in Latin America. Indicators include limited access to clean water, sanitation, doctors, and hospital beds.

Bolivia is the only country in South America without data on age-standardized mortality rates, although there are some data available on deaths from certain cancers. Based on International Agency for Research on Cancer data, Bolivia stands out as
one of the few Latin American countries in which breast cancer is not the leading cause of cancer deaths among women. Gynecological cancer (cervix uteri, corpus uteri, and ovarian) is the leading cause of cancer among Bolivian women and also is the greatest cause of cancer mortality among all Bolivians, men and women. This is especially tragic as most of these cancers are completely preventable or curable.

Bolivia’s highest cancer mortality is gynecological, and the second is urological (bladder, kidney, prostate, and testis). In third place is stomach cancer. Lung cancer is merely the ninth-most frequent cancer in Bolivia. Facing this projected health crisis, the objective is to provide preventive care and treatment to a population that often finds health care of any kind inaccessible and traditional methods more in accord with their culture and values.

Bolivia has a large indigenous population. The centrality of this previously marginal population has been a recent political phenomenon with the election of the nation’s first indigenous president, Evo Morales. There are three distinctive geographical and cultural regions outside the capital city, La Paz: the High Andean plateau, the region of the valleys, El Chapare, and the tropical Amazonian region. Cultural diversity is reflected in language diversity, with about 45 percent speaking only Spanish and 30 percent bilingual Spanish and an indigenous language. Ecological diversity is represented by traditions of medicinal plants and their use. Ethnographers report more than 2,000 different medicinal plants used by traditional healers. Their main use is for gastrointestinal problems. Despite the rapid spread of hospitals and health posts across the rural areas of Bolivia, their population continues to depend on traditional healers and herbal remedies. WHO cites up to 90 percent of the population of developing countries depending on these traditional sources to meet their health needs. The primary reason for preferences for these traditional methods is the low income of users, inaccessibility of modern facilities, and the perceived effectiveness of traditional healers over hospital doctors.

This developmental and cultural picture complicates the problems of preventive and treatment actions against cancer. The main concern in Bolivia is cervical cancer, which can be prevented through vaccinations, pap tests and human papillomavirus (HPV) tests. The Bolivarian women at risk of cervical cancer is estimated at 3 million. It is unlikely that programs of vaccination will be implemented anytime soon, for economic reasons. This is a major limitation in the developing world generally. It is estimated that most women in these countries do not receive medical services until they have an advanced cervical cancer with is untreatable and leads to an inevitable, tragic death.

However, Bolivian health authorities and doctors are working to control cancer through planning for installation of necessary diagnostic equipment and training of health professionals.

Keith R. Johnson
Oakton Community College

See Also: Developing Countries; Smokeless Tobacco; Women’s Cancers.

Further Readings

Bonadonna, Gianni

Gianni Bonadonna is a renowned Italian cancer doctor and scientist who has conducted groundbreaking research in the adjuvant treatment of
breast cancer. He also helped lead the battle to convince the surgical establishment of the treatment's efficacy. In addition, Bonadonna pioneered the development of a combination chemotherapy regimen that remains the gold standard for treatment of Hodgkin's disease, a cancer of the lymphatic system.

Born in Milan, Italy, in 1934, Bonadonna received his medical degree from the University of Milano in 1959 and completed his postdoctoral training at the Memorial Sloan Kettering Cancer Center in New York in the early 1960s. He went on to join the Instituto Nazionale des Tumori of Milan and became director of medical oncology in 1976. He was appointed head of the Department of Cancer Medicine in 1991 and served in that position until 1998, before becoming chair of the institute's Committee on Prospective Clinical Trials.

Bonadonna's important contributions to cancer research and treatment began in the early 1970s. Bonadonna and colleagues conducted a landmark clinical trial showing that an adjuvant combination chemotherapy of cyclophosphamide, methotrexate, and fluorouracil (CMF) improved survival in women who had their breast tumors surgically removed. As a result, CMF therapy became the first combination chemotherapeutic regimen for the treatment of breast cancer. Its discovery led to the beginning of a multidisciplinary approach to breast cancer treatment. Eventually, CMF therapy was shown to be not only effective but also to significantly reduce the risk of disease recurrence and death over an extended period of 30 years.

In 1995, Bonadonna and colleagues reported on a 20-year follow-up of an original group of women in his 1970s studies. These women had undergone radical mastectomies and were randomly assigned to groups that received no further treatment with CMF therapy for a 12-month cycle. The results showed that CMF nevertheless continued to provide significant benefits to the patients. In 2005, Bonadonna reported on a 30-year follow-up of these patients to show that the CMF regimen was long lasting in its benefits for patients who had both favorable and unfavorable prognoses.

Bonadonna also discovered a new combination chemotherapy for Hodgkin's disease in the early 1970s. The therapy used a combination of the drugs adriamycin, bleomycin, vinblastine, and dacarbazine (ABVD). A 1974 clinical trial conducted by Bonadonna showed that ABVD was superior to the commonly used mecloretamine, vincristine, procarbazine, prednisone (MOPP) chemotherapy in treating Hodgkin's disease. The results of another trial of ABVD published in 1982 showed that radiation therapy along with ABVD improved long-term outcomes compared to MOPP alone. Overall, ABVD therapy was shown to be easy to administer and had no severe side effects, findings that were confirmed in subsequent trials by other investigators. ABVD remains the most widely used conventional chemotherapy for the Hodgkin's disease, curing more than two-thirds of patients with advanced disease.

Another major contribution to cancer treatment discovered by Bonadonna and colleagues occurred in the late 1980s. Clinical trials conducted by Bonadonna indicated that primary chemotherapy before breast cancer surgery could reduce tumor size. The study also showed that conservative surgery could be an effective alternative to a radical mastectomy (removal of the entire breast as well as underlying chest muscle and lymph nodes of the axilla). Although it took some time to convince the medical community of the research findings, the medical establishment finally accepted that a less-radical surgery could effectively treat some breast cancers while maintaining the patient’s body integrity and self-image.

Bonadonna also founded the Fondazion Michelangelo (Michelangelo Foundation), a nonprofit organization located in Milan, Italy, devoted to advancing cancer research. The origins of the Michelangelo Foundation date back to 1993, when medical oncologists in Italy trained by Bonadonna began contacting him about participating in some of his clinical studies. Bonadonna was initially reluctant to the requests, primarily because he was concerned about a large group's ability to diligently follow research guidelines across groups.

Bonadonna eventually decided that it might be advantageous to get more oncologists collaborating on his clinical research. The cancer researcher reasoned that wider participation would benefit patients, who would no longer have to come to Milan for treatment and participation in clinical trials. Despite his devotion to research, Bonadonna remained dedicated to patients.

Bonadonna eventually invited approximately 15 medical oncologists from northern Italy for a meeting...
Bone Cancer, Osteosarcoma/Malignant Fibrous Histiocytoma

Bone Cancer, Osteosarcoma/Malignant Fibrous Histiocytoma

Osteosarcoma and malignant fibrous histiocytoma of bone (MFH-B) are cancers that affect bone tissue and together are identified with lots of similar and dissimilar characteristics. Throughout history, osteosarcoma and MFH-B have been presented as primary diseases of childhood and adolescence. The prevalence of these diseases in adulthood and old age is usually as a secondary tumor or metastatic disease. The two types of cancers exhibit a variety of similar clinical presentations and need treatment according to the prognostic factors. However, above all, there is a huge impact on social interaction and quality of life of the patient and family. Once these cancers are diagnosed, overall survival (OS) and event-free survival (EFS) of the patient guide further decision making and medical care course.

Definition and Types of Cancer
Osteosarcoma is a malignant tumor of bone tissue in which the neoplastic cells produce osteoid (new bone) and is sometimes accompanied with an excessive proliferation of vessels called telengectasias. The osteosarcoma can be located in

See Also: American Society of Clinical Oncology; Breast Cancer; Chemotherapy; Clinical Trials.

Further Readings
Bonadonna, Gianni. “Primary Chemotherapy to Avoid Mastectomy in Tumors With Diameters of Three Centimeters or More.” NCI Cancer Weekly (October 8, 1990).
the bone called central (medullary) or toward surface (peripheral). The World Health Organization (WHO) has classified osteosarcoma according to the histological features:

- Central tumors (medullary)
- Conventional central osteosarcoma
- Telangiectatic osteosarcoma
- Small cell osteosarcoma
- Intraosseous well-differentiated (low grade) Osteosarcoma
- Surface (peripheral)
- Parosteal (juxtacortical) well-differentiated (low-grade) osteosarcoma
- Periosteal osteosarcoma
- High-grade surface osteosarcoma

MFH-B (nowadays called undifferentiated pleomorphic sarcoma) is a malignant neoplasm composed of fibroblasts and pleomorphic cells developed on bone with a prominent storiform pattern. The histological characteristics of MFH-B are different than osteosarcoma but have the same clinical staging, and both have similar modes of treatment.

**Epidemiology**

Data from the National Cancer Institute mention an estimate of 4.4 per million new cases of osteosarcoma each year in people age 0 to 24 years. The U.S census bureau estimates that there were 110 million people in this age range in 2010, resulting in an incidence of roughly 450 cases per year in children and young adults younger than 25 years. Osteosarcoma accounts for approximately 5 percent of childhood tumors. In children and adolescents, more than 50 percent of these tumors arise from the long bones around the knee. Osteosarcoma can rarely be observed in soft tissue or visceral organs. MFH-B is relatively a rare tumor, which represents less than 2 percent of all primary malignant bone lesions.

**Etiology**

The main cause of these tumors has not been determined clearly; the origin of osteosarcoma and MFH-B is multifactorial. There are several risk factors involved in pathogenesis, like changes or mutations in our genes. Such genetic mutations in turn act as direct or indirect causes of osteosarcoma and MFH-B. Mutations can be inherited, such as...
mutation that turns off the TP53 tumor suppressor gene or the mutation in retinoblastoma RB1 tumor suppressor gene. Perhaps mutations can be acquired as well, such as radiation therapy in a past form of cancer, random errors that occur when cells reproduce at the time of the teenage growth spurt, or Paget disease of bone that causes rapid bone growth. All of these factors increase the risk of osteosarcoma and MFH-B.

Pathogenesis, Presentation of the Disease and Diagnosis

The clinical course of the disease is highly variable for many types of osteosarcoma and MFH-B, but each one leads to the same result and progression and varies with the time. The diagnosis usually requires a synthesis of clinical, radiologic, and pathologic features. Patients typically present with pain and swelling of the affected area. A plain radiograph reveals a destructive lesion with a moth-eaten appearance, a spiculated periosteal reaction and a cuff of periosteal new bone formation at the margin of the soft tissue mass. A computed tomography (CT) scan of the primary tumor is best for defining bone destruction and the pattern of calcification, whereas magnetic resonance imaging (MRI) is better for defining intramedullary and soft tissue extension. A chest radiograph and CT scan are used to detect lung metastases. A metastases to the bony skeleton should be imaged by a bone scan or by fluorodeoxyglucose positron emission tomography (FDG-PET). Almost all osteosarcomas and MFH-B are hypervascular. Angiography is not helpful for diagnosis, but it is the most sensitive test for assessing the response to preoperative chemotherapy (extent of necrosis). Pathologic diagnosis is established either with a core-needle biopsy or with an open biopsy with an appropriately placed incision that does not compromise future limb-sparing resection. Most osteosarcoma and MFH-B are high grade. The most important prognostic factor for long-term survival is response to chemotherapy.

Management and Treatment

Preoperative chemotherapy followed by limb-sparing surgery (which can be accomplished in more than 80 percent of patients) followed by postoperative chemotherapy is standard management. Current chemotherapy protocols include combinations of high-dose methotrexate, doxorubicin, cyclophosphamide, cisplatin, ifosfamide, etoposide, and carboplatin with leucovorin rescue. Meta-analysis of protocols for the treatment of osteosarcoma concluded that regimens containing three active chemotherapy agents (mainly cisplatin, doxorubicin, and methotrexate) were superior to regimens containing two active agents and, with four agents, were not superior than with three agents. As is known, surgical resection of the primary tumor with adequate margins is an essential strategy for patients with localized osteosarcoma or MFH-B, and more than 80 percent of patients with extremity osteosarcoma or MFH-B can be treated by a limb-sparing procedure and do not require amputation. In such cases, limb-sparing procedures are planned only when preoperative staging indicates that it would be possible to achieve wide surgical margins. Consequently, poor histologic response and close surgical margins have a high rate of local recurrence. After surgery, the reconstruction of the limb can be accomplished with many options including the following:

- Metallic endoprosthesis
- Allograft or allotransplantation
- Vascularized autologous bone graft
- Rotationplasty

There are several factors that involve optimal surgical reconstruction, which include the site and the size of the primary tumor, the ability to preserve the neuromuscular structures of the distal extremity, the age of the patient, and potential for additional growth. Other factors include the needs and desires of the patient and family members. One of the most important components is the delay in resumption of chemotherapy after definitive surgery, which is associated with increased risk of tumor recurrence.

For some patients, amputation is an optimal choice, but in the case of limb salvage, a pathologic fracture at diagnosis has worse outcomes. The local recurrence is considered high risk for death from osteosarcoma or MFH-B. In this case, there are various elements associated with an increased risk of local recurrence, including: nonparticipating patients in a clinical trial, limb-preserving surgery, pelvic primary site of tumor, limb-preserving surgery, soft tissue infiltration beyond the periosteum, poor pathologic response
to initial chemotherapy, failure to complete planned chemotherapy, and performance of the biopsy at an institution different from the institution performing the definitive surgery.

**Prevention and Education**

The risk of many adult cancers could be reduced by making certain lifestyle changes, but at this time, there are no known ways to prevent osteosarcoma or MFH-B. As mentioned before, there are conditions associated with osteosarcoma and MFH-B (Paget disease, radiation exposure, bone infarct, or bone trauma and fibrous dysplasia). The education is given to people to learn the first manifestations at the time of diagnosis in osteosarcoma and MFH-B, symptoms like joint tenderness or inflammation, pain or swelling of a part of an extremity, fractures due to bone weakness, and limited range of motion. Other findings during physical exam may suggest the presence of osteosarcoma or MFH-B and make additional tests to rule out or confirm the presence of disease.

Ghulam Ishaq Khan  
*Columbia University*  
Samuel Xavier Pimiento Rodríguez  
*Universidad Estatal de Cuenca*

**See Also:** Childcare and Cancer Risk; Drugs; Genetics; National Cancer Institute; Radiation Therapy

**Further Readings**

Fletcher, C. D. M., K. K. Unni, and F. Mertens, eds.  

Harrison, Tinsley.  

Mertens, et al.  
“Reclassification and Subtyping of So-Called Malignant Fibrous Histiocytoma of Bone: Comparison With Cytogenetic Features.”  

National Cancer Institute.  
“PDQ Osteosarcoma and Malignant Fibrous Histiocytoma of Bone Treatment.”  

“Study of Malignant Fibrous Histiocytoma: Clinical, Statistic and Histopathological Interrelation.”  

---

**Bone Marrow Transplants**

Bone marrow transplantation is the common term for the transplantation of hematopoietic stem cells found in bone marrow. The procedure was first established by a Johns Hopkins researcher, George Santos, in 1968, following his development of a chemotherapy cocktail using cyclophosphamide, which targeted cancer cells more specifically than radiation treatment did but had the effect of destroying healthy and necessary bone marrow tissue as well. The transplantation of stem cells from bone marrow into the chemotherapy patient helped undo some of the damage that had been done; Santos based the procedure on work by Georges Mathe, a French oncologist who attempted unsuccessful marrow transplants on Yugoslavian nuclear workers whose marrow had been damaged in a nuclear accident. Most of the standards of bone marrow transplants were subsequently developed at Hopkins.

Bone marrow is a flexible tissue in the interior of bones, comprising about 4 percent of the body weight of the average person. Bone marrow is an important part of both the lymphatic system, producing lymphocytes for the immune system, and of the cardiovascular system, producing red blood cells, platelets, and some white blood cells through hematopoiesis. There are two types of bone marrow: red marrow, medulla ossium rubra, made up mainly of the hematopoietic tissue, and yellow marrow, medulla ossium flava, consisting of stored fat cells. Bone marrow begins as fully red at birth and accumulates yellow marrow over time, being about half and half in most adults. Red marrow is found mainly in flat bones (such as the ribs, cranium, and vertebrae) and the rounded ends of long bones (such as the femur).

Bone marrow also can be divided between the hematopoietic tissue and the stroma, which includes all the marrow tissue not directly involved in hematopoiesis. Stroma includes yellow marrow,
connective tissue, macrophages, adipocytes, osteoblasts, osteoclasts, and endothelial cells. Some of these types of cells indirectly contribute to or enable hematopoiesis; for instance, macrophages deliver the iron that is necessary to produce hemoglobin. Bone marrow stroma also contains mesenchymal stem cells, which are multipotent stem cells capable of differentiating into osteoblasts, chondrocytes, myocytes, adipocytes, and beta-pancreatic islets cells. Though not as differentiable as embryonic stem cells, mesenchymal stem cells have been the subject of much research into the use of stem cells as sources of cures and remedies, particularly in the United States, where until recently, funding for human embryonic stem cell research was strictly constrained. Mesenchymal stem cells also contribute to the progression of cancer, particularly cancers that affect the lymph nodes, blood, or bone marrow, a mechanism that is also the subject of study.

Bone marrow is subject to damage by several different diseases, as well as cancer, and can be damaged by radiation therapy or chemotherapy, accounting for some of the symptoms of radiation poisoning as well as some of the complications and side effects of chemotherapy.

Bone marrow hematopoietic tissue contains hematopoietic stem cells (HSCs), the cells that differentiate into all other blood cells. These stem cells may be harvested, whether for transplant (bone marrow transplants are in fact hematopoietic stem cell transplants [HCST]) or in order to manipulate the stem cells to some other end. For instance, hematopoietic stem cells can be used to treat neurological diseases by inducing them to differentiate into neural cells, and there may be some potential for their use in the treatment of human immunodeficiency virus (HIV). Hematopoietic stem cell harvesting is a minimally invasive procedure performed under general anesthesia and may be either inpatient or outpatient depending on the circumstances.

Such transplants may be either allogenic, meaning that cells are harvested from one person and transplanted to another, or autologous, meaning they are transplanted back into the donor at a later date. HCSTs are used to treat several leukemias (acute myeloid leukemia, chronic myeloid leukemia, and acute lymphoblastic leukemia), especially in cases where the patient would not benefit from chemotherapy as well as Hodgkin’s and non-Hodgkin’s lymphoma, neuroblastoma, Ewing sarcoma, myelodysplastic syndromes, gliomas, thalassemia, aplastic anemia, Fanconi anemia, and immune deficiency syndromes. More than 50,000 transplants are performed each year, mostly in Europe and North America.

Bone marrow is generally extracted from the pelvis, though it can be taken from other bones if there is a need. Another possibility is to administer a drug that releases the donor’s HSCs into the bloodstream. After several days of such medication, the donor HSCs can be extracted through apheresis. The donor’s blood passes through an apparatus that directs it through a centrifuge that separates out the HSCs while returning the remainder to the body. Apheresis kits are single-use in order to prevent the risk of infection from contamination in the centrifuge or tubing. In autologous HSCT, harvested cells are then stored in a freezer until they are needed.

Side effects are minor; other than lingering soreness, most of those from a bone marrow extraction will be due to the anesthesia itself. In the case of apheresis, the process can be mildly uncomfortable, including chills and lightheadedness, and some donors experience flu-like symptoms and difficulty sleeping while taking the medication. Only about 15 percent of donors experience adverse reactions to apheresis. A very small number of donors experience severe reactions to one or more events in the donation process, requiring hospitalization; most commonly, these are cardiovascular-related events, including deep vein thrombosis and myocardial infarction.

Typically, the purpose of autologous HSCT is to safeguard the patient’s health through the preservation of HSCs, while the patient undergoes radiation treatments or high-dose chemotherapy, which in the course of destroying cancer cells, also destroys healthy bone marrow tissue and impairs the patient’s ability to produce new blood cells. The stored HSCs are then transfused back into his bloodstream and, upon being absorbed into the bone marrow, differentiate to form new healthy cells. Autologous HSCT avoids several of the risks of allogeneic HSCT— not just the possibility of rejection (a phenomenon known as graft-versus-host disease [GVHD]) but the risks faced during the immunocompromised period, which in this scheme is considerably shortened. In the treatment
of lymphoma, autologous HSCT has become standard for this reason.

However, the patient’s bone marrow may not always be healthy enough for autologous HSCT to be beneficial. Patients with acute myeloid leukemia, for instance, face an increased likelihood of cancer recurrence when undergoing autologous HSCT, and so allogeneic HSCT is preferred in these and some other cases. Allogeneic HSCT is a similar procedure, but the HSCs are harvested from a second person, a healthy donor. This requires finding a compatible match—close relatives are ideal, but unrelated donors may also have a matching human leukocyte antigen (HLA) type, which is necessary for the body to accept the donated tissue rather than treating it as foreign material. Rejection can be quite serious. In GVHD, rather than the body rejecting the foreign tissue, the white blood cells in the transplanted material attacks the host body’s cells, treating it as an infection. While more common with unrelated donors, there is a chance of this occurring even when the donor is an HLA-identical sibling, due to the presence of minor histocompatibility antigens—genetically different proteins from the donor’s T-cells. Damage is wreaked on organs, including the liver and gastrointestinal tract, the skin, the thymus, and the lungs, as well as on the bone marrow itself. Despite the risk posed by including T-cells in the transplant, they are often deliberately included because they assist in strengthening the immune system and preventing the more familiar host-versus-graft disease. Donor T-cells are especially efficacious in cancer cases, where they help the host system fight against tumor cells. Sometimes called the graft-versus-tumor effect, donor T-cells help to eliminate both tumor cells and, in the case of leukemia, malignant host T-cells. Studies have suggested the effect may be seen in breast cancer cases as well as myeloma, lymphoma, and leukemia cases. The mechanism is not well understood.

Acute GVHD presents in the first 100 days after transplant and is one of the main morbidity and mortality challenges faced by transplant. Common symptoms include rash and gastrointestinal problems, dry or irritated eyes, dark patches of the skin, or jaundice if the T-cells have attacked the liver; women may experience severe vaginal pain and scarring if the donor T-cells attack the mucosa. Chronic GVHD occurs after those first 100 days and can extend its attack to the exocrine glands and connective tissues. In either case, GVHD is usually treated with intravenous or oral steroids and immunosuppressants to reduce the immune response of the donor T-cells; glucocorticoids are commonly prescribed for acute GVHD and corticosteroids for chronic GVHD. Immunosuppressants also may be prescribed for several months after a transplant as a preemptive measure. Most patients enter a state of tolerance within a year after the HSCT.

Bone marrow transplant is one of the few transplantation procedures in which GVHD is more common than the reverse, due to the donor’s T-cells being included in the transplant. Host-versus-graft disease, often simply called transplant rejection or engraftment syndrome, is the more familiar situation of the host’s immune system treating the transplanted tissue as an infection. Recent work on transplant rejection following allogenic HSCT has focused on the possibility of mesenchymal stromal cells as a treatment.

The National Marrow Donor Program (NMPD) was established in Minneapolis in 1986 in order to encourage volunteer hematopoietic cell donation and umbilical cord blood donation for use in transplants. Between 1986 and 2013, more than 55,000 transplants were conducted with the NMPD’s help and that of the Be The Match donor registry, which it operates. NMPD covers the costs of donation (medical, travel and lodging as needed) that are not covered by the patient’s insurance; the donor’s cost is simply the time he or she needs to take off from work to travel and recuperate from the donation procedure. Marrow cells are obtained from the pelvic bones of living adult donors, while umbilical cord blood comes from the umbilical cord of newborn babies after the cord has been clamped and cut (and thus is no longer attached to the baby nor causes it any discomfort). The NMDP is the only federally funded, Congressionally authorized stem cell registry in the United States, but other, smaller donation registries exist throughout the country.

Bill Kte’pi
Independent Scholar

See Also: Leukemia, Acute Lymphoblastic, Adult; Leukemia, Acute Lymphoblastic, Childhood; Leukemia, Acute Myeloid, Adult; Leukemia, Acute Myeloid, Childhood.
Brain Stem Glioma, Childhood

Within a neuronal network, there exists a symbiosis between neurons and glial cells. Glial cells are classified as supportive cells, providing a structural and dynamic framework within which neurons are able to thrive. Glial cells are ubiquitous within the nervous system and in fact outnumber neurons of an approximate ratio of three to one. These supportive cells modulate synaptic activity and interactions between neurons in various neural structures with an end result to carry out a common function. In the brain stem, for instance, the nodal interactions drive the brain stem network to carry out cardiovascular, respiratory, and proprioceptive control. The brain stem serves as a conduit for many motor and sensory pathways as well as a passage for cranial nerves III through XII. Thus, damage to this crucial structure can result in significant consequences.

Brain stem glioma develops from glial cells of the brain stem. When the cells begin to proliferate and grow uncontrollably, they form a mass (tumor), which leads to symptoms. Tumors are further classified as either benign or malignant. Benign tumors are focal, and although they press on proximal structures, they do not spread. Malignant tumors, however, are invasive and can quickly dissipate to other areas—they are cancerous. Regardless of malignancy, tumors require treatment because they are capable of adversely interfering with function of any tissue they come in contact with. Tumors of brain stem glioma are of two types: diffuse intrinsic pontine glioma (DIPG) or focal/low-grade glioma.

Most brain stem gliomas (approximately 80 percent) occur within the pons region of the brain stem, whereas the remaining occur with the medulla, midbrain, and cervicomedullary junction. Furthermore, most of the brain stem gliomas within the pons are high-grade tumors with the capacity to spread. Brain stem gliomas occurring outside the pons, in contrast, are focal and low-grade tumors. Grading of tumors is based on the World Health Organization (WHO) grading system, which considers cellular irregularity, growth, and vascular involvement.

The frequency of brain stem gliomas is approximately threefold greater in the pediatric population than the adult. Current statistical findings are reporting a frequency of 20 percent for brain stem gliomas within all pediatric brain tumors. This number is greater than what was previously reported in the 1970s and 1980s, seemingly due to improvements in diagnostic techniques rather than a true increase in incidence. No gender or racial preference exists. Population analyses indicate a median age of five to nine years for diagnosis, with symptoms beginning between 2 and 13 years.

As with pediatric brain tumors in general, most cases have no known causes and are considered sporadic. However, there exist possible risk factors for brain stem glioma, which are largely genetic in nature. These include: Li-Fraumeni syndrome, neurofibromatosis type 1, nevoid basal cell carcinoma syndrome, tuberous sclerosis, and Turcot syndrome (associated with colon polyps). Models of genetic susceptibility syndromes (i.e., NF-1 and tuberous sclerosis) are currently studied in research to uncover the involvement of genetic predisposition and signal transduction pathways in the development of brain stem glioma.

Symptoms of childhood brain stem glioma are diverse and largely context dependent. Contextual factors include patient history (age and development), tumor classification, tumor location, and tumor proliferation. Most of the time, cranial
Brain Stem Glioma, Childhood

nerve palsies are the initial symptoms. Usually, cranial nerve VI and VII are involved. Later symptoms can include contralateral hemiplegia and ataxia, dysphagia, and hoarseness. Neck stiffness and discomfort have been reported in a number of cases and even can present with torticollis. Other symptoms include increased intracranial pressure and vomiting, intractable hiccough, facial spasm, personality change, and headache. Eventually, symptoms can become bilateral. On average, there is a six-month duration between symptom onset and diagnosis.

The main diagnostic tools for brain stem glioma are computed tomography (CT) scan and magnetic resonance imaging (MRI) with gadolinium. After a complete physical and neurologic exam, any suspect of brain stem glioma can be assessed preferably with an MRI. In this procedure, gadolinium is injected into a vein and will clearly demarcate cancerous cells. A biopsy is sometimes performed for diagnosis in cases where the MRI scan detects a focal/low-grade brain stem glioma. After the tissue is removed, the pathologists examine for cancerous cells. In these cases, if cancerous cells are found, the mass may be removed during the same surgery.

Standard treatment of brain stem glioma includes: surgery, radiation therapy, chemotherapy, cerebrospinal fluid diversion, and watchful waiting. Surgery, as discussed previously, simply removes the mass. Radiation therapy, considered the treatment of choice, uses radiation to exterminate and control cancerous cells. Radiation is not without consequences, however, and developmental side effects (i.e., growth stunt) from therapy are likely to result. Chemotherapy is under clinical trial for treatment, and because it utilizes drugs to fight cancerous cells, it is seen as a potential replacement for radiation therapy. Cerebrospinal fluid diversion shunts excess cerebrospinal fluid away from the brain to be absorbed by other body areas. Watchful waiting, as suggested, involves close monitoring of the patient and only administering treatment when symptoms begin or change.

Childhood brain stem glioma presents, unfortunately, with the worst prognosis of all childhood tumors. The median survival time ranges from 9 to 12 months. Recent research suggests that certain clinical, CT, and pathological findings are correlated with prognosis. Cranial nerve palsies were found to be correlated with malignant tumors, mitoses in histological findings with poor prognosis, Rosenthal fibers and calcification with better prognosis, and a hypodense tumor on the CT with a poor prognosis. Further experimentation is required to explore these methods as potential treatment predictors.

In conclusion, childhood brain stem glioma is a severe condition that requires urgent and prudent care. Many factors are to be taken into account when deciding treatment options. Much remains to be discovered with regards to the cause and treatment of this condition.

Krishna Subhash Vyas
Eva Olariu
University Kentucky College of Medicine

See Also: Brain Stem Glioma, Childhood; Brain Tumor, Brain Tumor, Cerebellar Astrocytoma, Childhood; Brain Tumor, Cerebral Astrocytoma/Malignant Glioma, Childhood; Brain Tumor, Medulloblastoma, Childhood; Brain Tumor, Supratentorial Primitive Neuroectodermal, Childhood.

Further Readings
Brain Tumor, Adult

Adult brain tumors involve cancer that grows in the tissues of the brain among people more than 18 years of age. There are approximately 130 different types of brain tumors. Brain tumors usually increase intracranial pressure (pressure in the skull) because of their size and weight. They may therefore cause symptoms such as headaches, vomiting, loss of appetite, seizures, visual changes, gait changes, and changes in cognition, mood, or personality.

Diagnosis of a brain tumor is made by taking a patient history, giving a neurological examination, and typically using magnetic resonance imaging (MRI) and computerized topography (CT) scans. These technologies have complementary roles—CT scans are particularly valuable for identifying bleeding on the brain that is less than one day old, calcification, and skull lesions. On the other hand, MRI is more sensitive for soft-tissue resolution. In some cases, a brain biopsy is necessary.

If the tumors start in the brain, they are called primary brain tumors; if the tumors start somewhere else in the body and spread to the brain, they are called metastatic brain tumors. Metastatic brain tumors are by far the most common—they outnumber primary brain tumors by a ratio of 10 to 1. When metastatic brain tumors occur, approximately 70 percent of cases involve multiple metastases.

Brain tumors account only for approximately 1 percent of all primary malignant cancers. (This statistic does not include benign tumors or those with brain metastasis from primary tumors in another part of the body.) Malignant brain tumors can be fast growing and aggressive, invading the surrounding tissue and spreading throughout the cerebrospinal fluid space surrounding the brain and spinal cord.

Between 20 and 40 percent of all cancer patients develop metastatic brain tumors. The most common primary cancers that metastasize to the brain are lung cancer, breast cancer, unknown primary cancers, melanoma, and colon cancer. Approximately half of all people with lung cancer and one-fifth of people with breast cancer develop metastatic brain tumors.

It is important to recognize, however, that tumors in the brain cannot automatically be assumed to be metastatic, even if a person has a prior history of cancer. They may be new primary tumors, and appropriate treatment may be able to stop their progression.

Few definitive causes of brain tumors have been identified. However, some of the risk factors that have been identified for adult brain tumors include a history of radiation therapy to the brain and certain conditions such as neurofibromatosis, Von Hippel-Lindau syndrome, Li-Fraumeni syndrome, and Turcot syndrome.

The role of mobile phones as a potential cause of brain cancer is highly contested. There is no medical consensus at this stage about the correlation between cell phone use and brain tumors.

Brain tumors constitute between 85 and 90 percent of all primary central nervous system tumors. Sometimes, patients do not experience any symptoms until the tumor has become quite large. At that stage, the tumor may quickly damage a person’s health. In other cases, symptoms develop slowly.
Brain tumors have high morbidity and high mortality rates. However, the precise effects of a particular brain tumor will depend on the size of the tumor, the grade of the tumor cells, the part of the brain in which it is located, and the age of the person at diagnosis. Outcomes are generally better for younger people.

It was estimated 23,380 new cases of brain tumors will be diagnosed in the United States in 2014. Also, approximately 14,320 people in the United States were expected to die from brain tumors in 2014.

Epidemiological studies suggest that the incidence of primary brain tumors is higher in Caucasians than African Americans, and the mortality rate is higher in men than women.

It is best for patients if an interdisciplinary team offers treatment. For brain tumors, such treatment teams usually include a neuro-oncologist, neurosurgeon, oncologist, radiation oncologist, neurologist, and social workers. Patients with brain tumors may report increased quality of life if they receive comfort measures and counseling and if they participate in support groups. If the prognosis is poor, it may be helpful to discuss advance directives, palliative care, hospice, and plans for a living will.

Treatment for adult brain tumors typically involves surgery to remove the tumor completely or, in the case of deep tumor, to remove as much of the tumor as possible while retaining cognitive function. Surgery is particularly important where it is necessary to have a resection of a single brain metastasis, and it is also necessary in the case of large, symptomatic, or life-threatening tumors. After surgery, radiation therapy and chemotherapy are usually used. The use of steroids is also common. If an individual with a brain tumor has been experiencing seizures, treatment also involves the use of anticonvulsants.

Clinical trials are being conducted currently with the use of alternatives to MRI for brain tumors. MRI scans do not show where the nerve pathways are in the brain, so diffusion tensor imaging (DTI) is being tested because it shows the white matter tracts and the nerve pathways. Although medical understanding of the role of molecular-genetic phenomena in the development of brain tumors has increased considerably in recent years, the exact cause of most brain tumors is unknown, and the mortality rate for brain tumors has remained essentially the same for the last 40 years.

Nevertheless, due to advancing scientific knowledge, researchers do have a much better understanding of tumor biology. Treatment guidelines are evolving. New drugs and new combinations of drugs are always being explored in the treatment of brain tumors. Antiangiogenesis drugs, which block the growth of new blood vessels to tumors, have shown some promise. In 2009, the U.S. Food and Drug Administration gave accelerated approval for one of these antiangiogenesis drugs, Bevacizumab, as monotherapy for some patients (those with progressive glioblastoma).

Other clinical trials have helped in the development of adjuvant treatment. Research is also being conducted on the best ways to treat low-grade gliomas so that they do not recur.

Patient advocacy groups are now organizing charity fun runs and walking events to raise funds, improve awareness, and promote the need for a breakthrough in scientific research. These events also give people a chance to meet others who have had similar experiences. Such events and support groups can provide adults with brain tumors a sense of community and also help reduce the sense of isolation that some people experience when dealing with this difficult experience. National groups such as the American Brain Tumor Association provide advocacy as well as support and information for patients, families, and health care providers.

Mark D. Sherry
University of Toledo

See Also: American Brain Tumor Association; Chemotherapy; Bone Marrow Transplants; Brain Stem Glioma, Childhood; Brain Tumor, Childhood; Childhood Brain Tumor Foundation; Radiation Therapy; Surgery.

Further Readings
Brain Tumor, Cerebellar Astrocytoma, Childhood

A cerebellar astrocytoma is a form of brain cancer that arises in the cerebellum, the posterior portion of the brain that controls balance, coordination of movements, and motor learning. In particular, an astrocytoma is a type of glioma, a brain tumor arising from cells of the central nervous system (CNS), either astrocytes, oligodendrocytes, or ependymal. Astrocytomas are defined as either low-grade (Grade I or II) or high-grade (Grade III or IV) gliomas based upon histologic review and how closely the cancer cells resemble normal astrocytes. Low-grade cerebellar astrocytomas are the most common form of brain cancer in children over 3 years, accounting for 10 to 20 percent of all childhood brain tumors and generally presenting before age 10. The grade of the tumor determines the prognosis, treatment, and potential for relapse.

Types of Astrocytomas
Astrocytes are the most abundant cells in the brain, acting to perform multiple functions including fluid and ion homeostasis, regulation of blood flow in brain, aid in the growth and repair of neurons, and formation of the blood–brain barrier, among others. When these cells lose the ability to regulate their growth, they become cancerous astrocytomas. In children, approximately 80 percent of all cerebellar astrocytomas are Grade I pilocytic astrocytomas. Pilocytic astrocytomas are slow growing and well demarcated, often forming a cyst, a closed pouch of cells with a clear distinction from other adjacent cells. An important characteristic of Grade I pilocytic astrocytomas is that they do not progress to Grade II gliomas. Additionally, due to the slow growth and predilection for certain environments, metastasis is not common. Pilocytic astrocytomas may also be associated with the genetic disease neurofibromatosis I, but within the cerebellum, most pilocytic astrocytomas are sporadic. It has been found that the majority of sporadic pilocytic astrocytomas arise from a duplication of a portion of a cellular chromosome, 7q34, which forms a genetic rearrangement where the BRAF gene is fused to the KIAA1549 gene within the cancerous cell. The BRAF gene is a proto-oncogene for the B-Raf protein within the RAS/MAPK signaling pathway. This signaling pathway controls the growth and division of cells, cell movement, and self-destruction of compromised cells (apoptosis). Mutation of the BRAF gene activates the genes oncogenic potential, capable of causing the unregulated cell growth known as cancer.

A smaller portion of childhood cerebellar astrocytomas are fibrillary, Grade II diffuse astrocytomas. Compared to pilocytic astrocytomas, Grade II diffuse astrocytomas are six to seven times less common and account only for approximately 20 percent of cerebellar astrocytomas. Most frequently, diffuse astrocytomas are found in the frontal or temporal lobes of the brain but can be found in the cerebellum. Unlike Grade I pilocytic astrocytomas, malignant progression of diffuse astrocytomas to Grade III anaplastic astrocytoma and Grade IV glioblastoma multiforme is possible, although it occurs only in 10 percent of children with this tumor. Grade II diffuse astrocytomas are also slow growing but differ from Grade I tumors by the invasion of the borders spreading into the adjacent brain tissue. Grade II is differentiated from Grade III anaplastic astrocytoma and Grade IV glioblastoma multiforme due to its microscopic histological and radiologic findings.

Symptoms and Diagnosis
Clinically, the symptoms associated with cerebellar astrocytomas are largely associated with their location within the brain. Due to the cerebellum’s role in balance and coordination, the most common symptoms are associated with loss of balance and lack of coordinated movements. Additionally, due to the skull’s requirement of stable pressure, a rise in intracranial pressure due to the tumor’s size or ability to block fluid movement generally causes nausea, headache, and vomiting.

Imaging studies are integral in diagnosing cerebellar astrocytomas and can be useful in determination of grade. Magnetic resonance imaging (MRI) is the primary diagnostic tool in determining disease staging and guiding surgical and treatment strategies. A computed tomography (CT) scan is then often utilized in order to determine whether there is cerebrospinal fluid blockage and further guide treatment strategies. Biopsy is a common procedure used to verify tumor histology in order to grade the tumor and stage the progression of disease.

When inspected through MRI, a pilocytic astrocytoma is defined as a cyst with a contrast-enhancing mural nodule. Microscopically, pilocytic
astrocytomas are identified by the presence of Rosenthal fibers and biphasic tissue structure. In order to differentiate the low-grade gliomas from one another, the Grade II diffuse astrocytomas are seen without well-defined borders and are nonenhancing. Histologically, the tissues appear hypercellular with angulated, irregular cellular nuclei. Grade III and IV high-grade gliomas both show enhancement without well-defined borders, and Grade IV can show necrosis. Histologically, Grade III tumors appear as Grade II tumors with mitoses, or cells with increased numbers of chromosomes. Grade IV tumors appear similar to Grade III tumor tissue, displaying either necrosis or increased blood flow and microvascular proliferation.

**Treatment and Prognosis**

Treatment for all grades of cerebellar astrocytomas includes some combination of surgery, radiation therapy, and chemotherapy. Low-grade cerebellar astrocytomas generally can be resected surgically, and when complete resection is achieved, cure rates are high, reaching 80 to 90 percent. When the location of the tumor makes resection a challenge without serious neurologic danger to the child, chemotherapy is used after incomplete resection. Radiation therapy is withheld in low-grade tumors due to the high cure rate with resection and chemotherapy as well as the severe side effects of long-term cognitive impairment, risk of stroke, and risk of secondary cancer. Treatment for high-grade gliomas generally includes all three of the common treatment modalities—surgery, radiation, and chemotherapy—often along with other emerging therapies or clinical trials. Due to their rapid rate of growth and high likelihood for metastases, the prognosis of high-grade gliomas is not favorable with less than 30 percent five-year survival rates. Certain biological gene markers, including p53 and epidermal growth factor receptor amplification or mutations, can be helpful in predicting clinical outcomes and response to therapy. Due to the invasive high-risk therapy options for these children, those who survive almost all have severe side effects of neurological and neurocognitive defects and susceptibility to stroke and seizure among others.

**See Also:** Brain Stem Glioma, Childhood; Brain Tumor, Cerebral Astrocytoma/Malignant Glioma, Childhood; Brain Tumor, Medulloblastoma, Childhood; Brain Tumor, Supratentorial Primitive Neuroectodermal, Childhood; Brain Tumor, Visual Pathway and Hypothalamic Glioma, Childhood; Ependymoma, Childhood.

**Further Readings**


Brain Tumor, Childhood

Brain Tumor, Cerebral Astrocytoma/Malignant Glioma, Childhood

The normal brain is made up of several cell types: neurons, the main functional cell of the brain, and glia, which play a supportive role to the neurons. Glia are further subdivided into different types, each type with a different function, including oligodendrocytes, which cover the axons of neurons with sheaths of myelin, and astrocytes, which serve many functions including taking up excess neurotransmitters and creating the blood–brain barrier. Gliomas are tumors of the glial cells, particularly astrocytes and oligodendrocytes. About two-thirds of all childhood brain tumors are gliomas.

Gliomas, like other tumors, occur when the mechanisms that keep cell growth in check go awry, resulting in uncontrolled growth and destruction of surrounding normal tissue.

Gliomas occur in the brain, which is particularly problematic because so many essential areas exist in a relatively small and enclosed space. A small amount of abnormal cellular growth can cause significant symptoms depending on the location of that growth in the brain.

Astrocytomas, or tumors presumably derived from astrocytes or their precursors, are the most common type of glioma. There are several types of astrocytomas, including pilocytic astrocytoma, which is generally considered the most benign of this group, fibrillary astrocytoma, anaplastic astrocytoma, and glioblastome multiforme, the most malignant of the gliomas.

As with most other forms of brain tumors, attempts for curative therapy in high-grade gliomas begin with surgical resection. Ideally, the goal of surgery is to achieve a gross-total resection, meaning that the surgeon has removed all visible tumor and, when scans are obtained after the surgery, no apparent tumor remains.

One of the difficulties in achieving a gross total resection is that, particularly for microscopic tumor cells, they are invisible on magnetic resonance imaging (MRI), or the neurosurgeon may extend beyond suspected tumor boundaries. This is because these tumors are infiltrative, meaning they tend to pass in and around normal brain structures. Some tumor cells may have already migrated to the other side of the brain, quite distant from the tumor seen on preoperative scan and at surgery. In certain cases, surgical resection is not feasible, and the surgeon may only obtain a biopsy to confirm the diagnosis.

Following surgery, patients are often treated with radiation therapy to the region of the brain where the tumor was evident on scans and at surgery. Radiation therapy is routinely limited to areas where the tumor was noted prior to surgery.

The role of chemotherapy in the treatment of high-grade gliomas has been somewhat more debated but is often utilized because of the high failure rate of surgery combined with radiation therapy in the treatment of high-grade gliomas. Chemotherapy has been aggressively utilized in very young children in an effort to delay the use of radiation therapy until the children are a little older.

Most patients with high-grade gliomas will eventually have a recurrence of the tumor, usually within three years of the original diagnosis. Disease may recur at the primary tumor site or at the margin of the resection site or radiation bed. They may also occur at other sites in the nervous system.

Krunal Patel
Independent Scholar

See Also: Brain Tumor, Cerebellar Astrocytoma, Childhood; Ependymoma, Childhood.

Further Readings

Brain Tumor, Childhood

Childhood solid neoplasms and cerebral tumors are the most common cause of cancer deaths
among children, and the four most common neoplastic disorders found in children include medulloblastomas, astrocytomas, ependymomas, and gliomas.

Medulloblastomas are highly malignant tumors of the central nervous system (CNS). In 2007, the World Health Organization (WHO) recognized five histological types under the following categories: classic, anaplastic, large cell, desmoplastic and nodular, and medulloblastoma with extensive nodularity. This class of neoplasms represents the most common solid tumor in childhood and is the leading cause of mortality, accounting for nearly 25 to 30 percent of primary CNS tumors in children younger than 18 years of age.

Molecular biology findings point to a group of negatively transformed stem cells capable of regenerating malignant cells and existent among tumor cell populations as the progressive factor. While current treatment options consist of chemotherapy, tumor resection, and radiation, the risks of treatment include severe neurological defects as well as secondary brain tumors.

Further gene profiling has subdivided the group into four categories based on pathways activated; these include the following: Wnt, Shh, Group 3, and Group 4. Moreover, overexpression of OTX2 was determined to be common across most medulloblastomas. These OTX2 mutations are linked with several disabling phenotypes, including those producing ocular and CNS abnormalities such as seizures, short stature, developmental delay, and pituitary hormone deficiency (CPHD).

Several variables are used to determine cancer type and prognosis, including age, completeness of resection, histological subtype, and genetic markers, which now contribute to treatment decisions and prognostication. Patients can be categorized by risk profile to coordinate treatment modalities as well. Across several groups in past years, new approaches to treatment have improved survival rates and reduced mobility significantly. Some of these advances in the treatment of medulloblastomas include restoring normal cerebrospinal fluid (CSF) flow and maximal tumor resection.

Pilocytic astrocytoma (PA) is the most common glial cell tumors arising in children. Sporadic cases have been linked to KIAA1549: BRAF gene rearrangements. Roughly a quarter of pediatric patients develop PA in the context of the neurofibromatosis 1 (NF1) inherited tumor predisposition syndrome. These tumors are disposed to forming in the optic pathway and brain stem. They also arise within the cerebellum, pointing to the involvement of additional inactivation or mutation events involving the NF1 tumor suppressor gene or KIAA1549:BRAF gene product.

Several etiologic theories exist involving the differential risks of preneoplastic neuroglial cell formation in different brain regions under which sporadic PAs form. The most central of these include transformed stem cells populations. These tumors are often seen with GFAP articulation and histological inclusions, including eosinophilic bodies and Rosenthal fibers. Microvascular growth and large amounts of microglia are often features of these cells. Additionally, the mitogen-activated protein kinase pathway, shown to be a hallmark of PAs is often constitutively active and dysregulated. Loss of tumor suppressor neurofibromatosis 1 (NF1) leads to many of these disorders. In individuals with loss of function mutations in NF1, optic and auditory nerves may be at risk.

Pediatric ependymomas arise throughout the craniospinal axis but are found most commonly along the vertebral system. The spine and meninges are deeply affected. Chief histological features include pseudo rosettes and spiral aura of cells around veins. Additionally, large, solid cytoplasmic inclusions and positive stains for GFAP are notable features on immunoassaying. They originate from glial cells, which give rise to ependymal cells during development. These tumors constitute half of all spinal cord gliomas, roughly 10 percent of pediatric intracranial tumors and approximately 15 percent of all cord tumors.

Ependymomas are the third-most common primary brain tumor in children. Intracranial ependymomas commonly arise within the sacrococcygeal region, mediastinum, and ovaries. Intracranial ependymomas are characteristically found in pediatric populations and tend to be rare in adults.

The vast majority of all pediatric ependymomas are intracranial. Supratentorial tumors account for only a third of ependymomas found in this region in pediatric patients. Supratentorial lesions form in the lateral or third ventricles but may also arise within the white matter or rarely in the cortex. Most pediatric spinal cord tumors account for a tenth of all ependymomas.
Pediatric high-grade gliomas (HGGs), which include glioblastoma multiforme, anaplastic astrocytoma, and pontine gliomas, among others, are difficult to treat and are associated with an extremely poor prognosis. Where there are no effective chemotherapeutic treatments for pediatric HGG, new treatment regimens are in active investigation. Differences between adult and pediatric HGG require additional studies in children.

Molecular science has revealed cell markers that are overexpressed in pediatric HGG include PDGFRα and P53. For example, upregulation of EGFR is distinguishable but to a lesser degree than in adult HGG. Unfortunately, key therapeutics including bevacizumab and tipifarnib have been shown to be less active in pediatric patients than that observed in adults. Gefitinib has shown greater effects. After promising phase I findings in children with primary CNS tumors, the integrin inhibitor cilengitide is being investigated in a phase II trial. Studies are underway in pediatric HGG with two EGFR inhibitors: cetuximab and nimotuzumab. Dendritic cell-based vaccinations, boron neutron capture therapy, and telomerase inhibition remain novel therapeutics under investigation.

Godfrey Ilonzo
Independent Scholar

See Also: Brain Stem Glioma, Childhood; Brain Tumor, Cerebellar Astrocytoma, Childhood; Brain Tumor, Cerebral Astrocytoma/Malignant Glioma, Childhood; Brain Tumor, Medulloblastoma, Childhood; Brain Tumor, Supratentorial Primitive Neuroectodermal, Childhood; Brain Tumor, Visual Pathway and Hypothalamic Glioma, Childhood; Ependymoma, Childhood.

Further Readings

Brain Tumor, Medulloblastoma, Childhood

Although cancer is rare in children, brain tumors are the most common type of childhood cancer other than leukemia and lymphoma. About one out of five childhood brain tumors are medulloblastomas (MBs). Childhood MB is a disease in which benign (noncancer) or malignant (cancer) cells form in the tissues of the brain, especially in the cerebellum, which is at the lower back of the brain, or posterior fossa and have a tendency to disseminate rapidly throughout the central nervous system (CNS). The cerebellum is the part of the brain that controls movement, balance, and posture.

Epidemiology
MB, as the most common brain tumor of childhood, represents 20 percent of all childhood brain tumors. They are most frequent in children between the ages of 3 and 8 and are slightly more common in boys (62 percent) than girls (38 percent). The disease is more prevalent in younger children than older children. Forty percent of patients are diagnosed before the age of 5, 31 percent are between the ages of 5 and 9, 18.3 percent are between the ages of 10 and 14, and 12.7 percent are between the ages of 15 and 19. The overall incidence rate of MB is approximately 1.5 and 0.62 per million population in the United States. Children (1 to 9 years of age) with MB had an incidence rate of 6.0, compared to 0.6 in adults; and therefore, children are 10 times more likely to be affected by an MB than adults.

Signs and Symptoms
General symptoms are: vomiting (most common) with or without nausea, headaches, clumsiness, difficulty with tasks like handwriting, gradual decline in school performance (impaired attention).

Diagnosis
The following tests and procedures examine the brain and spinal cord to determine if there is childhood MB or to locate exact traces of tumor cells before taking biopsy: computed topography (CT scan), a procedure that makes a series of detailed pictures using X-rays of areas inside the body, which then can be
visualized via a computerized system—a dye may be injected into a vein or swallowed to help the organs or tissues show up more clearly—and magnetic resonance imaging (MRI), a procedure that uses a magnet, radio waves, and a computer to make a series of detailed pictures of areas inside the brain and spinal cord. A substance called gadolinium is injected into the patient through a vein. The gadolinium collects around the cancer cells, so they show up brighter in the picture. The final step for diagnosis of an MB is made by the neurosurgeon taking a biopsy of the tumor. This is taken when the neurosurgeon makes attempts to remove the entire tumor.

Pathophysiology
MB is a cerebellar tumor arising predominantly from the cerebellar vermis. The histogenesis of MB remains controversial. One view suggests that the cell of origin derives from the external granular layer of the cerebellum. This is supported by the finding that the proliferation of precursor neurons in this layer is controlled by sonic hedgehog (SHH), whose receptor PTCH is mutated in a subset of sporadic MBs. Another hypothesis proposes that MBs have more than one cell of origin. This is based on studies showing differential immunoreactivity to a neuronal calcium-binding protein that is not expressed in the external granular layer and to a beta-tubulin isotype, which is expressed in the neuronal cells of the ventricular matrix and external granular layer. Numerous molecular alterations that appear to modulate the biological behavior of MB or its response to therapy have been reported. Recent integrated genomic studies have revealed that MB is composed of four distinct molecular and clinical variants: WNT, SHH, Group 3, and Group 4. Involving of genetic alterations in the pathophysiology of MB is exemplified in a study that suggests that MB expression of neurotrophin (NT3) may modulate the behavior of these tumors by inducing apoptosis, thereby retarding tumor progression and resulting in a more favorable prognosis.

As the tumor grows, obstruction of cerebrospinal fluid (CSF) passage through the fourth ventricle generally occurs, resulting in hydrocephaly. The tumor may spread contiguous to the cerebellar peduncle, or the floor of the fourth ventricle; anteriorly, to the brainstem; inferiorly, to the cervical spine; or superiorly, above the tentorium. It also may spread via the CSF intracranially or to the leptomeninges and spinal cord. Of all the pediatric CNS neoplasms, MB has the greatest propensity for extraneural spread, especially to bone and bone marrow; however, the rate of such events is less than 4 percent. It is currently thought that MB arises from cerebellar stem cells that have been prevented from dividing and differentiating into their normal cell types.

Mortality and Morbidity
Risk group stratification is continuing to evolve but is currently based on three principal features, including age, extent of postoperative residual disease, and the metastasis stage (M stage) derived from the Chang classification staging system. The average-risk disease group is defined as patients older than 3 years who are at stage M0 with less than 1.5 cm² of residual tumor postoperatively. The poor-risk disease group is defined as patients older
than 3 years who are at stage M1 through M4 or with more than 1.5 cm² of residual tumor postoperatively. Infants are defined as patients younger than 3 years. This group has the worst prognosis, regardless of M stage and extent of postoperative residual disease.

**Treatment**

With aggressive surgery, craniospinal radiotherapy, and chemotherapy, more than 50 percent of children with MB can be expected to be free of disease five years later. Using current treatments, 80 to 90 percent of those without disseminated disease can be cured; however, treatment for this disease often results in significant endocrinological and intellectual sequelae. Children greater than 4 years of age who have had a complete tumor resection receive a combination of craniospinal (brain and spine) radiation, followed by a four-month course of intensive chemotherapy. Because of the significant effects of radiotherapy on an infant’s developing brain, children less than 3 years of age receive high-dose chemotherapy immediately following surgery, with the aim to delay or even obliterate the need for radiation treatment.

The progress of using blood stem cell transplants instead of radiotherapy has impacted the overall survival rate of this disease. The overall five-year survival rate is the percentage of people who survive at least five years after the cancer is detected, excluding those who die from other diseases. For children with MB, this depends on several factors, including the risk level for this disease and age at the time of diagnosis. Survival rates for children who had a complete removal of their tumor during initial surgery have risen to 80 percent survival at five years from diagnosis, compared to 50 percent and 60 percent survival rates five years ago. The treatment of infants continues to be difficult (30 percent survival rate). This is because of the delay in the ability to deliver radiation to the entire brain and spine, resulting from the known detrimental effects it has on the developing brain.

Mohamad Reza Aghanoori
Shiraz University of Medical Sciences

**See Also:** American Brain Tumor Association; Childhood Brain Tumor Foundation.

**Further Readings**


**Brain Tumor, Supratentorial Primitive Neuroectodermal, Childhood**

One of the ways in which brain tumors are classified is according to whether they are located in the upper or lower part of the brain. Supratentorial tumors are located in the upper part of the brain, where the cerebrum—the center of thought, emotion, learning, and voluntary movement—is located. A primitive neuroectodermal tumor (PNET) occurs at the neural crest. The neural crest is a migratory cell population at the border of the neural plate, which is formed during neurulation—the folding of tissue that begins the formation of the central nervous system in the developing fetus. While the neural tube forms into the brain, spinal cord, retina, and posterior pituitary, the neural crest becomes ganglia, pigment cells, facial cartilage, the adrenal medulla, and other features. Most of the tissue of a
primitive neuroectodermal tumor comes from the neuroectoderm, the germ cell layer that develops into the nervous system. Primitive neuroectodermal tumors are rare and usually occur in children and young adults. The "primitive" part of the name refers to the fact that the neuroectoderm cells in the tumor have not developed or differentiated like normal neurons. PNETs are divided into two types: peripheral PNETs, which occur on the bone, and central nervous system PNETs, nearly all of which are supratentorial.

Primitive neuroectodermal tumors are part of the Ewing family of tumors (EFTs), all of which develop from the same kind of stem cell. Other EFTs include Ewing tumor of bone, extraosseous Ewing tumors, and Askin tumors (PNETs occurring in the chest wall). As with most childhood brain tumors, the causes of PNET are unknown.

Symptoms of PNET are typical of other brain tumors and include symptoms that may be mistaken for other illnesses—including sleepiness, nausea, vomiting, and headaches—as well as symptoms that are more immediately suggestive, like weakness or change in sensation that is specific to one side of the body, and unexplained weight changes. Changes in personality or behavior may or may not be noticeable depending on the age of the child. Once a tumor is suspected, a computed tomography (CT) scan or magnetic resonance imaging (MRI) is performed to locate it, followed by surgery. During surgery, part of the skull is removed, and a sample of tumor tissue is examined for signs of cancer. If the tumor is cancerous, the surgeon removes it during the same surgical session.

As with other cancers, prognosis is dependent on the size and spread of the tumor and how thorough the surgical removal is. The location and size of the tumor and the age of the child impact treatment options. There is no staging system for PNETs—instead, cases are discussed in terms of poor risk (if the tumor was near the center of the brain, if some of the tumor remains after surgery, if the cancer has spread, or if the child is under 3 years old), which have a high chance of recurrence, or average risk, if the child is over three, nearly all of the tumor was removed, and the tumor has not spread.

Risk groups can be determined through MRIs and chest X-rays as well as a bone scan—during which radioactive material is injected into the patient, which collects in the bones before being scanned—or lumbar puncture, also known as a spinal tap, a painful procedure by which cerebrospinal fluid is extracted from the spinal column.

In addition to surgery, radiation therapy and chemotherapy are used to treat PNETs, as with other brain tumors. Typically, surgery is followed by radiation therapy to the brain and spinal cord, especially if not all of the cancer was removed; radiation helps destroy the remaining cancer cells. However, radiation exposure can have significant effects on the development of the child brain, and so lower-exposure means may be used, or chemotherapy may be used in order to either replace or, commonly, delay radiation therapy. Children under 3 are especially poor candidates for radiation therapy.

The five-year relative survival rate for PNETs is 64 percent for children and 35 percent for adults age 20 to 25. There are only two known survivors over the age of 25. The oldest known PNET patient, 41-year-old Tim Young, underwent surgery for PNET of the spinal cord in 2008; he remains a survivor in 2014.

As with other cancers, there is a chance of PNET recurring. Recurrent childhood supratentorial PNET may come back many years later, and while it usually recurs in the brain or spinal cord, it can occur in other parts of the body instead, such as the lungs or bone tissue.

Bill Kte’pi
Independent scholar

See Also: Brain Stem Glioma, Childhood; Brain Tumor, Cerebellar Astrocytoma, Childhood; Brain Tumor, Cerebral Astrocytoma/Malignant Glioma, Childhood; Ependymoma, Childhood.

Further Readings
Brain Tumor, Visual Pathway and Hypothalamic Glioma, Childhood

Anterior visual pathway (optic) gliomas are brain tumors that arise in the structures that convey vision from the eye to the brain. Their origin is not from the nerve cells but from the stellate cells (astrocytes) that are supporting cells in the central nervous system. Optic pathway gliomas account for approximately 5 percent of childhood brain tumors; most patients are diagnosed before age 10. Optic pathway gliomas also can develop in adults, but the natural history is different in those cases, and the outcomes are poorer. This entry focuses on optic glioma in the pediatric population.

Children with optic gliomas typically present with visual impairment, although they can have a number of other problems depending on the tumor location. Symptoms can include abnormal eye movements, eye protrusion, headache, and even endocrine dysfunction. Sometimes the symptoms are not recognized until later in the disease course, especially in younger children because of their limited ability to communicate.

The tumor can be located anywhere along the visual pathway, the route that conveys information from the eye to the brain. From front to back, it includes the optic nerves, the optic chiasm (an X-shaped structure where the optic nerves join inside the skull and where parts of the optic nerves cross), and the optic tracts. The visual information is then transmitted to the posterior portion of the brain (the visual cortex), where higher levels of visual processing begins.

Nearly all childhood optic gliomas are benign and slow growing, and the prognosis for survival is good. The diagnosis usually is made from the appearance of a lesion on brain imaging. The symptoms, management, and prognosis of visual pathway gliomas depend largely on which of the visual pathway structures are involved and to what extent. The main goals in management of all visual pathway gliomas are to retain as much vision for as long as possible and to decrease any other potential complications associated with the disease or its treatment.

If only the optic nerve is involved, then the tumor is known as an optic nerve glioma. About a quarter of visual pathway gliomas are confined wholly to the nerve at the time of diagnosis. Gliomas confined to the optic nerve have fewer complications and higher survival rates than other gliomas of the visual pathway. They result in vision loss in one eye. One significant risk factor for developing an anterior visual pathway glioma is having a diagnosis of neurofibromatosis type 1 (NF1), also known as von Recklinghausen’s disease. This disease is dominantly inherited and is characterized by optic gliomas, nodules on the iris, bone abnormalities, and skin lesions. The cause is a mutation of a gene that encodes a protein known as neurofibromin, which acts in cell signaling. Patients with NF1 account for one in three patients with optic gliomas, and so any patient with a newly diagnosed optic glioma should be evaluated for this disorder. Usually, resection as a treatment choice is considered only for visual pathway gliomas that are confined to the optic nerve because it would be too invasive to try to remove tumors from other areas of the visual pathway, but resection of optic nerve gliomas usually is considered only when an eye no longer has vision and there is severe protrusion of the eye.

The optic chiasm is the next structure back from the optic nerves in the visual pathway. The hypothalamus, which controls metabolism and homeostasis, is located just above the chiasm. Because of their proximity, optic chiasm gliomas can involve the hypothalamus. Hypothalamic involvement can cause developmental delay and hormonal dysfunction, such as early puberty and weight changes.


Some chiasmal tumors also increase intracranial pressure by blocking the normal flow of cerebrospinal fluid, causing nausea, vomiting, lethargy, irritability, and headaches. Sometimes patients with these symptoms undergo shunt procedures to redirect the fluid. Optic chiasm and hypothalamic gliomas have the highest rate of death among the visual pathway gliomas.

Children affected by visual pathway gliomas are seen by a multidisciplinary team of physicians. The treatment options most often elected are chemotherapy and radiation. These treatments can be effective, but their adverse side effects do not warrant their administration unless functionally debilitating symptoms arise. Sometimes visual pathway gliomas spontaneously regress, so there is some controversy about the best way to treat these tumors. Asymptomatic tumors are typically observed with serial eye examinations and imaging studies.

Both chemotherapy and radiotherapy can stabilize or shrink these tumors, but chemotherapy is usually the first-choice treatment for children if observation is not favored. Chemotherapy involves the use of medications that disrupt the tumor cells’ ability to replicate. This can be an effective therapy, but side effects such as nausea, vomiting, and anemia can occur because the drugs do not differentiate between tumor and normal tissue. There are also patients who have tumors that progress or recur despite chemotherapy. Radiation therapy uses high-energy rays to kill and shrink the tumors. Although it is also effective, serious long-term side effects such as cognitive, hormonal, and vascular complications may occur as well as the formation of secondary tumors, especially in patients with NF1. Recent advances in radiation therapy allow for more specific targeting of the treatment to smaller areas, reducing damage to nearby tissues, but given the potential side effects, radiation therapy is often avoided as the initial treatment, especially in younger children. Surgery is also avoided if possible because the visual pathway and other nearby structures can be damaged during resection of the tumor, and resection of gliomas is in any case rarely feasible from a technical point of view.

The management of gliomas of the anterior visual pathway varies depending on the location of the tumor, the age at diagnosis, and the symptoms and is still a work in progress. Further research is underway to find better ways to manage these tumors. Newer technologies and surgical techniques may provide better options for future treatment of this disease.

Yoshihiro Yonekawa
Aubrey Gilbert
Simmons Lessell
Harvard Medical School

See Also: Brain Tumor, Cerebral Astrocytoma/Malignant Glioma, Childhood; Chemotherapy; Radiation Therapy.

Further Readings

Brazil

Brazil is the largest country in South America (it occupies about 47 percent of the South American continent). It has approximately 200 million inhabitants, therefore the largest population in the whole continent, encompassing at least five big ethnic groups. Compared to other countries, Brazil has a cancer rate that is lower than Europe, North America, and eastern Asia. The incidence of some cancers in the United States—for example, breast cancer—doubles those in the totality of South America. In the whole continent, there are some transformations, in principle attributable to the transition from a high incidence of infectious diseases to chronic conditions. That situation has resulted in an increase of the incidence of cancer. As a part of Latin America, Brazil reaches the level of epidemics in terms of cancer. Economic inequity, lack of prevention, and lifestyle are actively contributing to the increase of mortality rates.

In Latin America, although the incidence of cancer is lower than in Europe or in North America, the probability of dying of cancer is 60 percent higher than in those continents.
However, chronic diseases such as infections by candida, malaria in some regions like Amazonas, or hepatitis B still have an enormous impact on the population.

**History**
The perception of cancer, as in most countries, underwent a transformation between the 19th and 20th century. At the beginning, it was seen as something exceptional and therefore as a rare social problem. However, once the aging population pushed the incidence of cancer higher, specialized care and philanthropic approaches began to appear.

In the late 1910s, radiotherapy was applied in restricted cases in Brazil—usually limited to skin cancers. In fact, when the National Department of Public Health was created, its main goal was to control cancer, thanks to the connections between dermatology and oncology. Between the 1920s and the 1940s, Brazil made systematic efforts to control cancer in the whole country. In the early 1920s, philanthropic societies provided facilities for patient treatment. On its part, government made investments in order to inform the public and implement prevention programs. Following the examples of Europe and the United States, Brazil implemented in the 1920s the first anticancer policy in the sanitary system. In the decade of the 1930s, the first leagues to fight cancer emerged. Their purpose was to raise funds in order to build centers for diagnosis and treatment. In 1935, during the First Cancer Congress, several experts tried to convince authorities about the need of a generalized system of cancer control. In 1937, the first center of oncology was founded.

All those plans were virtually possible after the creation of the National Department of Public Health, consolidated at the end of the 1940s but was created in the 1920s, when cancer became a priority not only in terms of information to the population but also in a better understanding of cancer as a professional field. Until that moment, the efforts were rather few and not enough to reach the expected goals. However, that priority was relative; most experts were more concerned about infectious diseases with high impacts on the population, like malaria, syphilis, leprosy, or tuberculosis. In fact, many doctors believed that cancer was a transmitted disease, similar to leprosy.

**Brazil in Figures**
In Western countries, and in many developing countries, there are similar scenarios: Most cancers occur among male populations. Besides, in Brazil the highest mortality rates occur among men, especially in the case of lung, prostate, and stomach cancers. But there is a big difference in comparison to Western, developed countries, where cancer used to be the first or second cause of death. In Brazil, it is the third cause, just after vascular diseases and external causes. The highest average incidence was found in the region of Porto Alegre and São Paolo, and it is valid for both males and females.

Contrary to other worldwide trends, the most common malignant tumor in men is nonmelanoma skin cancer, followed by lung, colorectal, and stomach. Among women, skin cancer also is placed at the top of the most common malignant tumors, followed by breast, cervical, and colorectal cancer. Skin cancer (nonmelanoma), although it is the most common cancer, used to be surgically removed with no further consequences for the patient. The high rates of infection by human papillomavirus (HPV) are translated into a high incidence of cervical cancer. From an epidemiological point of view, some programs were implemented in the last years in order to study HPV transmission and to test (effective) vaccines. With regard to breast cancer and in the context of Latin America, Brazil, together with Peru, are countries with worse expectations for those patients due to late diagnoses, when cancers are at advanced stages and the results of the treatments rather poor.

According to the Unity of Prevention and Control of Cancer, from the Brazilian Cancer National Institute, whereas some type of cancers, like prostate, breast, and colorectal, are the consequence of an improvement of socioeconomic level, other malignant tumors—oral, cervical, and penile—are more associated with poverty.

The cancers caused by occupational agents apply to between 2 and 4 percent in the case of Brazil, affecting primarily the lungs, bladder, or skin or even causing leukemias.

In the case of developing countries, like Brazil, around 20 percent of the totality of cancers is attributed to some collateral effects of globalization—sedentary lifestyle, use of alcohol, and inappropriate diet. Despite all of this, it has a low rate compared to developed countries, where the average could be 30 percent.
It is estimated that about 1 million people are under risk of suffering some kind of cancer due to a specific attribute (age, gender, status, etc.) and that 520,000 new cases will be registered annually. In fact, the number of cases annually per 100,000 people is 171.3. The annual number of deaths reached 1,261,100, according to official data from 2013, and it is higher among men than among women.

One of the most important institutions is the José Alencar Gomes da Silva National Cancer Institute (INCA), which provides statistical data as well as general information for the population and specific information for patients. Its fundamental mission is to improve the quality of life of patients, detecting administrative mistakes that could be an obstacle in the process of a patient’s treatment.

The Brazilian Population-Based Cancer Registry (PBCR) was created in 1967 in Recife, followed by the registry of São Paolo two years later. Actually, the Brazilian Cancer Registry is the result of regionalized efforts—it covers a total of 27 states to collect data, to provide indicators, and to publish updated reports. It integrates with other health institutions or programs, like Mortality Information System (SIM), Health Care Management, and NCD Surveillance.

In the last years, some associations to give support to cancer patients have proliferated. The most relevant is the Brazilian Association for Supporting Cancer Patients (ABRAPAC), which gives practical information and advice to cancer patients in order to improve their quality of life not only in terms of treatments but especially in all collateral support (emotional support, how to face hair loss after chemotherapy, etc.). Besides, since 2000, the project Brazilian Association of People Suffering From Cancer (AMUCC) has been in operation, originally created to give support to women affected by breast cancer and later involved in projects related to all cancers and any kind of patient. Its main goal is to ensure the rights of cancer patients.

Finally, the Brazilian Society of Oncology promotes campaigns to fight risk factors of cancer related to lifestyle. They provide information to patients but also resources like specialized publications that can be consulted online.

See Also: Disparities Within Nations (Elimination of Cancer); Global Health Issues and Cancer; Organisation of European Cancer Institutes; Solar Radiation; Sun Exposure (Australia).

Further Readings

Breast Cancer

Breast cancer is a major public health problem in the developed world. It is the most common cancer among U.S. women and makes up a significant portion of illness, health care expenses, and loss of life. One in eight women is expected to develop breast cancer in her lifetime. Factors associated with increased breast cancer risk include family history of the disease, higher number of lifetime menstrual periods, and inadequate physical activity; generally, the disease is thought to result from a complex combination of genetic and lifestyle factors. One key to reducing the burden of breast cancer is to detect the disease at its precancerous or early cancerous stages. Tools for early detection include mammography, imaging, and self-examinations.

Studies suggest that breast self-exams lead to increased follow up of noncancerous masses and do not increase breast cancer death rates. The benefits of screening for early detection need to be balanced against the risks of increased anxiety among women whose screening results ultimately may turn out to be negative. Over recent decades, better treatment options for breast cancer have improved the outcomes for patients. The promising outlook for breast cancer is due in part to breast cancer advocacy, which grew immensely at the end of the 20th century. Community involvement has
increased awareness, support, and research funding for this common and deadly disease.

In 2015 in the United States, the American Cancer Society estimates that 231,840 new cases of breast cancer will be diagnosed in women and 2,350 new cases in men. The number of new breast cancer cases increased rapidly throughout the 1980s and since then has risen only slightly. This is likely to be a result of increased screening in the 1980s followed by the use of novel tools for early detection.

Despite increasing numbers of new diagnoses, early detection and improved treatments held the number of deaths attributed to breast cancer among women constant until 1990. Following this time, deaths due to breast cancer decreased substantially. The American Cancer Society reports that, between 1990 and 2003, deaths from all types of cancers in women decreased, and 40 percent of this decline was due to reductions in breast cancer deaths.

In 2015 in the United States, the American Cancer Society estimates that 40,290 women will die of breast cancer, as will 440 men. The disease is currently the second-most common cause of cancer deaths (second to lung cancer), representing an estimated 15 percent of all deaths due to cancer in women. However, among women age 20 to 60, breast cancer is the most common cause of cancer death; African American women are estimated to have the highest rates of breast cancer deaths compared to other women.

Risk Factors
Although we have learned much about a variety of factors that may influence the development of breast cancer, the true cause of breast cancer remains unknown. It is likely that breast cancer results from a combination of genetic and nongenetic factors. Thus, a woman who is at increased risk due to disease in her family may be able to modify this risk with changes in lifestyle factors, such as increasing her frequency of exercise.

Epidemiologic researchers conducting studies of large numbers of women compare characteristics of those who do and who do not develop breast cancer and have found some consistent results. Some risk factors are unfortunately not modifiable. These include being female (women are at much higher risk), being white (African American, Asian, Hispanic, and American Indian women have lower rates), increasing in age (older women are more likely to develop the disease), and having affected relatives (having a mother, sister, or daughter with breast cancer about doubles risk). In addition, starting periods at an early age and entering menopause at a later age increase a woman's risk of breast cancer; this is thought to be due a longer lifetime exposure to estrogens.

Other factors related to the risk of developing breast cancer may be considered modifiable. These include childbearing (women pregnant at an early age and pregnant more than one time are at a lower risk), breast-feeding (women with children who breast-feed seem to be at reduced risk), exercise (physically active women are at lower risk), avoiding alcohol (drinking up to five drinks a day may increase risk), and maintaining lower body weight (children with large weight gain may be at increased risk of later breast cancer and women who are obese after menopause are at increased risk).

There are also more complex, modifiable factors that should be considered in consultation with a physician. Hormone replacement therapy, specifically the use of estrogens combined with progesterone, after menopause has been shown to increase breast cancer risk. A woman’s use of oral contraceptives within the last decade may increase risk as well. There are also medical conditions associated with increased risk including radiation treatment in the chest area, abnormal breast biopsy, and certain formerly used hormonal treatments such as diethylstilbestrol (DES).

A physician should be consulted about the risks and benefits of medical treatments that may lead to modified breast cancer risk later in life.

Less-common factors may also influence a woman’s breast cancer risk. Studies are under way examining specific environmental pollutants that may influence risk at very high doses; however, no results to date are clear-cut. Approximately 7 percent of all breast cancer cases are thought to be due particularly to genetic changes passed down in families. A portion of these truly familial cases are due to changes in the genes, BRCA1 and BRCA2. Changes, or mutations, in these genes lead to an approximate 80 percent chance of developing breast cancer. While the search is under way for similar genes, and for genes conferring more modest increases in risk, it is likely that modifiable factors play a role even among families with these high-risk genes.
Screening and Early Detection

Like other cancers, the burden of breast cancer in terms of medical complications, expense, and most important, death can be reduced if the disease is detected at an early stage, for example, before it has spread to other organs in the body. Early detection of breast cancer can be attained by routine population screening and by easy access to care when any symptoms first develop, assuming symptoms are recognized by the woman experiencing them.

There has been great debate in the recent decade about the utility of monthly breast self-exams. One of the potential harms from breast cancer screening comes from false positive findings leading to unnecessary further testing and anxiety. Several studies, including a large randomized trial in China, suggest that breast self-exams lead to increased follow-up of noncancerous masses and overall do not increase breast cancer death rates.

The traditional approach to breast cancer detection is an annual physical examination by a physician. Many medical organizations, including the American Cancer Society and the American College of Radiology, recommend annual screening mammograms for women starting at age 40. Screening mammograms are X-rays of the breasts (generally two for each breast) done in women with no signs or symptoms of breast cancer in order to find very early stages of breast cancer before they can be found on a clinical exam. It is generally agreed that patients between age 40 and 50 years should be screened every 12 to 24 months. There have been several randomized studies showing the efficacy of annual mammographic screening in reducing breast cancer rates by about 20 to 30 percent in women after age 50. The benefit of an annual screening mammography in women age 40 to 50 or over 70 years is less clear. It is important to note that breast exams performed by clinicians with proper technique can detect up to 5 percent of cancers not picked up by mammograms.

One form of screening mammography uses digital mammograms (as opposed to standard film mammograms) wherein images are captured as in film mammography and then digitally manipulated for clarity. Digital mammography is preferred in women with denser breast tissue; dense breast tissue is seen mainly in women who have not yet entered or are in the midst of menopause. Digital mammography systems are two to four times more expensive than film mammography systems. Some institutions use computer-aided interpretation of mammography, although the benefits of computer interpretations, considering substantial increases in cost, remain to be proven.

Other means of detecting breast cancers are used to complement these methods. Ultrasound of the breast complements a mammogram in evaluating lumps detected by physical examination and can be useful in following up abnormal mammogram findings and is relatively inexpensive. Magnetic resonance imaging (MRI) is a technique that enables the diagnosis of breast cancer that cannot be seen in mammograms in up to 10 to 18 percent of cases. An MRI can be used to identify multiple areas of cancer in the same breast and define the extent of cancer. An MRI of the breasts is increasingly used as a screening procedure especially in high-risk women (such as those with BRCA1 or BRCA2 gene mutations) and in women with dense breast tissue. Because an MRI is expensive, requires injection of dye, has a lower specificity leading to increase rate of follow-up invasive procedures, screening MRI is not advised in average-risk women.
Breast Cancer

Diagnosis and Prognosis

A biopsy of any lump in the breast or a suspicious area on a mammogram is performed using a needle to draw cells from the lump and examine them under a microscope. Cancer diagnosis is then established.

At diagnosis, approximately 60 percent of breast cancers are localized (confined within the breast), 30 percent are regionally spread (e.g., to nearby lymph nodes), and 10 percent have metastasized (e.g., to the liver). African American women tend to be diagnosed at a more advanced stage, consistent with increased rates of breast cancer death in this group and indicative of fast-growing disease. Two types of breast cancer can be diagnosed: Ductal carcinoma in situ (DCIS) is diagnosed if the cancer has not invaded outside the mammary ducts, and invasive cancer is diagnosed when the cancer has spread outside the milk ducts.

When a breast cancer is diagnosed, the staging process begins, involving extensive testing to assess the extent of disease within the body. Medical history, physical examinations, chest X-ray, and blood tests are used as staging tests. If any of these tests are abnormal, then a bone scan (injection of a radionuclide substance intravenously and imaging the whole skeleton), computed tomography (CT) scan or a positron emission tomography (PET) scan are obtained as needed. Some of these tests are very costly and are therefore used only when specially indicated.

Recent data suggest that, on average, 89 percent of women diagnosed with breast cancer survive five years or more. Women diagnosed with Stage I breast cancers (tumors less than 2 centimeters with no lymph node involvement) can have an overall 10-year survival (proportion of patients living 10 years following diagnosis) of up to 95 percent, women diagnosed at Stage II (less than 2 centimeters with or without lymph node involvement) have an average 10-year overall survival of up to 80 percent, and those with Stage III disease (less than 5 centimeters or fixed tumor or several sentinel lymph nodes [SLNs] involved or with inflammatory changes) have 10-year overall survival of up to 50 percent with modern treatments.

Treatment Options

Women with early-stage breast cancer typically undergo surgery. Mastectomy (removal of entire breast) and breast conservation surgery (smaller surgery focused on limited area using a wide local excision or lumpectomy) confer similar prognoses. SLN sampling is routinely done during these surgeries, which involves the removal of the lymph node nearest to the affected area in the breast.

The SLN is examined for the presence of cancer cells, and if the SLN is positive for cancer metastasis, then a full dissection of auxiliary lymph nodes is performed. Tumors that are removed in surgery are tested for estrogen receptor (ER) and progesterone receptor (PR) status, which indicate the presence of these proteins in the nuclei of the cancer cells.

Following surgery, subsequent treatments may include radiation treatment, chemotherapy, or hormonal therapy depending on the size of tumor, lymph node involvement, type of initial surgery, menopausal status, and estrogen and progesterone (ER and PR) status. Patients with breast-conserving surgery undergo postoperative radiation therapy to prevent local recurrence of cancer. Currently, the standard radiation therapy is delivered over a period of approximately five weeks. Finding transportation to and from a radiation facility can be a financial burden for many patients.

Generally, for ER- and PR-positive tumors, hormonal therapy such as tamoxifen or aromatase inhibitors (which block adrenal gland production of estrogen) give maximum benefit in women who have gone through menopause. Even in premenopausal women, the hormonal therapy with removal or suppression of the ovaries may be of benefit. In selected patients with DCIS and ER- and PR-positive tumors, tamoxifen is prescribed for five years to prevent local recurrence and the prevention of a new breast cancer in lieu of or in addition to radiation. These treatments can prolong a patient’s life by anywhere from 20 to 40 percent in Stage II and III patients.

For advanced cancers (large tumors and lymph node-positive tumors), additional chemotherapy is recommended. The cost of chemotherapy further increases because patients need to receive growth factors to boost white blood cell counts or red blood cells to facilitate timely treatment. Recently, herceptin, an antibody to treat certain aggressive breast cancers, has been approved to be used along with chemotherapy. This is an expensive treatment requiring patients to return to the clinic at least every three weeks for a whole year.
The American Cancer Society provides navigators for newly diagnosed patients to help them through the process of treatment and accessing resources. A mentor program links current patients with survivors to provide one-on-one support—for example, accompanying patients to doctors’ visits to help them ask the right questions.

**Issues for Breast Cancer Survivors**

Both hormonal therapy and chemotherapy can cause significant side effects, including hot flashes, severe joint pain, and nerve damage requiring further interventions that can be costly. Patients without insurance may not be able to afford cancer treatments and supportive services.

Lymphedema can occur postoperatively, in which excess fluids build up in certain tissues and organs; lymphedema can adversely affect quality of life and decrease productivity at work. Fortunately, surgical advances removing only selected (rather than all) lymph nodes have reduced the burden of this condition.

The cost of breast cancer to patients and society including genetic testing, screening tests, and treatment of established cancer extends to follow-up testing to detect cancer recurrence. Randomized studies have shown that the majority of breast cancer recurrence is detected by a detailed history and physical exam with annual liver chemicals, mammogram, and chest X-ray monitoring picking up other recurrences. Expensive scans, such as CT, PET, and bone scans, and tumor markers in the blood are not currently recommended when following breast cancer survivors.

For breast cancer that has recurred or spread to other organs, there is no cure. However, these patients can live three or four additional years and be on continuous cancer treatments. Newer drugs such as antibody treatments offer more promise, but costs can be prohibitive, with several thousand dollars per monthly treatment, mostly borne by insurance carriers and Medicare. Many of these patients continue to be productive citizens and view life differently following their diagnoses.

Breast cancer survivors have noncancer issues to deal with as well. Having a mastectomy can be a life-changing event for many patients. Patients may be distraught by the loss of a breast and lose their self-image. Reconstruction of the breast has given hope and solace to women who choose to undergo plastic surgery; insurance companies have recently recognized that this is an important aspect of a breast cancer patient’s recovery and currently cover the costs associated with this operation.

Young women thrown into early menopause by chemotherapy and antiestrogen therapy may suffer from low libido and vaginal dryness, which can interfere with sexual relations and emotional relationships with partners. Belonging to survivor groups has been helpful to many women coping with these issues.

**Advocacy**

Women have proven that they carry a powerful voice. In the last half-century, breast cancer awareness has exploded. The month of October has been designated as Breast Cancer Awareness Month in the United States. Pink ribbons symbolizing breast cancer awareness are worn by patients, relatives, friends, and caregivers to remind people to go in for mammograms and contribute to breast cancer research funds. Major retailers such as Estée-Lauder and the Avon Foundation contribute a portion of their profits to breast cancer research.

Breast cancer survivors have lobbied and obtained reimbursement for breast reconstruction. Survivors attend national research meetings and conferences, and their opinions are heard and incorporated into clinical trials.

The Susan G. Komen Foundation is a successful organization started by the sister of a breast cancer patient. It sponsors annual events throughout the nation to raise hundreds of thousands of dollars to fund major research. Breast cancer advocacy groups such as this and the National Breast Cancer Coalition have paved the way for other cancer groups to be powerful advocates. However, much work remains to prevent and cure breast cancer; ongoing research with community involvement is essential to achieve this goal.

Ellen L. Goode
Prema P. Peethambaram
*Mayo Clinic College of Medicine*

**See Also:** Breast Cancer, Male; Breast Cancer and Pregnancy; Europa Donna, the European Breast Cancer Coalition; National Alliance of Breast Cancer Organizations; Screening.
Breast Cancer, Male

Male breast cancer is pathologically similar to female breast cancer but is much less common, while breast cancer is the second-most common cancer faced by women after skin cancer; less than 1 percent of breast cancer cases are male. It is one of the least common cancers among men, with men who live to 95 facing a 1 in 1,000 chance of developing it, compared to the one-in-eight chance of women.

Because breast cancer is overwhelmingly more common in women, most medical knowledge of male breast cancer, including screening and treatment methodologies, is generalized from female breast cancer. Both cancers are functionally the same but behave slightly differently due to the different conditions (hormonal and structural) of male and female bodies.

Risk Factors
Genetic factors are among the possible risk factors for male breast cancer. Like women, men carrying mutations of the BRCA gene—BRCA1 or BRCA2—face an elevated risk of breast cancer, though a man with BRCA mutation still faces a lower risk than a woman without it.

Male breast cancer in the family is itself a risk factor for female breast cancer—a woman whose brother has male breast cancer is 30 percent more likely to develop breast cancer herself than a woman whose sister has breast cancer.

Because most male breast cancer is ER+—meaning the cancer has estrogen receptors—high levels of estrogen, normally found in men only in small amounts, contribute a risk, and so substances that increase estrogen production therefore increase male breast cancer risk. Obesity can lead to elevated estrogen levels, as does cirrhosis of the liver (usually caused by chronic drinking or viral hepatitis) and certain medications for high blood pressure, stomach acid, or prostate cancer. A disproportionate number of men using the baldness treatment finasteride have been diagnosed with breast cancer, but a causal link has not been shown (numerous noncausal correlations could provide an explanation). It is believed that overconsumption of soy proteins increases estrogen levels as well. As with all cancers, there are environmental risk factors, including exposure to radiation or certain carcinogenic chemicals.

The rare hereditary condition known as Klinefelter’s syndrome carries some breast cancer risk. Affecting about one in 1,000 men, Klinefelter’s syndrome is characterized by the presence of an extra female X chromosome (XXY instead of the normal male XY), resulting in larger breasts, higher estrogen levels, smaller testicles, and sparse body hair. Men with Klinefelter’s syndrome have a breast cancer risk that is as much as 50 times that of other men.

Symptoms and Diagnosis
Most male breast cancer is diagnosed after age 60, and it is rarely screened for, except in men facing an elevated risk as a result of genetic factors or previous cancer diagnoses. Genetic factors may be determined by direct relatives having been diagnosed with breast cancer or ovarian cancer (which is linked to breast cancer in some genetic conditions).

Male breast cancer diagnosis usually begins with the discovery of a lump in the breast tissue during self-examination. Discharge from or alterations to the nipple or skin lesions, may less commonly present themselves. After a doctor confirms the presence of the lump, a biopsy is usually performed to determine whether the lump is cancerous; as with women, many lumps are benign.

Male breast cancer can manifest in most of the same types as in women, with ductal carcinoma (cancer of the ducts) similarly being the overwhelmingly most common form. Male breast cancer may also develop as intraductal cancer, Paget’s disease of the nipple, or inflammatory breast cancer, whereas lobular carcinoma in situ has not yet been seen. As in women, male breast cancer spreads through the lymph nodes and
bloodstream, and so it is described with the same staging system.

**Treatment**

Male breast cancer is rare enough that patients may not seek medical attention, assuming other benign causes of whatever symptom they are presenting. However, because the breast is typically much smaller, lumps are more noticeable and easier to find by accident. Cancerous lesions in men tend to be more advanced, because the smaller breast creates less distance for it to travel before reaching skin or muscle tissue, and so about half of male breast cancer patients are stage III or IV.

Treatment usually involves a mastectomy (removal of the breast) or lumpectomy. Though either surgery can leave the chest deformed, fewer pains are typically taken to preserve appearances than have become common in breast surgeries on women. Prophylactic mastectomies—removal of the breasts before any cancer has manifested—is sometimes performed on men with a number of breast cancer patients among their direct relatives.

Chemotherapy and hormone treatment, including tamoxifen for patients whose tumors are ER+, are also used, and radiation therapy often follows surgery in order to eliminate cancer cells that escaped excision. As with any other cancer, chemotherapy has significant side effects, including those caused by the destruction of healthy cells, while hormone therapy typically causes impotence and hot flashes as a result of hormonal imbalances.

Bill Kte’pi
Independent Scholar

**See Also:** Breast Cancer; Chemotherapy; Genetics.

**Further Readings**


---

**Breast Cancer, Sociocultural Differences and**

In the United States, breast cancer is the most commonly diagnosed type of cancer women face, and it is also one of the most deadly forms of cancer for women. Female breast cancer health care costs are the highest for any single cancer, consuming approximately 13 percent of U.S. total health care expenditures and are expected to increase in subsequent years. Specifically, it is estimated that, in the United States, more than $16 billion is spent yearly on female breast cancer treatment and care costs. One-third of this cost is incurred in the last year of life of a woman with breast cancer.

The importance of breast cancer has been highlighted on the national U.S. health care agenda. The National Cancer Institute (NCI), which is the cancer research and training branch of the National Institutes of Health (NIH), reported funding of breast cancer research in excess of $600 million in fiscal year (FY) 2012. A great deal of this research was spent on clinically related projects examining etiology, diagnosis, and treatment. So while there are great contributions being made to the clinical science of breast cancer, there is still much to be understood about the social aspects of the disease, whose two biggest sociodemographic risk factors are gender (being a woman) and age (getting older). For example, according to NCI, women represent more than 98 percent of the estimated incident (or new) cases in 2014. Additionally, the majority of women diagnosed with breast cancer are 65 or older (more than 40 percent); however, women under the age of 50 represent 25 percent of new cases. In addition to gender and age, other sociodemographic categories are important in terms of breast cancer incidence as well as mortality (death) rates.

**Sociocultural Differences in Breast Cancer**

The sociocultural perspective is a theoretical framework that social scientists use to help explain social phenomena, for example, breast cancer incidence and mortality rates, by describing how an individual or group response to phenomena might be influenced by social and cultural factors, such as race, ethnicity, or nationality. Regarding, racial
or ethnic differences in breast cancer, while whites represent the majority of incident cases, overall mortality rates for minority ethnic women are higher. Specifically, African American women are more likely to be diagnosed at later stages of the disease and subsequently have higher mortality rates than other racial or ethnic groups, regardless of age. While race and ethnicity have not been identified by the scientific community as being causal factors in the risk for breast cancer, mortality rates are considerably higher among minority racial and ethnic groups, which is a continued cause for concern.

According to research in the social sciences, there are a number of reasons for this racial and ethnic disparity in the mortality rate; however, two important contributing factors that social scientists point to are (1) cultural differences in beliefs about breast cancer and (2) cultural bias in health care experience. Both of these issues impact rates of detection and screening for breast cancer as well as adherence to treatment recommendations by health care professionals once diagnosed.

**Cultural Differences in Beliefs About Breast Cancer**

No longer seen as a social stigma to be kept hidden, breast cancer receives a great deal of money in research funding and now has become a popular topic within the discourse related to disease and illness. However, even with all of the new information available to the public and the recent positive attention the disease has garnered, cultural differences in beliefs about the disease and its outcomes persist.

A number of lay misconceptions about the disease have been identified from the perspectives of minority women, which include: breast cancer as contagion (spread through contact with another person), fatalism or unavoidable death (death from the disease is predestined and cannot be changed), breast cancer as a result of direct trauma to the breast (resulting in a lump), and breast cancer as a disease mainly of concern for white women (seeing white women as the face of breast cancer in the media). Moreover, cultural taboos about physical touch (e.g., breast self-exams), reluctance regarding open communication about body parts, and spirituality or religiosity in minority communities have been examined. To some degree, these issues factor into whether or not minority groups seek medical treatment, which subsequently explains the presentation of advanced stage of disease, when eventually diagnosed, and higher mortality rates among minorities.

**Cultural Bias in Health Care Experience**

In general the provider–patient relationship has been explored, with the preponderance of evidence reporting that positive relationships (i.e., trusting, shared communication) between health care providers and patients yield better patient outcomes, such as recurring visits to health care providers and adherence to treatment regimens. Racial (and cultural) bias among health care providers contributes to negative patient outcomes for marginalized groups, such as lower quality of life and higher mortality rates. In fact, based on a recent Institute of Medicine (IOM) report examining racial bias in health care, NIH disseminated a call for research examining racial and ethnic discrimination and its effect on the delivery of health care services. Communications from these sources (IOM and NIH) alert us to the continuing importance of race and culture in the health care experience.

Health care providers are not immune to cultural biases. Stereotyping is a learned behavior and practice within our social world. Some general examples of stereotyping within the field of health care are: racial and ethnic minority groups’ noncompliance with recommended medication and other treatment therapies and nonadherence to diet or exercise regimens. As a result of these cultural biases and stereotypes, minorities often find themselves having poor communication and brief interactions with their providers as well as receiving little information about their diseases or illnesses from their providers. These factors can lead to feelings of distrust and disconnect, which again influence the patients’ decisions to make routine visits to medical professionals and their subsequent health outcomes.

**Conclusion**

As with age and gender, breast cancer is also no respecter of race or ethnicity, which is evidenced by minority groups’ higher mortality rates. Early detection is an important way to increase chances for survival. However, misunderstandings and cultural taboos about breast cancer persist in our society.

Communication and understanding within the provider–patient relationship are key to
Breast Cancer and Pregnancy

Breast cancer that is associated with pregnancy can occur during pregnancy, in the first postpartum year, or during lactation. Breast cancer during pregnancy requires consideration of the health of both the mother and fetus in both diagnosis and management.

Epidemiology

Breast cancer is one of the most common cancers to be diagnosed during pregnancy; however, it is very rare to develop breast cancer during pregnancy. It is estimated to occur in one in 1,000 pregnancies. Breast cancer during pregnancy is becoming more common with more women delaying childbearing. No specific risk factors for breast cancer in pregnancy are known; risk factors are similar to non-pregnant women of similar age. First pregnancy later in life is associated with increased risk of breast cancer during the remainder of a woman's lifetime than pregnancy at an earlier age. First pregnancy is associated with substantial breast cell proliferation. First pregnancy has both a short-term adverse effect on risk and a long-term reduction in subsequent risk accumulation. The longer the interval between menarche and first pregnancy, the greater is a woman's breast cancer risk. Therefore, menarche to first pregnancy represents a window of time when breast tissue is particularly vulnerable to carcinogenic stimuli. Full-term pregnancy induces cellular and molecular changes well documented in animal and human models. Pregnancy induces decreases in the number of hormone-sensitive luminal cells and down regulation of the Wnt signaling pathway in basal stem and progenitor cells, making breast tissue less susceptible to carcinogens. Additionally, first pregnancy induces long-term hormonal changes, including reduced prolactin and estrogen levels and increased levels of sex hormone-binding globulin, which may provide further protection against breast cancer.

Diagnosis

Breast cancer in pregnancy usually presents as a painless lump. Diagnosing breast cancer in pregnancy is challenging and often delayed. During pregnancy, physical changes occur in the breasts...
such as enlargement, fullness, and increased tissue density. These changes make it difficult to detect small lumps or masses in the breasts. Early changes from breast cancer could be mistaken for changes that happen with pregnancy. Therefore, breast cancer in pregnant women is often diagnosed at a more advanced stage than for nonpregnant women. Other causes of a breast mass in pregnant or postpartum women include milk retention cyst, infection, noncancerous growths such as fatty tissue or blood vessels, and less commonly other cancers such as blood cancers.

The initial workup includes imaging studies such as an ultrasound and a mammogram of the breast. Mammograms do have small amounts of radiation exposure that is focused on the breasts. A lead shield is used during mammography to protect the fetus; however, it remains unclear what effect the small dose of radiation may have on the fetus. A magnetic resonance imaging (MRI) of the breast is thought to be safe and does not have any associated radiation; however, there is minimal data to support its efficacy during pregnancy. The contrast material used in MRI crosses the placenta; therefore, the use of contrast material is not recommended during pregnancy. A biopsy of the breast lump or the suspicious area on breast imaging is needed to confirm a diagnosis of cancer.

After diagnosis of breast cancer, further imaging may be required to assess if the cancer has spread to other parts of the body. A chest X-ray with abdominal shielding and a liver ultrasound may be used. If there are signs or symptoms of bone involvement, MRI without contrast can be used for evaluation. Positron emission tomography (PET) scans, computed tomography (CT) scans, and bone scans are often avoided during pregnancy because of radiation exposure.

**Treatment**

Treating breast cancer in pregnant women is complex because it involves treating both the cancer while protecting the fetus from harmful effects of treatment. In the past, there was concern about the hormonal changes of pregnancy and effects on the breast. However, studies have shown that pregnancy termination does not improve patient survival.

Treatment of breast cancer in a pregnant woman depends on the size, the location, the type of cancer, and how far along the patient is in the pregnancy. Treatment involves surgery, radiation therapy, or chemotherapy. Surgery could include either partial removal of breast tissue (breast conservation) or removal of the entire breasts (mastectomy). Surgery could be potentially safe for the fetus in all three trimesters. Certain types of anesthesia such as general anesthesia could have negative effects on the fetus, and this would need to be accounted for in planning the surgery.

The type of surgery performed may depend on ability to treat with postsurgical radiation. Breast-conserving surgeries would require radiation to prevent cancer from coming back. Radiation could have harmful effects on the fetus and is not recommended until after delivery. Radiation can cause miscarriage, birth defects, slow fetal growth, and increased risk of childhood cancer. How far along in the pregnancy a woman is would affect this decision regarding possibility for radiation treatment. A significant delay in starting radiation therapy could cause the radiation to be less effective in preventing the cancer from coming back. A woman diagnosed at the end of her pregnancy could have radiation treatment after delivery without much delay. In contrast, a woman in the earlier stages of her pregnancy would be unable to have radiation treatment without significant delay, and a mastectomy may be required. Lymph nodes also need to be removed from the axilla to check for cancer cells. Treatment must be individualized.

Chemotherapy may be needed either after surgery or by itself (before surgery) for advanced cancers. Decision to administer chemotherapy should follow similar guidelines as that for nonpregnant women. However, fetal age would affect the timing of chemotherapy. Chemotherapy is not recommended in the first trimester of pregnancy because this is the time for fetal organ development. Exposure to chemotherapy in the first trimester is associated with a 10 to 20 percent risk of congenital malformation. This risk declines to less than 2 percent in the second and third trimesters. Studies have shown that certain chemotherapies during the second and third trimesters do not increase risk to fetus. Chemotherapy can lower a woman's blood counts and result in infection or bleeding during delivery. Because of these risks, chemotherapy is not recommended after 35 weeks of pregnancy or within three weeks of delivery. Data on long-term effects of prenatal exposure to chemotherapy is limited.
Standard chemotherapy regimens for breast cancer with fluorouracil, doxorubicin, and cyclophosphamide during the second and third trimesters were not associated with fetal complications. The use of anthracycline chemotherapies such as doxorubicin have not been associated with birth defects. Additional chemotherapy may be offered after delivery.

Hormone therapy is often used in nonpregnant women with tumors that express estrogen or progesterone receptors. Hormonal therapy is not safe for the fetus and is associated with high rates of birth defects. Tamoxifen is the hormonal pill indicated for women before menopause. Tamoxifen is associated with high rates of birth defects and is not used in pregnant women. Aromatase inhibitors are hormonal pills used for postmenopausal women and do not work in women who are premenopausal. Aromatase inhibitors are not effective or safe to use in pregnant women.

Drugs that target HER2 such as trastuzumab (Herceptin) are used for nonpregnant women who have breast cancers that are HER2-positive. HER2 expression is also high in embryonic tissues. Drugs that target HER2 are not recommended during pregnancy due to safety concerns for the fetus.

**Breast-Feeding**

Breast-feeding is not recommended while a woman is receiving chemotherapy, hormones, or targeted drugs because these agents can contaminate the mother's milk. Breast-feeding is possible after treatment is completed but it may be difficult as a result of the surgical and radiation changes. Milk production from the nonaffected breast is not changed by surgery or radiation. If radiation treatment is administered, breast-feeding from the irradiated breast is not recommended because of risk of mastitis.

**Survival**

Pregnancy may cause a delay in diagnosis of breast cancer, resulting in the cancer being found in more advanced stages and thus more difficult to treat. Most studies have found similar outcomes among pregnant and nonpregnant women with similar stages of breast cancer.

See Also: Breast Cancer; Chemotherapy; Lymphoma, Hodgkin's, During Pregnancy; Lymphoma, Non-Hodgkin's, During Pregnancy; Radiation Therapy; Surgery; Women's Cancers.

Further Readings


---

**Bristol-Myers Squibb (United States)**

Bristol-Myers Squibb Co. (BMS) is a pharmaceutical company headquartered in the United States in New Jersey. The company conducts drug research and development, licensing, manufacturing, marketing, distribution, and sale of pharmaceuticals as well as other health care products. Its pharmaceutical business segment is the company’s primary source of revenues. The company has developed several cancer drugs, including drugs that show promise in boosting the immune system to fight cancer.
BMS was formed by the combination of the Bristol-Myers Company (Bristol-Myers) and the Squibb Corporation (Squibb). Squibb was founded in 1858 by a U.S. Navy doctor named Edward Robinson Squibb. William McLaren Briston and John Ripley Myers founded the precursor to Bristol Myers in 1887, when they purchased the Clinton Pharmaceutical Company, which was incorporated in 1887. The company was named the Bristol, Myers Company in 1899. In 1989, the two companies merged, creating the world's second-largest pharmaceutical company in the world at the time.

Squibb began to delve into cancer research in 1967 and discovered the drug hydroxyurea to treat leukemia and advanced ovarian cancer. The company was one of the few pharmaceutical firms willing to invest in research into anticancer drugs at the time. Most drug companies wanted to avoid the investment required for research and the risk of not seeing profits from their efforts in the near future. In the 1970s, Bristol-Myers received the rights to market some anticancer drugs developed by other drug companies, academic institutions, and various outside research institutes, including the National Institutes of Health.

In 1973, Bristol-Myers introduced the drug Blenoxane (bleomycin sulfate) as a therapy for squamous cell cancers, head and neck cancers, and non-Hodgkin's lymphomas. The following year, it began marketing Mutamycin (mitomycin) for tumors of the stomach and pancreas and for bone cancer. The company followed up in 1976 with Ceenu (lomustine) for Hodgkin's lymphoma and brain cancer. Then, in 1978, the company introduced the anticancer agents Platinol (cisplatin) and Lysodren (mitotane). In 1983, Bristol-Myers began marketing the drug Vepesid (etoposide) as a treatment. Following the merger of Bristol-Myers and Squibb in 1989, BMS received approval to market Paraplatin (carboplatin) as a therapy for recurrent ovarian cancer.

In the early 1990s, BMS was developing the anticancer drug Taxol (paclitaxel). Made from the bark of pacific yew trees and other similar sources, Taxol would be marketed first to ovarian cancer patients in 1993 following its approval by the U.S. Food and Drug Administration (FDA) in 1992. The approval gave BMS five-year exclusive marketing rights to the drug. Taxol would eventually be used to treat people with head and neck, lung, ovarian, and breast cancers, as well as advanced forms of Kaposi's sarcoma.

At one time, BMS had the only contract allowing a drug company to harvest bark from the endangered trees on United States territory. However, BMS was subsequently accused of overpricing by the U.S. Subcommittee on Regulation, Business Opportunities, and Energy. BMS argued that the price of $6,000 to $8,000 per complete treatment was not excessive. Nevertheless, the company would not supply the data used to set the price. In 1994, BMS researchers discovered a semisynthetic source of paclitaxel that could kill cancer cells with fewer side effects.

In 2002, BMS was accused of maintaining an illegal monopoly on Taxol and faced an antitrust lawsuit. The lawsuit maintained that, if not for the actions of BMS, generic forms of paclitaxel would have been available to more patients much earlier at much less cost. It was also pointed out that paclitaxel was developed by taxpayer money because it was largely developed by the government-funded National Cancer Institute. BMS conducted the late-stage clinical trials. The lawsuit was not the last or only lawsuit BMS faced in regard to Taxol and keeping the price inflated. The company agreed in 2003 to pay $670 million to settle various lawsuits by states, consumers, and competitors. Another lawsuit brought in 2007 led to the company settling for a payout of $125 million.

In 2001, BMS acquired a 19.9 percent stake in ImClone Systems, Inc., a biotechnology company working on a monoclonal-antibody drug to kill cancer cells. BMS went on to help codevelop and market the drug, called Erbitux. Initially, the drug failed to receive approval from the FDA, which finally approved the drug in 2004. ImClone was acquired by Eli Lilly Company, but BMS still co-marketed Erbitux in the United States.

In 2003, BMS acquired the cancer therapeutics company Kosan Biosciences. That same year, the company began a collaboration with Exelixis, a biotechnology company. The two companies would jointly work on developing and marketing a therapy for medullary thyroid cancer and another therapy for advanced solid tumor malignancies. BMS also entered into an agreement with Ono Pharmaceutical Co., Ltd., in 2009, to further BMS's rights to an investigational cancer immunotherapy based on the anti-PD-1 antibody. (PD-1 stands for...
programmed death receptor 1, an immune-cell pathway.) That same year, the company acquired Medarex, which was working on antibody-based treatments for cancer and other diseases.

In 2011, BMS received FDA approval for its anticancer drug called Yervoy to treat melanoma. Yervoy, an anti-PD-1 antibody-based drug, was the first drug shown to significantly extend the lives of patients with melanoma. The drug promotes efforts by the body’s immune system to fight tumors by stopping cancer cells from attaching themselves to PD-1 to escape being destroyed by the immune system. As a result, the immune system has a better chance of fighting and defeating the cancer. The company continued to work on immune-system-boosting drugs that seemed to offer more hope of prolonging life long term for cancer patients.

In 2014, a new drug called Nivolumab, also based on interaction with the PD-1 antibody, was under development by BMS and undergoing clinical trials. The drug has shown promise when used in combination with Yervoy to treat melanoma. However, another trial using the drug combination to treat non–small cell lung cancer showed less promise and also produced more side effects in lung cancer patients. Nevertheless, the ultimate goal in using these drugs is to replace traditional chemotherapy approaches to cancer and potentially establish a long-term cure for various cancers, most notably melanoma, lung cancer, and prostate cancer.

David Petechuk
Independent Scholar

See Also: Food and Drug Administration; Head and Neck Cancer; Lung Cancer, Non–Small Cell; Lung Cancer, Small Cell; Melanoma.

Further Readings
Noto, Anthony. “New Cancer Drugs Spark Deal Possibilities; A Segment of Oncology Has Piqued the Interest of Major Biotech Companies Such as Merck and Bristol-Myers.” Mergers & Acquisitions: The Dealmaker’s Journal (July 1, 2014).

Broad-Spectrum Ultraviolet (UV) Radiation

Ultraviolet (UV) radiation is electromagnetic radiation with a wavelength shorter than visible light and longer than X-rays, with a general range of 10 to 400 nanometers (nm). Because the lens of the human eye blocks light in the 300 to 400 nm range (and the cornea blocks light below 300 nm), UV light is not visible to most humans, with the exception of some young people and people with aphakia (who lack a lens); many birds, insects, and fish can perceive UV light with no difficulty. Both UV and visible light are part of the larger electromagnetic spectrum, the range of all possible frequencies of such radiation; the word ultraviolet refers to UV radiation's position on the spectrum beyond violet, just as infrared comes just before red, on the other side of visible light.

What differentiates ultraviolet light is not simply its invisibility to the naked eye (though in the absence of visible light, it can render some objects visible, as with black lights) but its excitation of molecular and atomic valence electrons, sometimes resulting in the ejection of electrons. This is called the photoelectric effect, which is responsible, for instance, for the dusty atmosphere of the moon (as charged dust levitates off the surface) and is used in night vision devices. UV radiation was discovered in 1801 when physicist Johann Wilhelm Ritter observed that paper soaked in silver chloride darkened when exposed to oxidizing rays (as opposed to the heat rays of the other side of the spectrum, now understood as infrared light). By the end of the century, short-wave UV light was shown to kill off bacteria and thus sterilize an environment—a use to which it is still put—and in 1960, it was shown to have damaging effects on DNA.
World Health Organization has classified ultraviolet light at all wavelengths as a Group 1 carcinogen, and it is responsible for at least 90 percent of all skin cancer cases.

UV can be subdivided into UVA (315–400 nanometer wavelength), UVB (280–315 nm), and UVC (100–280 nm), the last of which is less familiar to the layperson because UVC in sunlight is completely absorbed by the ozone layer and atmosphere and so is not a factor in sunburn or skin cancer risk from sun exposure. It is also useful to distinguish near ultraviolet (NUV, 300–400 nm), which is visible to birds, insects, fish, and some young humans, from middle (200–300 nm), far (122–200 nm), and extreme (10–121 nm).

The UV portion of the spectrum covers radiation with a variety of different effects. For instance, the photoelectric effect is possible only with UV at the shortest range of the spectrum (furthest from visible light), while mid-range UV can break chemical bonds. It is mid-range UV radiation, emitted by both natural light (sunlight) and some artificial lights, that is the most relevant to human health. It is responsible for sunburn, as UV rays disrupt skin cells and can damage DNA through photochemical reactions—resulting in pyrimidine dimers, the primary cause of melanoma skin cancer. Sunburn is often erroneously understood as being caused by the heat of the sun, but actually, it is UV’s chemical-bond-disrupting ability that is more relevant, which is key to realizing that sunburn—and damage leading to skin cancer—can occur on cloudy or cold days as well as the warm, sunny ones that were once celebrated as tanning days.

UV light accounts for about 10 percent of the light emitted by the sun (though the mixture is filtered by the atmosphere and differs at ground level) and is also produced by various artificial lights, including tanning lamps, mercury-vapor lamps (often used as streetlights as well as to illuminate large areas from overhead, such as in factories, parks, or sports stadiums; some retail stores use

Squamous cell carcinoma, which grows faster than basal cell carcinoma and is not as common, is nevertheless on the rise. It occurs most commonly on damaged skin or skin that has been subjected to chronic irritation, usually by ultraviolet (UV) radiation. UV can be subdivided into UVA, UVB, and UVC wavelengths. Melanoma is generally caused indirectly by DNA damage wrought by UVA radiation, while UVB radiation can cause skin cancer and squamous cell cancer. (MorgueFile)
color-corrected mercury-vapor lamps, but otherwise, the light emitted makes Caucasian skin look sickly and so is avoided in sales environments.

At ground level, sunlight is only about 3 percent ultraviolet, 44 percent visible light, and 53 percent infrared. Almost all of the UV light approaching Earth is blocked by the atmosphere; damages to the atmosphere, especially to the ozone layer, threaten to hamper this and significantly increase the amount of UV sunlight Earth life is exposed to, which at a minimum will increase the prevalence of skin cancer and other UV-inflicted DNA damage.

Though the role of the ozone layer in absorbing UV radiation, and the role of anthropogenic causes in depleting the ozone layer is subject to politicized debate, there is no debate about the impact of UV radiation on cancer. UVA and UVB have different carcinogenic effects; melanoma principally is caused indirectly by DNA damage wrought by UVA radiation, while UVB radiation can cause skin cancer and squamous cell cancer. Until recently, the carcinogenicity of UVA radiation was disputed or not well understood. It is now known that UVA's chemical effects on the body can include the generation of hydroxyl and oxygen radicals, which can go on to cause single-strand breaks in DNA and basal cell keratinocytes that lead to basal skin cancer.

UVB, on the other hand, produces pyrimidine dimers by exciting the DNA in skin cells such that aberrant covalent bonds form between pyrimidine bases. The body removes most of these dimers through nucleotide excision repair, but some may escape that process; and of course, the greater an individual's UVB exposure, the more dimers are formed, and the greater the odds that some of them will escape repair. Such dimers cause a mutation in DNA; when DNA is replicated, a CC dimer is read as AA instead, causing the replication mechanism to add a TT pair to the strand, a process called a classical C-T mutation. This is one of the most common ways skin cancer begins.

Because of UVB's effect on skin and resulting pyrimidine dimers, certain individuals with a hereditary condition called xeroderma pigmentosum are disproportionately affected by UV exposure. These individuals have inherited a defect in one of the 30 proteins used in the nucleotide excision repair process, resulting in a greater number of dimers escaping the repair process. Skin cancer is a common side effect.

Skin cancers caused by UV exposure include basal cell cancer, presenting as a pearl-shaped wound in an area of skin exposed to sunlight (often on the face); squamous cell cancer, usually appearing on the face in places with long-term sun exposure and presenting as scaly patches with open wounds, with a high chance of spreading; and melanoma, forming from the pigment-containing melanocyte cells, which looks like a mole in its early stages but can spread to other parts of the body and become fatal. Melanoma is most likely to form on the legs for women and on the back for men.

Less seriously, sunburn is also caused by DNA damage by UVB light, which is why sunburns are often pointed to as a skin cancer risk factor. The pain of a sunburn is thought to be the result of excitation of nerve tissue by overproduction of CXCL5 protein.

UV light's human health impact is not entirely negative. In fact, exposure to UV light is a necessary element of well-being: UVB induces vitamin D production in the skin at rates that make it much more significant to vitamin D availability than diet, promoting immunity and mood and helping to regulate blood pressure, calcium metabolism, insulin secretion, and cell proliferation. The cold-climate phenomenon of seasonal affective disorder, or the winter blues, generally is believed to be the result of insufficient UV exposure and consequent insufficiency of vitamin D: At northern latitudes (or southern ones in the southern hemisphere), there is so little daylight in the winter months and so little incentive to spend time outdoors (especially with exposed skin) that many people simply are unable to produce the amount of vitamin D required for good health. This even may have an impact on the prevalence of winter illnesses due to vitamin D's role in the immune system. UV light therapy also is used for treatment of certain skin conditions like vitiligo, eczema, and psoriasis.

Modern sunscreens are designed to block both UVA and UVB. Despite this, it is not yet clear from the research what protection sunscreen usage offers from melanoma and other skin cancers. Some studies have found melanoma more frequently in sunscreen users than nonusers, but critics of some of these studies have suggested that these comparisons need to take into account relative sun exposure—that is, nonusers may have lower rates simply because they have less sun exposure,
which does not speak to the effect of sunscreen usage among members of groups with heavy exposure (e.g., because of working outdoors). A correlation between sunscreen usage and melanoma would be expected, after all, provided sunscreen offers less-than-perfect protection simply because sunscreen usage correlates with planned UV exposure. More serious are the possibilities than sunscreen ingredients may themselves be carcinogenic—paraaminobenzoic acid (PABA) was banned due to its DNA damage—or cause other health problems. Sunscreen also interferes with vitamin D production.

Tanning beds pose a significant UV exposure risk, producing much more UV light than is found in ground-level sunlight, and regular users of tanning beds are at least 75 percent more likely to develop skin cancer. This is part of the rationale for the 10 percent indoor tanning excise tax included as part of the Affordable Care Act because, as with cigarette smokers, tanning bed users as a group are a greater drain on health care resources.

Bill Kte’pi  
Independent Scholar

See Also: Melanoma; Skin Cancer, Non-Melanoma; Sunlamps or Sunbeds, Exposure to.

Further Readings

Bronchial Adenomas/Carcinoids, Childhood

Bronchial adenomas are the most common primary pulmonary malignancy in children and adolescents, appearing mainly in adolescents. Adenomas are tumors, usually benign in adults, of epithelial tissue in the glands or with glandular characteristics. Bronchial adenomas are found in the bronchi—airway passages in the respiratory tract that bring air to the lungs from the trachea (windpipe). There are two main bronchi, left and right, of which the left is smaller around but longer. Each main bronchi divides into secondary bronchi (three in the right and two in the left) to deliver air to the lobes of the lung, and each secondary bronchi divides into tertiary bronchi to deliver air to a bronchopulmonary segment of the lung. These in turn divide into series of bronchioles. The bronchi are critical to the respiratory system and familiar to laypeople through bronchitis, a disease causing inflammation, as well as asthma, which is hyperreactivity of the bronchi. Even benign bronchial adenomas pose health issues and often result in recurring pneumonia in children.

Although benign, adenomas can become malignant adenocarcinomas, a broad class of tumors. When it develops in the distant bronchioles, this adenocarcinoma is called in situ pulmonary adenocarcinoma (AIS), formerly known as brochioloalveolar carcinoma, one of the four types of adenocarcinoma in the lung. A type of non–small cell lung cancer, AIS is a small tumor with an alveolar epithelial appearance and a scaly covering. It grows along preexisting airway structures without invading or destroying the underlying tissue or lymphatics, and so diagnosis is uncertain until after the pathological examination of the tumor during surgery. Prognosis is 100 percent if it can be completely removed in surgery. If the AIS progresses and becomes malignant, recurrence is frequent, as with other non–small cell lung carcinomas. Treatment is usually with a full lobectomy of the lobe containing the tumor.

More than 80 percent of childhood bronchial adenomas develop into carcinoid tumors, tumors that develop from an endobronchial stem cell with neuroendocrine differentiation. They may develop in the submucosal glands or the salivary glands. Usually, the first symptoms are similar to asthma or bronchitis and include coughing, wheezing, recurring pneumonia, and similar respiratory complaints. Lesions are visible to a bronchoscope, and a computed tomography (CT) scan can reveal the degree of obstruction and exact location and size of the tumor. Because even a benign tumor in this area is usually harmful—and
is, in any event, causing bronchial difficulties—a biopsy is not usually performed. The tumor is removed surgically, usually with adjacent lymph nodes removed as well. As with adenocarcinoma, a complete lobectomy is common in order to prevent recurrence.

Bronchial carcinoids can lead to Cushing's syndrome or carcinoid syndrome in less than 10 percent of childhood cases. Cushing's syndrome is caused by excessive cortisol steroids as a result, in this case, of the cancer being close enough to the pituitary gland to cause large amounts of adrenocorticotropic hormone, which in turn causes the adrenal glands to produce excessive cortisol. Cushing's syndrome is characterized by a distinctive “moon face” as the result of rapid weight gain in the trunk and face, as well as excessive sweat, thin skin, and stretch marks from the skin being pulled by the weight gain, insomnia, dry and brittle hair, acne, skin tags, and hypertension. Adolescents may also experience impotence and decreased libido due to hormone imbalance.

Cushing's syndrome can be treated with cortisol inhibitors like ketoconazole, but the symptoms will also fade after surgical removal of the tumor.

Carcinoid syndrome is a series of symptoms that accompany carcinoid tumors about 5 percent of the time. When carcinoid tumors cause the patient to secrete serotonin and kallikrein, the syndrome sets in, characterized especially by flushing of the head, throat, and upper chest, diarrhea that may be intense and debilitating, abdominal cramps, constriction of the bronchioles that can exacerbate respiratory problems caused by the tumor, nausea and vomiting, and in about half of cases, cardiac trouble as a result of serotonin-induced fibrosis of the valvular endocardium.

Diarrhea carries its own complications, including electrolyte imbalances, debilitating headaches, fatigue, and dehydration. As with Cushing's syndrome, the best remedy is the removal of the tumor causing the problem, but if surgery is not available immediately, symptoms may be treated through drugs that reduce serotonin secretion, radionuclide therapy, and antihistamines, as well as antiemetics to control diarrhea and nausea.

In some cases, the symptoms of Cushing's or carcinoid syndrome are the first events that cause the patient's parents to seek medical attention, and so the diagnosis of the bronchial carcinoid may be delayed as these other symptoms act to distract the diagnostician, particularly if the attending pediatrician is not versed in pediatric oncology.

Bill Kte'pi
Independent Scholar

See Also: Adrenocortical Carcinoma; Carcinoma of Unknown Primary; Lung Cancer, Non–Small Cell.

Further Readings

Bulgaria

In July 2014, Bulgaria’s population was estimated at 6,924,716, with a sex ratio of 0.92 male to 1.0 female. The population is experiencing a rate of decrease of 0.83 percent annually (2014 estimate), due in part to migration out of the country (2.89 out-migrants per 1,000 population in 2014). The population in the country was distributed in a
total of 255 cities and 5,047 villages. One-third of the population in the country live in the seven biggest cities, where the total population is more than 100,000 persons.

Health care in Bulgaria is provided by the National Health Insurance Fund, and visitors to the country can use their European Health Insurance Card (EICH) to access health care when needed. Politically, cancer patients often have been overlooked in Bulgaria. The treatment of Bulgarian cancer patients was exclusively an obligation of the government, and Bulgaria is the only European country whose largest hospitals do not always have a foundation associated with them to aid financially in times of illness and hardship, like a cancer diagnosis.

Unlike other European countries, whose health care systems try their best to support people and their relatives through cancer diagnosis and treatment, many diagnosed with cancer in Bulgaria faced a shortage of lifesaving medicines and lack of the support to cope with such an illness. Some accounts even point to prominent government figures stating forcefully that money should not be spent on a disease such as cancer due its high level of mortality. Front-page headlines were made by a former health care commissioner who referred to such patients as doomed. Much has been done to change this outlook in Bulgaria, including a recent patient-centered organization called the Bulgarian Cancer Association.

The Bulgarian National Cancer Registry (BNCR) was established in 1952. Its purpose is collecting, processing, and analyzing data on cancer incidence and death rate in Bulgaria. There exist 13 regional cancer registries, all part of the National Oncological Center Network. Collected data is then sent to the Central National Cancer Registry for analysis. Each year, BNCR publishes its yearbook, Cancer Incidence in Bulgaria, containing the most recent data on cancer incidence, mortality, and prevalence. The registry maintains the national database for cancer patients according to international standards and guidelines for cancer registration. It manages statistical and epidemiological analyses of cancer incidence, including survival rates, mortality, and survival. BNCR has been a member of the European Network of Cancer Registries (ENCR) and of the International Association of Cancer Registries (IACR) since 2000.

The number of cancer patients in Bulgaria increases typically by 2 percent a year, according to statistics released in Bulgaria on February 4, 2010, the World Day Against Cancer, noting that the theme of that year’s Day Against Cancer was that cancer can be prevented no matter what type.

In September 2011, the World Health Organization (WHO) consultants Jill Farrington and Jan Stjernsward traveled to Bulgaria and organized informational meetings in preparation for a workshop entitled Cancer Prevention, Treatment, and Rehabilitation funded by the WHO. The WHO consultants and their Bulgarian counterparts analyzed documents and met with officials on noncommunicable diseases, tobacco use, alcohol consumption, and nutrition. Colleagues from public health institutions were also welcomed to these meetings. The workshop took place in the capital of Bulgaria, Sofia. It was called to order by the Deputy Minister of Health Dr. Kiril Dobrev and the Acting Head of WHO Office in Bulgaria, Dr. Farman Abdulayev. This event gathered oncologists from various hospitals and medical offices in Bulgaria and formed working groups to discuss and develop the relevant documents on the national action plans on prevention, treatment, and rehabilitation of cancer.

In 2012, the Bulgarian Cancer Index indicated that the number of Bulgarian people newly diagnosed with cancer was 32,100, and the risk of getting cancer before age 75 was 23.8 percent. Last, the number of people dying from cancer each year in Bulgaria was 18,100 as of 2012. Risk factors included smoking, lack of exercise, obesity, an unhealthy diet, and excessive exposure to the sun or ultraviolet light.

Specific types of cancer are on the rise in Bulgaria, including breast, cervix, lung, and prostate cancers. According to WHO data recently published, breast cancer deaths in Bulgaria reached 1,428 or 1.67 percent of total deaths. The age-adjusted death rate was 19.55 per 100,000 of population, which ranks Bulgaria 54th in the world for breast cancer, 27th in the world for lung cancer, and 91st in the world for liver cancer.

By the year 2017, it is predicted that incidence rates of all cancers, except stomach cancer (change in risk factors and education contribute to the decline), will increase in Bulgaria. It is further estimated that, in the time frame from 2013 to 2017,
new cases of cancer will be 62 percent higher than from 1998 to 1992 in Bulgaria. Screening programs, educational and awareness programs, and changes in predicative factors will need to be further analyzed, and new programs should be introduced. Changing government and health care structure should also help these numbers change as time goes on.

Diane Ferrero-Paluzzi
Iona College

See Also: Chemoprevention; Diet and Nutrition; Obesity; Tobacco Smoking.

Further Readings

Burkina Faso is situated in west Africa. It is bordered on the north and east by Mali, east by Niger and Benin, and south by Benin, Togo, and Côte d’Ivoire. It is the 17th-most populous country in Africa and 61st-most globally with a population of more than 13.5 million.

French is the official national language, and there are 67 living indigenous languages spoken by respective ethnic groups in Burkina Faso. The most widely spoken include Bisa, Dagara, Gourmanchema, Jula, Kasem, Lobi, and Moore. Each ethnic group has its own rich traditions of ethnomedicine. For example, a traditional healer who uses medicinal plants for treating cancers and other ailments is called tip-tiim by the Mossi, who speak Moore. Most people in Burkina Faso, particularly those in rural areas, rely on traditional medicine and medicinal plants to treat common diseases.

There are many traditional medicinal preparations used in Burkina Faso. Most of these traditional medicines incorporate use of local plant materials, many of which have shown medicinal properties in laboratory studies. For example, extracts of medicinal plants traditionally used, such as Acacia macrostachya and Lantana ukambensis, demonstrated antiproliferative effects against cancer cells. Research also suggests that use of certain plants may help protect against cancer by reducing oxidative stress and stimulating enzymes and other processes that help the body fight carcinogens. For example, an extract from Nymphaea lotus, locally referred to as beli, demonstrated substantial antioxidant potential.

Medicinal plants are used in Burkina Faso to treat many health problems associated with cancers. For example, the stems and leaves of Cassia nigricans are used to treat uterine tumors; leaves of Ocimum americanum are used to treat stomach tumors; and the stems and leaves of both Lippia chevalieri and Lippia multiflora are used to treat liver pathologies. A root decoction of Hybanthus enneaspermus can be administered for abdominal pain.
There are serious deficiencies of modern pharmaceutical supplies, as opposed to traditional preparations, and in modern medical services for cancer and similar conditions in Burkina Faso. Burkina Faso also has a relative shortage of doctors, with about 920, at a density of 0.58 per 10,000 population. According to the World Health Organization’s (WHO’s) Health System Response and Capacity, as of 2010, there was no general availability of either chemotherapy or radiotherapy in the public health system in Burkina Faso.

Burkina Faso is a signatory to the Single Convention on Narcotic Drugs, Convention on Psychotropic Substances and United Nations (UN) convention against the illicit traffic in narcotic drugs and psychotropic substances; consequently laws exist to control narcotic and psychotropic substances and precursors. Annual consumption of controlled substances is highly regulated to curtail abuse. Accordingly, annual consumption of morphine is 0.00004627 milligrams per capita, fentanyl is 0.00002 milligrams per capita, pethidine is 0.00167 milligrams per capita, and phenobarbital is 60.01271 milligrams per capita. These factors make it very difficult to provide appropriate palliative care for cancers and other conditions.

Due, in part, to the shortage of medical services and supplies, health problems are endemic in Burkina Faso. The 10 leading causes of morbidity, in rank order, are malaria, respiratory diseases, skin diseases, diarrhea, intestinal worm infestation, accidents, pneumonia, eye infections, rheumatism, and urinary tract infections. The average number of cancer cases annually is 103.9 per 100,000 population.

Cancers account for a substantial amount of disability and suffering among those impacted. According to the WHO’s Disease and Injury Country Estimates, the age-standardized disability adjusted life year estimates for 2004, the 10 most prevalent cancers in Burkina Faso were led by liver cancer at 328 per 100,000 population; breast cancer at 248 per 100,000 population; cervical and uterine cancers at 141 per 100,000 population; prostate cancer at 104 per 100,000 population; trachea, bronchial, and lung cancers at 80 per 100,000 population; bladder cancer at 78 per 100,000 population; stomach cancer at 69 per 100,000 population; mouth and oropharynx cancers at 68 per 100,000 population; lymphomas at 62 per 100,000 population; and esophageal cancer at 62 per 100,000 population.

Modern medical supplies and services are generally, if available at all, in short supply in Burkina Faso. Both prescription and over-the-counter products are often unavailable. Consequently, health problems are endemic and limit development. For example, an estimated 300,000 people live with human immunodeficiency virus (HIV) in Burkina Faso, which ranks the country 18th highest in Africa and 25th highest globally. The mortality rate for HIV/acquired immune deficiency syndrome (AIDS) in 2010 was 62 per 100,000 population. Debate continues on the relative risks in Africa for respective cancer types for those infected with HIV. The age-standardized mortality rate for tuberculosis in 2008 was 51 per 100,000 population and for malaria in 2006 was 178 per 100,000 population, while that for cancers in 2009 was 130 per 100,000 population. Nine cancers are among the 50 leading causes of death in Burkina Faso.

Liver cancer is the 17th-leading cause of death; the age-standardized death rate for liver cancer in Burkina Faso is 18.18 per 100,000 population, which ranks it as the 14th-highest country globally for liver cancer deaths. Breast cancer is the 23rd-leading cause of death; the age-standardized death rate for breast cancer in Burkina Faso is 15.48 per 100,000 population, which ranks it as the 107th-highest country for breast cancer deaths. The remaining of these nine cancers and their age-standardized death rates are cervical (12.83), prostate (8.81), stomach (5.06), bladder (3.42), lung (3.20), colon and rectal (3.06), and lymphomas (2.95). Furthermore, according to the WHO’s Global Health Observatory Data Repository, in 2008, the age-standardized estimates of deaths from all cancers was 100 per 100,000 population for males and 101 per 100,000 population for females. As a consequence, life expectancy is only 44.2 years, which ranks Burkina Faso 40th in Africa and 211th globally. There is a clear and urgent need for improved cancer awareness, early detection programs, and health services infrastructure in Burkina Faso.

Victor B. Stolberg
Essex County College

See Also: Côte d’Ivoire; Developing Countries; Mali; Togo.
Burma (Myanmar)

Cancer in Myanmar (formerly Burma) stands among the country’s leading causes of mortality and morbidity. Decades of government neglect of the nation’s health system has served to exacerbate effective cancer controls. Although increasing economic growth and the lifting of economic sanctions have afforded significant opportunities to the health sector, notable challenges remain for the alleviation of noncommunicable diseases (NCDs).

While the majority of the population is composed of ethnic Burmans, 135 distinct ethnic groups are indigenous to the southeast Asian nation of Myanmar. In 1044 C.E., the various ethnicities were unified under a succession of Buddhist dynasties. In 1886, the country was conquered by Britain and subsequently incorporated into British India. After achieving independence in 1948, Myanmar’s government was characterized by a democratic republic until it was overthrown in a 1962 military coup d’état. Following a series of military governments, national elections held in 2010 have marked a transition to civilian, democratic governance.

During British colonial rule, Myanmar doctors were trained in European techniques and health care, and the nation came to be well regarded abroad. Due to cultural factors restricting Myanmar women from engaging in physical contact with males outside their families, nurses were mainly ethnic minorities, with many Myanmar women operating as pediatricians and gynecologists. Under Myanmar’s socialist governments, emphasis was given to achieving national health objectives. However, a lack of application of such principals led to extremely low government health expenditures that both significantly undermined the health care infrastructure and led to lack of available information on the country’s health situation. In recent years, expanding economic growth and the lifting of Western economic sanctions have resulted in significant improvements in health care, though the sector remains highly under-resourced.

As a developing nation with an agricultural-based economy, 75 percent of Myanmar’s 59.13 million citizens reside in rural regions. As a result of improvements in public services and standards of living, there has been a gradual decline in infectious diseases representing a major public health issue, in turn, leading to the increasingly epidemiologic significance of NCDs such as cancer. Cancer in Myanmar has been found to be one of the 10 foremost causes of mortality and morbidity. In 2008, cancer deaths per 100,000 inhabitants were estimated to be 123 among males and 115 among females. Due to an absence of public awareness, coupled with inadequate programs for early detection, the majority of cancer cases are not identified until late stages. This is particularly the case for children with cancer, an estimated 85 to 92 percent of whom are either undiagnosed or not receiving treatment. For the nation’s 18.84 million children (from birth to age 15) and an estimated 1,500 to 2,800 new pediatric cancer cases each year, there are merely two pediatric oncology centers in Myanmar, located at Yangon and Mandalay Children’s Hospitals. Pediatric patients and their families may have to travel for days for treatment.

While there is no pediatric cancer registry in Myanmar, the subnational Yangon Cancer Registry
(YCR) was founded in 1974 in order to determine the pervasiveness of cancer in the nation's capital. Between 1974 and 2001, there were a total of 85,298 registered cancer cases, including 40,486 men and 44,712 women. Morbidity for cancer in Yangon increased from 87 per 100,000 residents in 1981 to 1,172 per 100,000 residents in 1995. From 1974 to 2001, the most common types of cancer within the YCR were digestive tract, respiratory tract, female reproductive organs, breast (female and male), and oral cavity and pharynx. Among women, the leading cancers between 1993 and 2000 were cervix, breast, and lung.

Tobacco use, both by smoking and chewing, remains an important risk factor within attempts at cancer control. A 2001 study reported that 40 percent of Myanmar adults use tobacco. Since 2000, significant developments have occurred in the realm of preventative smoking measures, including the founding of the Myanmar Tobacco Free Initiative Project, the country’s joining of the World Health Organization (WHO) Framework Convention on Tobacco Control and the action of the Control of Smoking and Tobacco Products Consumption Law. Additionally, the government’s launch of the Myanmar Health Vision 2030, representing an ambitious plan to meet current and future health challenges, has focused on a commitment to national health education on the prevention of NCDs diseases such as cancer.

Despite a recent dramatic increase in government health expenditures, the overwhelming majority of health-sector financing comes from the private sector and external assistance. Prior to the lifting of economic sanctions, very few countries provided direct economic support due to restrictions implemented by national governments and the European Union. Rather, developmental health assistance was funneled primarily through international nongovernmental organizations (INGOs), domestic nongovernmental organizations (NGOs), and global partnerships. This has in turn raised notable challenges to the alignment of such assistance with national policies and programs. Currently, funding mechanisms that continue to bypass the government in direct support of INGOs and NGOs remain a threat to the further weakening of an already fragile health infrastructure.

However, national partnerships with United Nations’ (UN’s) organizations play a significant role in health activities. The main contributors in this regard include the WHO, the United Nations Development Program (UNDP), the United Nations Population Fund (UNFPA) and the Food and Agriculture Organization (FAO) of the UN. Furthermore, significant progress in the country’s health development has also emerged from government partnerships with INGOs and NGOs. Myanmar’s Ministry of Health has signed various memorandums of mutual understanding with 10 domestic NGOs and 31 INGOs regarding health development collaboration.

Despite the opportunities afforded by Myanmar’s current political-economic transition, significant challenges remain to cancer control efforts. While Myanmar’s economy is forecasted to grow quickly, increasing global integration inevitably entails NCD risks brought about by Western lifestyle influences, including those pertaining to smoking and obesity. Developmental assistance circumventing government health efforts may also further debilitate a fledgling health sector. Furthermore, reflective of developing nations more broadly, the majority of health costs are currently paid for by patients and their families.

Economic gains have yet to translate among Myanmar’s ordinary population. Associated with Buddhist cultural tradition, it is common practice for patients to provide gifts to their doctors. If economic prosperity is not felt at the level of the population, escalating costs of living could further inhibit people’s willingness to seek medical treatment. Moreover, growing ethnic tensions along the nation’s boarder region threaten to exacerbate the existing divide between access to health care infrastructure between Myanmar’s rural and urban populations. Consequently, without mechanisms to ensure equitability, achievements in Myanmar’s health sector may fail to meet the needs of the most impoverished members of the population while further aggravating existing inequalities.

Lara Lengel
Brett Rodrique Labbe
Bowling Green State University

See Also: Asian Diet; Developing Countries; Disparities Within Nations (Elimination of Cancer); Global Health Issues and Cancer; International Agency for Research on Cancer; World Health Organization.
Further Readings

Burundi

Burundi, officially the Republic of Burundi, is a landlocked country in the African Great Lakes region of southeast Africa. Much of its southwestern border is adjacent to Lake Tanganyika, however. The country is sometimes considered part of central Africa.

Burundi is one of the five poorest countries globally. It has one of the lowest per-capita gross domestic products (GDPs) of any nation in the world. The country has suffered from warfare, poor access to health care, and education and governmental corruption. Burundi is densely populated and experiences substantial emigration. After the president of Burundi was assassinated in 1993, more than 683,000 Burundi residents fled to neighboring countries, towns with poor sanitation, or rural villages with little access to services. According to the Global Hunger Index of 2013, Burundi has an indicator ratio of 38.8, making it the hungriest country in the world.

Health care in Burundi is handled by the World Health Organization (WHO), including the training of sanitarians, public health nurses, and public health services. Burundi students are trained in the Democratic Republic of Congo and in France. The WHO has helped Burundi tackle several campaigns against disease, including malaria, tuberculosis, and smallpox.

Because of its many large-scale problems, Burundi is distinctly lacking in its cancer education, care, and prevention programs. The population of Burundi is about 8.07 million people, with several thousand more men than women. The estimated number of new cancer cases in Burundi for the year 2008 was 5,860, including 2,369 cases in men and 3,491 in women, based on data from Globocan.

The five most common cancers in Burundi are gynecological (corpus uteri, ovary, and cervix uteri), breast, Kaposi’s sarcoma, hematological malignancies (Hodgkin’s lymphoma, multiple myeloma, non-Hodgkin’s lymphoma, and leukemia) and esophagus. If you segment the gynecological cancers, the other most common cancer cases in Burundi are prostate cancer, throat cancer related to smoking, and liver cancer caused by the hepatitis virus. The last two can be prevented mostly by changing one’s lifestyle, and the cervical cancer can be prevented by the human papillomavirus (HPV) vaccine.

Human Papillomavirus and Related Cancers
Burundi has a population of about 2.88 million women age 15 and older who are at risk for developing cervical cancer. Current estimates indicate that about 1,400 women each year in Burundi are diagnosed with the disease, with 1,080 women dying from cervical cancer each year.

Cervical cancer is the most frequently diagnosed cancer among women in Burundi. About 35.8 percent of women in Burundi are estimated to have HPV infections. And 76.5 percent of invasive cervical cancers are caused by HPV types 16 and 18.

Prostate Cancer
In some men, prostate cancer that is not treated can spread (metastasize) and cause death, and there is no real cure for prostate cancer today. Each year, about 150 Burundian men are diagnosed with prostate cancer, and hundreds more may have the disease and never be diagnosed. Every man who lives in Burundi is at risk for prostate cancer, though it occurs most often in men over 50 who are genetically predisposed to the disease. A simple blood test (prostate specific antigen [PSA] test) is the best way to discover an early diagnosis of the disease. Men
should start having prostate cancer screenings in their 40s as those who are diagnosed and treated early in the disease have a much smaller risk of dying from it.

**Lung Cancer**
Lung cancer often can be prevented through a lack of tobacco usage, and preventative campaigns can go a long way in reducing the risk of lung cancer in Burundi. Many Burundians with lung cancer are forced to go outside of the country to receive treatment. Often, this means traveling to India, where treatments are relatively cheap and the doctors are experienced. Of course, many people do not have the means to travel, and they are left in Burundi to suffer without access to the right kinds of medical treatment. Lung cancer is one of the most common killers in the world, and it is imperative that early diagnosis happens to reduce the risk of death for Burundians. Preventative campaigns must be put in place in the future, or Burundi runs the risk of increasing incidences of this disease.

**Challenges to Cancer Care**
Like many African countries, Burundi does not have enough doctors who specialize in cancer care to address the population. Newly diagnosed cancer patients need chemotherapy or radiation therapy, pathology, and surgery. The number of oncologists needed is based on the number of patients needing these services. For developing countries, the International Atomic Energy Agency (IAEA) recommends training radiation and clinical oncologists who can prescribe both chemotherapy and radiation for the major cancers. It is recommended that each city in Burundi have two oncologists on staff, adding up to more than 50 oncologists needed across the country according to WorldCon data. In addition, radiation specialists are also needed throughout the country. Right now, many cancer patients in Burundi must go outside of the country to achieve adequate treatment.

Other concerns surrounding cancer in Burundi include the fact that it is not considered one of the main health threats by the Public Health Ministry. Though the International Cancer Day is held every February 4 (along with a themed workshop in 2014), this is nearly the extent of the government’s involvement. The Burundian Alliance Against Cancer (Alliance Burundaise de Lutte Contre le Cancer), active since June 2008, believes that more should be done.

In Burundi, all many people with cancer can do is take pain medicine and wait for death. The Burundian Alliance has been driving campaigns of sensitization through which it also promotes prevention to address this issue. This is the only way that the alliance can attribute the same level of seriousness to cancer as the government currently does to human immunodeficiency virus (HIV) and acquired immune deficiency syndrome (AIDS).

**Conclusion: What Can Be Done**
Several studies have shown that cancer is increasing in developing countries, and holding vaccination campaigns (for HPV) for women in Burundi is one step that the country can take to reduce the risk of cancer for its women. Because there is a lack of oncologists and lack of funds for many patients to be treated in the country, prevention and awareness campaigns are the only currently feasible solutions. Much more has to be done for cancer in Burundi, and February 4 should not be neglected.

Katie Moss
Independent Scholar

**See Also:** Cervical Cancer; Prostate Cancer; Lung Cancer, Non–Small Cell.

**Further Readings**


Calcium

Calcium is a hard, white mineral. Its molecular weight is 40.08, and its melting point is 842 degrees C. Next to sodium and potassium, calcium is the third-amplest essential mineral in the human body, followed by magnesium.

An adult body contains on average 1.0 to 1.2 kilograms of calcium, 99 percent of which is in the skeleton (bone, teeth, and cartilage). Only 1 percent of body calcium is in the extraskeleton—for example, extracellular fluids (plasma and tissue fluid), cells, membranes, and tight intracellular conjunctions. Plasma calcium is vital for nerve conduction, muscle contraction, cardiac rhythm, and blood coagulation; therefore, its level is strictly controlled. When the plasma calcium levels start to fall, calcium is withdrawn from the skeleton. About 0.8 to 1.2 grams of calcium are absorbed from the gastrointestinal tract each day, while 0.9 gram of calcium is excreted from feces and 0.1 gram from urine. Children can absorb up to 75 percent of ingested calcium, compared with 30 to 40 percent absorption in young adults and 15 percent in adults. Excessive fat, phosphate, phytate in bamboo, and oxalate in spinach reduce calcium absorption from milk and soy.

Parathyroid hormone works with growth hormone to increase the plasma calcium levels. In contrast, thyroid calcitonin and cortisol mobilize calcium and magnesium out of the skeleton. These hormones work on the bone, intestine, and kidney to keep plasma calcium steady.

Calcium Balance and Health

The human body must maintain a proper balance of calcium for optimum health. Hypocalcemia refers to abnormally low levels of calcium, and its signs are osteoporosis, tooth pain or loss, back pain, irritability, magnesium deficiency, menstruation syndrome (painful uterine cramps), nightly leg cramps, and tetany.

Hypercalcemia occurs when there is too much calcium in the body, which can cause arteriosclerosis, blood clots, cardiac conduct abnormal, constipation, polyuria, hypertension, hyperparathyroidism, nausea, and kidney stone formation.

For good bone development, osteoblasts help collagen synthesis and facilitate calcium binding to hydroxyapatite in the bone matrix. Weight-bearing activities stimulate bone formation. Bisphosphine reduces bones breaking down. Other cofactors for bone strength are magnesium, zinc, fluoride, and vitamin C, which is essential for collagen cross-linking. To another end, osteoclasts destruct collagen and dissolve bone mineral. The dynamic balance in the bone is positive in most people before age 30, but thereafter, it starts to be negative. A sedentary lifestyle, acidic foods and beverages, refined grains and sugar, antidepressants, alcohol,
cigarettes, heparin, arthritis, and glucocorticoids weaken bone strength.

Osteoporosis is defined as a reduction of bone density. Radiology shows osteoporosis when bone density declines 30 percent or more. Osteoporosis Type I is a disproportional loss of trabecular bone in postmenopausal woman. Type II occurs in both sexes after age 75. After age 70, hip fractures double every five years and reach 2,750 incidences per 100,000 people per year, compared to 1,300 incidences of vertebral fractures at age 85. The probability of hip fracture in white women age 50 or over is 14 percent compared to 5 percent in white men. Bone density declines after age 65 at a regression slope similar to age-related weight loss. So, keeping muscle helps keep bone mass. After menopause, women have accelerated bone density loss, which is stabilized by age 60. No evidence shows accelerated decline in women age 65 to 74.

**Ideal Daily Calcium**

To attain ideal bone mass in adolescents, the recommended dietary allowance (RDA) extends the total daily allowance of calcium 1,200 milligrams up to age 24. The ideal daily calcium intakes are as follows: age zero to six months: 400 milligrams; age six to 12 months: 600 milligrams; age one to 10 years: 800 milligrams; age 11 to 24 years and pregnant or lactating women: 1,200 milligrams; age 25 years and up: 800 milligrams.

Calcium supplements are used by about 20 percent of Americans to reduce osteoporosis and premenstrual syndrome. Calcium was also used in some colon cancer and depression treatments. Because 87 percent of American adolescent girls lack calcium and many of them have painful menstruation, calcium-rich foods and weight-bearing exercise for 30 minutes a day are most useful at this age. Once cup of low-fat milk or yogurt contains 300 milligrams of calcium, cooked soybeans contain 450 milligrams, and cooked collard greens contain 280 milligrams. Isocaloric substitution of yogurt reduced central adiposity during certain calorie restriction trials. Fortified food means adding 25 to 100 percent of RDA per serving.

Among calcium supplements, CaCO$_3$ contains the highest calcium element (40 percent), followed by CaCl$_2$ (36 percent), calcium citrate (20 percent), calcium lactate (13 percent), and calcium gluconate (8 percent). Ideal CaCO$_3$ supplements should be quickly dissolved in the stomach. A supplement of 400 milligrams of magnesium cooperates with 800 milligrams of calcium (at a ratio of one to two) to optimize neuromuscular function, help bone health, and reduce calcium-related arteriosclerosis, nephrolithiasis, hypertension, and constipation.

Jin R. Baker

*Health and Food Institute*

**See Also:** Age; Diet and Nutrition; Food Additives.

**Further Readings**


Dawson-Hughes, Bess, Susan Harris, Elizabeth Krall, and Gerard Dalla. “Effect of Calcium and Vitamin D Supplementation on Bone Density in Men and Women 65 Years of Age or Older.” *New England Journal of Medicine* (September 1997).


**California Blood Bank Society**

The California Blood Bank Society, located in the state of California and abbreviated CBBS, is an organization that develops, educates, and inspires health care professionals in cellular therapy and
transfusion medicine to improve patient outcomes and practices.
To achieve these goals, CBBS holds regional seminars in Northern and Southern California for donor technicians, nurses, donor resource professionals, quality assurance professionals, laboratory technicians, medical technologists, administrators, physicians, and compliance staff. These seminars are held in the first or fourth quarter each year, and they are announced on the official CBBS Web site, which is currently under renovation.

The CBBS also holds its annual meeting, which includes many vendor exhibits and takes place in either Northern or Southern California. This meeting gives attendees the opportunity to network with their peers in a relaxed environment, while also attending quality seminars on a variety of topics related to transfusion medicine.

In addition, the CBBS publishes the CBBS Today journal twice annually. This publication focuses on issues affecting staff working in various areas of blood centers and hospital transfusion services, along with committee activities and the important issues of state emergency planning and safety/compliance. The CBBS employs between 1 and 10 individuals.

Also of mention is the organization's e-network forum, which provides health care professionals working in cellular therapy and transfusion medicine a safe and convenient place to conduct collegial discussions. This forum also acts as an announcement space for relevant meetings, news, and links. The forum began as an e-mail discussion group founded by Dr. Ira Shulman in 1998.

The American Association of Blood Banks
The CBBS is a member of a greater collection of organizations devoted to cellular therapy and transfusion medicine—the American Association of Blood Banks (AABB). The AABB is an international, nonprofit association that represents institutions and individuals involved in cellular therapies and in the field of transfusion medicine.

The AABB's mission is similar to the CBBS' in that it strives to advance the practice and standards of cellular therapies and transfusion medicine to increase patient and donor care and safety. It is committed to improving health by creating and delivering standards, educational programs, and accreditations to further these goals.

The core values of the AABB include integrity, the pursuit of excellence, a focus on the donor and patient, consensus building, innovation, and transparency. The AABB is composed of almost 2,000 institutions and 8,000 individual members, including researchers, scientists, doctors, nurses, health care providers, medical administrators, technologists, and so on. Members are located in more than 80 countries.

History of the AABB
Since 1957, the AABB has been creating standards for transfusion services and blood banks. Beginning in the 1980s and continuing today, standards have been and are being developed for immunohematology reference laboratories, perioperative services, cellular therapies, patient blood management, and relationship testing. The corresponding accreditation programs for these standards strive to improve the safety and qualities of the activities they cover.

The role of the standards and accreditation created and managed by the AABB promote patient quality and safety across various fields. These standards combine internationally accepted quality management system best practices with technical requirements appropriate for each field. These standards then form the basis for the AABB's accreditation program.

Accreditation With the AABB
To become accredited, a facility must meet compliance standards as outlined in the current edition of Standards, as well as the requirements outlined in the AABB's Accreditation Information Manual. The AABB accreditation program is internationally recognized as a symbol of quality.

There are many reasons to become AABB accredited. Facilities that achieve accreditation show the highest level of quality and have systems in place to keep improvements continual. The AABB accreditation program strives to improve the operational systems in place within a facility by improving the safety of testing, collecting, processing, administering, and distributing products.

The AABB accreditation process usually takes about six to nine months, though the total time to
achieve it depends on the state of the facility's preparedness and adherence to quality system requirements. The cost for accreditation depends on several variants, including the activities for which the facility is seeking accreditation and the size or volume of the facility.

Institutions interested in becoming members will be assigned a technical specialist from the accreditation department who will help and guide them throughout the process. This personal assistance will help ensure that all applicants understand what is expected of them at each step along the path to accreditation.

The AABB's accreditation program promotes the highest standard of care for donors, patients, and products in all of the various aspects of cellular therapies, transfusion medicine, relationship testing, and transplantation. The program supports the highest possible standards for clinical application; medical, technical, and administrative performance; and education.

The resulting accreditation program specifically assesses operational areas and quality systems for compliance with recorded standards. The basis for assessment includes compliance with U.S. Code of Federal Regulation, standards, and federal guidance documents. The assessment of operations is independent, and it helps in preparation for other inspections.

The program offers both peer review and educational opportunities. The overall goal of the program is to see that accreditation is recognized at both national and international levels.

Accreditation is granted for a variety of facilities and processes, including storage, testing, administration, collection/procurement, and processing for transfusion medicine activities (e.g., transfusion, donor center, immunohematology reference laboratories, molecular testing laboratories and perioperative); cellular therapy activities (e.g., cord blood, hematopoietic progenitor cell, clinical, and somatic cell); and Specialist in Blood Bank schools and relationship testing activities.

Conclusion

CBBS provides inspiration for medical professionals in the fields of cellular therapy and transfusion medicine to improve the safety and effectiveness of their practices. The CBBS is a member of the AABB—an organization also devoted to cellular therapy and transfusion medicine.

Katie Moss
Independent Scholar

See Also: American Society of Hematology; American Society of Pediatric Hematology/Oncology; Haemophilia Society (UK).

Further Readings


Cambodia

Cambodia remained relatively untouched by the Western world until the French colonization in 1863. Prior to colonization, medical practices were rooted in tradition, including herbal remedies and rituals performed by healers with morals, merits, and power derived from dhamma to care for both acute and chronic conditions. With the onset of French colonization came drastically different ideals of medicine, including the first vaccinations and medical doctors focused on medical care from a Western perspective, that is, acute and chronic care treated with medicines and treatment void of religious and spiritual dimensions. As hospitals and medical care implemented by the French colonizers became more prevalent, tensions between cultures (French and Khmer) kept many Khmer people from taking advantage of the newly introduced health care services provided by the French.

The infrastructure provided for health care services was short-lived due to political instability in the 1960s and 1970s that culminated in the Khmer Rouge victory over the Lol Nol regime, which led to the genocide war from 1975 to 1979 that wiped out
social infrastructures in an effort to create a commun-ist, agriculture-based society. Hospitals, schools, and other social services were destroyed in an effort to take Cambodia back to a state devoid of any colonial influences. Approximately 2 million people were targeted and killed during the genocide, especially well-educated doctors, lawyers, and educators. The aftermath of the genocide left Cambodia in a state of post-conflict turmoil that continued well into the 1990s. Although some hospitals and medical care were available, it was not until the late 1990s that medical care began to create infrastructure capable of providing care for patients. For cancer patients, care has been significantly lacking. It was not until 2010 that oncology became a specialty available to students receiving medical training in Cambodia. With the assistance of international organizations (INGOs) and nongovernmental organizations (NGOs), statistics are becoming more available regarding the prevalence and diagnosis of cancer.

According to the World Health Organization (WHO), with a population of 14,865,000 in 2013, cancer prevalence is approximately 13 percent, the third-most common disease behind communicable, maternal, nutritional conditions (37 percent), and cardiovascular disease (24 percent). The Ministry of Health, with assistance from the WHO and local NGOs, has made access to care for cancer patients a key focus of policy and strategies for increased diagnosis and care are in place. For instance, cancer care and prevention are objectives outlined in the Ministry of Health Strategic Plan 2008 to 2015, indicating the necessity to educate the general population on risk factors contributing to cancer as well as providing access to quality treatment. However, with limited funding (5.6 percent of gross domestic product [GDP]) for health care and statistics, indicating that preventative measures are limited in dissemination, issues such as social habits and socioeconomic issues continue to contribute to the high incidence of certain cancers.

According to Kimman, Norman, Jan, Kingston, and Woodward, the most common cancers for males are lung (29.7 percent), liver (25.8 percent), mouth and oropharynx (16 percent), and stomach (15.3 percent). In contrast, the most common cancers for females are cervical (27.4 percent) and breast (20.7 percent), followed by lung cancer at a much lower rate for females (8 percent) than men.

The stark contrast between the types of cancers between men and women can, in part, be attributed to sociocultural factors regarding proper behaviors for men and women. Cambodia is a male-dominated society in which certain behaviors, including drinking alcohol and smoking, are seen as acceptable for men but generally inappropriate for women. These factors further support the notion that social factors and consumption of alcohol and tobacco are significant contributors to the prevalence of lung, liver, mouth, and stomach cancer in the male population. In the case of women, high rates of human papillomavirus (HPV) and cervical cancer indicate that women, especially those involved in prostitution and drug use, tend to have high rates of the HPV, which contributes to the incidence of cervical cancer among the female population.

Out of a population of almost 15 million people, only 14,000 new cancer patients are being diagnosed each year. This rate mostly likely would be higher if proper diagnostics were made available to the population as a whole and if services were available in rural areas. Only two hospitals currently have public wards specializing in cancer care, the lack of access to local care contributes to the underdiagnosis of cancer. Wealthy Cambodians have the option to travel to regional health care facilities outside of Cambodia, most often Thailand and Vietnam. The access and affordability of health care in neighboring countries is not accessible to most Cambodians, but the proximity of the resources and moderately affordable cost for wealthy Cambodians make traveling for adequate care the best option for those who can afford it.

Late diagnosis also contributes to the high mortality rates of diagnosed people with cancer. More than 70 percent of cancers are diagnosed at Stages 3 and 4. Women with breast cancer, the second-most common form of cancer in women, have been shown to have one of the highest mortality rates. Smaller rates of women have incidences of oral cancers, but this appears to be higher in older women. Contributing to the incidences are the high rates of elderly women chewing betel quid, a compound of tobacco, betel leaves, and slaked lime. The practice of chewing this compound has been shown to increase the incidences of oral cancer.

Alternate forms of medical outreach are currently being implemented to help facilitate access
to care for populations outside urban areas. Telemedicine, the use of e-mail, and other forms of communication are being utilized to communicate with patients in rural areas. Based on preliminary results, use of these forms of communication has been found to reduce the amount of acute care services and increase patients adhering to prescribed care at higher rates. This is especially helpful with cancer treatment, including patient participation in remission follow-ups with medical staff.

While underdiagnosis and issues of care and remission care are significant in Cambodia, efforts are being made to increase the quality of care for cancer patients. As of 2014, the first National Cancer Center has been created in Phnom Penh. Efforts to include the latest technologies available in more-developed economies are paramount to the creation of a facility capable of providing quality care to cancer patients. Eav Sokha, head of oncology at the largest hospital in the capital city of Phnom Penh, Calmette Hospital, is a forerunner in providing adequate care for cancer patients. His insight into the vision of a cancer center has thrust his hospital into the spotlight as the most technologically advanced hospital in the country, with radiography machines, positron emission tomography (PET)–computed tomography (CT) scanners, and a Spectre gamma camera. While these machines are widely available in more-developed economies, the creation of this center is the first of its kind to provide diagnosis and care using these devices.

Although strides are being made to increase the health infrastructure to help diagnosis and treat cancer, Cambodia still has a long way to go in providing adequate care. Through the help of international organizations and NGOs, Cambodia is beginning to establish the necessary facilities and doctors to provide care that should help provide the Cambodian population with the necessary treatments to decrease cancer mortality and increase quality of care.

Whitney Szmodis
Sothy Eng
Lehigh University

Further Readings

Cameroon

The central African country of Cameroon is geographically located on the Gulf of Guinea, bordered by Nigeria, Chad, the Central African Republic, the Republic of Congo, Equatorial Guinea, and Gabon. As with many African countries, it has a history of colonization that is still evident in the 21st century. Cameroon was first colonized by the Portuguese in 1520, who established sugar plantations and began the slave trade; they were succeeded by the Dutch in the 1600s, followed by the Germans in 1884, then the British and French in about 1916. Current reports estimate the population of Cameroon at 24 million.

Cameroon has an estimated 250 ethnolinguistic groups and five major cultural groups spread across the region. This ethnic and cultural diversity influences the behavior patterns and perceptions related to seeking treatment for cancer and other diseases. As a result of colonization, the country is underdeveloped, and many of its indigenous citizenry living in rural areas are impoverished and undereducated, which adds to the country’s public health crisis.

Public Health
Cameroon faces the double burden of challenges from communicable diseases such as acquired

See Also: Breast Cancer; Liver Cancer, Adult (Primary); Lung Cancer; Non–Small Cell; Cervical Cancer; Stomach (Gastric) Cancer.
immune deficiency syndrome (AIDS) and human immunodeficiency virus (HIV) infection, malaria, tuberculosis, and noncommunicable diseases such as cancer. Adults and children are plagued by a variety of cancer types that include breast and cervical cancers for women, prostate and liver cancers for men, and Hodgkin’s and Burkitt lymphomas and leukemia in children. This combination of high rates of communicable and noncommunicable diseases in the same population creates an additional burden on already limited human and financial resources to remedy the problem. The high rate of tobacco use is also a major contributor to cancer rates.

Overall cancer is the second-leading cause of death in developing countries. In Cameroon, cancer accounts for 3 percent of all deaths from all ages annually, and the risk for both males and females prior to the age of 75 is 11 percent. Cameroon cancer statistics are generally unavailable at both national and institutional levels as there is no countrywide cancer registry; therefore, the numbers related to incidence rate and mortality are tracked infrequently and considered low.

Cameroon has two major government-run hospitals, Yaoundé General Hospital and Douala General Hospital, both of which have cancer centers with limited resources of equipment, medication, and staff. However, access to quality health services are beyond the reach of some of the primary victims of cancer in Cameroon who are more likely to be poor and have limited access to available health services due to provider location and the high cost of diagnosis and treatment.

National Cancer Control Plan
Cancer is recognized as a public health problem in Cameroon, and as such, Cameroon’s Ministry of Public Health established the National Cancer Control Committee (NCCC) and subsequently its National Cancer Control Plan (NCCP), which was initiated with the help of Dr. Anderson S. Doh, other citizens, and allies concerned with the growing cancer crisis in Cameroon. First published in 2004, this version of the cancer control plan was created with the assistance of the World Health Organization (WHO), American Cancer Society (ACS), International Agency for Research on Cancer (IARC), and the International Atomic Energy Agency (IAEA), among others.

According to NCCC officials, the cost of health services is beyond the means of the average Cameroonian. In addition to financial barriers, the NCCP details the following challenges to the growing cancer burden in Cameroon: cultural beliefs and myths regarding cancer, systemic poverty, and the fact that many cancer patients seek medical assistance only after the disease has reached an advanced stage. Other challenges are related to the role of traditional healers and some health workers treating the disease without proper training and necessary medical resources.

In June of 2013, an assessment of Cameroon’s cancer control measures was completed by the IAEA, which identified areas of continued concern for the NCCP and offered suggestions for improvement.

The Role of Missions and Nonprofit Organizations
Although cancer treatment facilities are few relative to the population, one source of major support in the burgeoning cancer pandemic comes from the Cameroon Baptist Convention Health Board, which provides free health care to rural populations of subsistence farmers and their families. Missionaries and medical professionals run clinics at the following hospitals: Banso Baptist Hospital, Northwest Province; Mbingo Baptist Hospital, Northwest Province; and Mutengene, Southwest province, along with their partners Stellenbosch University, Tygerberg Children’s Hospital, South Africa; and Beryl Thyer Memorial Africa Trust. They assist with cancer diagnosis and treatment along with other public health concerns.

In 2013, the Medical Mission of Hope was organized by two U.S.-based international organizations, the African Women’s Cancer Awareness Association, and the Michael and Mauritia Patcha Foundation and sought to provide professional medical services to those residing in the remote southwest region of Cameroon. A diverse pool of medical and nonmedical professionals from the United States and Cameroon contributed the human resources necessary to screen, diagnose, and treat breast, cervical, and prostate cancers. In addition to providing patient health education and awareness and medical training related to the current trends in cancer screening, diagnosis, treatment, and palliative care were provided to early career nurses, doctors, clinicians, and other allied health professionals.
With the growing number of cancer cases in Cameroon expected to surpass 20,000 per year by 2030, cancer prevention and detection in Cameroon has taken on a multifaceted and multi-institutional design that includes structural policy and fiscal changes, community advocacy, education, and individual behavioral change strategies. Key components to the success of prevention and detection are government subsidies and assistance from national and international philanthropic organizations. It is necessary for a developing country such as Cameroon to combat cancer through educational programs, diagnosis, and treatment.

Annette D. Madlock Gatison
Southern Connecticut State University

See Also: AIDS-Related Cancers; Anticancer Drugs.

Further Readings

Canada

Canada is one country geographically belonging to North America; it has a surface of 9,984,670 square kilometers and scarcely 35 million inhabitants, making it the biggest country in the Americas and the one with the lowest population density. Epidemiologically, it shares its registries with those from the United States through the North American Association of Central Cancer Registries, founded in 1987, whose main goal is to provide cancer registration standards in the region in order to obtain reliable and uniform data. Canada follows the general trend in North America in the sense of an increasing trend of prevalence of cancer cases due fundamentally to the combination of an early diagnosis and an improvement in survival.

Canada in Figures
In the last 15 years, the number of people living with cancer continues to rise, and this is especially valid for the leading cancers, like breast, prostate, lung, and colorectal, dominant cancers in Western countries. The differential reality in the case of Canada is that liver cancer incidence has tripled in the Canadian male population and doubled in females in the last 40 years. It is estimated that life expectancy of people suffering from this cancer is not higher than five years. One reason for this is that, when symptoms are detected, liver cancer is already spread to other organs. According to the report “Canadian Cancer Statistics 2013,” the immigration from regions of the world with a high incidence of infections like hepatitis B or C could partially explain the increasing incidence rate of liver cancer. On the other hand, bladder cancer also rose in the last decades, basically affecting Canadians over 70 years old. Smoking and occupational exposure seem to have to do with the increasing number of bladder cancer cases.

About two in five Canadians will suffer from cancer in their lifetimes, and one in four will die because of the disease. Most cancer cases are lung, breast, colorectal, and prostate (52 percent). Lung cancer is, so far, the main cause of cancer death. Canada, as opposed to the rest of Western countries, has a similar rate of lung cancer, which is second in importance, between men and women (13.8 percent for men and 13.3 percent for women).
Cancer affects more men than women, and definitely, the largest group of people diagnosed with cancer is older than 50 (about 88 percent). However, in 2009, cancer was also the main cause of death among children under 15. More than half of all cancer cases (63 percent) go beyond the five-year survival ratio, but it clearly depends on the type of cancer. In 2013, it is estimated that around 96,200 men were diagnosed with cancer and about 91,400 women. The most common cancer in men is prostate (24.5 percent) and breast in women (26.1 percent). Breast cancer notably rose through the 1990s. Although the causes are not totally clear, it is believed that progressive participation in mammography screening and other factors, like early age at menarche, late age at menopause, oral contraceptives, and late age at pregnancy had a direct link with the increase in the incidence.

The incidence of cancer is higher in the western region than in the eastern one. The Atlantic coast and Quebec have the highest incidence in the whole country. Risk factors like smoking and obesity are the main cause.

Cancer Registries
The Canadian Cancer Registry (CCR) is a kind of umbrella institution whose purpose is to collect information from all provincial and territorial Canadian cancer databases. Other organizations, like the Canadian Association of Provincial Cancer Agencies, are tools of control for cancer to make life easier for all citizens and create a network to collaborate with other institutions with similar goals and commitments. Its purpose is to ensure the quality of life of Canadians by reducing the burden of cancer in the country. It has existed since the 1980s, and it was the result of a common effort of diverse provincial, regional agencies that decided to work together. The community-based organization Canadian Cancer Society also has a fundamental mission to improve the quality of life of citizens and users, and it has agencies all over the country in a regional structure.

There are other institutions, such as the Canadian Research Data Center Network (CRDCN), that since 2000 have provided all kind of statistical information, health data among them.

Care and Services
Institutions like the Canadian Cancer Society provide information and guidelines about all the questions and needs affecting any patient of cancer. It highlights four fields of action: prevention, cure (treatment), follow-up or control, and palliative care, basically oriented to diminish the pain and suffering of the terminal patient and to improve his or her comfort. In its information, it also includes how treatments will affect the patient and a complete inventory of the side effects. At the same time, it offers help to families of cancer patients, thanks to the coordination of volunteers and people who have undergone the same experience, among other activities and initiatives.

In general, all the services are good, organized, and properly explained, and they give total priority to patients and their environments. In such a context, the Canadian Partnership Against Cancer has some programs that aim to modify lifestyles to
prevent cancer and other chronic diseases. And, as it was proven that old people were not receiving recommended cancer therapies, like young people were, some policies were launched in order to change this reality.

It is also emphasized that First Nations are an absolute priority in cancer control programs due to the difficulty of reaching remote, isolated, or rural regions.

Other interesting initiatives are related to the possibility of finding a specific trial by type of cancer, location, or even drug, which is a way of connecting citizens to all available and high-quality cancer resources.

Natalia Fernández Díaz-Cabal  
*Free University of Barcelona*

**See Also:** Canadian Association of Medical Oncologists; Canadian Association of Pharmacy in Oncology; Canadian Cancer Society; Canadian Red Cross; Canadian Society of Surgical Oncology; Canadian Urologic Oncology Group; Disparities Within Nations (Elimination of Cancer); Global Health Issues and Cancer; Organisation of European Cancer Institutes; Solar Radiation.

**Further Readings**
Dellaire, Graham, Jason Berman, and Robert Arceci.  
Elwood, J. Mark and Simon B. Sutcliffe. *Cancer Control*.  

**Canadian Association of Medical Oncologists**
The Canadian Association of Medical Oncologists (CAMO) is a national society of the Royal College of Physicians and Surgeons of Canada that contributes to the control of cancer through education, research, and clinical practice in screening, prevention, diagnosis, treatment, palliative and supportive care, and rehabilitation.

The association’s overall goal is to achieve and maintain excellence in scholarly and clinical activity among its members, creating a culture of respect and compassion for human dignity.

Each year, the association holds its annual scientific meeting. The 2015 CAMO annual scientific meeting was April 30, 2015, in Toronto, Ontario. Pricing for the event ranges from free for associate residents and fellows to $250 for individuals.

**Canadian Association of Medical Oncologists Goals**
The goals of CAMO are as follows: Support the continuing education and maintenance of its members’ knowledge base; serve as a national for the discussion of common interest issues for medical oncologists in Canada; provide a national forum at which medical oncology trainees can present their research; advocate for appropriate medical oncology content in the curricula of medical schools and other organizations revolving around health care training; promote postgraduate research and clinical training in the field of medical oncology; advocate on behalf of cancer patients requiring systemic therapy; and advocate with the federal and provincial governments of Canada and other agencies on the need for health human resources to provide systemic therapy services. CAMO strives to reach these goals through its annual scientific meeting and throughout each year.

**Benefits of Membership**
There are many great reasons for organizations and individuals to join the CAMO, including: committee appointment opportunities; CAMO support of regional oncology endeavors; investment in one’s career and support of his or her profession; a network of professional and social contacts in a similar field; a reduced annual meeting registration fee; communication with thousands of medical oncologists through the association’s dedicated Web site; opportunities for research fellowships; continuing professional development through the obtainment of the Royal College Maintenance of Certification program; committee appointments through various subcommittees of the Royal College (allowing
members to be directly involved in setting the conditions of employment and standards of practice at a national level in Canada); the retrieval of the results of ongoing studies of medical oncologists’ physician resource requirements; and maintained support of the Medical Oncology Royal College training program through representation of specialty committees.

**Canadian Association of Medical Oncologists Leadership**

The executive leadership of CAMO has included Dr. Christopher Lee as president, Dr. Hal Hirte as president elect, Dr. Bruce Colwell as secretary treasurer, Dr. Kara Laing (past president), and Alexi Campbell as executive director.

Committees and chairs have included the following: Dr. Michael Vickers, who has been chair of the annual scientific meeting, and Dr. Petr Kavan, who has been co-chair of the annual scientific meeting. Members of this meeting committee have included Dr. Christopher Lee, Dr. Kara Laing, Dr. Bruce Colwell, Dr. Rashida Haq, and Dr. Hal Hirte. The chair of the Continuing Medical Education platform has been Dr. Rashida Haq. The chair of Fellowship has been Dr. Kylea Potvin. The chair of Nominating has been Dr. Renaud Whittom, and members of the same have been Dr. Bill Evans and Dr. Charles Butts. Finally, Dr. Chris Lee has been chair of Human Resources.

**Related Canadian Oncology Societies**

The Canadian Association of Medical Oncologists is only one of several national medical societies across Canada. Other, related organizations include: the Colorectal Cancer Association of Canada (CCAC), the Canadian Cardiovascular Society, the Canadian Anesthesiologists’ Society (formerly the Canadian Anesthetists’ Society), the College of Family Physicians Canada, the Canadian Medical Association, the Libin Cardiovascular Institute of Alberta, and the College of Physicians and Surgeons of Ontario.

**Canadian Association of Medical Oncologists and Quality Improvement**

Presented at the 2014 American Society of Clinical Oncology (ASCO) annual meeting, a study on the role of quality improvement (QI), an essential component of oncology care, was presented via a 13-question online survey to members of the Canadian Association of Medical Oncologists. The study was given due to the fact that few QI studies involving oncology patients are published. The idea was to study the attitudes of Canadian medical oncologists toward QI and to determine causes for the low publication rate of how QI affects patients throughout medical oncology literature.

The 13-question survey given to members of CAMO employed a modified Dillman method and was administered in October 2013. Questions revolved around their attitudes toward QI, barriers to QI involvement and publication, and involvement in QI initiatives (based on criteria from the *Journal of the American Medical Association* in 2000).

The results were as follows: There was a 43 percent response rate (143 out of 332 participants), with 97 percent of oncologists agreeing that QI is an important part of their practice. However, only 49 percent of respondents had participated in QI in the past five years.

There were no significant differences between QI participants when comparing by community versus academic institution type, though administrators were more likely to be involved in QI than researchers or clinicians. The majority of QI participants focus on patient centeredness (67 percent), domains of safety (70 percent), and sufficiency of care (56 percent). Seventy-two percent of participants did not publish their findings due to lack of time. Other pinpointed indicators included uncertainty about how to get involved in QI initiatives, lack of interest, unfamiliarity with QI methodology, and no identifiable journals. QI participants were more likely to be aware of recent practice-changing QI publications than nonparticipants.

**Conclusion**

The Canadian Association of Medical Oncologists plays an important role in oncology in Canada and across the world. The organization continues to grow and expand, and its participation in oncological studies is of the utmost importance.

Katie Moss  
*Independent Scholar*

**See Also:** American Association for Cancer Education; American Cancer Society; American Society of Clinical Oncology; Canada; Canadian Association of Pharmacy
Canadian Association of Pharmacy in Oncology

The Canadian Association of Pharmacy in Oncology (CAPhO) is the national forum for oncology pharmacy practitioners and other health professionals in oncology pharmacy throughout Canada. CAPhO provides a forum for these individuals to meet colleagues, post professional papers, exchange views, discover oncology pharmacy resources, locate contacts in other provinces, complete continuing education courses, and more.

History of the Canadian Association of Pharmacy in Oncology

The first national oncology pharmacy symposium (NOPS) was in 1988, organized by Larry Broadfield and Rosemary Bacovsky, though there was a preceding meeting in 1986, which was organized by Mary and Rosemary Gannon in Toronto, Canada. This meeting has been pinpointed as the first meeting of oncology pharmacists in Canada. Attendees included Linda Chow, Flay Charbonneau, and Carlo DeAngelis, with about 20 attendees in total.

The CAPhO was formed by Larry Broadfield and John McBride, and the first executive committee consisted of Larry Broadfield as president, Jeff Barnett as vice president, and Julie Levesque as secretary and treasurer sometime in 1990 or 1991.

The NOPS meeting was slated to coincide with the National Cancer Institute of Canada (NCIC) clinical trials group (CTG) annual general meeting (AGM), and because of this, it went between Montreal and Toronto each year—getting larger each time. The first major highlight of the event was the hosting of International Society of Oncology Pharmacy Practitioners (ISOPP) III in Toronto in 1993.

At this symposium, a few of the influential members met and decided to form an international society known as ISOPP. John McBride became interested in the NCIC activities, so he discontinued his work with NOPS and created the NCIC Pharmacists’ Network. Larry Broadfield aided him in this task, but he also kept the NOPS meeting on track, with the help of several other members.

Julia Pacchiti was one of these members. She became heavily involved in the NOPS and eventually took over presiding over the meetings. In those years, Larry Broadfield became more involved in ISOPP, setting forth the first legal constitution, helping form the organization, and finally, becoming the third president of ISOPP.

After 25 years, many of the organization’s founders remain committed to its meetings as well as excited about oncology pharmacy. The organization’s members are active NOPS participants, and they continue to produce presentations, publications, and more. New members are always welcome.

CAPhO Advocacy

One of CAPhO’s initiatives is advocating for the field of oncology pharmacy. The organization asserts that “cancer has touched the lives of every Canadian. So has how we treat cancer.” It believes that cancer and cancer treatments must continually be present on the agenda of health care decision makers because oncology pharmacy is of the utmost importance to cancer treatment and oncology technicians and pharmacists are very important members of every cancer-related health care team.

CAPhO advocates for oncology pharmacy in several ways, including: determining target groups for advocacy issues; identifying issues and trends and legislative affairs that impact CAPhO members; being available to CAPhO members and the public who need specific data on oncology pharmacy; and forming, managing, and supporting advocacy initiatives and public relations efforts.
More About CAphO

CAphO is a member of the Canadian Cancer Action Network (CCAN) Associate Membership Program, and the organization works closely with CCAN to support national Canadian efforts to create a strong, sustainable cancer control model for the entire country. CAphO, as a member-directed association, promotes, advances, and supports oncology pharmacy practice.

CAphO has a focus on quality, providing safe and effective oncology pharmacy services to cancer patients throughout Canada. The association prides itself on its accountability and inclusivity to members, including technicians, pharmacy assistants, and pharmacists who are involved in oncology pharmacy services. CAphO is also intent upon engagement and collaboration with patients, health care providers, and organizations, along with professional development for these individuals through education, mentorship, and research.

The executive branch of CAphO is composed of technicians, pharmacists, pharmacy assistants and other health care professionals across Canada. Executive officers of the association include the president, president-elect, immediate past president, and president-elect. These officers are responsible to the executive committee and manage and operate the association. The executive committee is comprised of the chairs of the standing committees of the association, along with the executive officers. Committees are created to recommend policies and programs to the executive officers, and they are ongoing and permanent. Task forces are also formed to deal with specific issues, but they are dissolved once their work is complete. The organization’s bylaws provide a strict framework for the association.

CAphO’s communication is predominately in English, but its Canadian French-speaking members are also catered to through initiatives such as a translatable Web site and bilingual versions of several of its online continuing-education initiatives. CAphO represents the issues and professional interests of oncology pharmacy at a national level.

CAphO encourages new members to join their association as it believes it can efficiently represent the professional interests of those working in pharmacy in oncology. CAphO members in good standing also receive a substantial $150 discount off the registration fee for the association’s annual conference.

Presentations and posters from the annual CAphO Conferences are posted online each year. Members are encouraged to have continual participation in oncology basics, the first release of four oncology practice essentials online education modules, as well as the online education and resources section of its Web site.

CAphO publishes news and updates through its Twitter and Facebook social sites, CAphO Compass blogs through http://www.capho.org/blog and Clinical Pearls for Practice on the CAphO Compass blog. Members are invited to publish on the latter. CAphO also provides travel grants and awards to members as well as tools to promote the association and upcoming conferences.

Katie Moss
Independent Scholar

See Also: American Association for Cancer Education; American Cancer Society; American Society of Clinical Oncology; Canada; Canadian Association of Medical Oncologists; Canadian Cancer Society; Canadian Society of Surgical Oncology; Canadian Urologic Oncology Group.

Further Readings


Canadian Cancer Society

During the Great Depression, the King George V Silver Jubilee Cancer Fund raised $450,000 that in part funded the founding of the Canadian Cancer Society/Société canadienne du cancer (CCS/SCC)
in 1938. The CCS aims to end cancer and enhance survivors’ lives. The CCS has 140,000 volunteers and 1,200 staff under President and CEO Pamela Fralick. The CCS sponsored bone cancer amputee Terry Fox in his 1980 run across Canada to raise money for the CCS. The CCS raises money through its Relays for Life, Daffodil Balls, Days and Months and by selling items like the Thing-a-ma-boob key chains that teach women about breast cancer lump dimensions. The CCS has 11 regional divisions and two national offices (Toronto, Ottawa). The CCS is the largest national charitable funder of cancer research in Canada and its five foci are research, advocacy, prevention, information, and support.

In 1931, the Canadian Medical Association (CMA) recommended forming the CCS. The CCS was formed in 1938, initially funded via the King George V Silver Jubilee Cancer Fund. In 1947, the first CCS office opened in French Canada in Montreal. Also in 1947, the CCS and the Department of National Health and Welfare created the Canadian Cancer Society Research Institute (CCSRI).

The CCS has funded important cancer research. In 1951, Dr. Harold Johns developed Cobalt radiotherapy. In 1961, Drs. Ernest McCulloch and James Till proved that all blood cells come from bone marrow stem cells, allowing for future bone marrow transplants. In the 1970s, Dr. Anthony Miller showed how Pap smear tests reduce cervical cancer deaths in women age 30 to 64. In 1982, Drs. Martin Yaffe and Donald Plewes in Toronto helped develop digital mammography. The CCS has funded 753 peer-reviewed journal articles.

In 1980, the CCS supported Terry Fox’s Marathon of Hope. Fox, who had an amputation above the right knee after bone cancer, left Newfoundland on April 1980 and ran west, aiming to raise $1 million. The CCS set up fund-raising events in the cities and towns that Fox visited. Fox stopped running on September 1, 1980, in Ontario after 3,339 miles (5,373 kilometers) and 143 days when cancer spread to his lungs. A frustrated Fox told the press that the CCS did not organize fund-raisers in the small towns he ran through. However, Fox and his supporters raised more than $24 million by 1981. In 1994, the CCS held the first successful Daffodil Ball in Montreal. The ball is now Canada’s most successful cancer fund-raising gala. In 2000, a daffodil on a blue background became the new CCS logo. The previous CCS logo, two serpents intertwining a sword, is the current American Cancer Society (ACS) logo.

The CCS estimates a 60 percent cancer survival rate, up 35 percent since it began funding research in the 1940s. Cancer is the leading cause of death in Canada, comprising 30 percent of all deaths. About two in five Canadians will develop cancer in their lifetimes and one in four will die of the disease. More than 190,000 new cases of cancer (not including more than 75,000 nonmelanoma skin cancers) and more than 75,000 deaths will occur in Canada in 2014. More than half of all new cases are prostate, breast, lung and colorectal cancers.

In 2002, CCS integrated the 11 regional divisions into one new Web site. The CCS has a Twitter feed that promotes Daffodil Day and Month, Relay for Life, and tobacco and tanning cessation that features cancer survivors and allies as active participants. In 2012, CCS estimated that it doubled its followers on Facebook and Twitter over the previous year. In 2012, more than 5 million visited www.cancer.ca, including people in more than 200 countries. CCS operates online support networks at www.CancerConnection.ca in English and at www.ParlonsCancer.ca in French. CCS mobilized its online followers in 2013 to lobby Canadian Members of Parliament to vote for Motion No. 381 to deem asbestos a dangerous substance.

A toll-free telephone cancer information service was started in 1996 across Canada in both official languages (i.e., English and French). More than 1 million people have used the service since then. In 2002, Quebec started the J’ARRÊTE! (I QUIT!) Smokers’ Helpline. Similarly, Prince Edward Island (PEI), Nova Scotia, New Brunswick, Ontario, Manitoba, Saskatchewan, and Yukon co-fund the Smoker’s Helpline in both English and French with text messaging and interpreter services available in Ontario. In conjunction with these smoking cessation telephone helplines, a Canada-wide online and self-directed smoking cessation programs are available at www.smokershelpline.ca in addition to http://iquitnow.qc.ca (English) and http://jarrete.qc.ca (French). The latter two Web sites are specifically marketed in Quebec but accessible to all online participants. In addition to online communications, the CCS distributed nearly 1.5 million print materials in 2011.

In 2012, CCS spent $45 million on research, $71 million for programs and services for people with
Canadian Red Cross

The Canadian Red Cross/Croix-Rouge Canadienne (CRC) belongs to the International Red Cross and Red Crescent Movement (IRCRCM), an aid organization originating from the Geneva Convention. The CRC was first active during the Northwest Rebellion of 1885. During World War II, the Canadian government gave the CRC control of blood services until 1998, when a tainted blood controversy led to the creation of a new Canadian blood agency. Currently, the CRC offers assistance during natural disasters and conflicts both domestically and internationally, in addition to community health and safety programs.

In 1862, Swiss humanitarian Jean Henry Dunant called for a volunteer society to aid those affected by war after having worked with this population in Northern Italy. In 1863, the Geneva Society for Public Welfare convened a committee that, by 1864, led to 12 nations signing the original Geneva Convention to give aid workers wartime neutrality under the flag of the Red Cross (also called the Geneva Cross). This became the IRCRCM, a movement now operating in 189 countries. Dunant was awarded the first Nobel Peace Prize in 1901.
Canadian Red Cross

sharing it with French economist and arbitrator Frédéric Passy.

Canada first flew the Red Cross flag in 1885, during the Northwest Rebellion at Batoche, Saskatchewan. Dr. George Sterling Ryerson, a wartime surgeon, affixed his hand-sewn flag to his horse-wagon ambulances. The Metropolitan Toronto Reference Library now owns this flag, which is on display in the Canadian Red Cross (CRC) national office in Ottawa. Ryerson founded the Canadian branch of the British Red Cross (BRC) in 1886, the first overseas branch of the BRC. The organization initially provided monetary support during the Spanish–American War in 1898 and material support for the South African War in 1899. The Canadian Red Cross Society Act was passed by Canada's parliament on May 19, 1909, formally establishing the organization.

During World War I, CRC volunteers provided $35 million in relief funds and donations for soldiers and civilians overseas. The CRC funded six European wartime hospitals, recreation huts and ambulance convoys. Starting in the early 1900s until 1984, the CRC operated one-nurse medical outposts in remote northern Ontario. One such nurse, Rene Caisse, gained attention for promoting an herbal remedy named Essiac in 1922 to treat cancer, which she learned from local Aboriginal Canadians. This outpost infrastructure is credited with shaping how medical services in isolated areas would eventually be delivered.

During World War II, 3 million CRC members delivered $80 million of monetary and material relief. Notably, the CRC provided food packages to overseas prisoners of war. At the time, hundreds of aid agencies were competing to control this type of aid, but the CRC is recognized as leading the effort. Starting in 1940 and continuing during World War II, the Canadian federal government gave responsibility for Canada's blood supply to the CRC, a largely volunteer organization, because of its medical experiences and its nationwide network. Canada's health care system was in development at this time. After World War II, the CRC served veterans, orphans, and refugees and administered Canada's blood service. At the height of its program, the CRC accepted blood from more than 1 million volunteer donors each year.

In March of 1983, the Red Cross organization issued advisories urging members of high-risk groups (i.e., those diagnosed with human immunodeficiency virus/acquired immune deficiency syndrome [HIV/AIDS] and men who have sex with men) not to donate blood. By March of 1985, the U.S. Food and Drug Administration (FDA) approved the first commercial HIV blood-testing kits, and by November of 1985, the CRC was using the test. However, from 1980 to 1985, HIV-infected blood was made its way into the CRC-administered blood system along with hepatitis C (HCV)–infected blood collected from 1980 to 1990.

Experts argue that 2,000 individuals were infected with HIV and 30,000 with HCV from CRC-distributed blood and blood products and that 8,000 will eventually die as a result. From 1994 to 1997, a government inquiry into the tainted blood scandal was convened. Chaired by Justice Horace Krever, it was popularly called the Krever Inquiry. One of many recommendations of the Krever Inquiry was that Canada's blood program be managed by an agency separate from the CRC and the Canadian government.

In September 1998, an organization eventually called Canadian Blood Services (CBS) was created to manage Canada's blood and blood products service except in Quebec, where Héma-Québec (HQ) was created. Both CBS and HQ are regulated by Health Canada. Control of the CRC's Unrelated Bone Marrow Donor Registry, established 1989 to treat blood and bone marrow cancers, was similarly given to CBS and HQ.

Currently, the CRC is run by a 15-member board of directors and serves four domestic regions (i.e., Western, Ontario, Québec, and Atlantic) and several other countries, with its 428 branches and a national office in Ottawa. The CRC works with local communities, the Canadian government, and humanitarian organizations. The CRC provides food, shelter, first aid and support in disasters and crises plus programs in communication, first aid, water safety, community health, violence, bullying and abuse prevention, humanitarian law, family restoration and refugee services.

In Canada, the CRC responds to natural and manmade disasters and also offers financial support and transportation assistance to cancer and patients who are seriously ill through its HELP program. Internationally, the CRC collaborates to offer programs for preventing AIDS among intravenous drug users in rural Asia and mother-and-child
health services, including cancer screenings, in South America.

Gordon Alley-Young  
Kingsborough Community College

See Also: Bone Marrow Transplants; Screening, Access to; Transportation.

Further Readings

Canadian Society of Surgical Oncology

The Canadian Society of Surgical Oncology (CSSO) has several goals, including: encouraging the creation of surgical oncology training programs in surgical departments in universities across Canada; facilitating communication among oncology surgeons; cooperating with other organizations, including CAGS, the Royal College of Physicians and Surgeons of Canada (RCPSC), and Canadian Oncology Societies (COS) in activities designed to achieve similar objectives; fostering the development of education in cancer for undergraduate, graduate, and continuing medical education; encouraging the development of research in oncologic surgery; and promoting the optimum treating of cancer patients through a multidisciplinary treatment approach. Each year, the society holds its annual scientific meeting. In 2014, the meeting took place in May at the Eaton Chelsea Hotel in Toronto.

Membership in the Canadian Society of Surgical Oncology
Active membership is available for any individual who holds a valid certificate in a surgical specialty or subspecialty, who is a practicing medical practitioner, and who is engaged in the field of cancer or a related field. Senior members include surgeons age 65 or older who have or are currently practicing in the field of surgical oncology or a similar field. Senior members also include members of the CSSO who have retired from active work and wish to continue to participate in the society's activities. Senior members have all of the privileges and rights of the society and are excused from paying any dues.
Honorary members of the CSSO include any individuals who are deemed worthy due to their contributions to the field of oncology or his or her services to the CSSO. Honorary members are proposed by the members of the executive of the society, for memberships may be nominated. If they are then elected by the society's members, they will obtain all of the privileges of the society. They do not need to pay dues, and they may not hold office.
Associate members include scientists, physicians, or other health care workers engaged in the treatment, investigation, or experimental field of surgical oncology, and they are permitted to all of the privileges and offices of the society, except for the positions of president elect and president.

Sampling of Topics Discussed at the 2014 Canadian Society of Surgical Oncology Annual Meeting
Breast Cancer in Manitoba: Do Surgical Oncologists Practice Differently? Under this topic, the application of Canadian guidelines for the management of breast cancer (published in February 1998) were explored, specifically, the statements that breast conservation is the preferred procedure for early-stage breast cancer; the testing of axillary nodes should be standard procedure for invasive breast cancer, though some admissions are allowable; a minimum of 10 nodes should be identified when an axillary node dissection (AND) is done for invasive breast cancer; and axillary surgery should not be completed for ductal carcinoma in situ (DCIS).
The objective of the study was to compare the practices of surgical oncologists to other surgeons in Manitoba with these guidelines in mind. The results for the population-based study showed that breast cancer patients in Manitoba’s surgical care was more consistent with Canadian guidelines when performed by surgical oncologists compared to other surgeons.

Identification of Colorectal Cancer Opinion Leaders for a Knowledge Transfer Program in Ontario. Asserting that accurately staging patients with colorectal cancer (CRC) is imperative because this has a direct effect on diagnosis and treatment, this presentation presented a population-based study in which researchers demonstrated that 73 percent of stage II CRC in Ontario, Canada, are stage based by testing an inadequate amount of lymph nodes. In response to this assertion, researchers devised a multimodal strategy combining continuing education strategies in formal (lectures) and informal (opinion leaders) forums. The study was sent out to 1,243 surgeons and pathologists in Ontario. The study utilized a modified Hiss and Stross OL identification method, and each physician received four formal mailings (containing incentives). Physicians were requested to identify a surgical or pathology OL for CRC and the chosen community leader. The results showed that, although 75 percent of Ontario CRC is done in community hospitals, a disproportionate number of OLs are employed at academic centers.

Rectal Cancer Outcomes Are Affected by Referral Patterns of General Surgeons. This study explored the idea that, in British Columbia, registration of malignant disease in a cancer registry is mandatory, yet despite this fact, referral to a multidisciplinary assessment team is not. Because of this, general surgeons who manage rectal cancer patients have an important role in choosing patients who would benefit from referral to the British Columbia Cancer Agency (BCCA) for multidisciplinary treatment. The study evaluates referral patterns of general surgeons in selecting patients for multiple adjuvant therapies that are based on published guidelines by provincial cancer management. There were 495 patients identified as being treated for rectal cancer, and their referral rates were evaluated. The study shows that surgeons preferentially referred patients to BCCA based on the stage of their cancer. Of 153 Tis or T1 patients, 17 (11 percent) were referred to BCCA, whereas 75 percent (70 out of 93) of patients with T3 lesions were referred. Overall, the results from the survey stated that patients with advanced-stage cancer are more likely to be appropriately referred to multidisciplinary care. These patients have a survival advantage when compared with patients who do not undergo multidisciplinary treatments.

Katie Moss
Independent Scholar

See Also: American Association for Cancer Education; American Cancer Society; American Society of Clinical Oncology; Canada; Canadian Association of Medical Oncology; Canadian Association of Pharmacy in Oncology; Canadian Cancer Society; Canadian Urologic Oncology Group.

Further Readings

Canadian Urologic Oncology Group

The Canadian Oncology Group (CUOG) is a clinical research investigator network that is owned and operated by its members. The consortium is a national group of leading community- and academic-based urologists, radiation oncologists, and medical oncologists who are committed to furthering urology research, including pharmaceutical trials, throughout Canada.
CUOG is a nonprofit, nonshare corporation that has a cooperative relationship with the Canadian Urology Association (CUA). The corporation partners with the Canadian Urology Research Consortium (CURC) on mutually held oncology studies.

Canadian Urologic Oncology Group Clinical Trials
CUOG pursues clinical trials in tandem with the pharmaceutical industry to discover medicines and cures to undermine urological disorders such as: prostate cancer, renal cancer, bladder cancer, and testicular cancer, among others. CUOG offers enhanced research options, which strive to bring better quality of life to Canadians.

Value of Canadian Urologic Oncology Group
The CUOG creates value by: managing and creating national resources to benefit physicians, the public and pharmaceutical industry; assisting rapid accrual to clinical trials; setting standards for clinical trial performance and research; collectively offering enhanced treatment options; creating awareness campaigns and building continued medical education; incorporating an efficient professional business approach based on credibility, fairness, and transparency; and providing a uro-oncologic focus and specific expertise.

CUOG measures its success on a number of factors, including: giving back knowledge, networking clinical trial performances, managing enhanced clinical trial productivity, publishing research, attracting industry players, being self-sufficient and credible, creating international outreach to the uro-oncology community, and leading urology clinical research to achieve innovation and excellence in clinical care.

Affiliation to the Canadian Urological Association
The CUOG is affiliated with the Canadian Urological Association (CUA), which exists to promote the highest standard of urologic care for Canadians and to advance urology as a science.

The CUA is a Canadian, member-based organization dedicated to enabling urologic oncologists to provide the highest possible standards of care by: fostering excellence in the practice through research, advocacy, support, and practice tools and education; providing continuous professional development for Canadian urologists; providing leadership in public education for urologic conditions; representing the urologic community in Canada in relationships with international and national societies and governments; and leading evidence-based clinical practice.

Recent Studies and Publications by Canadian Urologic Oncology Group
CUOG Randomized Trial of Neoadjuvant Androgen Ablation Before Radical Prostatectomy: 36-Month Post-Treatment PSA Results. This study’s purpose was to test the hypothesis that neoadjuvant androgen ablation prior to radical prostatectomy decreases the likelihood of biochemical progression at 36 months. Two hundred and thirteen patients with localized prostate cancer were chosen at random to a 12-week course of 300 mg of cyproterone acetate daily followed by surgery (CPA, n = 112) or radical prostatectomy alone (Sx, n = 101). Biochemical progression was determined for the entire group and by baseline prostate-specific antigen (PSA), clinical stage, pathologic stage, and Gleason Score.

The results of the study showed that the probability of biochemical progression at 36 months was about the same for both groups. Also, CPA patients with baseline serum PSA between 25 and 50ng/mL had a lower probability of biochemical progression. In terms of Gleason score, no difference was seen in the probability of biochemical progression between groups. The results did show a trend for a higher probability of progression in the neoadjuvant arm in patients with negative and positive surgical margins.

In conclusion, neoadjuvant androgen ablation with CPA reduces the positive margin rate meaningfully but does not result in a difference in biochemical progression at three years. This could be because of insufficient power of the trial to demonstrate a small benefit, a lack of sufficient follow-up, or a true lack of benefit of neoadjuvant androgen ablation prior to radical prostatectomy.

CUA-CUOG Guidelines for the Management of Castration-Resistant Prostate Cancer (CRPC): 2013 Update. Castration-resistant prostate cancer (CRPC) includes a variety of disease types, from patients with metastases and significant debilitation due to cancer symptoms to patients without metastases or systems with rising PSA levels despite androgen deprivation therapy (ADT). This
scholarship studied the management of castration-resistant prostate cancer.

CRPC is defined by disease progression despite ADT and the progression of preexisting disease, and it may exist as either a continuous rise in serum PSA levels, or the presence of new metastases. Advanced prostate cancer has been identified under same names over the years, but it was only recently discovered that extra testicular androgen production plays a significant part in the resistance of prostate cancer cells to surgical or medical castration therapy.

A variety of management techniques were explored for the different varieties of CRPC and patient struggles, including secondary hormonal manipulations with first-generation nonsteroidal antiandrogen and specific medications like docetaxel. The researchers in this study recommend that, based on the results of randomized, controlled trials, men with metastatic CRPC and clinical or biochemical evidence of progression should receive treatment with docetaxel 75 mg/m² IV every three weeks with five milligrams oral prednisone twice daily should to improve disease control, symptom palliation, overall survival and quality of life.

Denosumab and zoledronic acid are also pinpointed as exceptional treatments. In men with CRPC and bone metastases, denosumab (120 mg) or zoledronic acid (four milligrams IV) every four weeks is recommended to prevent disease-related SREs, including pathological fractures, surgery or radiation therapy, or bone or spinal cord compression.

Researchers point out that there were some other positive drug associations for CRPC, but they were not thoroughly explored for this study.

Katie Moss
Independent Scholar

See Also: American Association for Cancer Education; American Cancer Society; American Society of Clinical Oncology; Canada; Canadian Association of Medical Oncologists; Canadian Association of Pharmacy in Oncology; Canadian Cancer Society; Canadian Society of Surgical Oncology.

Further Readings


Cancer Association of South Africa

The Cancer Association of South Africa (Cansa) has positioned itself as the leading nonprofit organization dedicated to representing the interests of all South Africans affected by cancer. Cansa was established in September 1931 by 75 delegates representing 24 different organizations and four individuals who gathered at the first National Cancer Conference to share their concerns regarding the increasing rate of cancer in the country. The main topic on the agenda was how to end suffering and gain control of the disease. The outcomes from the conference have developed and evolved over decades and include the establishment of a national cancer registry, special cancer centers and clinics, and educational programs throughout the country.

Located at the southern tip of the African continent South Africa is a large nation with a population close to 52 million people and 11 official languages in 10 provinces. Priding itself on representing all people, each province is represented on Cansa’s board of directors. The entire board consists of a president, vice president, and council of governors, board chairperson, vice chairperson, provincial directors, provincial council, chief executive officer, and executive directors. The provincial directors and council work to develop and implement initiatives tailored to each individual province. Researchers and a Cansa committee are also part of the association leadership. The Cansa workforce consists of 350 staff members and 5,000 volunteers.
With the history of apartheid looming in the nation’s background, CANSA has instituted an extensive code of conduct that explicitly defines its policy of nondiscrimination. A Social and Ethics Committee, a subcommittee of the board of directors, was established in 2010. The role of this committee is to assess and address all ethical risks within CANSA and promote and integrate ethics throughout the association.

CANSA's self-reported purpose is to lead the fight against cancer in South Africa by offering a unique, integrated service to the public that involves holistic cancer care and support to all people. CANSA's mission is to enable research, educate the public, and provide support to all people affected by cancer.

With more than 30 care centers around the country, CANSA utilizes its staff and volunteers to implement various health programs to support cancer patients and their families. In its efforts to support and reach all South Africans, CANSA created a multilingual cancer coping kit, which it distributes free to cancer patients in need. These audio recordings are available in four of the 11 major languages spoken in South Africa: English, Afrikaans, isiZulu, and Sesotho. The coping kits are designed to give a message of hope. Other programs include: cancer screening, cancer treatment, and cancer prevention, 12 CANSA care homes that serve as a home away from home for out-of-town cancer patients, CANSA–TLC lodging for parents and guardians of children undergoing cancer treatment, and individual counseling and support groups.

CANSA is committed to research and in partnership with the Medical Research Council and National Health Laboratory Service through the Cancer Research Initiative in South Africa spends more than an estimated $562,028 (R6 million) annually on various types of cancer research in South Africa. The research findings are used to refine existing programs, develop new ones, create public awareness, and support CANSA’s role as advocates for public health policy in South Africa.

CANSA truly believes that the most effective weapon against cancer is knowledge. In their mission to educate, CANSA works to create public awareness of known cancer-causing agents, which contributes to cancer prevention by not containing known carcinogens.

CANSA's advocacy role includes influencing South African policy makers by lobbying and developing position statements. An example would be CANSA's Position Statement on Patient Rights Including the Rights of Caregivers. The preamble to this statement acknowledges that every inhabitant of South Africa will need to access health care services.

Every single South African citizen in contemporary society has a constitutional right to access health care, and this was not always the case. Historically, for the majority of the South African population, public health services that were offered were often of questionable quality. A person's racial classification had a significant impact on his or her ability to access health care services as well as the quality of health care that was provided. Many people's rights were violated—particularly black South Africans—especially their rights to equality, dignity, and privacy.

The preamble to the position statement goes on to recognize that the end of apartheid did not automatically result in an end to all of these inequalities. Many inequalities still exist and are strongly influenced by service delivery and socioeconomic factors such as class and income. In South Africa, race, class, and income remain closely linked. Since 1994, various laws and policies have been put into place to make sure that the rights of all people who need access to health care services are respected, protected, promoted, and fulfilled. These laws and policies are specifically aimed at improving access and the quality of public health services as well as ensuring that more people are able to access private health care services.

This specific position statement speaks to the commitment CANSA has to all people as stated in its purpose and mission. They are committed to systemic and societal change in cancer care, prevention, research, and education. CANSA offers to all communities, cancer survivors, and those affected by cancer solidarity a message of hope and the opportunity to get involved in the fight against cancer by providing access to information and education.

Annette D. Madlock Gatison
Southern Connecticut State University
Cancer Communication

Cancer Communication is the study and application of the use of strategically designed messages delivered through carefully selected media to convey relevant health information to targeted audiences (of health care consumers, cancer survivors, health care providers, researchers, patients, at-risk populations, and others) to educate members of these key audiences about cancer prevention, treatment, and control. Carefully designed cancer communication efforts are used to encourage cancer screening and early detection activities, reduce cancer morbidity and mortality, and enhance the quality of life of those who are confronting cancer. Cancer communication is a relatively young, but an increasingly important and rapidly advancing, area of applied research and intervention.

The powerful influences of communication on cancer prevention, treatment, and control was publicly reinforced in 1999, when the American Society of Clinical Oncology (ASCO), the largest and most prominent professional society for cancer care research and practice, identified communication as a key clinical skill for oncology practice. That same year, 1999, the National Cancer Institute (NCI), the largest and arguably the most influential institute in the U.S. Department of Health and Human Services’ National Institutes of Health, declared cancer communication to be one of the institute’s primary areas of emphasis, an “extraordinary opportunity” for concerted research and outreach activity. NCI’s identification of cancer communications as an area of extraordinary opportunity led to major investments in funding for large-scale cancer communication research initiatives that have advanced the science of cancer communication, encouraged introduction of new cancer communication programs at major medical and research centers, and fostered development and implementation of improved cancer communication policies and practices that influence cancer prevention, detection, diagnosis, treatment, survivorship, and end-of-life care.

Closely related to the NCI’s announcement of the Extraordinary Opportunity in Cancer Communications in 1999, the NCI introduced a new organizational unit that focused on promoting cancer communication research, the Health Communication and Informatics Research Branch (HCIRB). The HCIRB was established as part of the behavioral research program within the NCI’s Division of Cancer Prevention and Population Sciences. It became the focal unit within the NCI for developing and implementing new research programs to fulfill the overarching goal of the extraordinary opportunity in cancer communication to apply new cancer communication programs, policies, and technologies to reduce the national burden of cancer in the United States. The HCIRB staff were charged with developing and conducting major new cancer communication research programs and did this through the introduction of a number of large-scale and innovative intramural and extramural NCI research initiatives.

The cornerstone initiative of the NCI’s extraordinary opportunity in cancer communication and a major source of national data about cancer communication in the United States was the introduction of a repeated measure surveillance research tool, the Health Information National Trends Survey (HINTS) research program. HINTS is a nationally representative, biennially repeated, cross-sectional survey of the American public’s access to and use of relevant health information. It was developed to complement and build upon several other major national federal surveys, including the Behavioral Risk Factor Surveillance Survey (BRFSS), the National Health Interview Survey (NHIS), and the National Health and

See Also: Psychosocial Care/Support; South Africa.

Further Readings
Nutrition Examination Survey (NHANES). HINTS has become an important source of information tracking the state of public knowledge about cancer prevention and control.

Since its first administration in 2003, HINTS has been conducted every two to three years to identify and track how well different segments of the U.S. population were being informed about relevant cancer issues (such as risks and causes of cancers, symptoms and screening methods, and the best forms of cancer treatment). HINTS research identifies which cancer topics are most confusing to different groups of people, where different segments of the population currently get cancer-related health information, and how they would prefer to access relevant health information. In essence, HINTS tracks national cancer communication information access, use, needs, and opportunities.

As the HINTS acronym suggests, this major research initiative provides important insights (hints) about the best ways to meet the American public’s health information needs. HINTS provides researchers, public health promotion professionals, and health policy makers with a continuing source of surveillance data to compare trends in health information usage over time. The survey also provides health communication scientists with periodic opportunities to conduct fundamental research into the basic relationships among cancer-related communication, knowledge, attitudes, and behavior.

In addition to the HINTS research program, the NCI introduced several other important cancer communication research initiatives as part of the Extraordinary Opportunity in Cancer Communications program. Some of the most influential cancer communication initiatives include the Centers of Excellence in Cancer Communication Research, the Digital Divide Pilots, the Health Communication Intervention Research Program, the Multimedia Technology and Health Communication Small Business Innovation Research and Small Business Technology Transfer (STTR) program, and the Cancer Information Service Research Consortium Program.

The Centers of Excellence in Cancer Communication Research (CECCR) initiative provided large-scale funding to establish a cohort of major trans-disciplinary (combining multiple disciplinary research perspectives) research centers to conduct cutting-edge research to rapidly advance cancer communication research and practice. In 2003, the four original CECCR research centers were funded by the NCI for five-year terms. In 2008, the NCI renewed the CECCR grants for the four original research centers for another five-year term and funded a fifth (new) CECCR research center. Each of the CECCR research centers conduct several large, interrelated cancer communication research projects (on issues such as the effective use of online cancer information systems, the influences of news coverage of cancer information on health beliefs and behaviors, communication strategies for reducing cancer health disparities with minority populations, and patient-centered cancer communication) to advance knowledge, research methods, theory, and applications as well as to initiate new novel research projects and train the next generation of cancer communication researchers.

The NCI introduced the Digital Divide Pilot Projects to fund four demonstration research programs to test innovative and culturally sensitive communication strategies for implementing effective online health education programs to promote cancer prevention and control with vulnerable populations (poor, low literacy levels, elderly, immigrant, rural, urban, and minority populations). These demonstration projects illustrated best practices for narrowing the digital divide and helping at-risk groups access and use relevant health information online to promote cancer prevention and control. Similarly, the Health Communication Intervention Research Program funded seven innovative cancer communication intervention research studies to increase understanding about how targeted and tailored communication interventions can be used to promote cancer prevention and control as well as to reduce the burden of cancer, particularly among those disproportionately affected.

The diversity in theoretical approaches and intervention modalities used in these studies contributed broadly to understanding of the role of communication in health promotion and disease prevention. The NCI’s STTR programs fund science-based, theory-driven, user-centered grants and contracts with the goal of translating cancer research across the cancer continuum into programs, interventions, systems, networks, and
products needed by professionals and the public to reduce cancer risk and improve the quality of life of cancer survivors. Still another influential NCI cancer communication initiative was the Cancer Information Service Research Consortium Program, which created an innovative collaboration between the NCI's Cancer Information Service (CIS) health education information dissemination program and NCI’s HCIRB. The NCI funded a large multi-study program project grant (PO1) that engaged both NCI staff and external researchers to conduct applied studies evaluating the effectiveness and impact of the CIS educational and outreach programs; the use of tailored educational materials and interventions for targeted groups of consumers, the use of online information systems and resources; cancer information-seeking patterns; and communication strategies for promoting informed cancer prevention, detection, and treatment decision making.

Through these NCI initiatives and related studies, a large body of cancer communication research has illustrated that strategic communication can raise awareness about cancer risks, prevention strategies, and early detection and give people the information they need to make informed cancer-related decisions. Moreover, effective cancer communication can influence people to engage in recommended health behaviors that can improve their health, such as stopping smoking or undergoing screening for certain types of cancer. Cancer communication research has shown that, while the use of targeted media campaigns can produce behavioral change, the influences on relevant health behaviors are increased when communication efforts are supplemented by other community-based educational efforts. The theoretical basis of this effect is that increased knowledge and understanding alone do not motivate a person to change entrenched health behaviors. Other
factors, such as self-efficacy, skills to implement the change, convenience, and social and cultural mores all influence decisions and the ability to make relevant behavioral changes.

A large body of cancer communication literature demonstrates the powerful influences of communication interventions on a broad range of health behaviors and health outcomes. Research has shown the important influences of intrapersonal, interpersonal, group, organizational, and societal communications on health knowledge, behaviors, and outcomes. Similarly, studies have shown the positive influences of increased patient communicative involvement in treatment on desired health outcomes. Studies illustrate the positive influences of social marketing and diffusion-based strategies in encouraging at-risk populations to adopt important cancer-prevention behaviors.

Cancer is a complex array of different kinds of health challenges, with many different sites, stages, causes, screening strategies, treatment strategies, and responses to treatment. Due to the broad range of different cancer conditions and issues, a great deal of specific information needs to be conveyed to different individuals depending on their unique situations. To add to this complex information environment, active programs of cancer research are generating new information about the biological mechanisms underlying different forms of cancer, new screening and diagnostic techniques, and new forms of treatment and care for different cancers. It is imperative that cancer communication programs provide complete and up-to-date information about the key cancer issues of concern to specific audiences.

Cancer information is often highly emotionally charged due to the serious, often life-threatening, nature of many forms of cancer. Receiving a diagnosis of cancer can be a major shock to most people. It is important that cancer communication programs are strategically designed to address the important psychological and socioemotional issues surrounding different individuals’ experiences with cancer. Care must be taken to coordinate content and relational aspects of communication to inform people about cancer and cancer treatment without confusing or upsetting them.

To further complicate cancer communication programs, we must recognize the complexities of effective communication. Cancer communication messages must be designed and delivered to match the communication skills, needs, and predispositions of specific audiences. To influence entrenched health behaviors, messages need to be relevant and compelling, with health information that provides direction and rationale for making the best health-related decisions and adopting health-preserving behaviors.

Communication is central to providing high-quality cancer care, from primary prevention to survivorship. Interpersonal, group, organizational, and mediated communications are critical parts of cancer prevention, control, and care. The process of communication is central to each of the stages of the continuum of cancer care (prevention, detection, diagnosis, treatment, survivorship, and end-of-life).

Communication is the primary process for promoting cancer prevention. Cancer-prevention efforts typically involve designing and implementing strategic communication campaigns to promote healthy behaviors (such as refraining from smoking or using tobacco products, following a low-fat, high-fiber diet, and engaging in a program of regular exercise). Cancer prevention efforts typically involve the development and distribution of persuasive and informative cancer education programs and materials, as well as the development of behavioral intervention programs, to influence health behaviors that are often entrenched.

Communication is the primary process for informing and motivating people to seek screening for early detection of cancers. Communication is essential for encouraging audiences to engage in early detection and screening behaviors, to promote the development and adoption of screening programs in different health care and organizational settings, and for monitoring cancer trends to determine the best opportunities for screening and cancer detection. Promotion of early cancer detection and screening often involves the use of communication campaigns, educational materials, and behavioral intervention programs.

Communication is the critical process used for gathering and interpreting diagnostic cancer information from patients (often by checking suspicious symptoms, collecting health histories, or examining biological evidence of cancer). Due to the complexity of many cancer diagnoses, interpersonal and group communication are often used
as indispensable social processes for interpreting and clarifying diagnostic information (such as by eliciting second opinions, engaging in multidisciplinary consultations, and conducting tumor boards). Once a diagnosis is reached, human communication is the channel for presenting the diagnosis and plans for treatment to patients. Care must be taken to communicate cancer diagnoses as clearly and as sensitively as possible to help patients overcome the initial shock of receiving a cancer diagnosis, understand the intricacies of the diagnosis, and begin evaluating different plans for treating the condition.

Cancer treatment is an active and, ideally, a collaborative communication process between health care providers and consumers. Providers must explain treatment options and refinements to treatment strategies to their patients to help them make informed decisions about the best available programs of treatment. Once an initial cancer treatment regimen is implemented, the patient’s response to specific treatments must be carefully monitored and evaluated, so the treatments can be refined to produce the best effects and cause the least possible discomfort to the patient. Interpersonal and sometimes group communications are essential processes for seeking information about patients’ responses to treatments and making informed decisions about revised treatment strategies.

There is a growing population of long-term cancer survivors today due to advances in early cancer detection and improved cancer treatments. A recent report in the journal *Cancer Epidemiology, Biomarkers & Prevention* stated that, as of January 2012, there were approximately 13.7 million cancer survivors in the United States, a number that is expected to rise by 31 percent to 18 million by 2022. Cancer survivors have unique communication needs to help them cope with the many uncertainties of living with cancer. For example, cancer survivors typically have to cope with the fear of their cancer recurring. Survivors also need to access social support and relevant information to help them live with side effects of cancer treatments. Peer support from others who have adapted to living with cancer often can help cancer survivors overcome both physical and psychosocial challenges and enable them to readjust to their everyday lives.

Communicating with patients and their loved ones during the end-of-life process is often a very challenging part of cancer care for all involved parties. Death is not easy for most people to communicate about, yet the uncertainties surrounding death demand sensitive and caring communication. The quality of communication at the end of life is critical to providing effective cancer care for patients who are dying. Increasing attention in recent years has been directed toward the role of communication in palliative cancer care, especially at the end of life. The hospice movement also has focused attention on the unique communication needs of cancer patients and their loved ones during the transition to end of life.

There is a great need for cancer communication research to direct cancer prevention and care. For example, in cancer prevention and detection, we need to conduct controlled trials that compare different forms and intensities of communication-based behavior change interventions and examine the use of tailored, interactive, computer-based health communications programs that can contribute to an improved understanding of these new technologies.

Research on consumer–provider communication can help identify strategies for increasing accurate exchange of relevant health information, promote cooperation in the cancer treatment process, and enhance the quality of care for people confronting cancer. Further cancer communication research is needed greatly to fill in knowledge gaps about information needs in cancer prevention and control as well as to capitalize on the unusual opportunity presented by advanced communication technologies to help achieve cancer prevention and detection goals.

A significant increase in the size of the cancer communication research enterprise is needed to develop the next generation of research and interventions. At the same time, the enterprise must be informed by a greater understanding of the mechanisms by which these communications work. New cancer communications research should both increase knowledge and identify practical strategies for enhancing cancer communications and improving prevention and control of cancer. The challenge ahead is to develop cancer communication research programs that can help reduce cancer risk, incidence, morbidity, and mortality.
and promote the highest quality of life for people confronting cancer.

Gary L. Kreps
George Mason University
Lisa L. Sparks
Chapman University

See Also: Hospice Care; National Cancer Institute; Survivors of Cancer.

Further Readings

Cancer Council Australia

The Cancer Council Australia (CCA) undertakes a broad range of activities. Cancer councils, in general, are the leading independent funders of cancer research in Australia. In 2014, research grants from these organizations surpassed $65 million. Cancer councils directly funded $42.9 million in research, with an additional $22.2 million contributed by research funding partners. Each year, more than 100,000 Australians contact cancer councils for information and advice.

Cancer councils manage a network of cancer support groups, programs, and services to help improve the quality of life of people living with cancer, cancer patients, and their families and caretakers.

Goals and Values of Cancer Council Australia

The CCA works with the Clinical Guidelines Network (CGN), a countrywide network of health professionals that works to develop guidelines to provide the best evidence-based treatment and care for cancer patients. The CCA also works closely with its clinical partner, the Clinical Oncology Society of Australia, to ensure recommendations on cancer care and to incorporate the advice of experienced cancer specialists across various scientific and medical disciplines.

Cancer Council Australia advises the government on the needs of its stakeholders and establishes an independent voice for improved cancer control policy. The council also publishes the country’s National Cancer Prevention Policy, which advocates for a rigorous and comprehensive national approach to cancer prevention. This policy makes specific recommendations for governments and nongovernment organizations to take national action to create strategies and programs to help reduce the incidence of cancer.
In addition, CCA organizes events, works with its corporate partners to raise money to support cancer control activities, and receives donations and bequests to work with its corporate partners. The CCA has many network affiliations with national and international cancer organizations to help further shared goals.

**History of Cancer Council**

Over its 50-year history, CCA has transformed from a small secretariat to a strong federal body that has become Australia's strongest independent authority on cancer control.

The CCA began in 1961 as the Australian Cancer Society, when the existing six state cancer councils agreed to create a federal body to promote cancer control at the national level. Cancer organizations in the Northern Territory and the Australian Capital Territory (ACT) were then formed and signed on as members of the society. In 1997, the eight jurisdictional members agreed to expand the society, renaming it the Cancer Council Australia and appointing an expert chief executive officer, Professor Alan Coates. In May 2006, Professor Coates retired and was followed by Professor Ian Olver.

**Cancer in Australia**

Each year, about 128,000 new cases of diagnosed cancer in Australia, and those numbers are expected to rise to about 150,000 by the year 2020. One in two Australian men and one in three Australian women will be diagnosed with cancer by the time they turn 85. Cancer is a leading cause of death in Australia. In 2011, more than 43,200 people died from cancer in Australia. Cancer accounts for about three in 10 deaths in Australia. Compared to three decades ago, about 19,000 more people die from cancer each year—predominately due to population growth and aging. However, the death rate has fallen by more than 16 percent.

In terms of survival, 66 percent of Australian people diagnosed with cancer are still alive five years after diagnosis. The survival rate for many common cancers has increased by 30 percent in the past 20 years.

The most common cancers in Australia (not including nonmelanoma skin cancer) are colorectal, prostate, melanoma, breast, and lung cancers. Together, these cancers account for more than 60 percent of cancer cases diagnosed in Australia. More than 434,000 people in Australia are treated for one or more nonmelanoma skin cancers each year, with 543 people dying in 2011.

Cancer costs the direct health system in Australia more than $3.8 billion each year. In 2000 and 2001, 22 percent of all health research funds in Australia ($378 million) were spent on cancer research.

**Skin Cancer in Australia**

The CCA’s early detection and prevention programs aim to aid people to quit smoking, engage in physical activity, protect themselves from the sun, and eat healthier foods to decrease the risk of cancer.

About 95 to 99 percent of skin cancer occurs when skin cells are damaged by overexposure to ultraviolet (UV) radiation from the sun. Each year in Australia, skin cancer accounts for about 80 percent of all newly diagnosed cancers. Each year, general practitioners have more than 1 million patient consultations regarding skin cancer. Australia’s incidence of skin cancer is one of the highest in the world, two to three times the rates in the United States, the UK, and Canada. The main types of skin cancer are: basal cell carcinoma, melanoma (the most dangerous form), and squamous cell carcinoma.

Two in three Australians will be diagnosed with some form of skin cancer by the time they are 70. Over the past several decades, the incidence of skin cancer has risen in Australia. From 1982 to 2010, diagnoses for melanoma increased about 60 percent. Nonmelanoma skin cancer is the most common type of skin cancer, and it is more common in men. Each year, more than 434,000 people are treated for one or more forms of this type of cancer.

Melanoma is the most common cancer in Australians age 15 to 44 and the third-most common cancer in Australian women and men in general. In 2010, 11,405 people in Australia were diagnosed with melanoma, and in 2011, 2,087 people died from skin cancer in Australia. The majority of these deaths were due to melanoma, compared to nonmelanoma skin cancers. The five-year relative survival rate for melanoma is 94 percent for Australian women and 90 percent for Australian men.

The CCA markets a range of high-quality, affordable sun protection products that support the council’s activities, among its other beneficial initiatives.

Katie Moss

*Independent Scholar*
Cancer Drugs, Costs and Benefits of

The high costs or prices charged for cancer drugs are a major policy concern for physicians whose patients cannot afford to follow therapy and for health insurance or payments plans. This entry summarizes evidence that the prices charged do not correlate with added clinical benefit or with the net research costs to companies.

In 2013, a group of more than 100 oncologists coauthored a remarkable article in *Blood* on the ways in which the very high prices charged by drug companies for patented cancer drugs burdened their patients and became barriers to effective therapy. This is a particularly American story because laws allow and even encourage companies to charge much higher prices that in other affluent countries and because American insurance companies uniquely charge patients a co-payment of about 20 percent of the prices for cancer and other specialty drugs. As cancer drugs, by 2013, were priced at $100,000 or more for a year's supply, even well-insured patients had to pay $20,000 or more from their after-tax household budgets. Patients may have to take one to three anticancer drugs continuously. High prices and co-payments contribute to medical bankruptcy being common in the United States. Outside the United States, the financial burden of high prices for cancer drugs is widely discussed in many other countries that do not have these special features.

Just Price
One moral framework for pricing and social justice invoked by oncologists is *justum pretium*, or just price. This refers to the fair value of a commodity when it affects the lives or health of individuals. Examples include the price of bread during famines, the price of life-saving vaccines, and treatments for chronic medical conditions, such as cardiovascular conditions, hypertension, diabetes, tuberculosis, or multiple sclerosis. This is why medical services are treated as a publicly funded social good in most countries: Prices and costs are dealt with at the systemic level and not as charges to patients, except for some co-payments that usually have low, annual caps. Just prices should reflect some mixture of the benefit of the commodity when critically needed and affordability. The oncologists estimate that effective cancer drugs cost about $400,000 to $800,000 per additional year lived, several times the commonly used worth assigned in several countries because the prices are not just.

Do Prices Reflect High Research Costs?
The two key factors said to affect prices are the costs of research and the added value of new cancer drugs. Pharmaceutical companies commonly explain that they must charge high prices because research involves high risks and costs exceeding $1 billion.

The most widely cited average cost of research and development (R&D) that has a semiofficial status comes from the pharmaceutical industry’s leading policy institute, the Tufts Center for the Study of Drug Development. For more than 30 years, the same team of health economists, led by Joseph DiMasi, has had unique access to R&D costs submitted by companies in confidence to the center. They reported that the average research costs to get a drug to market was $1.3 billion in 2012, including all costs of failures.

An independent analysis of this estimate by Donald Light and Rebecca Warburton found that it was based on several factors or calculations that increased the figures substantially from the initial cost data from the companies. It is difficult to know what these data represent because the sample of companies is small and not disclosed. Those data cannot be verified, and the sample is both small and not random. Neither the names of the drugs nor their classes are disclosed.

See Also: American Cancer Society; Australia; Canadian Cancer Society; Green, Adele; Sun Exposure (Australia).

Further Readings

Cancer Drugs, Costs and Benefits of

The high costs or prices charged for cancer drugs are a major policy concern for physicians whose patients cannot afford to follow therapy and for health insurance or payments plans. This entry summarizes evidence that the prices charged do not correlate with added clinical benefit or with the net research costs to companies.

In 2013, a group of more than 100 oncologists coauthored a remarkable article in *Blood* on the ways in which the very high prices charged by drug companies for patented cancer drugs burdened their patients and became barriers to effective therapy. This is a particularly American story because laws allow and even encourage companies to charge much higher prices that in other affluent countries and because American insurance companies uniquely charge patients a co-payment of about 20 percent of the prices for cancer and other specialty drugs. As cancer drugs, by 2013, were priced at $100,000 or more for a year's supply, even well-insured patients had to pay $20,000 or more from their after-tax household budgets. Patients may have to take one to three anticancer drugs continuously. High prices and co-payments contribute to medical bankruptcy being common in the United States. Outside the United States, the financial burden of high prices for cancer drugs is widely discussed in many other countries that do not have these special features.

Just Price
One moral framework for pricing and social justice invoked by oncologists is *justum pretium*, or just price. This refers to the fair value of a commodity when it affects the lives or health of individuals. Examples include the price of bread during famines, the price of life-saving vaccines, and treatments for chronic medical conditions, such as cardiovascular conditions, hypertension, diabetes, tuberculosis, or multiple sclerosis. This is why medical services are treated as a publicly funded social good in most countries: Prices and costs are dealt with at the systemic level and not as charges to patients, except for some co-payments that usually have low, annual caps. Just prices should reflect some mixture of the benefit of the commodity when critically needed and affordability. The oncologists estimate that effective cancer drugs cost about $400,000 to $800,000 per additional year lived, several times the commonly used worth assigned in several countries because the prices are not just.

Do Prices Reflect High Research Costs?
The two key factors said to affect prices are the costs of research and the added value of new cancer drugs. Pharmaceutical companies commonly explain that they must charge high prices because research involves high risks and costs exceeding $1 billion.

The most widely cited average cost of research and development (R&D) that has a semiofficial status comes from the pharmaceutical industry’s leading policy institute, the Tufts Center for the Study of Drug Development. For more than 30 years, the same team of health economists, led by Joseph DiMasi, has had unique access to R&D costs submitted by companies in confidence to the center. They reported that the average research costs to get a drug to market was $1.3 billion in 2012, including all costs of failures.

An independent analysis of this estimate by Donald Light and Rebecca Warburton found that it was based on several factors or calculations that increased the figures substantially from the initial cost data from the companies. It is difficult to know what these data represent because the sample of companies is small and not disclosed. Those data cannot be verified, and the sample is both small and not random. Neither the names of the drugs nor their classes are disclosed.
If one accepts the data as reported, the independent analysis of the $1.3 billion estimate found three ways in which the estimate was made higher. First, half the estimate is not research costs but rather an estimate of profits that companies would have made if they had not invested their money in research but instead put it in a fund that returned 11 percent compounded per year. There are good reasons for subtracting these profits foregone as not real research costs, which brings the average down from $1.3 billion to approximately $650 million. Second, taxpayers subsidize about half of company R&D through various credits and deductions. This brings the net company costs down to about $325 million. Third, the original authors explained that the R&D costs submitted were based on the most costly fifth of new drugs developed by the companies, but then these estimates were misattributed to all drugs. Correcting for this misattribution brings the average down by about 30 percent to $230 million.

Other factors exaggerate the true net costs of R&D to companies. Because a few costly projects always distort the average cost, one should use the median, which the original article estimates is 26 percent less than the average. This brings the average down to $170 million. Another striking problem is that no accurate estimate of basic research costs to discover new drugs exists because they vary so much, from nearly costless discovery by chance to decades of frustrating efforts costing millions before the correct target and strategy are discovered. For their $1.3 billion estimate, the economists backed in an unverifiable figure for basic research and discovery that made up a third of the total R&D cost estimate. Removing this basic-research inflator brings the net median corporate research costs down to $125 million, plus the highly variable costs of basic research that are paid largely by taxpayers.

Because more than 84 percent of all basic research for discovering new drugs comes from the public and charitable sources, who bear the high risks and failure rates of discovery and early development, net corporate costs for discovery are modest. Companies spend only about 1.3 percent of their total sales revenues on basic research, after deducting taxpayer

By 2013, cancer drugs were priced at $100,000 or more for a year’s supply, and even well-insured patients had to pay $20,000 or more from their after-tax household budgets. High prices and co-payments contribute to medical bankruptcy being common in the United States. The two key factors said to affect prices are the costs of research and the added value of new cancer drugs. (MorgueFile)
subsidies, and the rest goes to developing minor variations or testing. By the time the most promising drug candidates are put into clinical trials, the company risk for a drug success has dropped from one in several hundred to only one in five. The corrected estimate of $125 million in net, corporate development costs, plus discovery, is based on the same R&D figures submitted by self-selected companies that were used to arrive at the $1.3 billion estimate as well as the same failure rates, trial sizes, and trial lengths. The dollars that companies have put into research over the past 15 years have generated six times more in revenue. Andrew Witty, the chief executive of GlaxoSmithKline, stated that the $1 billion cost to develop a drug is “one of the great myths of the industry.”

In the case of cancer drugs, most of the basic research and many clinical trials are paid by the National Cancer Institute and foundations. Further, Salomeh Keyhani found that clinical trials for cancer drugs are smaller and shorter than trials for most other diseases. For these reasons, the net R&D costs to major companies for their own cancer research are unlikely to be higher than for other drugs.

Prices and Clinical Benefits
The group of more than 100 oncologists reported that most of the new cancer drugs provide few or no clinical advantages over existing ones, so the high prices do not reflect added clinical value. Prices charged do not seem related to added clinical value. For example, Gleevec, or imatinib, is widely regarded as the most important pharmaceutical breakthrough for cancer patients in a generation. When imatinib was approved in 2001, its potential benefit in prolonging life was unknown. In his book Magic Cancer Bullet, Daniel Vasella, then chair and chief executive officer of Novartis, explained how the company reluctantly decided to develop imatinib as a goodwill gesture. He discussed the need for healthy profit margins and set the price high at $30,000. Vasella estimated that, with a prevalence of 30,000 patients in the United States, the annual revenue from U.S. sales would be about $900 million, more than enough to recoup the costs of development within two years. After that, the remaining costs of production would be low.

Contrary to most cancer drugs, imatinib transformed the lives of patients with chronic myeloid leukemia (CML) and other cancers. The annual all-cause mortality in CML declined to just 2 percent. If the price reflected added clinical value, Gleevec should have cost several times more than the price of other cancer drugs, or conversely, their prices should be much lower. Instead, Gleevec continued to be priced about the same as much less-effective cancer drugs. Because Novartis earned back its R&D costs by 2005, it has steadily raised the price of imatinib to about $100,000 a year in the United States but not in other affluent countries. Pricing in this case and in general seems to reflect what countries allow. Moreover, the annual increased prevalence of CML (because of the reduction of mortality from 10 to 20 percent down to 2 percent) and additional uses approved by the Food and Drug Administration have greatly expanded the market base beyond 30,000 to about 250,000 patients. Thus, Novartis could make $1 billion a year if the price of imatinib were $4,000. Patients and advocates have made numerous appeals to lower its price.

A different kind of consideration than the low correlation between prices and benefits is the general improvement in five-year survival rates. More effective drug therapy is commonly credited with this overall gain. However, the impressive gains in five-year survival rates for Americans appear due largely to earlier diagnosis so that the five-year count starts earlier. Patients used to have palpable tumors when diagnosed, but more recently, diagnosis is based on microscopic abnormalities. The five-year survival rate is not actually a rate but just the proportion of individuals alive five years after diagnosis, and it has risen as more patients are diagnosed earlier. Even if new screening and treatment strategies were ineffective, the five-year survival rates would increase. Researchers at Dartmouth Medical School and elsewhere have found little relationship between the increases in five-year survival and mortality rates from cancer. The fact that diagnosing and treating cancer is so profitable in the United States provides powerful incentives to promote earlier diagnosis and claim it saves lives.

Factors Affecting U.S. Prices
Some economic experts argue that, in a free market economy, pricing is based on what the market will bear. It is unclear, however, what this metaphor means when sellers have monopoly rights to charge what they like for life-saving drugs. Large data sets from wholesalers like Express Scripts document
that, as in the example of imatinib, sellers keep raising prices on older as well as newer patented cancer drugs, a practice not allowed in most other countries.

A widely believed claim holds that companies must charge Americans more for patented drugs because they cannot recover R&D and other costs at the prices allowed in Europe, Canada, and other affluent countries. These countries are said to be foreign free riders on American patients and payers. An analysis of company and government reports found, however, that companies do recover all costs in other affluent countries. They charge more and make extra profits in the United States because there is no pressure from the buyer side of the market to restrain them, as there is in normal markets.

The foreign free rider argument does not make logical sense either because it assumes the pharmaceutical market is divided off into national cost and revenue silos so that companies can lose in one silo (e.g., Canada) and profit in another (e.g., the United States). But, the pharmaceutical market is international. A cancer drug developed in England at great expense, for example, gets sold throughout the world, so one cannot match up those English costs to English revenues at English prices and claim that the company lost a fortune because the English prices were not high enough. What matters are global sales at a variety of prices, with U.S. prices being two to three times those in other affluent countries.

In the past five years, companies have doubled the prices in the United States for cancer drugs already on the market. This strategy could be called market spiral pricing. Most oncologists say they would prescribe a cheaper drug if there were two or more with similar efficacy and toxicity profiles at different prices, but prices are similar enough through market spiral pricing that there is not enough drug price sensitivity to allow oncologists or patients to select drugs based on costs savings. Market spiral pricing contributes to cancer patients deciding not to begin the treatment recommended or drop it because of costs. Very high prices threaten universal access to critical care for patients facing death.

Three obstacles to affordable prices in the United States for cancer drugs are the lack of cost-effectiveness studies to encourage value-based pricing, pay-for-delay contracts, and clauses preventing Medicare from trying to get the best price within a therapeutic class. A fourth problem stems from creating many small, narrow classes so that many cancer drugs are first in class within them. Cost-effectiveness studies are done much more widely outside the United States than within. As such studies begin at the Patient Centered Outcomes Institute, clauses inserted into federal law impede their results being used in making purchasing decisions.

Pay-for-delay contracts, in which the patent-holding company pays several million dollars a year to a generic company not to put its competing drug on the market, are being allowed despite their antitrust nature, and they contribute to keeping U.S. prices more than twice those allowed by other affluent countries.

The 2003 Medicare Reform Act included clauses added to prohibit Medicare from negotiating drug prices. When the law was implemented, there was a substantial increase in pharmaceutical company profits. Peter Bach is a senior oncologist and leader in drug policy research at the Memorial Sloan Kettering Cancer. In a valuable review, he concluded that rising prices and overall spending for cancer drugs in the United States is due largely to a unique legislative and regulatory framework that shields cancer drugs. For example, to hold costs down, Medicare commonly uses techniques such as coverage limitations for payment, blended-price reimbursement that rewards interchangeable drugs that charge less, and formulary flexibility.

However, special clauses and rulings prohibit Medicare insurance formularies from not including or selecting drugs for cancer and other life-threatening conditions. The buyers’ hands are legally tied. U.S. regulations also prohibit the use of interchangeability by regarding all cancer drugs as unique and sole sourced. Blended-price reimbursement that rewards interchangeable drugs that charge less is blocked. Oncologists and patients concerned about the high prices of cancer drugs in the United States may not appreciate these legal obstacles to having prices reflect added clinical value.

Donald W. Light
Rowan University School of Osteopathic Medicine
Hagop Kantarjian
University of Texas MD Anderson Cancer Center

See Also: Advertising; Anticancer Drugs; Drugs; Experimental Cancer Drugs; Marketing, Drug.
Further Readings


Cancer Therapy Evaluation Program

The Cancer Therapy Evaluation Program (CTEP) was formed by the National Cancer Institute (NCI) within the Division of Cancer Treatment and Diagnosis (DCTD). Its mission is to improve the lives of cancer patients by finding better ways to treat, control, and cure cancer. To this end, CTEP funds a robust national program of cancer research and sponsors clinical trials to investigate new anticancer agents, placing importance on translational research and the practical application of scientific findings.

CTEP uses a scientific process to accomplish its goals. Basic scientific findings are first identified based on scientific criteria and therapeutic needs. New anticancer agents fitting specific criteria are then selected, and clinical trials are developed. Next, the agents are investigated in clinical trials. Finally, promising new cancer treatments are meticulously compared to the most efficacious existing treatments in clinical trials to define the best treatments for specific types of cancer. Importantly, the goal is to find an effective treatment for a disease rather than to find a function for a particular research agent.

CTEP is organized into nine distinct branches and offices, each with its own functions and responsibilities. The Office of the Associate Director (OAD) oversees the other eight branches and CTEP as a whole. Since 2008, Jeffrey Abrams, MD, has served as the associate director. He also currently serves as the NCI’s acting director for clinical research.

Each of the other eight branches has its own branch chief and specific duties and functions.

The Clinical Grants and Contracts Branch’s (CGCB) main function is to oversee translational research grants and cooperative agreements, specifically in the fields of clinical oncology, surgical oncology, and pharmacogenomics, that is, how a person’s genes affect his or her response to drugs.

The Clinical Investigations Branch’s (CIB) function is the scientific oversight, coordination of, and collaboration with all programs, organizations, and forms of research supported by CTEP.

The monitoring and auditing of all clinical trials sponsored by CTEP’s Division of Cancer Treatment, NCI, as well as some cancer prevention trials sponsored by the DCTD, is the responsibility of the Clinical Trials Monitoring Branch (CTMB). In order to ensure that trial data is accurate and in compliance with regulatory guidelines, this branch provides guidance and oversight for the conduct of clinical trials and serves as a liaison with the Food and Drug Administration (FDA), among other regulatory groups.

The Investigational Drug Branch (IDB) manages a cutting-edge research therapeutics program, including phase I, phase II, and phase III trials. The branch is comprised of three sections, each with its own portfolio of research agents under study.

The Pharmaceutical Management Branch (PMB) is responsible for providing pharmaceutical assistance and oversight for CTEP-sponsored trials. Their main functions are providing information related to all aspects of IND (Investigational New Drug) agents, approving the use of IND agents and the subsequent distribution of these agents to participating investigators and institutions, and handling special situations involving the use and supply of CTEP IND agents. In addition, this branch registers all investigators and other staff taking part in CTEP clinical trials and manages these records.
Candlelighters Childhood Cancer Foundation

Candlelighters was officially formed in 1970 by a group of parents of children with cancer. Today, it is named the American Childhood Cancer Organization (ACCO). ACCO is a national organization as well as one of numerous local chapters. For decades Candlelighters and ACCO have served...
as the premiere cancer support groups for families whose children have received a cancer diagnosis. Commonly, a parent member will visit the family of a newly diagnosed child in the hospital during the first admission, bringing educational, emotional, and hospital orientation resources and a parent’s perspective. The support of Candlelighters continues according to each family’s interest. Publications and meetings provide families with information on treatment options, education of the child with cancer, and sibling support. Today, Candlelighters also focuses on strong legislative advocacy for the child with cancer, and although it has changed its name, its central mission has not changed.

Candlelighters and ACCO was started by a group of parents in the Washington, D.C., area in 1968. In that year, Grace Ann and Larry Monaco had an 18-month-old daughter Kathleen who was diagnosed with acute lymphoblastic leukemia. At this time, most children still died rather quickly from cancer, and there were no patient advocates. The Monacos met with other parents of children with cancer being treated at Children’s National Medical Center. Fortunately, it was a powerful group of families that led those first parent meetings, which included scientists, journalists, government workers, and lawyers. There were 25 people in the original group of parents. They built a lobbying campaign for clinical trials and appropriations for childhood cancer research.

By 1970, the original group of parents met regularly at the Rayburn building and invited speakers including the noted pioneer on death and dying Elizabeth Kubler Ross. Meetings were taped, and a newsletter also started in that year. Candlelighters officially formed in 1970 under the name Candlelighters Foundation.

The parent leaders continued to lobby Congress as well as the National Institutes of Health and the National Cancer Institute. Largely because of this lobby, Congress began to allocate money toward childhood cancer research. This parent group also created the Childhood Cancer Ombudsman Program under the Candlelighters name in 1970. By the mid-1970s, Candlelighters had an office in the American Cancer Society. In the early 1980s, Candlelighters separated officially from the American Cancer Society, including their funding. Candlelighters began to build a network among local organizations of parents of children with cancer across the country. A handbook first created by Martha Nathanson in 1986 and updated in 2000 (You Are Not Alone) is still an important resource for families with a child who has cancer.

By the mid-1980s, Candlelighters began to broaden the board of directors to families outside the Washington, D.C., area. The national office expanded and began to develop more educational materials, notably Educating the Child with Cancer. By the 1990s, the work of the group included running the ombudsman program, providing financial advice and medical referrals and searches, and leadership training workshops for parent leaders. Also in this period, the American Cancer Society and Candlelighters ended their financial arrangement, which led to restructuring in Candlelighters. Candlelighters successfully rebuilt its organization. There are approximately 50,000 families in the membership, and advocacy continues to be a large part of the group both locally and nationally. Today, the mission of ACCO is to provide information and support for children and adolescents with cancer and their families, to provide grassroots leadership through advocacy and awareness, and to support research leading to a cure for all children with cancer. Because cancer impacts the entire family, the goal of the ACCO continues to be providing pediatric cancer family support. Their motto is “because kids can’t fight cancer alone!”

Robin L. Rohrer
Seton Hill University

See Also: Childhood Cancers; Leukemia, Acute Lymphoblastic, Childhood; Leukemia, Acute Myeloid, Childhood; Lymphoma, Non-Hodgkin’s, Childhood.

Further Readings
Carcinoid Cancer Foundation

The Carcinoid Cancer Foundation was first founded as the Carcinoid Tumor and Serotonin Research Foundation in 1968 after the National Institutes of Health’s (NIH’s) funding for rare cancers ceased. The name change took place in 1995. This organization is a nonprofit charted by the state of New York, and its goal is to encourage and support research and public education about carcinoid and similar neuroendocrine cancers through fund-raisers, educational efforts aimed toward both physicians and patients, helping patients find doctors, and other efforts to improve the care and early discovery of this disease.

A carcinoid is a type of neuroendocrine tumor that grows slowly. They are found most often in the midgut, but metastasis sometimes happens. These tumors also may occur in the lungs and anywhere else in the body but are most often found in the intestines. Since the growth rate is so low in these types of tumors, one could grow for years before any symptoms presented. These tumors usually appear in hormone-producing cells within the small intestine or digestive tract, and they also can appear in the sexual organs and pancreas. The tumor also can create other symptoms such as flushing, diarrhea, and in some cases, heart failure. It is difficult to diagnose at times as the tumors can be too small to identify, and sometimes surgeons make discoveries while in the operating room.

The Carcinoid Cancer Foundation hosts lectures and conferences to gather together physicians and other individuals in order to educate them about these tumors. They also provide resources for the newly diagnosed and individuals who are currently battling this type of cancer. They have events to raise awareness and fund-raisers to assist patients. They connect patients with doctors and provide a lot of helpful information about diagnosis, treatment, nutrition, videos of patient conferences, and other encouraging or helpful resources.

Carcinoid tumors can be difficult to diagnose. If the tumors begin in the gastrointestinal (GI) tract, the substances the tumors produce are released into a blood vessel that carries them to the liver, where enzymes destroy them. Because of this, tumors may not show any symptoms until they have grown much larger or have invaded the liver as well, sometimes destroying it to the point that a liver transplant would be required.

The survival rates for individuals who have been diagnosed with carcinoid tumors depend heavily on what stage and location the tumor is in when it is discovered. A localized tumor means that the tumor has not spread, and the five-year survival rate (chances of the person surviving five or more years) is more than half in all locations. A carcinoid in the rectum, for example, has a 90 percent rate of survival if it is localized when it is found. Regional carcinoma has spread to other areas in the region, whereas distant cells have made it into the lymph nodes or to other distant sites when they are discovered. Distant tumors have the lowest rate of survival.

Tumors in the stomach, duodenum (beginning of the small intestine), appendix, and rectum are much more likely to be discovered before the cancer spreads. Tumors found in other parts of the small intestine and colon usually have grown into nearby tissues or lymph nodes and are already considered distant before they are ever discovered. The symptoms of these tumors can vary from nausea to diarrhea and abdominal pain, which all can be symptoms of more-benign ailments.

Through educational seminars and the collection of information available to carcinoid cancer patients, physicians and patients can be more aware of these medical ailments and know more of what to look for. Because carcinoid tumors are so slow in growing and generally take a long time to spread, nearly half of all of the tumors are found in an early stage before any problems have cropped up. These tumors usually are found accidentally while in treatment for some other problem. They also may be found during surgery on the GI track to alleviate other disease. It is most likely to be found during upper endoscopy or colorectal cancer screenings.

Treatment for carcinoid tumors depend on several factors, such as whether it can be completely
removed by surgery, has moved to other places within the body, has come back from remission, or has not improved with treatment. The Carcinoid Cancer Foundation provides resources to help explain the treatment options in more detail for newly diagnosed patients.

There are several different types of therapy used for treatment: surgery, radiation, chemotherapy, and hormone therapy. Treatments typically require surgery. There is endoscopic resectioning, which is an endoscope with a tool to remove tumor tissue. Local excision is surgery to remove both the tumor and a bit of the tissue around it. In more serious cases, the organ that contains the cancer is totally removed, and a liver transplant may be required.

Treatment for carcinoid syndrome may also be necessary, such as hormone therapy to lessen flushing and diarrhea. Interferon may be used to stimulate the immune system for the same reasons. Medication may be given for diarrhea, skin rashes, and easier breathing and prior to receiving anesthesia for the medical procedure.

With the difficulty present in trying to diagnose and treat this type of tumor, the education offered by the Carcinoid Cancer Foundation is invaluable. This foundation raises money to further research in this field as well as offering resources to connect the newly diagnosed with support groups, doctors, information about diet changes that assist with the treatment, and other information, such as what a patient should do if insurance refuses to pay for the treatment. Carcinoid cancer may currently be one that is difficult to recognize, but thanks to the efforts of individuals working for the Carcinoid Cancer Foundation, research will continue to be done on this matter.

Michael Fox
Independent Scholar

See Also: Carcinoid Tumor, Childhood; Carcinoid Tumor, Gastrointestinal.

Further Readings


Carcinoid Tumor, Childhood

Difficult to diagnose, carcinoid tumors are slow-growing and rare but can be completely cured if caught early. Most start in the gut (pancreas, rectum, intestines, colon, and stomach). About one-third of the tumors of the small intestine are carcinoid. About one-half of malignant tumors of the small intestine are carcinoid. Carcinoid tumors are also found in the lungs, liver, appendix, ovary, and other areas. These tumors are relatively rare in pediatrics. When they do occur, some of the more aggressive types are associated with increased mortality in this age group.

Generally, less than 1 percent of all cancer cases in the United States involve children. Approximately 10,450 children (under the age of 15) and approximately 5,330 adolescents (age 15 to 19) will be diagnosed with cancer per year. Most will be treated successfully. The number of deaths from pediatric cancer, from the year 1975 to 2010, has decreased by greater than 50 percent. Yet, it is the second-leading cause of death. Approximately 1,350 children (under the age of 15) and 610 (age 15 to 19) will die from cancer per year in the United States.

Carcinoid tumors are the most frequent tumor in the gastrointestinal tract of children and the most frequent primary pulmonary tumor. The appendix is the most common site in the gastrointestinal tract. Carcinoid tumors found in the appendix of pediatric patients are often found during removal of the appendix. Some pediatric patients will present with abdominal pain; however, symptomology is not always present. Carcinoid tumors are more likely to occur in female patients with an incident rate of 2 to 1.5.

Carcinoid tumors are neuroendocrine tumors. They are found in the cells of the nervous and endocrine systems. Because of this, they can secrete excess hormones (e.g., histamine, serotonin)
Carcinoid tumors, childhood

Carcinoid tumor, childhood describes the symptoms associated with carcinoid tumors in the liver. Symptoms can include: redness in the face or neck, warm feeling in the face or neck, fast heartbeat, difficulty breathing, diarrhea, and sudden drop in blood pressure. Carcinoid syndrome is less likely present in pediatric patients as the cancer typically is not present in the liver. However, the larger the tumor, the more likely the liver will be involved.

Carcinoid tumors are diagnosed and staged through a variety of tests that may include: physical exam; physical history; blood chemistry (white blood cell, red blood cell, hemoglobin, and platelet counts); and a 24-hour urine test (urine is collected over a 24-hour period to measure higher- or lower-than-normal substances). The 24-hour urine test is also used when diagnosing carcinoid syndrome.

Treatment for carcinoid tumors typically includes surgical removal and when necessary further interventions. If the tumor occurs in the appendix of children, treatment might include removal of only the appendix, if the tumor is small. When a larger tumor is present, surgery to remove the appendix, lymph nodes, and even part of the large intestine is possible. If the carcinoid tumor has spread, chemotherapy or radiation therapy may also be required. The best chance for a cure is a complete removal of the carcinoid tumor. Approximately 18 percent of pediatric disease will involve a tumor of the appendix.

Carcinoid bronchial tumors in the pediatric population are often treated by resection of the bronchial region. The vast majority will undergo a lobectomy, which is an open surgical procedure. However, some are better treated by other means, and this is due to the specific location of the carcinoid tumor. Recent proposals in treatment of bronchial tumors include sparing as much bronchial tissue as possible utilizing bronchoscopic treatment.

A bronchoscope is a thin, lighted instrument that is inserted through the mouth or nose and is capable of removing small portions of diseased tissue without the need for an open surgical procedure. This method, however, can result in the need for a second resection and may increase the risk for recurrence of the disease. If the disease does recur, a lobectomy may be recommended.

Even though carcinoid tumors can be removed typically with surgery, they must be monitored appropriately. Patients of any age, especially if carcinoid syndrome is associated, are at risk for carcinoid heart disease. Some people develop this disease because carcinoid syndrome can cause a thickening of the heart valves. This makes it difficult for the valves to function. They may leak, as well. Symptoms of this disease can include shortness of breath (especially during physical activity) and fatigue. This disease may lead to heart failure. Surgical repair of the heart valves may be indicated.

It is recommended that parents talk with both the treating physician and primary care physician to develop an ongoing plan for follow-up care. Ongoing computed tomography (CT), magnetic resonance imaging (MRI), observation, screening, and follow-up care are recommended for not less than three months with the treating physician. Treating physicians may also recommend enrollment in clinical trials. Primary care physicians should regularly examine, administer appropriate tests, and monitor recovery for the remainder of childhood. A transition plan into adulthood may include good health guidelines, including not smoking, healthy diet, healthy weight, and regular exercise.

Treatment for cancer is associated with long- and short-term physical side effects; additionally, any cancer treatment in childhood should include a discussion and plan for cognitive and developmental side effects. The follow-up plan should also address quality of life in these areas as well as any emotional concerns. The family should keep an organized and detailed health record with the idea in mind that the child will one day be responsible for his or her own health care. Few children will remember treatment with enough detail to inform physicians in his or her ongoing care. This record can then be given to the child as he or she reaches adulthood. The information will be valuable to any treating physician through adulthood.

Jessica Anne Hammer
Independent Scholar

See Also: American Academy of Pediatrics, Section on Hematology/Oncology; Carcinoid Cancer Foundation; Carcinoid Tumor, Gastrointestinal; Thymoma, Childhood.
Carcinoid Tumor, Gastrointestinal

Carcinoid tumors are best treated when diagnosed early. They are often cured through surgery. Most grow and spread at a slow rate, but because of this, they often do not cause symptoms for multiple years. They start to grow in hormone-producing cells in a variety of organs. However, they are most prevalent in the gastrointestinal tract (i.e., stomach, intestines, appendix, liver, and pancreas).

Thirty-nine percent will occur in the small intestine; 15 percent in the rectum; 7 percent in the appendix; 5 to 7 percent in the colon; 2 to 4 percent in the stomach; 2 to 3 percent in the pancreas; and 1 percent in the liver. Approximately 12,000 persons are diagnosed with a carcinoid tumor in the United States. Of those, about 8,000 occur in the gastrointestinal tract. Approximately 50 percent of all small intestine cancers are carcinoid tumors. However, carcinoid tumors represent only 1 percent of the cancers that occur in the gastrointestinal tract.

Most symptoms of carcinoid tumors are vague and may be similar to symptoms of other conditions. Abdominal pain, bleeding, cramping, bloody stools (typically dark and tarry), or constipation may be present in gastrointestinal carcinoid tumors. Carcinoid tumors may lead to two conditions: carcinoid syndrome and Cushing’s syndrome. Approximately 60 percent of persons with a carcinoid tumor will eventually develop carcinoid syndrome. Heart palpitations, abdominal cramps, shortness of breath, wheezing, flushing of skin, rash, diarrhea, neurosis, and psychosis are all possible symptoms of carcinoid syndrome. When all of these symptoms occur at the same time, it is referred to as a carcinoid crisis. It is a serious complication and can be life-threatening. It can occur suddenly or be brought on by stress, anesthesia, or chemotherapy. Strenuous exercise and alcohol consumption can make these symptoms worse. Cushing’s syndrome may include high blood pressure, high blood sugar, weight gain, muscle weakness, increased facial and body hair, and thinning of the skin.

A high-magnification micrograph of a tumor in the small intestine. About one-third of all the tumors found in the small intestine are carcinoid. (Wikimedia Commons)
There are a number of identified risk factors associated with carcinoid tumors: genetic syndromes (i.e., MEN1 or neurofibromatosis type 1); female gender; African American heritage (gastrointestinal carcinoid tumors); Caucasians (lung carcinoid tumors); stomach conditions that reduce the amount of acid in the stomach; smoking; and age (gastrointestinal carcinoid tumors are most often diagnosed between the ages of 55 and 65). It is important to note that some people with risk factors never develop carcinoid tumors, while others with no risk factors will.

Physicians have a variety of tests to diagnose and stage tumors. Some of these tests also assist in determining the most effective treatments. Most often, a biopsy will be performed to make a definitive diagnosis. Physicians will most often consider: age and medical condition; previous test results; type of tumor suspected; and signs and symptoms.

Blood and urine tests are typically the first step. Physicians use these to look for excess hormones and other substances that carcinoid tumors may produce. Physicians may use X-ray, computed tomography (CT), magnetic resonance imaging (MRI), or a positron emission tomography (PET) scan to visualize suspected tumors. The imaging may include an injection of radioactive material that is attracted to carcinoid tumors. Endoscopy is typically used when gastrointestinal carcinoid tumors are suspected. Endoscopy can visualize nearly the entire digestive tract from the esophagus to the rectum.

When testing is complete and the results are cancerous, physicians will then stage the cancer. Staging describes where the tumor is, where it has spread, and if it is affecting other parts of the body. Knowing the stage helps the physician decide treatment and predict prognosis. There are different stage descriptions for each of the different types of carcinoid tumors. There are three general stages utilized for staging of gastrointestinal carcinoid tumors: localized (the tumor has not spread outside of the affected organ); regional spread (the tumor has spread to adjacent tissues); distant spread (the tumor has spread to tissues or organs not adjacent to the initially affected organ); and recurrent (a tumor that returns after successful treatment).

Treatment for the various stages depends on a number of factors, including possible side effects, patient's preference, and overall health. A localized stomach carcinoid tumor is often removed through the use of an endoscope. Surgery is recommended for both small and large intestine carcinoid tumors. An appendectomy is recommended for carcinoid tumors of the appendix. Carcinoid tumors of the rectum are removed with electro-fulguration (destroys the tumor with an electric current). When regional spread occurs, the primary carcinoid tumor is removed and the tissues and lymph nodes in the immediate area. If distant spread occurs, it is call metastatic cancer. Surgery at this stage typically alleviates symptoms but not necessarily all of the cancer. In this case, chemotherapy, immunotherapy, targeted therapy, or radiation therapy may be recommended. Each of these may also be utilized in conjunction with surgery.

Radiation therapy uses high-energy X-rays to destroy cancer cells. Usually, there are a specific number of treatments over a specific period of time. Radiation therapy can be external or internal. Chemotherapy uses drugs to destroy the cancer cell, usually by destroying the cell's ability to grow. This method also utilizes a specific number of treatments over a specific period of time. Immunotherapy helps the body to boost its natural defenses to fight the tumor. Targeted therapy is meant to target the tumor's specific genes, tissues, or proteins that assist with its growth or division. This treatment limits the damage to surrounding healthy cells.

Remission occurs when the cancer can no longer be detected and there are no longer any symptoms. Remission can be permanent or temporary. If it does return, it is called recurrent cancer. If it does reoccur, it can come back in the same place, nearby, or in another place. These are referred to as a local recurrence, regional recurrence, or distant recurrence, respectively.

Recovery is not always possible. In this case, the disease is called advanced or terminal cancer. Making sure symptoms are as controlled as possible and pain management is in place occurs at this stage. It is at this time that patients and families may discuss final wishes, who will make medical decisions, and what kind of life-saving interventions are desired or prohibited by the patient. If the patient has less than six months to live, hospice may be a good choice. Hospice is designed to increase or maintain quality of life, provide
nursing care and technical assistance, and any special equipment required. Hospice care can be provided in the home or in a facility.

Jessica Anne Hammer
Independent Scholar

See Also: American College of Gastroenterology; Bile Duct Cancer, Extrahepatic; Carcinoid Cancer Foundation; Pancreatic Cancer; Rectal Cancer.

Further Readings

Carcinoma of Unknown Primary

Carcinoma is cancer that develops from epithelial cells, the tissues that line cavities and surfaces in the body, as opposed to sarcomas, which develop from nonhematopoietic mesenchymal cells, and leukemias and lymphomas, which develop from hematopoietic cells. Carcinomas have among the highest mutation frequencies, depending on the type of tissue they develop from and whether, as in the case of lung cancers, that tissue is regularly exposed to DNA-damaging agents like tobacco smoke.

About 4 percent of cancers are cancers of unknown primary origin (CUP), meaning that a metastatic cancer—a cancer that has spread beyond its point of origin—has been discovered, but doctors are unable to determine where it originated. Though CUP properly refers only to those cancers whose origin remains unknown after a thorough and exhaustive investigation—the aforementioned 4 percent—those metastatic cancers that are unknown at first but eventually have their origin located are still important to research and to understanding CUP because they represent the same general phenomenon (cancer metastasizing before symptoms present) and may be caused by the same mechanism.

Most CUP cancers are adenocarcinomas: carcinomas that began in glandular tissue either lining or covering organs in the body. Adenocarcinomas can originate in the breast, lung, pancreas, prostate, stomach, liver, and colon most of the time. Adenocarcinomas, two-thirds of which are well differentiated, account for 90 percent of CUPs, while the remainder are squamous cell carcinomas, undifferentiated malignant neoplasms, neuroendocrine tumors, and mixed tumors.

A number of symptoms may present, including pain that does not go away, a cough or hoarseness that doesn’t go away or worsens, bleeding or discharge, fever, night sweats, loss of appetite or rapid weight loss, constipation, diarrhea, increased urgency in urination, or a lump.

Because CUP is a type of cancer rather than a specific cancer, symptoms can vary considerably, but usually, the cancer is discovered because of a swelling on the body or a mass discovered during medical imaging (either in response to other symptoms or because of some other condition). The defining feature of CUP is that it has spread sufficiently far beyond its origin without causing sufficient symptoms to necessitate a doctor’s visit. Characteristically, tumors in a CUP patient form in unusual areas—this is one reason it is difficult to determine their origin. A full physical examination of the body, including rectal and pelvic exams, and whole-body imaging are necessary to be sure that all tumors are identified. A computed tomography (CT) scan of the chest, abdomen, and pelvis is conducted, which may indicate a helpful pattern of spread. Cancer found in the upper body, for instance, likely originated above the diaphragm such as in the lung, while the pancreas and liver are more likely origins for cancer found in the lower body.

The reason the origin is important is because not all cancers are the same. A tumor in the breast that originated in the lungs is not, ideally, treated the same as a tumor that originated in the breast. Based on their origins, different cancers respond to different treatments. For this reason, immunohistochemical testing can sometimes identify the
cancer's origin by determining the expression of protein markers by the cancer cells and matching that pattern to a known cancer. Even this works only 25 percent of the time.

Treatment and prognosis vary considerably, though the prognosis is generally poor due to the metastasis. The standard modalities—chemotherapy, radiation treatments, surgery, and hormone therapy—are usually employed, often in combination, depending on the location of the tumors.

Research continues to investigate whether there is a common factor or mechanism that could account for the CUP phenomenon, making some cancers more likely than others to spread quickly but asymptptomatically. There are some indications that CUP not only runs in families but is associated with families with a history of lung, kidney, and colorectal cancers.

Bill Kte’pi
Independent Scholar

See Also: Colon Cancer; Kidney (Renal Cell) Cancer; Lung Cancer, Non–Small Cell; Lung Cancer, Small Cell.

Further Readings
Percival, Mary-Elizabeth and A. Dimitrios Colevas.
Scheidhauer, K., N. Avril, and V. M. Bonkowsky.
Taylor, M. B., N. R. Bromham, and S. E. Arnold.

Careers

The concept of career comes from a person’s work. Work that is specialized through a division of labor is a job. The division of labor creates work that is suited to workers’ abilities, skills, and interests. They can become very good at the work they do through training and experience. A career is more than a job, although it is often confused with a steady job of some kind.

It is the linkage of jobs so that the worker progresses in a planned process of increasing skills and responsibilities. This process takes place within a large organization with many different kinds of work organized in a logical way. As the sociologist Max Weber described it, employees’ jobs are linked in a series of steps. The result is the traditional organizational hierarchy, each step leading to a higher position on the career ladder. The bureaucracy groups jobs and careers into departments and divisions. There is even a department in charge of creating careers. The development of job descriptions, hiring and job placement, and training and career planning is done by human resources.

A worker’s career leads to first-line supervisor, to the manager of such supervisors, and on up the administrative ladder to the president. This is the line. A worker could spend a lifetime moving up step after step. Promotions would take place within the organization rather than bringing someone from outside.

While much that Weber described has been found to fit real organizations, there are problems with his theory. Not all work takes place within this administrative line. A second type of work has been found, carried out by the staff. Staff workers are experts who cannot be trained within the organization due to their highly specialized skills. No one in another job can become a doctor or nurse by receiving training from the office of human resources. Organizational studies have found friction and other problems from an organization
following two contrary operating principles: the specialized authority claims by professional staff and the administrative authority of the bureaucratic line. In a hospital, the question is this: Who runs the organization? Is it the doctors or the hospital administrator?

We see that medical work is organized into professions. When we think of a career in health care, the image of a profession comes to mind. In fact, there are a very large number of specialists doing skilled work, all of which is licensed to do a particular piece of the very broad category of health care. Each type of health care work has laid claim to being a profession. Work only partially recognized is a semi-profession.

The way professions work is very different from the rational bureaucracy. Yet, the professional career also consists of a series of steps. They are a throwback to the medieval guilds of craftspeople and retain many of their ancient features of loyalty to peers, not an employer.

The bureaucratic organization recruits from the general public. The guild gained its recruits from its members’ children. This process emphasized the guild’s unity. The recruit was an apprentice who worked in the home of a craftsperson for seven years. While the apprentice was not paid, he or she received training while living with the craftsperson’s family. This stage is like the college study required by health professions. Then came the stage of the journeyman, eventually becoming established as a craftsperson. The last stage was master craftsman. Each stage required peer acceptance of the candidate, usually by submitting a piece of work that demonstrated the candidate’s skills. These stages live on in the degrees granted by universities and the thesis that demonstrates the graduate’s scholarship.

The difference between the profession and the organizational career lies in the profession’s lack of integration with other work. Each profession operates in isolation. A nurse’s aide does not move up to become a nurse with training and experience. A nurse cannot become an emergency medical technician or become a doctor. A nurse could become a doctor but by starting at square one, getting admitted to medical school. Health care professions have their own stages of acceptance, but once a candidate is accepted into the profession, there is no organized plan to become another kind of professional. In the way organizations operate, these professionals are staff. However, they can move into the positions of the line, as when a nurse becomes the nursing supervisor or a doctor a hospital administrator. Also, there are new skills and specializations that professionals can gain within their professions. A doctor can become a surgeon, and a nurse can become a surgical nurse.

While an organization can hire anyone who is able to do the needed work and can be trained to do it, this does not hold true in hiring professionals. The profession, as did the guild, recruits and trains the professional. Only members can do its work when accepted by their peers and licensed. Professionals decide who to accept as trainees and what standards to require for licensure. Nearly every profession requires a college degree and many more advanced training. While professionals claim that their special knowledge can only be transferred through such education, they also are restricting membership to candidates who have the background that enhances the prestige of the group (profession).

During World War II, the U.S. Army required thousands of health professionals. Among these were pharmacists. As a large organization with power to organize and train its human resources, the army studied the pharmacy occupation logically and found that a good pharmacist could be trained in six weeks. The leaders of the profession loudly complained for their prestige was being undermined. They did admit that the requirement at the time for a college degree to be a pharmacist was not necessary, but it was good for the profession. The problem is that what is good for a profession, in raising the requirements for entry, may be bad for the public, in restricting the number of practitioners, raising the prices that practitioners can charge and holding back the profession from needed change.

This problem has led to a system of health care in the United States that is disorganized and fragmented, with hundreds of different kinds of specialized work being done by professions that do not work together to achieve organizational goals but separately to advance their power and prestige. Each profession works to control its work and who can do it. So, the nursing profession has control over medications. No nurse’s aide can give a pill to a patient, for that is the nurse’s job. Similarly,
Caregivers

Cancer patients often require care from informal caregivers who provide both emotional and instrumental support. Caregivers are often family members who provide, among other responsibilities, assistance with activities of daily life and coordination of medical care. Thus, a caregiver is one who attempts to meet the physiologic and psychosocial needs of the individual. Caregiving comprises an enormous unpaid contribution to health care, and the burden of caregiving brings increased psychological and medical morbidity to the caregiver. Only recently has research begun studying the impact of this distress and exploring interventions that support cancer caregivers to promote better outcomes for families managing a cancer diagnosis.

The Scale and Value of Care Provided

In 2009, roughly 42 million caregivers across all United States patient groups provided an unpaid contribution to health care of $450 billion, a value that approached federal Medicare spending for the same year. This represents an estimated 40,300 million hours of care, most often provided by immediate family members. In the UK, 6 million unpaid caregivers provide a £57 billion ($97 billion) contribution to health care—similar to the annual cost of the entire National Health Service. Collectively,

Keith R. Johnson
Oakton Community College

See Also: Hospitals; Technology, New Therapies.

Further Readings


Caregivers are a fundamental component of cancer treatment—providing approximately 50 percent of the total care needed for patients treated for cancer in developed countries.

Demographics
There were 14.5 million people living with cancer in the United States in early 2014. This number is projected to grow to 19 million by 2024 with similar growth in cancer survivorship expected worldwide. The number of people living with cancer is increasing in part due to earlier detection, improved treatment outcomes, and a resulting shift from the treatment of cancer as an acute illness to its treatment as chronic. As less-intensive treatments have become available and as managed care attempts to reduce health care costs, cancer is increasingly treated in an outpatient setting. As a result, additional involvement from family caregivers is increasingly being required to fill new responsibilities in the health care system.

A spouse or partner of the patient with cancer most often fills the role of caregiver. The second most common caregiving situation for those with cancer is provided by adult children of the patient, with daughters providing the majority of care. Most caregivers are female; however, a rise in prevalence of male caregivers across all types of caregiving has been continuing for many years, with men serving as caregivers for 39 percent of patients in the United States in 2007, reflecting a 25 percent rise in male caregiving since 1987.

The average lost income of caregivers in the United States during the two years after a cancer diagnosis was $47,710, with breast cancer representing the least costly at $38,334 and lung cancer representing the highest caregiving cost of $72,702. The typical caregiver in the United States loses $110 in wages and benefits a day.

Caregiver Burden
Caregiving for a family member with cancer often requires a full-time commitment, with caregivers responsible for monitoring and managing symptoms, tracking and administering medications, conducting basic medical procedures, and providing emotional support. This support is provided despite caregivers having only minimal training. Additionally, care providers often supply transportation for the patient and assist with medical decision making. This care typically occurs in the context of significant role changes at a time when the patient is not able to accomplish activities of daily living. For example, a spousal relationship can transition into providing extensive medical care. The caregiver is frequently required to take on other roles (home finances, cleaning, family transportation, etc.) along with the myriad aforementioned duties of providing care to the patient. These multiple roles and additional workload occur in the context of a grief reaction to the patient’s cancer diagnosis and, in many cases, reduced emotional support from the family member facing cancer. Caregivers are often unprepared for these new roles and increased emotional demands. As such, this confluence of events has been shown to produce a substantial psychological, physical, and financial impact on lay caregivers.

Psychological Impact of Caregiving
Caregivers have been shown to experience significant psychological distress. Indeed, the levels of caregivers’ emotional distress have been shown to be higher than those experienced by the cancer patient. Between 18 and 58 percent of caregivers experience levels of depression that meet diagnostic criteria. Similarly, anxiety is common among cancer caregivers and is observed to reach levels of clinical significance in 20 to 50 percent of family caregivers. Other commonly reported emotions include fear, hopelessness, and loss of control as a result of caregiving.

A number of factors have emerged that predict poorer psychological functioning in caregivers of cancer patients. For example, psychological distress worsens with disease progression, metastatic disease, graver prognosis, increased length of patient illness, and when caring for patients reporting greater distress. Personal caregiving needs, such as helping the patient shower, have been found to increase emotional burden on caregivers than more than nonpersonal needs such as transportation. Family caregivers of advanced cancer patients, those with less than a high school education, and those who experience more disruption of their life experiences are at highest risk for anxiety and depression.

Female caregivers report higher levels of distress, a higher burden due to caregiving, and less self-esteem than male caregivers. It has been theorized...
that this may be due to the influence of gender-role socialization where, in many cultures, women are expected to serve as primary caregivers. Therefore, women may be seen as fulfilling an already expected familial role, whereas men may receive additional positive appraisal from others for filling a gender atypical role. Adult children who are caregiving for a parent have been reported to experience higher levels of distress than spousal caregivers. In addition, caregiving distress has been shown to be higher in younger caregivers.

Studies of patient–caregiver dyads suggest that the quality of communication predicts the amount of emotional distress, depression, hopelessness, and caregiving burden experienced by the dyad. Patient–caregiver dyads that communicate well about their relationship and express authentic concerns about cancer experience lower amounts of emotional distress. Protective buffering is the practice of hiding worries or concerns to protect the other from emotional or physical distress. In caregivers, it often presents as a lack of willingness to bring up fears related to cancer or death and dying as well as not discussing burdensome aspects of caregiving. Protective buffering has been shown to increase distress in partners and lower relationship satisfaction in patients and caregivers undergoing cancer treatment.

Despite the large amount of psychological distress exhibited by caregivers, positive emotional experiences and benefit finding are also reported. For example, a deeper connection to the patient, enhanced experience of meaning in life, and improved self-worth or feelings of increased self-efficacy in the caregiver role are noted. These are often provided as examples of posttraumatic growth or the development of positive psychological change as the result of challenging life experiences.

**Physical Impact of Caregiving**

The physical effects of being a family caregiver for those with any chronic illness have been well documented, affecting sleep, fatigue, cellular immunity, markers of cellular aging, wound healing, cardiovascular disease, hypertension, and mortality.

Sleep disturbance is the most common symptom of distress among the caregivers of early-stage cancer patients. Between 31 and 95 percent of family caregivers of advanced cancer patients report severe sleep problems. Specifically, they report a lack of restful sleep, limited sleep duration, and frequent sleep disruptions due to restlessness of patient bed partners and nighttime caregiving needs. Caregivers also report daytime dysfunction from sleep deprivation. Caregivers may be cautious about taking sleep medications for fear of not being able to address the needs of patients during the night.

Fatigue is a common concern for long-term caregivers. There may be physiologic or psychological etiologies to this fatigue. The demands of multiple roles, emotional distress, anticipatory grief, sleep deprivation, and limited time for rest and recovery all contribute to the development of fatigue. Fatigue is related to caregiver burden, with fatigue increasing along with increasingly demanding caregiver schedules and perceived burden of the caregiving role. In patients with advanced cancer, fatigue has been shown to be interrelated with psychological morbidity, specifically with the level of depression, anxiety, and sleep concerns.

Medical risks conferred to caregivers are caused by increased allostatic load—chronic stress causing wear and tear on the body. Family caregivers experience wide-ranging negative impacts on biomarkers that are established indicators of health. These include reduced cellular immunity, slower wound healing, cytokine dysregulation, autonomic and neuroendocrine disruption, and elevated markers of inflammation and cellular aging.

The well-documented increase in inflammation may be tied to cardiovascular risk. For example, spousal caregivers of cancer patients have an increased risk of coronary heart disease and stroke, which is greater for patients diagnosed with a high-risk cancer, such as lung and pancreatic cancer. Caregiving has also been identified as an independent predictor of hypertension onset, with caregivers being 36 percent more likely to develop hypertension than noncaregivers. Caregiving lasting longer than one year has been associated with a more than doubled risk for hypertension. Elderly spousal caregivers for all types of patients who report strain in their role as a caregiver have a 63 percent increased incidence of mortality when compared to noncaregiver controls. Being a spousal caregiver has been established as an independent risk for mortality.
Support for Caregivers

Lack of resources for basic needs, employment, and finances often represent major sources of concern for caregivers. Families may lose one household income due to cancer, and the other, in full or in part, is lost due to work leave while caregiving. In the United States, the Family and Medical Leave Act (1993) provided one of the first legal protections for caregivers, allowing unpaid medical leave to allow for caregiving provided to a spouse, parent, or child. The Affordable Care Act (2010) granted additional provisions to expand Medicaid benefits for personal attendant care to help provide relief to family caregivers among the lowest income families in the United States. In Europe, caregivers similarly experience many unmet financial needs. Research in Italian and British populations has reported that many families spend a significant portion of their savings in providing care for loved ones at the end of life. Internationally, only 16 countries provide legally mandated paid caregiving with compensation rates ranging from 50 to 100 percent.

Care for the Caregiver: Interventions

Given the psychological morbidity and health consequences of caregiving, caregivers are in the unusual position of being in need of care themselves while providing care at the same time. However, cancer treatment is almost exclusively focused on patients. The focus on patient care can be all encompassing for oncologists, and identification of the unmet needs of the caregiver is often limited. As a result, many caregivers only receive intervention during times of crisis, when their needs are more likely to be outwardly visible to the oncology team and their support system.

Caregivers often value self-reliance and independence and may be reluctant to seek help. Other caregivers are narrowly focused on care for the patient and do not seek supportive services, possibly due to their perception that these services would distract from the care they provide. Indeed, support services that require them to leave the proximity of the patient may be prohibitive. Caregivers also report that they rarely have the time to take care of themselves due to the demands of providing care for their cancer patient.

Research has provided some insight into what interventions are most acceptable and effective at meeting the needs of caregivers. Randomized controlled trials have attempted to isolate intervention components in caregivers of cancer patients. These include, but are not limited to, interventions providing education and training about patient care, including information about the cancer and treatment, those that teach coping, communication and problem-solving skills directed at the caregiver, and those that provide a supportive therapeutic relationship for caregivers.

Interventions that give caregivers information about cancer, what to expect, treatment guidelines for patient care, as well as symptom management have been demonstrated to reduce caregiver distress, increase caregiver confidence and self-efficacy, and improve patient outcomes. It should be noted that many of these components are now considered standard of care. In addition to these targets of caregiver intervention, skill-based training that provides coping skills for managing emotional distress, communication, and problem-solving therapy are effective for many cancer caregivers. These interventions reduce symptoms of anxiety and depression, promote active coping over passive or avoidant coping, and ultimately, reduce caregiver burden.

Interventions providing supportive therapeutic relationships for caregivers are often integrated with other types of interventions. Social support provided by a group setting has been found to help caregivers. Similarly, caregivers with greater perceived social support report an enhanced ability to cope with caregiving as well as less emotional distress, reduced markers of inflammation, and reduced caregiver burden. Home-based caregiver respite services have been demonstrated to reduce the experience of caregiver burden in end-of-life cancer care. However, many caregivers are uncomfortable leaving the patient’s side toward the end of life. Most regrettably, financial support for these interventions is limited.

Conclusion

Caregivers of cancer patients exhibit significant psychological and physical distress, which often go unaddressed. Emerging evidence suggests that informational and skill-based interventions, along with increased psychosocial support, may mitigate the burden of caregiving; however, much of this work is nascent and integrating evidence-based interventions for caregivers into the standard of
Celebrities and Cancer

Celebrities have long held the public's interest, be it with their dating lives, legal troubles, or health and well-being. They can be influential in the public's perception of illness, bringing humanity to a specific disease and raising awareness to new treatments and screening procedures. For the last 50 years, celebrities have been candid about their cancer diagnoses with the public, making it an accessible topic and broadening the larger discussion in society. With this openness, celebrities have worked to create important cancer awareness organizations that reach out to the public.

Important Celebrity Stories

One of the first celebrities to share her story about cancer was Shirley Temple Black, known best as the curly-haired, adorable child star. She came forward in 1972 with her breast cancer diagnosis and resulting mastectomy, something that had never been done before because it was a privately fought disease at the time and rarely spoken about in public. When Temple Black died in 2014, her public declaration, made early in the fight against breast cancer, was one of the most discussed parts of her life even though she had won accolades as an actor and had served as an ambassador for the United States.

Betty Ford became another important early public figure with breast cancer. Her announcement was made even more important because her diagnosis came while she was first lady of the United States in 1974. Then in 2000, Katie Couric, an anchor on the Today Show, underwent an on-air colonoscopy to raise awareness for life-saving cancer screenings. Couric's husband had died in 1998 of colon cancer, and her public action was done to demonstrate to the audience that colonoscopies were not painful procedures but rather simple, necessary screening techniques that could save lives. She created something known as the Couric Effect, whereby gastroenterologists saw an increase in patients having routine colonoscopies after her public appeal. The audience found the demonstration of the procedure compelling and were touched by her story about losing her husband to a form of cancer that is more easily treated if caught early.

Suzanne Somers, known for her role on Three's Company and as the spokesperson for health and fitness products like the Thighmaster, was diagnosed with breast cancer in 2001. She underwent some traditional treatments for her cancer but also chose to publicly discuss her refusal to have chemotherapy and her decision to use alternative medicine and healing practices. The public discussion that ensued from her decision was somewhat critical of Somers's advocacy against traditional medical treatments, which was seen
then discussed on the show that this is the kind of growth that, if left untreated, could turn into colon cancer, and that Oz's diagnosis showed the importance of regular colonoscopies. This kind of early polyp is not uncommonly found, and some in the medical establishment were concerned that Dr. Oz was making this sound like an emergency and could be creating unnecessary panic in audiences. In 2011, Dr. Oz did a follow-up colonoscopy for the television show to underscore the importance of continued contact with your physician and the necessity of following up on these medical crises. Both points of contact with audiences raised awareness for these simple screening procedures that can help detect cancer early in growth, much in the same way that the Couric Effect helped do so 10 years before.

The death of famous celebrities also brings awareness to cancers that have high mortality rates. When Patrick Swayze died in 2009 from pancreatic cancer, followed by Steve Jobs in 2011, people at home saw that having money can buy excellent treatment, but it cannot save you from a cancer that is not as easily detected. In 2013, another public discussion about breast cancer began when Angelina Jolie announced in the New York Times that she had undergone genetic breast cancer screening tests that lead to a double mastectomy. She had two close female family members who had died of breast or ovarian cancer and decided that that warranted some very expensive screening tests. After her announcement, physicians spent the next few days telling the public that most people were not within the parameters to warrant this kind of screening and that they should work with physicians to better understand individual health situations and family histories to know if this would be effective. The major test that Jolie underwent costs close to $3,000 without insurance, and doctors worried that the test might become some sort of status symbol to the public, unnecessarily overused out of panic or status enhancement.

The importance of early detection and treatment and of seeking multiple opinions for a cancer diagnosis were highlighted in the case of actress and producer Rita Wilson, who announced in April 2015 that she had been diagnosed with breast cancer (invasive lobular carcinoma) and had a bilateral mastectomy followed by reconstructive surgery. Wilson, who is married to actor Tom Hanks, issued a press release emphasizing the importance of early detection of cancer and the value of seeking a second medical opinion. In her case, she was aware that she
had lobular carcinoma in situ and had been monitoring the condition through annual mammograms and breast MRIs. However, after a friend suggested she get a second opinion, she was diagnosed with invasive cancer and underwent the mastectomy.

**Celebrity Organizations**

While there are many well-known health-focused organizations that involve celebrities, three in particular were created by celebrities, court major celebrity brand ambassadors, or allow the public to connect with celebrity causes.

In 1982, Nancy Brinker created the Susan G. Komen Foundation after her sister’s death from breast cancer. The Komen foundation is known for its Race for the Cure, held both regionally and nationally, which raises money for breast cancer and has also heavily participated widely in the breast cancer economy, which encourages purchasing products where proceeds go toward the treatment or awareness for breast cancer. Over the years, many celebrities have supported and highlighted the Komen foundation and its events.

The Avon Foundation for Women, created in 1992, supported cancer research funding and later added the Avon Walk for Breast Cancer. The Avon Foundation has given millions of women the opportunity to create community and raise money for cancer treatment. Avon has long courted celebrity ambassadors like Reese Witherspoon and does numerous events across the country every year that encourage women not only to sell their cosmetic products but also to support breast cancer awareness and treatments.

In 1996, Lance Armstrong discovered he had testicular cancer that had spread to several other places within his body. As a famous cyclist who had won the Tour de France multiple times, he was open with the public about his diagnosis. He founded the Livestrong Foundation for cancer research and funding and started a worldwide trend in 2004 by selling yellow plastic wristbands to raise money for his foundation. Many other types of cancer now have wristbands in different colors that serve as fund-raisers for not only large foundations and groups but also for family-run support groups and other disease fund-raisers. Further, the Livestrong Foundation now has a Web site that offers extensive general health information as well as a multitude of information about cancer and medical research.

In May 2008, nine women working in the entertainment industry, including Katie Couric, cofounded the organization Stand Up to Cancer, which funds cancer research differently than most other models: These producers and executives wanted an organization that connected high-profile celebrity personas with cancer fund-raising. Stand Up to Cancer mainly works through celebrity magazine advertisements and television fund-raising specials that include a telethon to raise money for cancer research. Featured celebrities speak about their experiences and their family members’ experiences with cancer, perform for the audience, and answer the phones for callers pledging funds. These funds are then directly given to promising researchers, cutting out the middlemen of traditional funding arms.

Supporting a charity or cause is practically a requirement for the celebrity persona. The Web site Look to the Stars: The World of Celebrity Giving promotes celebrity humanitarian and philanthropic work and allows celebrities to associate their names with specific organizations. The site exists to encourage visitors to support the causes of the celebrities whom they love, respect, and admire through financial contributions, donations of time, or attendance of events, many of which revolve around either types of cancer or rare diseases.

**Conclusion**

Many other celebrities not mentioned specifically here have fought cancer and spoken publicly about their experiences. Michael C. Hall and hockey player Mario Lemieux battled Hodgkin’s lymphoma; actor Robert De Niro and figure skater Scott Hamilton both underwent treatment for prostate cancer; Michael Douglas overcame throat cancer; talk show host and celebrity wife Sharon Osbourne fought colon, breast, and ovarian cancers; and film critic Roger Ebert finally succumbed to thyroid and salivary gland cancer after a very public struggle.

There is a seemingly unending list of celebrities in all avenues of fame that have done their best to shed light on their particular form of cancer, to bring awareness to their fight, to give fans a way to support them, and to raise funds for treatment. Audiences and fans pay attention to these stories, the current status of treatments, and their survival rates. The personal stories of celebrities are a major way that information is communicated about cancer and has proven to have an effect on audiences in participation, fund-raising, and awareness campaigns.

Jessica Bodoh-Creed

*California State University, Los Angeles*
Celgene (United States)

Celgene is a global biopharmaceutical corporation that focuses on the discovery, development, and marketing of drugs for cancer as well as immune and inflammatory diseases. Founded in 1986 by David Stirling and Sol Barer, Celgene operates worldwide with offices in the United States and Europe. Celgene’s subsidiaries and global partnerships with other pharmaceutical companies, medical institutions, and government agencies across six continents make it one of the largest biopharmaceutical corporations in the world. The company strives to be at the forefront of research and development of new treatments for cancer and inflammatory diseases and to provide all patients in need access to its therapies, regardless of their location or ability to pay for them.

Throughout its 30-year history, Celgene has been known for its pioneering research and development of drugs targeting various cancers. In the 1990s, Celgene began exploring uses for the drug thalidomide, despite its notoriety as the cause of birth defects in thousands of children born in Europe during the 1950s and 1960s. For more than a decade, Celgene developed and tested a derivative of thalidomide known as Revlimid for possible treatment of cancer. Revlimid was first given to human immunodeficiency virus (HIV) patients who had developed a type of cancer known as Kaposi’s sarcoma and subsequently to patients with multiple myeloma. After years of research and clinical trials, Revlimid received Food and Drug Administration (FDA) approval in 2006 as a second-line cancer therapy. Thalomid, another form of thalidomide, was also approved as a first-line therapy for multiple myeloma that same year. Other drugs developed by Celgene have included Focalin XR, used to treat attention deficit hyperactivity disorder (ADHD); Vidaza for acute myeloid leukemia; Abraxane for non–small cell lung cancer; and Otezla, the first oral therapy for active psoriatic arthritis.

In 2003, with its acquisition of Anthrogenesis, Inc., Celgene extended its research and development efforts to encompass stem cell therapy. Celgene Cellular Therapeutics (CCT), a subsidiary of Celgene, was formed to discover and develop new therapeutic uses for stem cells. Celgene’s work in this area has been part of a new field in medical research and treatment—regenerative medicine. Regenerative medicine aims to treat a variety of diseases through the use of stem cells and tissue to repair or replace damaged, defective, or dying cells and tissues in the body. Through the transplantation of stem cells harvested from human placenta, umbilical cords, and amniotic fluid, diseases such as cancer might be defeated at the cellular and molecular levels. Today, CCT is testing various types of stem cell therapies on autoimmune, vascular, and neurodegenerative diseases. To obtain the stem cells and tissue needed for its research, CCT established LifebankUSA, a biobanking business that collects, stores, and disseminates umbilical cord blood and placenta blood and tissue. CCT uses the materials from LifebankUSA in a variety of research projects, from cord blood transplants to treat blood diseases, to organ and tissue regeneration, to wound care products. An example of the last is Biovance, a dehydrated, topically applied wound covering, produced from human amniotic membrane taken from the placenta of a normal, full-term pregnancy. Biovance was created by the Organ and Tissue Therapeutics unit of CCT, which is dedicated to engineering biomaterials that could repair or replace tissue and even organs. Biovance is just one of many products that have the potential to revolutionize patient treatment and medicine itself.

In 2010, Celgene continued its global expansion by establishing the Celgene Institute for Translational...
Research Europe (CITRE) in Seville, Spain. CITRE was Celgene’s first dedicated research and development site outside the United States and was designed to foster collaborative research between Celgene and the European research community. CITRE is incorporated as Celgene Research St. Louis University (SLU) and is a Spanish company financed by private U.S. capital. CITRE’s 25 staff members are scientists drawn from Spain and other European countries, and the institute has formed partnerships with many European cancer research organizations, including university medical schools as well as European government agencies. CITRE also has its own accredited tissue biobank, which houses tissue samples collected from patients who have participated in multicenter Celgene clinical trials held across Europe under the direction of the CITRE Clinical Trials unit.

In addition to its work in developing new therapies for cancer and inflammatory diseases, Celgene also has been active in making a number of its proprietary drugs available to people in impoverished areas of the world who suffer from other deadly diseases such as visceral leishmaniasis (VL), malaria, hemorrhagic fevers, tuberculosis, and HIV. In 2009, Celgene Global Health (CGH) was founded. CGH partners with nongovernment organizations (NGOs), global academic institutions, product development companies, contract research organizations, and other pharmaceutical companies to determine whether their drugs might be effective against the aforementioned diseases. Laboratory facilities are set up, testing and clinical trials are run, and CGH supports the strengthening of health infrastructures in developing countries so that new treatments can be delivered to as many people in need as quickly as possible. One example of a successful collaboration is that between CGH and Advinus Therapeutics Ltd., a pharmaceutical company, to find and disseminate better treatments for those with VL. VL is a parasitic disease that affects 500,000 people annually, and current treatments are difficult to administer, toxic, and costly. Celgene is not only committed to pursuing more effective therapies for cancer in the developed world but also to helping those in the developing world who suffer from lesser-known and often neglected diseases that are just as deadly.

Over the past several decades, the fight against cancer and other diseases has become a global one, and Celgene has been at the forefront of that trend in its search for safer and more effective treatments for cancer as well as its commitment to enabling patients from all over the world and all walks of life obtain access to its therapies. In both developed and developing countries, Celgene has established itself as a pioneer in the discovery and development of new and better therapies for cancer and other deadly diseases.

Carin Halper
Independent Scholar

See Also: Clinical Trials; Drugs; Marketing, Drug; Leukemia, Acute Lymphoblastic, Childhood; Myeloma, Multiple; Pharmaceutical Industry; Technology, New Therapies.

Further Readings


Cell Phones

Given that cancer is a complex disease, often requiring skillful diagnosis and application of multiple treatment modalities, there are great opportunities for utilizing mobile phones in creative and innovative ways to benefit cancer care. Technological
progress and growing availability and use of cell phones have allowed for extensive and diversified health care applications and opened up new vistas for the use of mobile phones in cancer care. These more-advanced mobile devices are equipped with high-resolution cameras, Internet-based equipment, global positioning devices, and major computing capabilities.

Cancer Prevention and Detection
Consideration of cancer-related use of mobile phones reveals relatively few studies focusing on cancer prevention efforts. Nevertheless, the availability of high-resolution cameras has allowed for encouraging cancer screening applications. Such applications hold particular promise in low-income countries and at remote locations, where traditional screening techniques are not readily implemented. One such example of a successful application of mobile telemedicine has been reported for cervical cancer screening. Physicians and nurse midwives in the United States reported promising results for remote evaluation of cervical cancer among 95 human immunodeficiency virus (HIV)-positive women in the Botswana. Studies also introduced smartphone applications that offer detailed examination of skin cancers or reminders for checking on skin spots for users.

Cancer Treatment and Care, System-Based Prospects
It is well known that the treatment of cancer poses major challenges to care coordination and delivery. In a useful review of the role of information technology in promoting patient-centered cancer care, the authors offer a useful model of patient, provider, and system-relevant applications of information technology in cancer care. They point to the promise of electronic registries, a national cancer database, and electronic health records for actual delivery of cancer care. It is argued that the technology is currently available for integrated uses of Web technology in diagnosis, treatment decisions, and symptom management. Exemplifying the potential value of such systems, they discuss that an optimal information technology-enabled system could help providers and patients in handling side effects of cancer treatment.

A notable project, HealthDesign, specifically targets mobile phone users. Personal health records (PHRs) can collect data about patients’ health behaviors in their daily lives and help to make health care decision. For example, breast cancer patients participating in this project can use their mobile phones as tools for customizing care planning. Accordingly, patients could report symptoms and problems that they experienced by accessing an advanced or smartphone-based symptom reporting system. This system could transfer the data into the patient’s electronic health record, allowing the health care team to offer outreach to the patient by e-mail or telephone. They also advocate the value of computerized decision support at the point of cancer care.

Patient-Focused Prospects
Major uses of patient-focused interventions in cancer care include psychosocial interventions aimed to improve quality of life among cancer patients. This approach is exemplified in a successful intervention with early-stage breast cancer survivors and their partners. The intervention involved telephone health education and interpersonal counseling delivered in eight weekly one-to-one sessions. Patients and their partners used video-phones for communication. Patients who were within one year of cancer diagnosis and who were currently receiving treatment were included in this study. Findings indicated that survivors’ and partners’ psychological well-being improved in the telephone and videophone interpersonal and counseling treatment groups but not in the group receiving health education.

Potential benefits of mobile phones apply throughout the spectrum of cancer survivorship and can be particularly useful in enhancing doctor, patient, and caregiver communication. Success also has been reported in the use of mobile phones to create a more supportive home environment through use of telehealth in palliative cancer care.

General Health-Related Uses of Mobile Phones Applicable to Cancer Patients
As we consider the applicability of mobile phones in cancer care, it is useful to note that some of the relevant applications have not been studied in the specific context of cancer. Nevertheless, there is widely supported utility of mobile phone use in general self-care or management that is relevant to cancer care. General intervention
includes self-management of illness, health-promotion activities such as exercise, and patient empowerment.

The most widely studied mobile phone-based interventions relate to encouragement and monitoring of physical activity. Activity-related interventions involving mobile phones can help clinicians and researchers monitor factors such as walking speed and energy used during exercise. For example, mobile phones can monitor participants’ daily activities and encourage them to increase physical activity. Although interventions have not specifically targeted cancer patients, they offer encouragement to engage in physical activities that can benefit cancer patients. It is notable that the majority of participants in interventions were sedentary or overweight individuals. There was also some focus on specific diagnostic groups such as diabetics or patients with heart disease. However, conditions such as overweight and heart disease may be related to cancer.

Reflecting useful functions of activity monitoring, it has been argued that decline in daily activities after hospitalization could reflect medical complications that need to be attended to in order to avoid rehospitalization. Another salient use of smartphones relates to pain management interventions. Most applications offering pain management are not specifically tailored to cancer patients, even though pain is a frequent symptom experienced by this group. Pain-related applications generally offer information about pain management and in some cases suggest techniques, such as exercise or meditation, to counteract pain.

**Uses of Mobile Phones by Health Care Providers**

Physicians and other health care professionals, such as pharmacists, have even greater access to mobile phones than do patients. A number of studies have focused on utilization of mobile phones in the care provision and professional communication. In a study focusing on the use of smartphone apps by medical providers, the most commonly used apps by physicians included drug guides (79 percent), with a much smaller percentage (18 percent) using medical calculators.

Smartphone applications are also increasingly used by physicians for managing their medical practices. Although some of these applications relate to billing and other office procedures, uses of smartphones extend to transforming doctor–patient relationships. Specific patient-friendly examples include more convenient appointment scheduling and patient access to medical records. These advances would be particularly beneficial to cancer patients who often see multiple specialists. Patients also can benefit from mobile phone applications that assist them in finding appropriate specialists and providing them with global position system information about the proximity of the location of these doctors.

**New Directions**

Many of the promising applications of information technology, and specifically of mobile phone use, have not yet come to fruition. Nevertheless, developments are occurring at a rapid rate. There is likely to be extensive growth built on the modest examples that are currently being implemented in practice. Although we offer optimistic prospects, it is important to note that many of these examples we offered represent funded research projects and interventions and are not yet available on a broad scale to patients receiving cancer care.

A systematic review of smartphone applications for prevention, detection, and management of cancer offers some useful insights about parameters of current use. It is notable that the majority of these applications, 46.8 percent (N = 295), targeted breast cancer with an additional 26.4 percent offering applications relevant to cancer in general. The most frequent applications focused on efforts to raise awareness about cancer and provide educational information about cancer (58.6 percent). There was far more limited attention to early detection (11.5 percent) and disease management (3.7 percent).

Moreover, even as we introduce the topic of mobile phone use for health care applications, it is important to emphasize that the proliferation of this technology has not been accompanied by quality control. There is insufficient data reviewing existing applications by professionals to support use by the patients.

Further, it should be noted that the distributions of smartphone usage and basic cell phone usage are unequal among different income groups. High-income countries have a particularly strong penetration of smartphones, while in lower-income countries, cell phones are utilized mostly as basic text messaging systems. While the majority of the market focused on smartphone applications
for cancer care services, there is limited research on text messaging (SMS), multimedia messaging (MMS), and voice calling based on basic cell phones. Creative applications for basic cell phone users present useful prospects for cancer patients who cannot obtain smartphones.

Eva Kahana
Minzhi Ye
Case Western Reserve University

See Also: Breast Cancer; Skin Cancer, Melanoma; Stress.

Further Readings

Central African Republic

Deemed by the United Nations as a failed state in permanent crisis, the Central Africa Republic (CAR) has been described as one of, if not the, grimmest, most dangerous places on Earth. Health and humanitarian experts indicate the level of the health crisis in the CAR is catastrophic.

As one of the most impoverished and perilous places on earth, the former French colony has experienced intense economic, political, and ethno-religious instability, particularly since December 2012, when armed rebel groups advanced on the capital city of Bangui. The protracted crisis and violence in the CAR, which increased in 2013, following the overthrow of President Bozizé, have affected all 4.6 million people living in the nation. The United Nations has indicated risk of genocide is high, and politicized ethno-religious cleansing targeting Muslim and Christian communities is an immense concern. These incidents and concerns, coupled with the violent activities of fighters loyal to Joseph Kony's Lord's Resistance Army, have deeply affected the internal security and health care in the country.

The humanitarian needs have continued to escalate in CAR since December 2012. As reports are changing daily, it is difficult to provide definitive details of the devastation in all areas, including health care. Reports have indicated at least 42 percent of the nation's health facilities have been deeply damaged and 50 percent looted as a result of the crisis, resulting in a shortage of medical staff and about 68 percent shortage of medicines. The World Health Organization (WHO) reported the health care and medical system has completely collapsed. Essential services, including schools and medical facilities, have been abandoned, ransacked, shut down, or completely destroyed in the sectarian violence, leaving no medical help for those who have been subject to the injuries, sexual violence, and torture directly resulting from the violence.

In addition, the ongoing state of emergency, lack of safe drinking water, acute malnutrition, and poor sanitation and hygiene have increased the burden of a range of communicable, waterborne diseases including, but not limited to, cholera, hepatitis A, hepatitis E, shigellosis, diarrheal disease, and typhoid fever vector-borne diseases including, but not limited to, malaria, yellow fever, dengue, Chikungunya; and sexually transmitted infections (STIs) including human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS); and particularly due to population displacement and the overcrowding in resettlement camps, diseases associated with displacement and crowding, including vaccine-preventable disease such as acute respiratory infection, measles, diphtheria, pertussis, meningococcal disease, tuberculosis, and polio.

With the burden on the health system and facilities in the country (only approximately 46 percent of people have access to health services in the CAR), priority is given to provision of primary and secondary health services, improving government infrastructure and capacity, and increasing the capacities of communities to prevent or control
diseases and promote health. Thus, in the short
term, the Health Cluster of the humanitarian com-
community of which the WHO is the leader, is focused
on helping achieve these health priorities, including
improving the management of noncommunicable
diseases such as cancer.

Prior to the protracted crisis, the WHO esti-
mated that 27 percent of all deaths in the CAR were
due to noncommunicable diseases, most notably
cardiovascular diseases, diabetes, chronic respira-
tory disease, and cancer. The nation’s Ministry of
Health had no policy, program, or plan to address
noncommunicable diseases.

The latest estimations prior to the crisis reported
that there were 92.86 per 100,000 cancer cases in
the CAR and an estimated 2,774 cancer cases per
year. Deaths resulting from cancer were estimated
at 74.25 per 100,000 or 2,171 total deaths per year.
The common types of cancer in the CAR are breast
(18.2 percent), cervical (11.2 percent), prostate
(9.7 percent), non-Hodgkin's lymphoma (7.3 percent),
liver (6.4 percent), bowel (4.6 percent), leukemia
(3.4 percent), ovarian (2.8 percent), Kaposi's sarcoma
(2.4 percent), lip (2.3 percent), esophagus (2.2 percent),
and stomach (2.2 percent), among others. Cervical
cancer is the second-most common cancer among
women in the CAR. About 311 diagnoses of cervical
cancer are made each year, resulting in 223 deaths.
The high incidence of cervical cancer in the country
is due to the prevalence of the human papillomavirus
(HPV), which is known to cause the cancer. Cancer
accounts for about 83.1 percent per 100,000 non-
communicable disease deaths in men and about
75.6 percent in women in the CAR, representing a
total of 121 per 100,000 adult deaths per year.

Diabetes, hypertension, obesity, smoking, alco-
hol, and use of solid fuels including coal and char-
ocol are some of the noted risk factors for cancer
mortality and morbidity in Africa generally and the
CAR specifically. The CAR currently has no national,
population-based cancer registry and no integrated
policy or action plan for cancer. Early diagnosis of
cancer is key to treatment and survival. However, in
the CAR due to scarcity of medical equipment and
medical technicians, most cancers are diagnosed
late or underdiagnosed, which inhibits treatments.

See Also: Angola; Cameroon; Chad; Congo,
Democratic Republic of; Developing Countries;
Disparities Within Nations (Elimination of Cancer);
Global Health Issues and Cancer; Guinea; International
Agency for Research on Cancer; World Health
Organization.

Further Readings
Africa Research Bulletin. “Central African Republic:
Humanitarian Crisis.” Africa Research Bulletin:
Economic, Financial & Technical Series, v.51/2
(2014).
Duprez, Renan, et al. “Human Herpesvirus 8 Serological
Markers and Viral Load in Patients with AIDS-
Associated Kaposi's Sarcoma in Central African
Republic.” Journal of Clinical Microbiology, v.43/9
(2005).
Green, Andrew. “Aid Groups Warn of 'Catastrophic'
Institut Català d’Oncologia. Central African Republic:
Human Papillomavirus and Related Cancers,
Fact Sheet 2013. Barcelona, Spain: Institut Català
d’Oncologia, L’Hospitalet de Llobregat, 2014.
O’Shaughnessy, Patrice. "A Nursing Career Built on
Sankaranarayanan, Rengaswamy, et al. “Cancer Survival
in Africa, Asia, and Central America: A Population-
World Health Organization (WHO). Public Health
Risk Assessment and Interventions—Conflict and
Humanitarian Crisis in Central African Republic.
World Health Organization (WHO) Regional Offi  ce for
Africa. Prevention of Cervical Cancer. République
Centrafricaine Publications. Brazzaville, Republic of

Central Nervous System Lymphoma, Primary

Primary central nervous system (CNS) lymphoma
is considered a type of non-Hodgkin's lymphoma.
Non-Hodgkin's is a term that applies to malignant
cancer that affects the lymph nodes. Lymph
nodes, or the lymph system, make up the body's
autoimmune response to infections. White blood cells that are carried in the lymph tissue both help to fight and prevent infections. When lymph tissue is compromised, it becomes difficult for people to fight infections or withstand chemotherapy treatment, which also weakens the immune system.

CNS lymphoma is a rare type of malignant cancer that affects the lymph nodes or lymphatic systems. CNS lymphoma can start in either the brain, spinal cord, meninges, or even the eye. Secondary CNS lymphoma is also rare and refers to cancer of the CNS that has spread from other parts of the body to the brain or the spinal cord.

Diagnosis of CNS lymphoma is particularly difficult as there is no standard method currently in practice. Presurgical diagnosis can be determined through brain scans and imaging software. If the tumors are operable, tissue biopsies are also a viable method of diagnosis. Last, the analysis of cerebrospinal fluid (CSF) can determine whether or not there is a presence of malignant cells. While the causes of this type of cancer is largely unknown, some occurrences have been linked to those who already have compromised immune systems, like those with acquired immune deficiency syndrome (AIDS) or other autoimmune deficiencies or diseases.

Symptoms of CNS lymphoma include fever, headaches, seizure, paralysis, numbness, weight loss, and loss of appetite. Patients may not necessarily experience all of these systems, and they may experience different symptoms as well.

There are various treatments that are available for CNS lymphoma, but treatment options and prognosis generally depend on the stage of the cancer as well as the age and state of health of the person with the disease.

Treatment options include chemotherapy, radiation, steroids, and some clinical trials. The success of these treatment options is different for everyone and is also dependent on age, health, cancer stage, and severity. Surgical removal is also a method of treatment; however, in the majority of cases, the lesions are inoperable due to size and placement.

Aggressive chemotherapy paired with stem-cell transplants has proven to be an effective form of treatment according to recent cancer studies. Patients who respond best to this treatment option typically are not seriously immunocompromised.

Methotrexate (MTX) and cytarabine (AraC) were found to be the most effective chemotherapy treatment options for patients suffering from primary CNS lymphoma. Radiation of the entire brain has also proven to be viable, along with stem-cell transplantation.

These treatment options, however, are the most effective for those patients in the early and less-aggressive stages of CNS lymphoma. The patients who responded best had undergone high doses of either MTX or AraC followed by stem-cell transplantation therapy or radiation treatment followed by high doses of MTX. In general, people who were given radiation or chemotherapy alone did not respond as well as those who received dual treatments. Response to treatment was generally better with the MTX than with the AraC; however, AraC remains a viable treatment option especially if combined with MTX. As with most high-dose chemotherapy treatments, response to treatment is generally better in younger adults with immune systems that are less compromised.

Steroid treatment is also used in conjunction with chemotherapy and other treatments; however, steroid treatment is not a long-term solution, and it is used to shrink tumors and masses in the brain. Steroids can improve neurological functions that may be affected by the stress or pressure caused by the tumor. Steroid treatment can be used during chemotherapy and radiation; however, most oncologists stop the use of steroids in order to gain more accurate diagnosis and to avoid the possibility of weakening the immune system further as steroids can have immunosuppressant effects.

Individuals with acquired immune deficiency syndrome (AIDS) make up a significant percentage of those who develop primary CNS lymphoma. While CNS lymphoma is still a fairly rare disease, reported incidents have increased since the 1980s, with the onset of the AIDS pandemic. The prognosis for patients with AIDS is generally poorer than those who have human immunodeficiency virus (HIV) alone. Studies focusing on the connections between CNS lymphoma and the AIDS virus have been linked to another virus called Epstein-Barr (EBV). EBV is a herpes-like virus that was found in CSF from patients with both AIDS and CNS lymphoma. While it is clear that there is some kind of connection between these viruses, further studies hope to find information that is more concrete.

Overall, patients that respond well to treatment for CNS lymphoma do not experience prolonged
periods of remission, especially if they are already immunocompromised. Doctors struggle to discover new methods of treatment largely because there is trouble crossing the blood–brain barrier. The term blood–brain barrier refers to the layer of blood circulating between the cerebral fluid and the CNS. Research, while progressive, still remains particularly difficult due to the rarity of the disease as well as the inability to conduct a greater scale of clinical trials.

Haylee Massaro
Independent Scholar

See Also: Chemotherapy; Lymphoma, Hodgkin’s, Adult; Lymphoma, Non-Hodgkin’s, Adult; Radiation Therapy.

Further Readings

Cervical Cancer

Cervical cancer develops in the cells of the female cervix, the organ connecting the vagina to the lower uterus. Globally, it is the second-most common cancer in women, resulting in more than 500,000 new diagnoses and 270,000 deaths each year. In the United States alone, there are more than 12,000 new cases and 4,000 deaths from cervical cancer annually. Mortality rates are much lower in the United States and other developed countries than in less-developed parts of the world. Much of this disparity results from high rates of routine gynecologic health care in high-income nations that leads to detection and treatment of precancerous lesions and early-stage cervical cancer. Although mortality rates have significantly declined over the past 30 years, major public health organizations, such as the World Health Organization, continue to consider cervical cancer to be a serious health threat to women.

Cervical Cancer and the Human Papillomavirus

The development of cervical cancer and precancerous lesions is almost exclusively linked to the human papillomavirus (HPV) as a predecessor to the disease. The virus infects cells on the outermost layers of the skin and mucous membranes, making the infection easily transmittable through skin-to-skin contact. As a result, the infection is commonly spread through sexual contact. Globally, HPV is the most commonly transmitted sexual infection, with a lifetime risk of infection as high as 75 percent for most individuals. HPV is also the most common sexually transmitted infection in the United States, with more than 14 million new infections among Americans each year. There are more than 120 identified strains of HPV, 13 of which have been conclusively linked to cervical cancer. Of these cancerous strains, two types (strains 16 and 18) are responsible for causing 70 percent of cervical cancers.

Because it is an infection, the body’s immune system responds to the introduction of HPV. Most infections self-resolve within several years of infection. However, infections that persist or recur are more likely to develop into cervical cancer. In females with healthy immune systems, it can take 10 to 20 years for a chronic HPV infection to develop into cervical cancer. In women with compromised immunity, such as human immunodeficiency virus (HIV)-positive individuals, this development may occur in as little as five to 10 years. While cervical cancer is often symptomless in early stages, symptoms of
advanced-stage cancer may include irregular menstruation, weight loss, fatigue, back or pelvic pains, vaginal discharge, or swelling in one leg.

Related Risk Factors
Additional risk factors such as tobacco use, diet, obesity, and genetic predisposition have been identified as possible mediators of cervical cancer. In other words, these factors may increase the risk of cervical cancer for individuals with HPV infections. For example, it is possible that smoking increases risk of cervical cancer by suppressing the immune system, allowing a high-risk HPV infection to persist and advance into cancer.

Screening and Detection
For years, gynecological screening (most often with the Pap test) has served as the primary mechanism through which HPV-associated lesions and other precancerous symptoms are identified and subsequently treated. However, screening for HPV only works to identify the presence of the HPV virus and the development of abnormal cervical cells but cannot determine whether such cells are likely to clear up or persist and develop into cancer. Ultimately, screening can help detect the virus but cannot prevent HPV infections from developing in the first place. A major concern is that, often, HPV infections are symptomless and may not be identified in the absence of routine screening practices. When regular screening is not available, cervical cancer may go undetected for years, until symptoms appear during advanced stages of the disease. Therefore, health advocates are increasingly pushing for a combined approach consisting of prevention, screening, and treatment together in order to combat HPV as an individual and public health issue. In particular, over the past decade, substantial interest in has grown in the use of vaccines as an HPV prevention strategy. Early results suggest that this strategy may prove to be an effective course of action in preventing HPV infection and, subsequently, reducing the incidence of cervical cancer.

Prevention Through Vaccination
Two HPV vaccines are currently available: Cervarix (produced by GlaxoSmithKline) and Gardasil (produced by Merck & Co.). In 2006, the United States Food and Drug Administration (FDA) approved the first HPV vaccine, Gardasil, for females age nine to 26. In 2009, the FDA approved Cervarix for females 10 to 25. Although the two vaccines share many similarities, they have several key distinctions. Cervarix has been approved for use in women starting at age 10 and immunizes patients against HPV types 16 and 18, the two strains most commonly associated with a variety of HPV-related cancers. Gardasil is the more commonly employed of the two vaccines and is currently approved for use starting at age nine. Gardasil is a quadrivalent vaccine as it immunizes against four common HPV types (6, 11, 16, and 18). The vaccine is given in three doses over the course of six months. Overall, HPV vaccination holds the strongest potential to reduce incidence of cervical cancer when administered to girls and young women prior to sexual debut.

In addition to increasing initial vaccination uptake, public health officials are also concerned with how to encourage females to complete the vaccination series once the first shot has been received as individuals often fail to receive subsequent doses.
Given what is currently known about the vaccine, the endorsement the vaccine has received from the medical community and federal health agencies, and the prevalence and severity of HPV-related health outcomes, the HPV vaccine offers an effective first step toward significantly reducing this public health concern. The introduction of the HPV vaccine has been called an important public health achievement. In particular, the vaccination provides the potential for widespread cervical cancer prevention in populations without routine access to female health screening. However, current vaccination rates are far below recommended targets for adolescents and young adults. As a result, public health officials continue to emphasize a comprehensive prevention and detection approach to reduce the impact of cervical cancer.

Melinda Krakow
Jakob Daniel Jensen
University of Utah

See Also: Screening; Vaccines; Women’s Cancers.

Further Readings

Chad

The Republic of Chad is a landlocked country in the middle of Central Africa. It is surrounded by Sudan, Libya, Cameroon, Nigeria, Niger, and the Central African Republic. Chad’s climate is composed of desert and savannah regions, and Lake Chad is the country’s largest wetland and the second largest on the continent.

As in the other countries of Africa, the major types of cancer in Chad are related to infectious agents. These include cancers of the urinary bladder, the Kaposi’s sarcoma, the liver, and the cervix. In addition, in 2008, cervical cancer made up 21 percent of the newly diagnosed cancers in African females, while liver cancer was the leading type of cancer for African males, at 11 percent. Though cancers related to dietary patterns, obesity, and tobacco use are most prominent in America, these cancers are becoming more common in developing countries, such as Chad, as well.

In 2012, according to Treat the Pain, more than 4,700 people died of cancer in Chad, with 80 percent of these individuals reporting they were facing moderate to severe pain before they expired.

In comparison, overall in Africa, 715,000 new cancer cases and 542,000 cancer deaths occurred in the year 2008. These numbers are projected to nearly double (1.28 million new cancer cases and 970,000 cancer deaths) by the year 2030 because of the aging population and unhealthy lifestyle factors.

Prostate Cancer

Another large cancer concern in Chad (and across the world) is prostate cancer. According to the GLOBOCAN 2002 database, 416 new cases of prostate cancer will be discovered in Chad each year, with deaths amounting to more than 350 annually. Many more men have prostate cancer and do not know about it. Men are typically diagnosed with prostate cancer between the ages of 50 and 65, and those who have a family member with the disease are at a higher risk.

A regular physical examination and a prostate specific antigen (PSA) blood test are necessary for early diagnosis of prostate cancer. Men should start prostate checkups starting around age 40.

Cervical Cancer

Chad has a population of 3.33 million women age 15 and older. These women are at risk of developing cervical cancer, and current estimates indicate that about 630 women each year are diagnosed with the disease, with about 464 deaths from the same each year.

According to the HPV Center, cervical cancer is the second-most common cancer among women in Chad between women age 15 and 44. Data is not currently available on the human papillomavirus
(HPV) burden in the general population of Chad. However, in Africa in general, about 25 percent of women in the general population are estimated to carry the HPV infection. And 71.3 percent of invasive cervical cancers come from HPV infection types 18 and 16. If prostate cancer is diagnosed and treated early, the mortality risk is small. If prostate cancer is diagnosed late and has spread to other portions of the body, then it is incurable.

**Cancer Care and Prevention**

Across Africa, cancer continues to receive low public health priority despite the fact that it is increasing in prominence across Chad and many other countries. This is predominately due to larger public health issues, such as acquired immune deficiency syndrome (AIDS) and human immunodeficiency virus (HIV) infections, along with tuberculosis and malaria. Other issues may include a lack of awareness of the current and future burden of cancer among the general public, international health agencies and policy makers. Additional effort should be given to raise cancer awareness and promote early detection and prevention in Chad and other African countries.

Most of the cancer incidences in Chad are diagnosed at an advanced stage. In addition to the factors listed, this also may be due to the stigma associated with a cancer diagnosis. Survival after a diagnosis is much lower throughout Africa than it is in the developed world, especially for cancer types that are greatly affected by improved treatment and screening. African patients also have limited access to quality treatment in a timely manner.

As an example, the five-year survival rate for breast cancer is less than 50 percent throughout several African countries, compared to nearly 90 percent in the United States.

Prevention of exposure to cancer-causing agents and risk factors (such as tobacco use, infections, and obesity) is extremely important across Chad and is the most cost-effective solution. Tobacco use, in particular, is extremely preventable. Tobacco-related cancers account for about 6 percent of cancer deaths throughout Africa.

Currently, about 10 percent of African men and 20 percent of African women smoke, which does not initially raise alarm. However, cigarette consumption in Africa is rapidly increasing due to the adoption of new social behaviors and increased marketing from tobacco companies. Smoking among teens is much higher, with smoking prevalence among boys being higher than adults in many African countries.

Obesity awareness is also a top concern. Along with physical inactivity and an unhealthy diet, obesity has been associated with the increased risk of several cancers, including uterine corpus, liver, stomach, colorectal, breast, and kidney cancers. The prevalence of obesity and physical inactivity is increasing in several African countries, especially in urban areas, as a result of increased consumption of calorie-dense food and lower energy expenditures in daily life.

**Conclusion**

There are many risk factors influencing cancer incidences and mortality rates in the Republic of Chad. Unfortunately, because Chad is a developing country, there are limited resources available for those with cancer, and many hospitals are inaccessible to the general population.

Late diagnosis is also an issue, as this often leads to elevated mortality rates. It is extremely important that Chad, along with other African countries, invests in cancer education for its residents. The medical community in Chad must also recognize the fact that cancer is a large health burden for the country; it cannot always be outweighed by communicable diseases such as HIV and AIDS. Prostate cancer and cervical cancer in particular must have educational and preventative programs surrounding them—preferably sponsored by the country’s national health institutions as this is the only way that Chadians will not face an elevated risk of these and other cancers for years to come.

Katie Moss
Independent Scholar

**See Also:** Cervical Cancer; Developing Countries; Prostate Cancer.

**Further Readings**

American Cancer Society. “Cancer in Africa.”

ICO Information Centre on HPV and Cancer. “Human Papillomavirus and Related Cancers, Fact Sheet 2013.”
The Chao Family Comprehensive Cancer Center

In the United States, cancer is the second-most common cause of death. In 2014, approximately 1,665,540 new cancer cases are expected to be diagnosed. Of those cases, 585,720 Americans are expected to die, almost 1,600 people per day. In order to fight and understand this disease, the National Cancer Institute (NCI) designates and partners with comprehensive care centers in order to adequately treat and advance the treatment of many different types of cancer. One of these esteemed centers is the Chao Family Comprehensive Cancer Center (CFCCC) at the University of California, Irvine (UCI) which is located in Irvine, California. Here, the CFCCC translates leading-edge scientific findings into clinical cancer treatment and prevention of cancer on all levels.

The Chao Family Comprehensive Cancer Center

The UCI Cancer Center was established in 1989 as a university-based cancer center. In 1994, it was designated for excellence by the NCI. The center achieved comprehensive cancer center status in 1997, making it one of only 41 in the nation. It was later renamed in honor of the Chao family and is now recognized for excellence in cancer treatment, prevention, research, education, and awareness. The CFCCC is affiliated with the UC Irvine Health School of Medicine and the university’s schools of basic sciences.

Located in the UC Irvine Medical Center, the CFCCC integrates research, prevention, and the most advanced diagnostics, treatment, and rehabilitation programs and technologies to provide the best possible care for patients and their families. World-class multidisciplinary teams of UC Irvine Health surgeons, radiation oncologists, medical oncologists, pathologists, nurses, rehabilitation therapists, pharmacists, social workers, and dietitians treat every kind of cancer, including rare and aggressive forms. New patients are offered the best in beginning care, including a comprehensive clinical evaluation with a wide range of diagnostic technologies.

The CFCCC provides the most advanced diagnostic and treatment technologies, including Arc radiotherapy, a groundbreaking method of delivering powerful, targeted radiation faster and more precisely than with conventional radiotherapy. This therapy advances the standard of care with uncompromised treatment in killing or slowing the growth of cancer cells in two minutes or less. Arc plans were found to be equivalent or better at target coverage for all targets and superior in protecting critical structures including the spinal cord, brain stem, eyes, optic nerve and chiasm, parotid glands, and brain.

The center is funded by the NCI, the National Institute of Health, and other public agencies, in addition to a variety of private sources. The CFCCC also offers eight shared resource facilities to help foster innovative educational clinical and epidemiologic research on the causes, treatments, and effects of cancer and allied diseases. These resources include Biobehavioral Shared Resource Facility, Biostatistics Shared Resource, Experimental Tissue Shared Resource Facility, Genomics High-Throughput Facility, In-Vivo Functional Onco-Imaging, Optical Biology Core, Transgenic Mouse Facility, and the collaboration with the Children’s Hospital of Orange County, where an overwhelming amount of children (85 percent) are enrolled in clinical trials at the CFCCC.

Research and Outreach

The CFCCC is at the forefront of research. At any given time, there are approximately 80 to 100 research trials open on the different types of cancer treated at the CFCCC. The purposes of these trials include treatment, prevention, screening, diagnostics, quality of life, and supportive care. Currently, there are 102 open trials with research focusing on cancers such as
as melanoma, liver, colon, pancreatic, prostate, brain and nervous system, and eye and orbit; however, the most predominant type of cancer being researched in the open trials is breast cancer in females.

Though the CFCCC treats all kinds of cancer, the NCI and its designated comprehensive care centers have made translational research a major focus, meaning the transformation of scientific discoveries made in laboratory, clinical, or population-based research into clinical applications that can reduce the cancer burden. At CFCCC, their translational research efforts are focused on four areas of strength: skin, prostate, colon, and women’s cancers. These teams have led to advancements in cancer surveillance, screening and prevention, diagnostics, therapeutics, survivorship and quality of life, and global benchmarks of success.

The CFCCC is also involved in conducting non-traditional research in its effort to find new, effective ways to treat and cure cancer. Notably, the CFCCC’s infusion center has implemented a music therapy program to treat pain, anxiety, and nausea in patients undergoing chemotherapy. The benefits of this program have shown to lessen the proposed treatments, including depression. Funded research is focused on conducting innovative studies such as finding the best time of day to receive radiation treatment to reduce hair loss, stem cell research to advance basic studies to improve cancer, and brain disease treatments. There is also a study measuring kava, a plant grown in the South Pacific, and its ability to cure cancer. The efforts of UC Irvine, CFCCC’s affiliate, have also resulted in advancements in treatments, specifically funding the development and creation of an ovarian cancer app for tablet computers. This advanced approach to treatment will help newly diagnosed ovarian cancer patients learn about and understand the trade-offs among chemotherapy options.

The CFCCC is also involved in national and international outreach that extends to several countries in the Middle East, Russia, Korea, Japan, and China through sponsorship by the NCI. Through the establishment of consortiums, the CFCCC can work to reduce the incidence and impact of cancer through solicitation and support of collaborative research.

The prevention and treatment of cancer heavily overlaps with the need for advancements in research. As the second-leading cause of death, cancer is a disease that requires time and dedication to find a cure. Through the collaboration of the NCI and designated comprehensive cancer centers like the CFCCC, cutting-edge research can help save lives. By focusing on treatment, prevention, research, education, and awareness, the CFCCC and its partners are able to offer the most-advanced diagnostic and treatment technologies and non-traditional, groundbreaking research as possible cures and preventions for all types of cancer.

Narketta Sparkman
Hope Comer
Old Dominion University

See Also: Chemoprevention; National Cancer Institute; University of Southern California/Norris Comprehensive Cancer Center; University of Wisconsin Carbone Cancer Center.

Further Readings

Chemical Industry

The chemical industry is a key source of toxic exposure to carcinogens for both employees and for people living in nearby neighborhoods. Increasingly, researchers are discovering that the burden of environmental toxin-associated cancers has been greatly underestimated. Due to the
large number of variables and the typically long lag time between exposure and diagnosis, cancer epidemiology is exceedingly difficult. The patient may not show any symptoms of cancer for 20 to 30 years from the time of exposure. Physicians may not know there was an occupational exposure and thus do not make the cause-and-effect connection; the connection goes unreported to cancer epidemiologists. Cancers may be diagnosed years after exposure. Due to a highly mobile population, patients may no longer reside in the area in which they were exposed.

One study found that between 4 and 6 percent of cancer deaths in the United States (about 34,000 people annually) are caused by occupational exposure to carcinogenic compounds. A large proportion of these occupational-related cancers is likely preventable. The rate of workplace-associated cancers has declined, however, with the implementation of greater employee safety controls and governmental regulation of industry practices.

Much of the knowledge about toxic effects levels of industrial compounds comes from research into cancer incidence and prevalence among these populations. Occupational studies are better able to quantify exposures than ambient studies because exposures are often known. Researchers can pinpoint exactly what compounds the worker was exposed to and in what dosage. Chemical exposures in the workplace are typically both prolonged and high dose. They may be either discrete events or long term.

Population-based case-control studies of current and former chemical-manufacturing employees have found increased levels of cancers in these groups. Oftentimes, cancer risks from specific chemicals are identified first among industrial workers. For example, occupational exposure to benzene, a known carcinogen, has been found to put workers at a two- to threefold increase of risk for acute myeloid leukemia and acute nonlymphocytic leukemia relative to the general population. Occupational factors seem to play a significant role in the incidence of bladder cancer, and workers exposed to asbestos are at significant risk of lung cancer. One study found that women employed in the plastics industry were at significant risk for endocrine disruption leading to breast or reproductive cancers. There is strong evidence to support claims that industrial chemicals, for example, inorganic acid mists, benzene, 1,3-butadiene, and formaldehyde, elevate risks for the development of a variety of cancers in exposed populations.

The chemical industry today produces an estimated 70,000 products in nine major areas: petrochemicals; synthetic organic chemicals; inorganic chemicals; resins and synthetic rubber; pesticides, fertilizers, and other agricultural chemicals; pharmaceuticals; paints, coatings, and adhesives; cleaning compounds; and other products, including inks, explosives, and photographic chemicals. Safety data on all of these compounds are not always available or even known. Oftentimes, the science to support safety simply has been done, and as more compounds are developed, the science is unable to keep pace with industry.

Determination of whether or not a particular substance is carcinogenic is time-consuming and often politically contentious. Controversies surrounding some compounds last decades or more without resolve, and the standards of proof have become increasingly difficult to meet. Early toxicological research quantified the levels of toxins at which a person would be expected to die. When animals survived toxicology studies, the compounds were considered safe. If the animals developed cancer, the compound was considered to be carcinogenic. This is no longer the standard for this type of research.

There are increasingly calls for human studies, the rational being that, as humans and animals have differing physiologies, a compound that might be carcinogenic in animals may have no effect on humans or vice versa. A human is not a rat; different compounds have different effects in different species. As it would not be ethical to expose humans to compounds to determine if they are carcinogenic, most human studies involve large-dose exposure accidents of employees in industrial settings. Most compounds known to be carcinogenic were identified in this manner.

Certain occupations in themselves have been identified by the International Agency for Research on Cancer as carcinogenic due to the high incidence of cancers in people employed in these settings. These include employees in aluminum production, auramine manufacturing, coal gasification and indoor coal emissions, coal-tar distillation, coke production, underground hematite mining, iron and steel founding, isopropyl alcohol
manufacturing, magenta manufacturing, painters, and those in the rubber manufacturing industry.

**Determining Levels of Toxicity**

Regulatory agencies, such as the Environmental Protection Agency and state-level environmental agencies in the United States, delimit both short- and long-term health effects for exposure to many different compounds. Short-term limits delineate at what dosage acute, high-dose exposures cause health effects. These are typically averaged over an hour. Long-term limits delineate thresholds at which health effects from low-dose, chronic exposure are expected. These typically are averaged over one year. It should be noted that the specification of the limits are often politically contested and that these levels can vary widely from agency to agency. These levels are informed by research on workplace exposures, occupational health research, and research into industrial accidents, as well as industry data.

Employees experience chronic exposure to known compounds as well as occasional acute events (such as in the case of a spill or leak). This known quantitative aspect allows researchers to more clearly identify cause-and-effect variables along with exposure safety limits relative to research into ambient chemical effects. As with any cancer research, cause and effect can be difficult to determine due to the significant lag between exposure and diagnosis. This lag can impact worker health negatively, delay the recognition of problematic practices, delay the implementation of safety controls, and impede worker compensation. The more prolonged the time effect, the more difficult it is to demonstrate clear cause-and-effect relationships.

Such research has also allowed for intragroup analysis. For instance, many research studies have pointed to excess breast cancers in women employees exposed to chemicals in manufacturing (such as in the plastics industry). There also may be disproportionate exposure among lower-wage workers in more dangerous positions within the factory.

**Employee Safety**

Numerous bio-monitoring studies of employees working in the chemical industry have found elevated chemical burdens and associated health impacts relative to the general population. Contaminants are released during the normal course of production. Workers are exposed to chemical compounds via inhalation of gases, vapors, and dust, as well as through direct physical contact with toxic substances. Exposure is related to the assigned tasks of the worker as well as the levels of safety measures taken by the company. Occupational chemical exposures are more likely to be both higher dose and prolonged than ambient exposures.

Exposed workers can be at much greater risk for cancer than others in the general population. Thus, while the population at large might benefit from the product itself, they do so at the expense of the workers’ health. These types of disproportionate exposures bring up issues of environmental justice and equity.

Workers in the chemical industry are subject to multiple chemical exposures—rarely are they exposed to only one compound at a time, and the synergistic effect of those compounds is typically unknown. They may have an additional burden if they reside in the vicinity of a polluting plant or if they have significant chemical exposures outside of the workplace (including tobacco related). Working conditions of course vary by location and are influenced largely by factors such as the physical layout of the plant, the availability and training in the use of personal protective safety equipment (such as protective clothing, respirators, and other gear), monitoring of employee health, environmental protection controls, ventilation, and regulatory powers.

Research has demonstrated significant reduction in workplace exposures via safety controls and regulatory oversight. Even with safety measures intact, however, breaches in safety protocols, improper use of equipment, and faulty or inadequate equipment can all lead to workplace exposures. In addition, industrial accidents are always possible as well as the possibility of unrecognized hazards in the work environment.

**Regulation**

Researchers have repeatedly demonstrated decreases in risk with improved safety measures, lending credence to regulatory intervention. As regulatory systems vary by jurisdiction, worker safety controls are haphazard, with significant differences in worker protections globally. Some researchers argue that globalization and free-trade
agreements have severely hindered the implementation of worker safety measures and that chemical manufacturing plants are more likely to be physically placed in areas with fewer restrictions as a cost-saving measure for the parent corporation. Industry representatives counter that such protections are both costly and oftentimes overprotective and that some measures are so extreme that their plants would be unable to implement them and be forced to close. Criticisms of industry practice go beyond worker safety to alleged involvement in regulatory lobbying and active suppression of scientific research.

Poor working conditions, lax enforcement of safety measures, and inadequate safety controls all result in an increased toxic burden for both the employees and the residents in surrounding neighborhoods.

**Sacrifice Zones**
Residential areas neighboring polluting industry are often referred to as sacrifice zones. Generally speaking, these neighborhoods are comprised of poor or racial ethnic-minority residents with low levels of social capital. As in the case of employee exposures, questions about environmental justice and equity are raised for residents of sacrifice zones. Researchers have repeatedly demonstrated increased cancer risks for people living in close proximity to chemical plants and other industrial activity. This risk is compounded with the potential for industrial accidents, such as leaks and explosions.

Examples of this type of exposure include pesticide use in heavy agriculture, industrial waste and by-products, air and water pollution from refining and other industrial factories, exposure to particulate matter, along with many others.

Jessica Smartt Gullion  
*Texas Woman’s University*

**See Also:** Electrical Industry; Glass Industry; Nuclear Industry; Paper Industry.

**Further Readings**

---

**Chemoprevention**

Cancer is a disease in which anomalous cells are created, attack vigorous tissue, and grow overpoweringly. The progression from a normal and healthy cell to a cancerous cell takes numerous years. Cancer may be predisposed by genetic, dietary, and behavioral factors. Cancer chemoprevention is the use of natural, synthetic, or biologic substances to repeal, subjugate, or prevent the expansion of cancer. Synthetic substances are made in a laboratory.
Biologic substances are from a living source. Individuals who have a genetic predisposition risk of acquiring cancer, encompassing those with a previous diagnosis of cancer, an inherited cancer syndrome, or a family history of cancer, typically use chemoprevention. Chemopreventive agents, unaccompanied or combined, can help prevent the development of cancerous cells or delay the development. Chemoprevention is not used to treat existing cancer but may be used in persons whose cancer is in remission in order to decrease the possibility of acquiring new cancers. Chemoprevention is the attempt to prevent cancer from developing by using substances that interfere in the process of carcinogenesis by utilizing natural (biologic) or laboratory-made (synthetic) substances to prevent cancer.

It should be recognized that chemoprevention is a contrast of chemotherapy. Chemoprevention is utilized well in advance of cancer developing to avert cancer or to inhibit precancer in vulnerable individuals, conceivably. In contrast, chemotherapy attempts to execute already infected cancerous cells. As explained, chemoprevention utilizes organic inventions originating from foods or synthetic products created in scientific labs. Due to the long-term usage of chemoprevention, it is imperative for the agents to be nonpoisonous, effectual, administer friendly, and affordable. Subsequently, there are a limited amount of agents recommended for extensive clinical use as lengthy clinical trials lasting up to 15 years are still in progress. Chemoprevention strategies are often based on the results from clinical studies to provoke change and scientific findings. For instance, scientists completed the debut map of the genetic makeup of the human genome in 2002. Because of the human genome map, cancer research has advanced precipitously. Epigenetic events, also known as the modifications in gene expressions absent certain DNA attachment, may perpetuate cancer chemopreventive drug production targeting tumor suppressor genes.

Chemoprevention Drugs
Again, chemoprevention should not be confused with chemotherapy. Chemotherapy's purpose is to defeat cells, especially cancer cells, to prevent cancer progression. Conversely, chemoprevention involves administering innocuous agents to considerably healthy persons who may be highly susceptible to cancer. Chemopreventive agents can act in two ways; they can prevent or stop genetic mutations that lead to cancer, and they can prevent or stop processes that lead to excessive replication of damaged cells. The National Cancer Institute has made chemoprevention research a top priority.

Even though chemoprevention may be a postponement for cancer, it does not protect an individual from being diagnosed with cancer in the future. In this regard, chemoprevention for cancer may be similar to drugs used to prevent heart disease or stroke, such as statins or antihypertensive drugs, which are not 100 percent protective. Chemopreventive drugs include but are not limited to tamoxifen (Nolvadex), an estrogen blocker that reduces the risk of developing breast cancer. Tamoxifen is the first chemoprevention drug to obtain Food and Drug Administration (FDA) approval and is the most recognized chemopreventive drug. Studies have shown that tamoxifen reduces a highly vulnerable woman's chances of developing breast cancer by as much as one-half. Raloxifene (Evista) lowers the risk of acquiring breast cancer in women who have been through menopause. Finasteride (Propecia or Proscar) and similar drugs lower prostate cancer risk by reducing the amount of dihydrotestosterone (a male hormone) produced by the body. Aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs) lower the risk of many types of cancer in people with an average risk of cancer.

Chemoprevention Benefits
Decreasing the risk of cancer is often a benefit of chemoprevention, although undesirable symptoms are a risk. Nutritional factors and lifestyle modifications are significant components in chemoprevention. It is projected that, through dietary improvements, there could be a 50 percent reduction in colon and rectal cancers, a 25 percent reduction in breast cancer, and 15 percent reductions each in prostate, endometrial, and gallbladder cancers. Cancers of the stomach, esophagus, pancreas, ovaries, liver, lung, and bladder also may be influenced by nutritional elements. Nonetheless, these improvements undoubtedly should derive from the diet instead of from dietary supplements. For example, in 2003, the U.S. Preventive Services Task Force disseminated a report that evidence was not conclusive enough to recommend for or against use of vitamin supplements to aid the prevention of cancer. The task force was anti-supplementation.
with beta-carotene because of higher occurrence of lung cancer among those who used certain levels of beta-carotene supplements.

Phytochemicals from food are a source of many chemopreventive agents. Garlic alone contains 30 cancer-preventing compounds including selenium. Broccoli contains indole-3-carbinol as well as phenethylisothiocyanate, a sulfur-containing compound. Soy products contain phytoestrogens such as genistein. Tea, both black and green, contains an abundance of polyphenols such as the catechins that have antioxidant and anticancer activity. Compounds in tea also have antiestrogen activity and can modulate detoxification enzymes. Curcumin from the spice turmeric is gaining attention as a chemopreventive agent. It is both an anti-inflammatory agent and an antioxidant. Laboratory animals have shown curcumin inhibition toward colon, breast, and stomach cancer.

Chemoprevention Risks

Due to the fact that chemopreventive drugs can be administered in high dosages and for extended lengths of time, the risk of side effects is augmented. The Carotene and Retinol Efficacy Trial (CARET) study in the 1980s discovered that beta-carotene actually increased the risk of lung cancer in males who smoked. Continuing use NSAIDs to avert colon cancer can lead to medical consequences such as gastrointestinal issues and liver toxicity. Recent recommendations are to intensify consumption of fruits, vegetables, and fiber in the diet instead of taking supplements.

Some chemopreventive agents can have acute side effects in certain patients, which is a problem when considering long-term management of a drug to vigorous people who may or may not acquire cancer. Because of this, most chemopreventive agents are suggested primarily for people at high risk of developing cancer because they are most likely to benefit from treatment. People who are susceptible to developing cancer consist of those with a family history of cancer. An inherited genetic mutation, such as Familial Adenomatous Polyposis (FAP) and other factors (ethnicity, obesity, smoking, etc.) increase cancer risk. Unfortunately, chemopreventive agents do come with risks and side effects. For instance, tamoxifen has been shown to increase the risk of developing endometrial cancer, cataracts, and blood clots, which is why the drug is considered most beneficial to women under the age of 50. Countless persons ridicule the thought of ingesting a drug for a disease they do not yet have and may never acquire. Moreover, a plethora of doctors either disagree with the published studies regarding chemopreventive drugs or are unaware of the studies’ results.

Chemoprevention Clinical Studies

Altogether, drugs or other substances that have shown evidence of lowering cancer risk are tested in clinical trials. Clinical trials are research studies in people. A chemoprevention study tests a new chemopreventive agent to learn whether it is safe and effective and actually delays or prevents cancer. Often, substances that seem to prevent cancer in the laboratory setting with animals do not prevent cancer when tested in human subjects. In some circumstances, chemoprevention was shown to cause harms, some of which were critical or even life threatening. As mentioned, beta-carotene, a substance found in carrots, squash, and similar vegetables, was thought to help prevent cancer. However, when tested in clinical trials, it raised the risk of lung cancer in participants who smoked. Another clinical trial of selenium and vitamin E for prostate cancer showed that neither selenium nor vitamin E lowered the risk of prostate cancer, and there was even evidence that men who took vitamin E had an increase in prostate cancer.

The National Cancer Institute suggested that approximately 400 compounds are being studied as potential chemopreventive agents, chiefly in laboratory research. More than 40 of these compounds are being studied in clinical trials. Some of these agents are being investigated as single agents; others are being tested in combinations of two drugs. Chemoprevention trials look at possible ways to prevent cancer with interventions that include drugs, vitamins, diet, hormone therapy, or other agents.

Clinical trials often reveal that chemopreventive agents do not work for all patients. This is consistent with other drugs utilized for cancer treatment or for the prevention of other diseases, such as heart malady. When evaluating the results of chemoprevention clinical trials, it is imperative to consider the demographic makeup (family history, environmental and social background, etc.) of the participants. Frequently, people with known, increased risks for cancer, such as those who smoke or have a family
history of cancer, are tested; as such, the results of the study may be atypical and may not be applicable to everyone. For instance, in the tamoxifen clinical trials, the participants were at high risk for acquiring breast cancer.

Clinical trials are currently investigating chemoprevention for people at high risk of certain cancers, for example, to inhibit breast cancer in the second breast of women who has already been treated for breast cancer, for women who have never had breast cancer but are determined to be at elevated risk, or to prevent colon cancer in people with a genetic predisposition for cancer. People not at an exceptionally increased risk can use behavioral and dietary modifications for chemoprevention. Beginning in the 1980s, the National Cancer Institute has acknowledged well over 1,000 natural and synthetic chemicals agents with some degree of cancer preventive element. As of today, more than 400 potential agents are under investigation for their ability to prevent cancer, and at least 40 compounds or combinations are experiencing human clinical trials.

Types of Chemoprevention

Breast Cancer. Antiestrogens can lessen the growth effect estrogen has on several breast cancers. Tamoxifen and raloxifene are two antiestrogens that have been proven in clinical trials to avert breast cancer in women at high risk for the illness. Because of these trials, the FDA has approved tamoxifen as a preventive therapy as well as a treatment cancer. Additional antiestrogens, counting soy isoflavones, are still being investigated. The synthetic retinoid, fenretinide, also exhibits potential in averting breast cancer. Also under investigation is indole-3-carbinol from broccoli.

Colon Cancer. The research of chemopreventive drugs is said to be a shorter process because there are more distinguishable tumor markers recognized for colon cancer. The relapse of cysts rather than the expansion of malignant cancer can be employed as an outcome. Inflammation has been linked to cancer for a lengthy stint, and the anti-inflammatory remedies sulindac and sulindac sulfone in addition to particular cyclooxygenase-2 inhibitors are proving valuable in counteracting colon cancer. Adjoining fruits and vegetables to the pattern of eating correspondingly give the impression from epidemiological studies to have a protective end product on colon cancer.

Prostate Cancer. Both antiandrogens and antiestrogens are important in obstructing prostate cancer. Finasteride is being researched as an antiestrogen to avert prostate cancer in men at risk of this cancer. Finasteride is a prescription drug that can decrease the levels of dihydrotestosterone, which is connected with prostate growth and perhaps cancer. It has been utilized to cure enlarged prostate. Finasteride is currently being explored to avert prostate cancer in men over the age of 55 years. Men at an amplified risk for prostate cancer include those with a history of prostate cancer, those with a high-fat diet, increasing age, and those of African American lineage. Soy products and indole-3-carbinol may also be efficient for this reason. Lycopene, a vitamin A-like compound found in tomatoes and other red fruits and vegetables is associated with a decreased risk of prostate cancer. Selenium and tea are both possible chemopreventive agents that deters prostate cancer.

Skin Cancer. In recent years, the prevalence of skin cancer has noticeably increased, possibly due to the acceptance of sun tanning. Complexes under investigation for the hindrance of skin cancer take into account of compounds from tea, silymarin from milk thistle, vitamin A, and coumarins found in a number of plants.

Natural Chemoprevention

Research indicates cancer is the most dreaded of all diseases. The public instantaneously connects the cancer disease with perishing. Dissimilar from other killer diseases, cancer usually causes a slow death involving pain, suffering, mental anguish, and a feeling of ineptitude. Furthermore, the mental and physical stress it puts on loved ones and caretakers are beyond reckoning. There are 76 trillion cells in the human body that must persistently undergo reproduction if the body is to remain active and operating correctly. Every few days, many of these cells reproduce, while others reproduce after a much longer period. As each old cell reaches the end of its life cycle, it reproduces and is replaced by a fresh, young cell. The natural death of the old cell is called apoptosis. An innate type of gene called the
P53 gene (natural biological clock) controls the rate of death of cells.

It is a known fact that most cancers are initiated by the action of free radicals. Free radicals are unbalanced atoms or molecules with at least one unpaired electron. These unpaired electrons want and need a partner. Subsequently, the unbalanced free radicals, which have the ability to magnetize electrons from other atoms or molecules, go about snatching electrons from stable atoms. This taking of an electron from another atom means that the free radical is now stable and is no longer an unrestricted radical. Nevertheless, the atom or molecule from which the electron was stolen is now injured, and it becomes an unrestricted radical. This sets off a domino-style chain reaction of damage within the body. In their hasty exploration for electrons, free radicals do a lot of structural harm to healthy cells. Aggregate free radical damage initiates the plasma membrane of the cell to collapse and stop functioning. When this happens, transportation of nutrients, oxygen, and water into the cell and removal of waste products and toxins out of the cell become compromised, leaving them at risk. This causes the cell to either die from starvation or die in a sea of accrued toxic waste. Otherwise, if the DNA of the cell is also affected, it can cause the cell to reproduce improperly and, in so doing, causing a cell mutation. The mutated cell is now genetically indecorous and, as such, does not perform as a normal cell. The P53 gene of the cell is affected, and the natural biological clock discontinues, often eliminating apoptosis (natural cell death). Without apoptosis, the mutated cancer cell does not expire. As a way to ensure its growth, a cancer cell steals nutrients from surrounding cells and starts to rapidly replicate in geometric progression (2, 4, 8, 16, etc.). With time, the cancer cell progresses into a cancerous mass or a tumor. Cancerous cells from the mass or tumor can be transferred to other tissues or organs where they entrench and begin to grow and reproduce, also known as metastasizing.

Orthodox approaches treat cancer as a localized disease to be treated in a localized manner by cutting out the tumor, exposing it, or saturating the body with toxic as well as carcinogenic drugs in order to destroy the tumor. Natural healing methods consider cancer to be a systemic disease. Rebuilding the body’s natural immunity is emphasized to strengthen its natural ability to destroy cancer cells. Data on cancer, which has been corroborated by the National Academy of Sciences, the U.S. Department of Health and Human Services, the National Cancer Institute, and the American Cancer Society, discovered that 80 to 90 percent of all cancers are produced because of lifestyle influences that include but are not limited to smoking, alcohol, lack of exercise, exposure to chemicals, environmental factors, and dietary and nutritional practices.

Natural and technologically produced toxins surround everyone. These ecological contagions exist in the air taken in daily, the foods eaten, and the water intake of everyone. In the contemporary, industrial world, humans cannot escape these toxins. Today, people are exposed to more toxins in 15 minutes than their great-grandparents were exposed to during a lifetime. The majority of these toxins are considered cancer-causing carcinogens, and as implausible as it seems, the most toxic atmosphere to which humans are exposed daily is the setting in the personal home. Given that lifestyle, environmental factors, and nutrition are the most common risk factors for developing cancer, it seems logical that many of these cancers can be demolished, substantially decreased, or their growth eradicated by reducing or eliminating the risk causes. Certain risk factors, such as air and water, are difficult to manage. Nonetheless, people have virtually total control over some of the other known risk factors such as smoking, alcohol, intake of chemicals and drugs, and diet and nutrition.

In 60 percent of women’s cancers, diet and nutrition appear to be factors. Dietary and nutritional factors make up about 40 percent of men’s cancers and about 75 percent of cardiovascular diseases. There is some discourse on diet and what foods to consume to decrease potential cancer maturity: a reduction in the intake of fat, red meat, smoked meats, or meats preserved with nitrates and elimination of white sugars from daily food intake as well as white flour products and soft drinks. Ironically, it is not common for doctors to counsel cancer patients or those who are at high risk for cancer about nutrition. Nonetheless, research shows that ingesting the correct foods and supplements may avert cancer and improve the immune system and energy levels in addition to giving the body a real chance to avert cancer or improve itself. In essence, a healthy diet strengthens the immune system, slows tumor growth, protects against further
metastasis, and reduces the side effects of radiation and chemotherapy.

Time after time, research has shown there is a considerable reduction in cancer risk in those who eat the necessary amounts of fruits and vegetables. Only 9 percent of Americans eat the recommended five daily servings. Studies have discovered that the antioxidants in fruits and vegetables bestow additional guards against free radically induced cancer. Low blood levels of antioxidants are connected with an increase in death rates from many types of cancer. One of the most assuring parts in cancer prevention involving nutrition is in the area of chemoprevention. Chemoprevention is the concept that natural substances found in completely fresh foods could provide powerful weapons against cancer and against other chronic diseases too.

Keep in mind that chemoprevention is not to be confused with chemotherapy. In place of toxic poisons, chemoprevention employs nutriceuticals to develop optimal health and to counteract cancer and other chronic and degenerative diseases. Remember, a nutriceutical is a food substance or part of a food that provides medical or health benefits, including the prevention of or treatment of disease. They are naturally occurring compounds found in plants, algae, microbials, and other biological sources that support specific bodily health functions. As mentioned, one of the most powerful nutriceutical chemopreventatives for cancer is an extract from red raspberry seeds called ellagic acid. Ellagic acid contains a naturally occurring phenolic compound that has very strong antioxidant properties. Ellagic acid has the ability to inhibit mutations within a cell’s DNA. It is also known to cause cancer obstruction, which has the ability to develop apoptosis or normal death in various types of cancer cells. Moreover, studies have found that it has antibacterial and antiviral properties. Ellagic acid is a super antioxidant and a potent anticarcinogen that protects the cells against free radical damage.

Chemopreventive agents have been identified that interact with all stages of carcinogenesis: initiation, promotion, and progression. These agents function by deactivating carcinogens, inducing enzymes, or functioning as antioxidants. Carcinogens are cancer-causing agents. As the chemopreventive agents continue to work toward preventing cancer, they may constrain tumor enlargement by acting as stimulating apoptosis or dominators. In essence, chemoprevention is a way to prevent or delay the development of cancer by taking medicines, vitamins, or other agents.

Tamikia Lott
Old Dominion University
Gail Seymour
Tennessee Department of Human Services

See Also: Alternative Therapy: Diet and Nutrition; American Cancer Society; Beta-Carotene; Chemotherapy; Daily Life; Diet and Nutrition; National Cancer Institute; Raloxifene; Tamoxifen.

Further Readings

Chemotherapy

Anticancer or antineoplastic chemotherapy generally entails the administration of one or more drugs with the intent to stop further growth of tumor cells (cytostatic) or to kill them altogether (cytotoxic). Chemotherapy is often used with surgery or radiation to treat cancer when the disease has spread, has come back (reurred), or when there is a high probability that it could recur. Chemotherapy may be administered in several forms including by pills, injection, or catheter. Chemotherapeutic drugs enter the bloodstream and travel through the body
Chemotherapy is a treatment that kills mostly cancer cells, but they may also affect some healthy cells in the process. This treatment commonly has adverse side effects that may include a temporary loss of the body’s natural immunity to infections, hair loss (alopecia), digestive disorders, and a general feeling of illness.

Cancer as a Disease of Cells
Cancer is a disease of cells characterized by a shift in control mechanisms that regulate the rate at which cells divide and differentiate. Normal cells undergo a constant life cycle, usually referred to as the cell cycle. This results in cellular growth and reproduction. Cancer cells follow a similar cell cycle, and chemotherapeutic drugs are generally designed to attack specific phases in the cell cycle that cancer cells may be going through. Cells that undergo neoplastic transformation divide rapidly and excessively, forming local tumors that can compress or invade adjacent normal structures. Cytotoxic chemotherapy drugs target rapidly dividing cells. Understanding how these drugs function helps doctors predict which drugs are likely to work well together. Doctors also can effectively plan how often doses of each drug should be given based on the timing of the cell phases. Although chemotherapy drugs attack reproducing cells, they cannot tell the difference between reproducing cells of normal tissues (that are replacing worn-out normal cells) and cancer cells. The damage inflicted on normal cells can result in side effects.

Determinants of Treatment
Chemotherapy is often the first choice for treating many cancers. It differs from surgery or radiation in that it is almost always used as a systemic treatment. This means that the medicine often travels through the entire body rather than being confined to one area or organ. This is important because chemotherapy can reach cancer cells that may have spread to other parts of the body. In some cases, it is the only treatment used in an attempt to cure, control, or palliate cancer. This is termed as adjuvant chemotherapy, which is administered with the intention of preventing the growth of cancer cells remaining in the body after surgery or radiation. Alternatively, it may be used as neoadjuvant therapy, which is used to shrink a large tumor that can be subsequently removed by surgery or can be treated more effectively with radiation.

The first and primary determinant of treatment is the microscopic or histologic diagnosis. Different cancers respond differently to different chemotherapeutics depending upon their location, size, natural history, aggressiveness, and tendency to spread. Thus, the histologic diagnosis, usually made by biopsy or surgical excision of a primary tumor, is a critical first step for treatment planning. Doctors also look for abnormal presentations of common tumors that warrant further investigations and more intense therapy. Treatment in cases lacking a precise histologic diagnosis is usually directed against the most-responsive tumor type within the realm of possible diagnoses. In some cases, tumor subtypes also may be important in deciding treatment options (e.g., as in the case of non-Hodgkin’s lymphoma) as these subtypes have different patterns of clinical response to treatment.

Tumor stage based on the extent of the disease is the deciding next step. This includes an evaluation of whether the tumor is curable by local treatment measures such as surgery or radiation therapy. Doctors also consider whether the cancer has involved lymph nodes and whether those can be removed surgically. Lymph node involvement usually indicates an aggressive tumor, especially if it is involved early in the disease process, necessitating establishment of more aggressive chemotherapy. Spread of the cancer to neighboring or distant organs is termed metastasis and is generally associated with poorer prognosis. In this case, surgeons may consider the possibility of resecting the primary tumor along with the metastasis (especially if they are not too many and are surgically reachable), provided the patient stands to benefit significantly from the extensive surgery. Chemotherapy is almost always recommended in such cases.

The ultimate decision is based on a thorough understanding of the disease process, the clinical pharmacology of the drugs, and the potential benefits and risks of alternative forms of treatment. The oncologist then evaluates all parameters and
decides whether a realistic opportunity for curative treatment exists. A decision to treat with curative intent demands a high degree of adherence to drug dosage and scheduling requirements and an acceptance of treatment-related side effects. When cure is not a realistic expectation, a decision to treat must be based on an expectation for prolonging the patient's life or an improvement in quality of life. When the potential for benefit is low, chemotherapy is usually offered only after frank and thorough discussion of the likely outcome.

**Drug Classes**

Chemotherapeutic drugs are classified based on their action on chemicals or processes within cancer cells and the specific phases of the cell cycle they affect. This knowledge helps oncologists decide which drugs are likely to work well together and, if more than one drug will be used, to plan the exact dosing cycles and intervals for each drug. In fact, using combinations of drugs belonging to different classes are the mainstay of most treatment strategies for advanced cancers. This involves administration of two or more drugs simultaneously or sequentially to obtain maximum response while minimizing the impact of resistance of cancer cells to any individual agent.

Alkylating agents directly damage DNA to prevent the cancer cell from dividing. These agents work in all phases of the cell cycle. Examples of this class include nitrogen mustards (mechlorethamine, chlorambucil, cyclophosphamide, ifosfamide, and melphalan), platinum compounds like cisplatin and carboplatin, triazenes like dacarbazine and temozolomide, and the alkyl sulfonate busulfan. Nitrosoureas like streptozocin and carmustine act in a similar way to alkylating agents. They interfere with enzymes that help copy and repair DNA and are not cell cycle-phase specific. However, unlike many other drugs, these agents can travel from the blood to the brain and are often used to treat brain tumors.

Antimetabolites are a class of drugs that interfere with DNA and RNA growth and damage cells during the S phase of the cell cycle. Examples of antimetabolites include folate analogs like methotrexate and pemetrexed, purine analogs like 6-mercaptopurine, and pyrimidine analogs like 5-fluorouracil, capecitabine, gemcitabine, and cytarabine.

Antacyclines like daunorubicin, doxorubicin, and mitoxantrone are antitumor antibiotics that work in all phases of the cell cycle and interfere with enzymes involved in DNA replication. A major problem is the toxic effects on heart muscle, which may require lifetime dose limitations.

Topoisomerase inhibitors interfere with the topoisomerase enzymes that are crucial for accurate DNA replication. These include topoisomerase I inhibitors like topotecan and irinotecan and topoisomerase II inhibitors like etoposide and teniposide.

Mitotic inhibitors are derived from natural products and include vinca alkaloids like vinblastine, vinorelbine and vincristine, and taxanes like paclitaxel and docetaxel. They can stop mitosis or inhibit enzymes from making proteins needed for cellular reproduction. These work primarily during the M phase of the cell cycle but can cause cellular damage in all phases. Peripheral nerve damage can be a dose-limiting side effect.

Adrenocorticosteroids like prednisone are natural hormones that are useful in treating some cancers and other illnesses. They are often combined with other chemotherapeutics to increase their effectiveness.

Sex hormones, or hormonelike drugs, alter the action or production of female or male sex hormones and are used to slow the growth of breast, prostate, and endometrial (uterine) cancers, which normally grow in response to natural sex hormone levels in the body. These drugs interfere with the normal action of sex hormones required by the cancerous growth or prevent the body from making the hormones. Examples include antiestrogens like tamoxifen and toremifene; aromatase inhibitors like anastrozole, letrozole, and exemestane; progestins like megestrol acetate; antiandrogens like flutamide; and gonadotropin-releasing hormone analogs like leuprolide.

More recently, chemotherapy has diversified to include targeted therapeutics that work primarily on cancer cells but not on normal, healthy cells. These attack cancer cells with mutant versions of certain genes or cells that express too many copies of a particular gene. This results in more specific targeting of cancer cells while reducing the unwanted side effects of conventional chemotherapy by sparing the normal cells. Examples include the protein tyrosine kinase inhibitors imatinib, gefitinib, and erlotinib and the proteasome inhibitor bortezomib.

Immunotherapeutic agents represent yet another recent and atypical group of chemotherapeutic
agents that either stimulate the body’s own immune system to fight the disease or use immune system components like antibodies created outside of the body. A major class of drugs in this field includes monoclonal antibodies, which are artificially made proteins that can target and inactivate specific molecules in cancer cells that are crucial to their development. Some examples of drugs in this class include cetuximab and trastuzumab, which interfere with the conduction of intracellular signals, bevacizumab, which interferes with new blood vessel development that can feed tumor cells, and rituximab, which targets a protein found on the surface of cancer cells in lymphomas.

Side Effects
Chemotherapy administration involves finding a balance between destroying cancer cells in an effort to cure or control the disease while sparing normal cells to limit unwanted side effects. As explained earlier, because cancer cells grow and divide more rapidly than normal cells, many anticancer drugs are designed to kill growing cells. However, certain healthy cells also need to multiply quickly, and chemotherapy can affect these cells too. This damage to normal cells is usually the cause of side effects. The fast-growing, normal cells most likely to be affected include blood cells forming in the bone marrow and cells in the digestive tract (mouth, stomach, intestines, and esophagus), reproductive system (sexual organs), and hair follicles. Some anticancer drugs may also affect cells of vital organs such as the heart, kidney, bladder, lungs, and nervous system. The type and severity of side effects depend on the type and dose of chemotherapy and how the body reacts to the drugs.

Fatigue is the most common symptom reported by cancer patients on chemotherapy. The exact cause is not always known and may be due to the disease, low blood counts, lack of sleep, pain, stress, and poor appetite among others. It usually appears suddenly, and patients feel worn out and drained. It is often not relieved by rest and may last for days, weeks, or months. However, severe fatigue does go away gradually as the tumor responds to treatment. Some people may also experience flulike symptoms for a few hours to a few days after chemotherapy. This may be especially seen in patients receiving chemotherapy in combination with biological therapy.

Nausea and vomiting are also common complaints while receiving chemotherapy. However, this is less common with newer drugs and is less severe when they do occur. In addition to standard chemotherapy, powerful antinausea drugs are often prescribed to most patients. As with fatigue, these side effects are not always predictable and may depend on the type of drug administered and the intrinsic physiology of the patient.

Diarrhea may result when chemotherapeutic drugs affect the rapidly dividing cells lining the intestine. As with nausea and vomiting, medications are available to control this side effect, but persistent diarrhea may warrant administration of intravenous fluids to replace the water and nutrients lost. Often, these fluids are given on an outpatient basis and may not require hospitalization. On the other hand, certain anticancer drugs, pain medicines, and other medications can cause constipation. This may also be the result of decreased activity or if the diet lacks enough fluid or fiber. Laxatives or stool softener are usually prescribed with caution in these cases, especially if the patient’s white blood cell count or platelets are low.

Some anticancer drugs can cause sores in the mouth and throat, a condition called stomatitis or mucositis. Chemotherapy drugs can make these tissues dry and irritated or cause them to bleed. Patients who do not eat well after beginning chemotherapy are more likely to get mouth sores.

Hair loss is another common side effect of chemotherapy, but not all drugs cause hair loss. Because the base of hair follicles has rapidly dividing cells, drugs that kill fast-growing cells often have this accompanying side effect. When hair loss does occur, the hair may become thinner or fall out entirely. It can occur on all parts of the body, including the head, face, arms and legs, underarms, and pubic area. The hair usually grows back after the treatment is over. At times, however, the hair may grow back a different color or texture.

Chemotherapy can cause minor skin problems like redness, rashes, itching, peeling, dryness, acne, and increased sensitivity to sunlight. Certain intravenous anticancer drugs may cause the skin along the vein to darken, especially in people who have dark skin. These areas usually fade a few months after treatment ends. Nails may also become darkened, yellow, brittle, or cracked and may develop vertical lines or bands. A more serious complication
Chemotherapy is called radiation recall. This happens in some patients who receive chemotherapy after radiation and develop red patches on the skin that was exposed to the radiation. The skin over the area may also blister and peel. This reaction may last hours or even days. Treatment is generally topical.

Chemotherapy can reduce the bone marrow’s ability to make red blood cells that carry oxygen to all parts of the body. When there are too few red blood cells, body tissues do not get enough oxygen to do their work, resulting in anemia. Anemia can make the patient feel short of breath, weak, and tired. This can be countered by medicines like erythropoietin, which can boost the growth of red blood cells. Extreme cases may also require blood transfusions. Bone marrow suppression also reduces the white blood cells being made that are in charge of fighting many types of infections. This increases the susceptibility of the patient to contract infections, usually from bacteria normally found on the skin and in the mouth, intestines, and genital tract. Anticancer drugs can also affect the bone marrow’s ability to make platelets, a blood component that helps stop bleeding by making the blood clot. Decreased platelet levels cause patients to bleed or bruise more easily than usual, even without an injury. Reduced white blood cell and platelet levels may be countered by the administration of colony-stimulating factors, drugs that help raise the numbers of these cells.

Chemotherapy drugs can also cause side effects related to the central and peripheral nervous system. Drugs may interfere with certain functions of the brain, causing tiredness, confusion, and depression. These feelings generally go away once the chemotherapy dose is lowered or the course is completed. Peripherally, the drugs can damage nerves, leading to burning, numbness, tingling, or shooting pain, most often in the fingers or toes. This can, however, be relieved by special pain medications.

Chemotherapy may occasionally affect sexual organs (testes in men and vagina and ovaries in women) and functioning. These side effects depend on the drugs used and the person’s age and general health. In males, chemotherapy may reduce sperm count and motility. These changes can result in infertility, which may be temporary or permanent. In females, anticancer drugs can lower the amount of hormones produced by the ovaries, leading to irregular or complete cessation of menstrual periods while on chemotherapy. It may also cause temporary or permanent infertility and premature menopause. Although pregnancy may be possible during chemotherapy, it is not advisable because some anticancer drugs may cause birth defects. Doctors advise female patients of childbearing age to use some method of birth control throughout their treatment.

Normal cells usually recover once chemotherapy is completed, so most side effects gradually go away after treatment ends, and the healthy cells have a chance to grow normally. The time it takes to recover from side effects depends on the overall health of the patient and the type of chemotherapy administered. However, while most people have no serious long-term complications from chemotherapy, some drugs may cause permanent changes or damage to the heart, lungs, nerves, kidneys, and reproductive or other organs. Another major complication with certain types of chemotherapy is the development of secondary malignancies that present many years later. The most frequent secondary malignancy is acute myelogenous leukemia. Certain alkylating agents and ionizing radiation are considered to give rise to this condition. With improvements in the

A patient receives chemotherapy through a port in the chest area. Chemotherapy may be administered in several forms including by pills, injection, or catheter. (National Cancer Institute/Rhoda Baer)
clinical efficacy of various chemotherapeutic drugs resulting in prolonged survival and in some cases cure of cancer, the issue of how secondary cancers may affect long-term survival has assumed greater importance.

**New Classes of Chemotherapeutic Agents**

With increasing knowledge on the molecular biology of cancers, several new classes of chemotherapeutic agents are being synthesized for use in various types of cancers. These agents are being designed to specifically attack cancer cells while leaving the normal cells unharmed. Experimental treatments with the most promising laboratory results are usually moved into clinical trials. During such a trial, more and more information is gained about an experimental chemotherapeutic, and its risks and benefits are evaluated.

Clinical trials are sponsored by a variety of organizations including medical institutions, foundations, voluntary groups, and pharmaceutical companies in addition to federal agencies such as the National Institutes of Health, the Department of Defense, and the Department of Veterans Affairs. All clinical trials have strict guidelines about who can participate and how the study can be conducted. In addition, all trials in the United States are legally required to be monitored by ethics committees and must report their results in accessible forums. A drug that completes a trial successfully is then approved by the Food and Drug Administration for prescription to patients.

Modern research is revealing several new uses of chemotherapy and other agents that hold even more promise for curing or controlling cancer. New drugs, new combinations, and new delivery techniques will improve our ability to cure or control cancer and improve the quality of life for people with cancer. As mentioned previously, targeted therapies are being developed to specifically attack a particular target on cancer cells. These drugs may have fewer side effects than standard chemotherapeutics and may eventually be used along with them. Monoclonal antibodies are being designed to guide chemotherapeutic agents directly to the tumor. Such antibodies (without attached chemotherapy) can also be used as immunotherapy drugs to strengthen the body’s immune response against cancer cells.

Research is also focusing on the targeted delivery of drugs to cancer cells. Liposomal therapy involves using chemotherapeutics that are packaged inside synthetic fat globules called liposomes. These help the drug penetrate cancer cells more selectively and decrease possible side effects. Examples of liposomal medicines already in use are Doxil (the encapsulated form of doxorubicin) and DaunoXome (the encapsulated form of daunorubicin).

Chemoprotective agents also are being developed to protect against specific side effects of certain chemotherapeutics. Agents are being developed that, when given along with chemotherapy, may help overcome drug resistance. Cancer cells often become resistant to chemotherapy by developing the ability to pump the drugs out of the cells. These new agents inactivate the pumps, allowing the chemotherapy to remain in the cancer cells longer, thereby hopefully enhancing their efficacy.

**Personalized Medicine: The New Frontier**

Scientists are now able to sample small amounts of tumor tissues obtained from biopsies to analyze the genetic makeup of individual patients’ cancers. Such information on which specific genes within cancer cells are mutated can be valuable to oncologists who can then assess the relative benefits of chemotherapeutics as their sites and mechanisms of action are known for most of them. This combined approach of assessing the molecular profiles of individual tumors and matching them with the most efficacious drugs is now leading to the personalization of therapeutic regimens. As researchers learn more about the biology of tumors and invent better chemotherapeutics that can specifically target cancers while sparing normal cells, the future is set to witness a radical change in this field wherein more effective chemotherapies with fewer side effects will be combined with or totally replace existing ones, leading to more targeted and rational patient management.

Anirban P. Mitra

*University of Southern California*

**See Also:** Anticancer Drugs; Chemoprevention; Clinical Trials; Experimental Cancer Drugs; Radiation Therapy.

**Further Readings**

Chabner, Bruce and Dan Longo, eds. *Cancer Chemotherapy and Biotherapy: Principles and*
Childcare and Cancer Risk

Parents and caregivers are often concerned about the cancer risk of their children. Helping children to avoid environmental hazards and other risks is, of course, beneficial to reducing children's risks of childhood cancer. Studies have suggested that children enrolled in childcare, such as preschool or day care, have a reduced chance of contacting certain childhood cancers. Children who attend day care, preschool, or play groups have a 30 percent lower risk of developing the most common type of childhood leukemia than those who do not.

Leukemia is the most common cancer found in children in wealthy nations. Leukemia affects approximately one in 2,000 children. Incidence of leukemia has been on the increase for the past several decades. Acute lymphoblastic leukemia accounts for more than 80 percent of all leukemia cases. Most often occurring in children age two to five years, acute lymphoblastic leukemia is often fatal. Acute lymphoblastic leukemia is characterized by the body's overproduction of lymphoblasts, cancerous, immature white blood cells. For patients with acute lymphoblastic leukemia, the bone marrow overproduces lymphoblasts, which continuously multiply, causing damage and death by inhibiting the production of normal cells. For a patient with acute lymphoblastic leukemia, the production of red and white blood cells and platelets is inhibited in the bone marrow and can spread to other organs. Researchers suggest that, for most types of childhood leukemia to develop, a genetic mutation must first take place in the womb. This genetic mutation is then followed by a second trigger during childhood that results in 1 percent of the children with that genetic mutation then developing the disease.

A child suffering an infection, or the timing of that infection, is one of the suspected triggers that might cause one child to develop acute lymphoblastic leukemia. In order to resolve this issue, scientists examined some of the environmental variables that separated those children who developed acute lymphoblastic leukemia and those who did not. Researchers asked parents questions about their child's day care, preschool, and playgroup attendance. The parents were also asked about their child's other forms of social interaction with other children. The various research studies that investigated the effect of social interaction with others on acute lymphoblastic leukemia varied in several ways. The timing, duration, and extent of social contact were investigated and in the age groups and types of leukemia studied. At the end of the process, the researchers in a variety of studies found some indication that social interaction with other children provided a protective effect against contacting acute lymphoblastic leukemia. No study found that children with a greater amount of social contact had an increased risk of being diagnosed with acute lymphoblastic leukemia.

Benefits of Interaction

Children are exposed to a multitude of infections when they have regular interaction with peers in settings such as day care or preschool. As a result, children who attend some sort of childcare are more likely to develop stronger immune systems. This stronger immune system serves to assist the children's immune systems to fight the development of the most common form of childhood cancer, acute lymphoblastic leukemia. This strengthened immune system seems to develop over time. Those children who are new to childcare appear to be the first to contact easily spread illnesses such as those involving the upper respiratory system or viral or gastric diseases. This contrasts with those children who have been in group childcare settings for some time as these children appear better able to manage exposures.

Certain differences appear to exist, however, among children from different racial or ethnic groups. While Caucasian, non-Hispanic children who were enrolled in childcare, day care, or preschool had significantly lower rates of being
diagnosed with acute lymphoblastic leukemia than other Caucasian, non-Hispanic children, this benefit was not enjoyed by children from other ethnic groups. Specifically, Hispanic children who were also enrolled in childcare, day care, or preschool contacted acute lymphoblastic leukemia at the same rate as other Hispanic children who were not enrolled in such services. Further research needs to be conducted to determine how such enrollment affects children from other ethnic groups, such as Asian or African American students.

**Childcare for Siblings of Cancer Patients**

The siblings of children with chronic illnesses such as cancer have been observed as having more adjustment or behavioral problems than do the siblings of healthy children. These adjustment problems are independent of the seriousness of the illness suffered by the sibling. Siblings of children with cancer face major stress themes in their lives, including change, fear of death, and loss. These children also deal with anxiety, social isolation, and fear for their own health. While families of children with cancer obviously place a great emphasis upon the needs of the child facing cancer, the needs of their other children are also significant and must be met. Day care, childcare, and preschool programs can provide excellent options for such families.

The siblings of cancer patients seem most affected by diminished contact with their parents, an understandable condition when considering the increased energy expended on the child facing cancer. This lack of contact may lead to eating and sleeping disorders as the sibling of a cancer patient attempts to find other ways to cope with the loss of his or her parents’ attention. Not surprisingly, this lack of contact most severely affects children who are below school age as they have fewer coping skills and also do not have the support and distraction provided by teachers and peers. When such children are enrolled in a quality childcare program, however, their ability to cope with these problems increases.

The childcare, day care, or preschool in which the sibling of a cancer patient is enrolled should be made aware of the situation facing him or her. Quality programs will help the child to discuss and come to terms with his or her feelings and provide him or her with the support necessary to feel validated and valuable. Merely enrolling in a childcare, day care, or preschool program will provide the siblings of cancer patients with a distraction and a new social set that will assist them in being able to better deal socially with the world around them.

**Support for Families of Cancer Patients**

Families faced with a diagnosis of childhood cancer have a variety of support systems that exist to help them. This support is often necessary for the child diagnosed with cancer, his or her parents, and other children in the family. The American Childhood Cancer Organization (ACCO), for example, provides a variety of services to those families facing childhood cancer, including support for parents and siblings. The ACCO, formerly known as the Candlelighters Childhood Cancer Foundation, was formed in 1970. As it was founded by parents of children with cancer, ACCO is aware of the many needs facing the family after receiving a diagnosis of cancer. ACCO works to advocate for these children’s needs and to support research that increases every child’s chances of survival. It also provides a wealth of materials and resources that can positively affect siblings and parents in such a situation.

The ACCO provides a variety of services intended to assist those children facing cancer and their families. These services include the distribution of books and other materials that provide information regarding the treatment options and late effects of childhood cancer. The organization also maintains a toll-free hotline and Web site where families can connect with volunteers and experts to receive referrals, support, and information regarding childhood cancers. Local affiliates of the ACCO often provide support groups where children facing cancer and their families can meet and discuss their situations with others. These services include peer support groups, in-hospital visits, and assistance programs. Siblings of children with cancer can benefit greatly from such assistance as it can help them better understand what they are feeling and how to best interact with others. Organizations such as the ACCO also advocate with policy makers and Congressional representatives to assure that childhood cancer research is given a high priority when legislative decisions regarding funding are made.

Stephen T. Schroth
Towson University
**See Also:** Childhood Cancers; Lymphoma, Hodgkin’s, Childhood; Lymphoma, Non-Hodgkin’s, Childhood; St. Jude Children’s Research Hospital.

**Further Readings**


---

**Childhood Brain Tumor Foundation**

The Childhood Brain Tumor Foundation is one of several foundations that address the needs of children with cancer and their families by providing education and other sources of financial support. The Web site for this foundation is www.childhoodbraintumor.org. The foundation is located in Maryland. The development of this foundation over the past 17 years has added to knowledge through Web-based education and materials and provided research opportunities to improve prognosis for children with pediatric brain tumors.

This organization is a nonprofit whose aims are to improve the quality of life and prognosis for children with pediatric brain tumors and find a cure for the spectrum of medical conditions addressed by the umbrella concept of pediatric brain tumors. Funding for the organization's activities is raised through private donations and community projects (walks to raise money for the organization, galas, etc.). Funding raised by this organization is primarily disbursed through research grants. Additionally, there is an educational section of this Web site that provides critical information about pediatric brain tumors, such as age of onset, prevalence, and medical information.

Another section of the Web page provides the stories of children with brain tumors. These stories and in-memory-of dedications shine a light on the courage that children and their families find to cope with the stress of childhood brain tumors. The stories and memoirs are filled with ideas for hope and fighting for recovery that could both inspire and support parents and children struggling to deal with the devastating impact of brain tumors for children. There also are links to Web sites that provide information about pediatric brain tumors (e.g., neurological information about this disease) and current research centers and initiatives in the field. Those seeking referrals for medical treatment can also find some guidance to treatment centers on the Web site.

Supporting research through grant funding is an important part of the mission of the Childhood Brain Tumor Foundation. Proposals for funding must address the organization’s goals of finding a cure, improving medical outcomes for children with brain tumors, or improving the quality of life for children with brain tumors. Grant proposals are evaluated using a system patterned after the grant review criteria established by the National Institutes of Health, where value also is placed on innovation, scientific merit, and research design of applications for funding. The Web page presents a review of abstracts from a variety of funded projects. The majority of the projects have a medical focus, aimed at understanding biological and genetic underpinnings of brain tumors to spur the field toward cures for these diseases. Some funding is also directed toward improving quality of life as well as assisting children in coping with the late effects related to radiation and other medical treatments for brain tumors.

Laura Nabors
*University of Cincinnati*
Childhood Cancers

Childhood cancers refer to those that occur in children, generally defined as taking place in young people from birth to age 14, although the upper age is sometimes used with those as old as 19. The most common childhood cancers are leukemia, brain tumors, and lymphoma, although a variety of other types of cancer can and do afflict children. Tremendous effort and funds have been devoted to finding cures for childhood cancers, and as a result, the survival rates for many of these have risen dramatically over the years. A variety of organizations exist to help children with cancer and their families to obtain treatment, cope with the disease, and to face other issues that may arise.

Globally, more than 175,000 incidents of childhood cancer are diagnosed each year, and nearly 100,000 childhood cancer cases result in death annually. In the United States, only accidents cause more deaths among children than cancer. Each year 16 out of every 100,000 children are diagnosed with some form of cancer, and three out of 100,000 children will die from the disease. This translates into approximately 12,000 new cases of childhood cancer in the United States each year, with approximately 1,300 deaths of those between birth and 14 years of age. In developing nations, the statistics involving childhood cancer are grimmer. In developed nations, childhood cancers have a mortality rate of approximately 20 percent, whereas in developing nations, the mortality rate often ranges from 80 to 90 percent.

Globally, the disparity between childhood cancer mortality rates in developed and undeveloped nations is an issue of concern. When examining the variation in childhood cancer incidence among nations, the greatest difference occurs when high-income countries are compared to low-income ones. Within this difference, however, a variety of factors may cause the disparity between the two groups. The differences in cancer mortality rates between high-income and low-income nations may result from differences in the capacity to diagnose cancer, differences in risks among different racial or ethnic population subgroups, differences in environmental or other risk factors, or a combination thereof. Researchers study these differences in an attempt to provide children living in particular countries the most appropriate treatment possible.

Types of Childhood Cancer

A variety of cancers are found each year in children. Children between the ages of one and four are most frequently diagnosed with childhood cancers, but those between the ages of 10 and 14 are the group most likely to die from cancer. Certain types of cancer are more prevalent in children than others. The most common types of cancer diagnosed in children are leukemia (34 percent of diagnoses), brain tumors (23 percent), and lymphoma (12 percent). Other types of cancer, although less common than leukemia, brain tumors, and lymphoma, are also seen regularly in children. These cancers, and their rates of diagnoses, include neuroblastoma (7 percent), Wilms tumors (5 percent), non-Hodgkin's lymphoma (4 percent), rhabdomyosarcoma (3 percent), retinoblastoma (3 percent), osteosarcoma (3 percent), and Ewing sarcoma (1 percent). Research is ongoing with all of these forms of childhood cancer both so that their causes might be better understood and so that treatment options might be tested and ultimately provided to patients around the globe.

The causes of most cases of childhood cancer are unknown. In between 5 and 15 percent of childhood cancer cases, a variety of familial and genetic factors can be identified as contributing to the disease. When physicians and researchers determine
that genetic factors are at play in a case of childhood cancer, the chance that an interplay between genetic and environmental factors must also be examined. Approximately 10 percent of the occurrences of childhood cancer involve environmental factors, which might include exposure to certain substances, such as medications, tobacco, or other known carcinogens. In the remainder of childhood cancer cases, however, the causes of the cancer are unknown, meaning that for more than 75 percent of these diagnoses, the causes of the cancer are unknown.

Those working with childhood cancer understand that there are significant differences between working with adults facing cancer. First, children have different, and sometimes unique, reactions to exposures to environmental hazards. Unlike adults, children must often rely on others to protect them from toxic environmental agents. Second, children's immature physiological systems often make them unable to clear or metabolize hazardous environmental agents with which they come in contact. As a result, adults must sometimes take additional steps when a child has been exposed to potentially hazardous materials. Third, the growth and development of children occurs in phases known as developmental windows. This can result in certain critical windows of vulnerability, during which a child who is exposed to certain hazardous materials may respond more adversely than a child who is not within that window. Special care must as a result be taken for children at certain ages. Fourth and last, children's longer life expectancies mean that a longer time exists for cancer processes to manifest with long latency periods. This means that children exposed to certain materials have an increased risk of developing some cancer types later in life due to early life events.

Assistance
Children and their families faced with a diagnosis of childhood cancer have a variety of support systems that exist to help them. The American Childhood Cancer Organization (ACCO), for example, provides a variety of services to those facing childhood
cancer and their families. The ACCO, formerly known as the Candlelighters Childhood Cancer Foundation, was formed in 1970 by parents of children with cancer. The ACCO works to advocate for these children's needs and to support research that increases every child's chances of survival.

The ACCO provides a variety of services intended to assist those children facing cancer and their families. These services include the distribution of books and other materials that provide information regarding the treatment options and late effects of childhood cancer. The organization also maintains a toll-free hotline and Web site where families can connect with volunteers and experts to receive referrals, support, and information regarding childhood cancers. Local affiliates of the ACCO often provide support groups where children facing cancer and their families can meet and discuss their situations with others. Organizations such as the ACCO also advocate with policy makers and Congressional representatives to assure that childhood cancer research is given a high priority when legislative decisions regarding funding are made.

Stephen T. Schroth  
*Towson University*

**See Also:** Adrenocortical Carcinoma, Childhood; Association of Oncology Social Work; Childhood Brain Tumor Foundation; St. Jude Children's Research Hospital; Survivors of Cancer, Families of.

**Further Readings**


---

**Chile**

The Republic of Chile is a South American country that is located between the Pacific Ocean and the Andes mountains. Chile is considered one of South America's most stable and prosperous nations; however, it still must support the burden of cancerous diseases.

In Chile, cancer is the second cause of death after cardiovascular diseases, making up 20 to 25 percent of deaths annually in the country. In 2008, cancer killed 22,000 people in Chile.

The most common forms of cancer in Chilean men, according to the Chilean Ministry of Health (based on a population of 100,000), are stomach cancer at 26.9 percent, prostate cancer at 20.9 percent, lung cancer at 19.1 percent, colorectal cancer at 6.7 percent, liver cancer at 6.2 percent, and gallbladder cancer at 6.2 percent.

In women, the most common forms of cancer are breast cancer at 16.9 percent, gallbladder cancer at 15.3 percent, stomach cancer at 13.2 percent, lung cancer at 11.2 percent, colorectal cancer at 8.4 percent, and cervical cancer at 7.6 percent.

Cancer incidence is higher among the elderly and middle-aged in Chile, and despite the lack of studies addressing death incidences among different ethnicities, there is evidence of gallbladder cancer being more prevalent in the indigenous population.

**Risk Factors**

Statistical analyses show that risk factors for cancer (gastric, in particular) in the Chilean Provinces include latitude, fertilizer, and rainfall. Results indicate that one major factor influencing stomach cancer mortality rates for Chileans is exposure to sodium nitrate in the form of fertilizer. In terms of gastric cancer, sodium nitrate plays a factor, and studies indicate that the farmers exposed to this compound are experiencing higher death rates.

Male workers in actual contact with the soil, such as farmers (31.2 percent) and miners (18.7 percent), accounted for almost half of all male deaths (837 cases) from stomach cancer in Chile.

Folate depletion is associated with an increased risk of colorectal carcinogenesis. A temporal association between folic acid fortification of enriched cereal grains and an increase in the incidence of colorectal cancer in the United States and Canada has, however, been reported recently.

Studies have shown that colon cancer, may correspond with the beginning of the country's mandatory flour fortification program, which requires 220 micrograms of synthetic folic acid per 100 grams of wheat flour. Studies show an increase
of colon cancer after this program was put in place. Additional Chilean studies indicate that a high risk of bladder cancer is also an issue in the country due to very high levels of arsenic in Chilean drinking water back in the 1950s and 1960s. These findings are not surprising, researchers say, because the cancer would take decades to surface. It is very important that the Chilean health care system promote screening for this type of cancer.

Though the arsenic problem has been under control for more than two decades, people in the region of Antofagasta, in particular, are showing high bladder cancer rates, at 16 cases per 100,000 for men in the region, compared with less than six cases per 100,000 individuals for the other parts of Chile. For women, the bladder cancer rate is 13.5 percent and 2.5 percent, respectively. Finally, studies have shown that there may be a correlation between hypertension and breast cancer in Chilean women. Hypertension is widely spread across Latin America, and reducing this treatable disease may help reduce the risk for breast cancer in the future.

Challenges to Cancer Care
One major challenge for the oncology community in Chile is that many cancer specialists prefer to work for the private health care system in the country due to the fact that it offers higher salaries when compared to the public sector. Many oncologists migrate to the capital city of Santiago to work in these specialized private health care branches. An additional challenge is the lack of specialists in palliative care treatment.

The Chilean public health care system handles 75 percent of the country’s population. The public system has fewer resources than the private system, including less access to targeted therapies and pharmaceutical drugs. Poorer patients often do not have access to the private system, and low-income patients living in distant villages have even fewer opportunities and less access to specialized treatments than low-income patients living in large cities. Chile’s national records indicate there are only 61 registered medical oncologists with specialized degrees and 45 specialists in radiation oncology. The exact number of additional specialists is currently unknown.

Patients who cannot be treated in small cities are sent to the capital, though the country recommends that all large hospitals have their own specialized cancer treatment centers. The National Cancer Institute serves the capital, Santiago, but this location only serves particular areas of the city.

The percentage of cancer-related mortalities is still high despite recent progress on poverty. However, there are bright spots. The National Cancer Institute of Chile was recognized for bringing the survival of patients with cancer to 70 percent over the past five years.

Conclusion
The need for further education and prevention efforts surrounding cancer in Chile is pronounced. Fortunately, there are some efforts currently in place to encourage this education. Beginning in 2006, the Chilean Oncology Foundation has worked with the American Society of Clinical Oncology (ASCO) to present educational courses and symposia in Chile. The organization held its first Multidisciplinary Cancer Management Course (MCMC) in Santiago in 2006. In 2010, it held a second event in conjunction with the Train the Trainer course.

In addition, the Simposio Latinoamericano Gastroenterología Oncológica (SLAGO), or Latin American Gastrointestinal Symposium, was organized as ASCO–SLAGO joint symposiums in 2007, 2009, and 2011. Also in 2011, the first long-term international fellowship (LIFE) was awarded to a Chilean oncologist—Cesar Sanchez, MD—by the ASCO Cancer Foundation. These awards contribute to the development of cancer prevention and treatment in Chile. With positive moves in this direction, the cancer situation in Chile could improve in the near future.

Katie Moss
Independent Scholar

See Also: Breast Cancer; Colon Cancer; Stomach (Gastric) Cancer.

Further Readings
Hirsch, S., et al. “Colon Cancer in Chile Before and After the Start of the Flour Fortification Program
China

With a population of nearly 1.38 billion, China accounts for 19.3 percent of the world population and is the most populous country in the world. Because incidences of cancer often vary between less-developed and developed regions, China faces unique challenges from both domestic and international perspectives. Cancer is the leading cause of death in urban China and the second in rural China (after cerebrovascular disease), accounting for 27.79 percent and 23.62 percent of total deaths, respectively. Compared to other more-developed countries, many of the high-risk factors faced by Chinese people involve lifestyle factors (e.g., smoking). Additionally, the growing industrialization, Westernization of dietary practices, and other unique social determinants (e.g., demographics, ecological, environmental, and cultural variables), and genetic factors have contributed to cancer problems in China. In 2009, the central government announced a ¥850 billion ($128 billion), three-year health care reform plan aiming to provide affordable and universally available health care by 2020. Some of the reforms include plans to expand the medical insurance system, reimbursing essential therapies and upgrading health care facilities in local communities and rural areas.

Common Cancers and Risk Factors

Patterns in cancer incidences can provide insights into the impacts of lifestyle on cancer development. From 1973 through 1975, the top three deadly cancers were stomach, esophageal, and liver cancers. By 1990 to 1992, the top three were stomach, liver, and lung cancers. A comparison of major cancer sites between the China and the United States showed that China has higher cancer incidence rates in four sites amongst males (i.e., nasopharynx, esophagus, stomach, and liver) and six sites among females (i.e., nasopharynx, esophagus, stomach, liver, gallbladder, and cervix uteri). The cancer trends in China indicate that risk factors for cancer such as the deterioration of the environment and Western lifestyles have increased in China since the 1970s, whereas the aging population became a contributing factor as of the 1990s.

Cancer mortality in China has also been increasing rapidly and continuously since the 1970s, with urban China seeing higher rates than rural China. Currently, lung cancer is the leading cause of cancer deaths in urban areas, followed by digestive tract cancers (liver, gastric, esophageal, and colorectal cancer). In contrast, liver cancer is the leading cause in rural areas, followed by lung cancer and other digestive tract cancers.

Lung cancer increased 465 percent between the 1970s and the 2000s. The World Health Organization (WHO) estimated that, by year 2025, more than 1 million Chinese would be diagnosed with lung cancer each year. A major risk factor of lung cancer is smoking. As the largest tobacco producer and consumer in the world, China now has more than 350 million tobacco smokers, among whom are 15 million regular smokers and 40 million casual smokers between 13 and 18 years old. In recent years, although the smoking rate among males (around 60 percent) has decreased, it has increased among female smokers (around 4 percent), with greater increases among young females.

Liver, stomach, and esophageal cancers are the three next deadliest in China in since the 2000s. China accounts for almost 50 percent of the world’s liver cancer cases. Hepatitis B, a causal factor for liver cancer, is highly endemic in China, with a 2006 survey noting an HBsAg carrier rate of 7.18 percent in the overall population (i.e., an estimated 93 million HBV carriers, including 30 million patients with chronic hepatitis B).

Other infectious agents also contribute to high cancer rates in China. For example, *Helicobacter pylori* (H. pylori)—induced gastritis is the single strongest risk factor for stomach cancers. In China,
several reports have shown that *H. pylori* prevalence rates remain around 60 to 70 percent since the 1990s. In contrast, the infection rate is estimated to be around 25 percent in the West due to improved hygiene and widespread antibiotic use. A randomized clinical trial in Shandong, China, found that a short-term treatment with antibiotics to eradicate *H. pylori* was able to reduce gastric cancer incidents by almost 40 percent during a 15-year period.

Nutritional deficiency is believed to play a major role for esophageal cancer development, especially in high-risk areas in China. Other researchers also found that environmental carcinogens (e.g., nitrate nitrogen), dietary practice (e.g., drinking tea at high temperatures), and genetic factors contributed to the high incidence rate of esophageal cancer.

Nasopharyngeal cancer (NPC) is extremely common in southern China, accounting for 18 percent of all cancers in China. It is also known as Cantonese cancer because it occurs in about 25 cases per 100,000 in this region, 25 times higher than the rest of the world. Researchers argued that early childhood exposure to Epstein–Barr virus (EBV) infection and salt-preserved fish in southern China pose significant risk factors. Researchers have also suggested genetic susceptibility and shared environmental risk factors together may also contribute to the high incidence rate in southern China.

**Organizations and Events on Cancer**

Cancer control programs in China focus on prevention, early diagnosis, and treatment. In addition to hospitals that are responsible for general cancer care, nonprofit organizations also play major roles in cancer prevention. The Cancer Foundation of China (CFC) accepts nationwide donations and sponsors public service, education, and cancer research. The Chinese Society of Clinical Oncology (CSCO) focuses on enhancing continuing education in clinical oncology and developing advanced training programs, with targeted services in rural areas.

Similarly, the Chinese Anti-Cancer Association (CACA) is dedicated to the prevention and treatment of cancers by coordinating and supporting professionals across all cancer-related fields. Every two years, CACA hosts the Chinese Conference of Oncology (CCO), China’s most comprehensive and influential conference in oncology. In 1995, CACA designated the week of April 15 to be National Cancer Week. Since then, public events aiming to disseminate cancer-related information and knowledge have been held during this week to raise public awareness and to seek public support. The past annual themes included healthy lifestyles, fighting cancer together, food and cancer, caring cancer patients, early detection and treatment, breast cancer, antismoking, among others.

**Chinese Media Reports on Cancer**

Cancer information is widely broadcasted through mass media in China, with television and newspapers being the most common venues. In urban or suburban areas, the Internet is a common alternative, while in remote areas, radio provides a higher reach. Cancer information presented in mass media includes statistical reports, status reports, cancer trends, the latest cancer treatment and research, and human interest cancer-related stories.

In China, mass media is essential in raising public awareness about health-related issues. For example, cancer village is a social phenomenon first identified through media, resulting in significant shifts in public attitudes and governmental policies. In 2009, *Phoenix Weekly* had the cover story titled “Hundreds of Places in China With High Carcinogenic Risk,” which documented heavily industrialized rural communities that experienced higher cancer rates and cancer-related deaths than the national averages. A so-called China Cancer Village Map was drawn and, together with related stories, spurred great concerns from the government and the public, which in turn promoted more media coverage. After years of research and debates, the Chinese government officially acknowledged the existence of cancer villages in 2013. The public was educated about the issue, and citizen involvement was encouraged. Mass media played a critical role in the process, publicizing these environmental hazards and highlighting China’s struggle to balance public health and economic growth.

In China, entertainment education, providing health-related information through films and television programs, remains a powerful form of health outreach. For example, a highly acclaimed Chinese movie in 2008 named *If You Are the One* followed the story of the main character, who was diagnosed with melanoma. He conducts a living funeral for himself before his death and commits suicide by later jumping into the sea. The movie left a huge impression on many audiences and introduced
melanoma to the public, motivating a large num-
ber of audiences to visit hospitals to have their
moles examined and removed. Media also provided
extensive reports from medical experts, dispelling
common misconceptions.

Media has also played a significant role in cov-
ering Chinese celebrities in the 21st century who
have suffered from cancer. A good example is Luo
Jing (1961–2009), a famous anchor of the national
news program Xinwen Lianbo on CCTV. Luo was
diagnosed with lymphoma in 2008 and died the
following year. Social media is playing an increas-
ingly important role for cancer education as well.
A prominent computer scientist, Li Kaifu, was
diagnosed with lymphoma in 2013. He posted a
Weibo, the Chinese equivalent of Twitter, announc-
ing his fight against cancer. His story was reported
by numerous media outlets and became a popular
topic in the public sphere. Stories of celebrities with
cancer provide rich resources and opportunities for
public awareness and education.

Guoyu Wang
Elaine Hsieh
University of Oklahoma

See Also: Hepatitis B; Lung Cancer, Small Cell;
Media; Nasopharyngeal Cancer.

Further Readings
Chen Haoquan and Ding Sheng. “To Learn. The Outline
of Cancer Prevention and Control Programming
(2005).
Hatton, Celia. “Can China Tackle Soaring Cancer Rates?”

Chlorine

Chlorine (Cl₂) is a nonmetallic chemical element.
It appears as a greenish-yellow gas that is slightly
soluble in water and has a suffocating or choking
odor. Chlorine, in combination with other chemi-
cals, is an ingredient in commonly used household
cleaners and disinfectants and is used to disinfect
water, purify metals, bleach wood pulp, and make
other chemicals. Although chlorine is known to
have health effects such as irritation of the eyes
and lungs, less is known about chlorine and cancer.
Over the past three decades, however, studies have
linked chlorinated water and swimming pools to
increased cancer risk.

Chlorine is found in nature in the form of salt
(sodium chloride) in seawater, and an estimated
10(16) tons of chlorine are present in the world’s
oceans and saltwater seas. Chlorine is also found in
minerals in the Earth’s crust. It was discovered in
1774 by Karl Wilhelm Sheele, an 18th-century Ger-
man-Swiss chemist, via experiments that created a
reaction between hydrochloric acid and manganese
(IV) oxide. Chlorine was first used as a disinfectant
in 1850 when John Snow, who helped pioneer the
field of hygiene, used chlorine to disinfect London’s
water supply during a cholera outbreak when he
tracked down a well in Soho that he identified as
the source of the sickness.

Chlorine’s widespread use as a disinfectant, how-
ever, did not begin until the early 1900s. Eventually,
chlorine was developed to create a new standard
for water purification in the Western world. This
advance, designed to kill harmful microorganisms
in water, was hailed as one of the 20th century’s
major public health achievements. Chlorine is still
the most widely used chemical to disinfect public
drinking water in the United States.

Chlorine has not always been used to benefit
people. It was developed by the Germans as a weapon
and, with the outbreak of World War I, became one
of the first poisonous gases used in warfare. Soldiers
exposed to chlorine gas suffered severe burning of
the lungs and other body tissues.

Despite the beneficial uses of chlorine, various
health concerns about the element, particularly in
water supplies, have been raised. The first concerns
in the scientific community about the relationship
between cancer and chlorine in drinking water
were raised in 1974. Scientists discovered that the
combination of chlorine and organic compounds
could produce dangerous hydrocarbon by-prod-
ucts. Nevertheless, a number of follow-up studies
produced no definitive evidence that chlorination
of water increased cancer risk.

Then, in 1992, chlorinated drinking water was
linked to increases in rectal and bladder cancer
rates by researchers at Harvard University and the Medical College of Wisconsin. The risks were considered small. For example, the findings, published in the American Journal of Public Health, were drawn from the 1970s, when municipal drinking water supplies typically used higher levels of chlorine to treat water. Still, according to the 1992 study, approximately 9 percent of all bladder and 18 percent of all rectal cancer cases were associated with the long-term drinking of hydrocarbon by-products. Overall, this estimation translated into more than 20,000 new cases each year.

Chlorine reacts with other natural compounds in water to form four primary chemical by-products, trihalomethanes, haloacetic acid, bromate, and chlorite. All four are regulated by the Environmental Protection Agency (EPA) in terms of parts per billion allowed in municipal drinking water supplies. The trihalomethanes (THMs) are a group of four chemicals: chloroform, bromodichlorometh, dibromochlorometh, and bromoform. These chemicals are formed when chlorine in water reacts with naturally occurring organic and inorganic matter. THMs produce free radicals in the body that are considered extremely carcinogenic.

According to a report by the U.S. Council of Environmental Quality, people drinking chlorinated water have a 93 percent higher risk of getting cancer than people who drink water without contain chlorine treatment. Furthermore, the Environmental Defense Fund has noted that, despite the low level of THMs in drinking water supplies, scientists are concerned that their presence may increase the risk for many types of the human cancers in the United States. For example, a 2009 study conducted in Hartford, Connecticut, found that female breast cancer patients had significantly higher levels (50 to 60 percent) of organochlorines (chlorination by-products) in their breast tissues when compared to women without breast cancer.

Studies have also shown that there are other areas where even a higher health danger from exposure to chlorinated water may exist. Approximately two-thirds of human exposure to chlorine occurs in the shower, where people inhale steam and water is absorbed into the skin. A 2010 study report also pointed to indoor chlorinated swimming pools as potentially inducing DNA damage that could lead to cancer. In addition to the normal creation of chemical by-products produced by adding chlorine to water, chlorine in swimming pools can also react to various other substances, including urine and cosmetics, often found in public swimming pools.

Research has shown that chlorine can increase the risk of bladder cancer for pool swimmers. The study found that people who were in the water for 40 minutes experienced an increase in risk markers for DNA damage that could have potential carcinogenic effects. According to the researchers, swimming pool water is not worse than tap water in terms of producing potentially harmful by-products. However, swimmers are exposed to a massive dose of these by-products.

As for drinking water, the World Health Organization (WHO) developed guidelines in the later 1990s for the amount of THMs that are acceptable in water supplies. Although some studies show increased levels of some carcinogens in drinking water supplies, many scientists, including those at WHO, warn against the wholesale disuse of chlorinated water. For example, Peru stopped using chlorine in its water supplies. Shortly afterward in 1991, a cholera outbreak led to more than 300,000 Peruvians contracting cholera during the epidemic, which researchers showed was partly due to the water supply.

There has been an ongoing debate about whether or not using chlorine to disinfect water supplies actually increases the risk for some cancers, especially bladder and rectal cancers. Many scientists, including those at the EPA and the WHO, believe health risks due to the concentration of chlorine by-products in the water supply produced by the use of chlorine is minimal compared to numerous risks associated with inadequate disinfection of water supplies. Furthermore, the EPA has not classified chlorine for carcinogenicity. Nevertheless EPA regulations have continued to further limit THMs and other chlorine by-products in drinking water due to chlorination.

Many scientists, including those at the National Cancer Institute (NCI), continue to investigate the issue, and more recent studies have shown associations between long-term exposure to drinking water by-products with increased risk of rectal and bladder cancers. In addition, NCI collaborated with researchers in Spain for the Spanish Bladder Cancer study, which examined exposure via drinking, showering or bathing, and swimming pool use.
The study showed an overall twofold increase of bladder cancer in people who had estimated household levels of THMs above 49 milligrams per liter. Meanwhile, various carbonated and other filters have been devised to reduce the amount of chlorine exposure in home water supplies. However, their effectiveness in removing chlorine THMs remains in question, and some methods are absolutely not effective in reducing the amount of THMs.

In addition to preventing or reducing bacteria and other infectious agents in water supplies, chlorine is also used in some therapies. For example, the drug cisplatin is used to treat testicular, bladder, and ovarian cancers that have spread. Cisplatin contains a platinum atom with two chlorine atoms. Once the drug arrives at the cancer cells, the chlorine atoms separate from the cisplatin molecules and give way to two binding positions that attach to the cancer cells’ DNA, thus helping stop the cancer cell from multiplying and tumors from further developing. Some alternative medicine proponents have also touted the use of chlorine dioxide solutions to help cure cancer. However, the medical establishment has pointed out the dangers of taking such solutions, which are often equivalent to industrial-strength bleach and have the potential to result in respiratory failure.

David Petechuk
Independent Scholar

See Also: Bladder Cancer; Breast Cancer; Chloroform; National Cancer Institute; Rectal Cancer; Water Treatment; World Health Organization.

Further Readings


Chloroform

Chloroform is a trihalomethane, one of four chloromethanes. It is a naturally occurring organic compound with a history of industrial uses, though because of its health effects and contribution to ozone depletion, it is being phased out as a component of refrigerants. Chloroform is naturally produced by both seaweed and fungi. It does not bioaccumulate in marine life, so its production by seaweed does not mean it is found in seafood. It is also produced synthetically. Industrially, chloroform is used mainly to make chlorodifluoromethane, which is used as a propellant and refrigerant, mainly in developing countries that are not signatories to climate change treaties limiting the use of hydrochlorofluorocarbons. The Montreal Protocol, to which the United States is signatory, requires the United States to reduce its consumption of hydrochlorofluorocarbons, and it has been phased out mainly in favor of propane and blended mixtures. The Environmental Protection Agency classifies chloroform as a Group B2 probable human carcinogen.

Trihalomethanes like chloroform are not only environmental pollutants that deplete the ozone layer and pose risks to the water supply, but most of them are known to be carcinogenic. Chloroform is produced through a haloform reaction in swimming pools when the chlorine in the water comes into contact with organic substances—not just urine, but the sweat, hair, and microscopic skin particles that are inevitably washed from swimmers’ bodies.
into the water. Some of the chloroform becomes vaporized in the air and may be inhaled, but most of the absorption is actually through the skin. Studies have found that adolescents who spend a lot of time in public pools—which host a greater number of swimmers than most home pools and thus more haloform reactions generating chloroform—have demonstrably lower testosterone levels.

Chloroform is perhaps most familiar from popular culture, in which a staple of crime fiction since the late 19th century has been the use of a chloroform-soaked rag by a criminal to induce their victim to pass out almost instantaneously (usually with no ill effects upon waking up). This pulp-fiction trope was inspired by the real-life uses of chloroform in turn-of-the-century crimes, both to render victims unconscious in order to rob them and as an instrument of murder. Even today, chloroform is sometimes used by pedophiles to incapacitate their child victims. However, the effect is not as rapid as is depicted in film and television. It takes at least five minutes of inhaling chloroform fumes to pass out, which is unsurprising when one reflects on the fact that even anesthesia in safe doses does not knock the patient out instantly.

The soaked rag trope was also, to be fair, influenced by the 19th-century use of chloroform as an anesthetic, first in Europe, and briefly in the United States, before its health effects were noted. Like other early anesthetics, it was also used as a recreational drug to induce euphoria.

Chloroform is, however, quickly absorbed and metabolized by the body (and eliminated mainly by the lungs). Either inhalation or ingestion causes depression of the central nervous system at high enough doses, followed by coma, respiratory depression, and death by respiratory or cardiac failure. Use as anesthesia was discontinued because some patients experienced nausea, vomiting, or jaundice. In people who have died as a result of chloroform poisoning, liver necrosis is observable in the autopsy.

Chloroform is believed to cause liver and kidney cancer and has been shown to cause tumor formation in rats. Ingesting amounts of chloroform in small doses over a prolonged period of time, because of chloroform in the workplace, in the water supply, or airborne because of evaporation from nearby water sources containing sufficient chloroform, forces the liver and kidneys to gradually take damage as they process too much chloroform, eventually inducing DNA damage during mitosis and the formation of a tumor. Chloroform can be found in drinking water for reasons similar to its presence in swimming pools: The chlorine used to make the water potable interacts with biological materials. This may find its way into food and beverage products that use chlorinated or tap water in their production. People who live near hazardous waste sites, sanitary landfills, swimming pools, or pulp and paper mills may have chloroform in their drinking water from groundwater seepage or may have it in their air.

There is no definite information about the cancer risk of chloroform inhalation. Studies are firmer on the probable association between chlorinated drinking water, which contains chloroform, and cancer of the large intestine, rectum, or bladder, but there are no studies of human consumption in which chloroform is isolated from the other constituents of chlorinated drinking water. Nevertheless the EPA, which is fairly conservative on such matters, considers chloroform carcinogenic in all routes of exposure.

Bill Kte’pi
Independent Scholar

See Also: Chemical Industry; Pollution, Air; Pollution, Water.

Further Readings
City of Hope

The City of Hope National Medical Center, located in Duarte, California, is a clinical research center, hospital, and graduate medical school. A private not-for-profit organization, the City of Hope was originally founded to treat tuberculosis patients and is well-known for its research prowess, especially with regard to cancer and cancer-related conditions. Founded by Jewish groups, the City of Hope provides nonsectarian services to patients from across the United States. Working with a variety of partner institutions and organizations, the City of Hope is home to the Beckman Research Institute of City of Hope.

Tuberculosis was a major health concern during the latter parts of the 19th and early 20th centuries. As tuberculosis (also known as consumption) is a highly infectious disease that often attacks the lungs, the public desired treatment options for tuberculosis patients, both to provide them with relief and to protect uninfected members of the public. To that end, a variety of treatment centers sprang up in the southwestern United States as a result of the belief that the arid climate there would provide health benefits to those afflicted with tuberculosis. The Jewish Consumptive Relief Association in 1913 raised funds to purchase 10 acres of land in Duarte, California, a rural community located approximately 15 miles northwest of Los Angeles. In 1914, two tents were erected, one for tuberculosis patients and the other for medical providers. This sanatorium, which was immediately successful, soon became known by the nickname City of Hope.

Through the end of World War II, tuberculosis treatment remained the focus of the City of Hope medical providers. Vaccines that inoculated individuals from tuberculosis were introduced at the end of that conflict, at which time the City of Hope’s focus turned to other medical problems. Beginning in 1946, City of Hope Executive Director Samuel Golter began a series of actions intended to transform the institution from a sanatorium into a full-service medical center, supported by a research center and graduate education. The institution’s formal name was changed from Los Angeles Sanatorium at that time, and the research center was founded in 1952, with the graduate school of biological sciences first accepting students in 1953. Golter’s successor, Ben Horowitz, assumed leadership of the City of Hope in 1953 and helped to grow the institution’s cancer research and treatment capacities. With an annual budget of $600,000 when Horowitz assumed control in 1953, the City of Hope’s annual budget had grown to more than $100 million by the time he retired in 1981.

Research

In 1983, the City of Hope received a grant from the Arnold and Mabel Beckman Research Foundation. These monies were used to establish the Beckman Research Institute of City of Hope, which is now the label used for all of the larger institution’s research efforts. Already named a clinical cancer research center by the National Cancer Institute, the Beckman Research Institute permitted the City of Hope to expand its research efforts greatly. The City of Hope has great expertise with specific types of cancer, including that of the brain, breast, gastrointestinal system, gynecologic areas, thorax, and urological systems.

The City of Hope has also conducted extensive work with patients suffering from leukemia and lymphoma. In addition to its cancer research, the City of Hope has also been a leader with regard to studies involving other diseases and medical conditions, including diabetes and human immunodeficiency virus (HIV) infection and acquired immunodeficiency syndrome (AIDS).

Researchers at the City of Hope have been responsible for several breakthrough discoveries that have received international attention and that have greatly influenced patient care throughout the world. For example, scientists at the City of Hope were the first to produce synthetic insulin, work that was later licensed to Genentech for development into commercial products including pharmaceuticals. A founding member of the National Comprehensive Cancer Network, the City of Hope works with 20 other U.S.-based cancer treatment centers to develop clinical practice standards for patient oncological treatment. Membership in this network also permits City of Hope researchers the opportunity to cooperate and collaborate with scientists at other member institutions, including St. Jude’s Children’s Research Hospital, Fox Chase Cancer Center, and the University of Texas MD Anderson Cancer Research Center.
Patient Care and Outreach
Despite this growth, the City of Hope has maintained an emphasis upon patient care that is unusual among other research-centered hospitals. The City of Hope views itself as a bench-to-bedside institution. This means that the City of Hope practices what is also sometimes referred to as translational medicine. In these situations, a hospital engages in biomedical and public health research that aims to improve the health of individuals and the community. Unlike institutions that are purely committed to research, however, the City of Hope and like hospitals then translate findings made in their laboratories into diagnostic tools, medicines, procedures, policies, and education that can benefit the patients they serve. The City of Hope’s hospital offers 183 beds to serve prospective patients. Patients who are admitted to the City of Hope are served by more than 675 registered nurses and 30 licensed practical nurses. Annually, the City of Hope also provides more than 145,000 outpatient visits and 3,260 inpatient surgeries. For patients in need of these services, the City of Hope also provides 40 temporary, on-site residential housing units, which provide palliative and hospice services as needed.

The City of Hope maintains several centers and institutes that assist it in its efforts to provide outreach regarding its discoveries. In addition to the Beckman Research Institute, the City of Hope is also the home to the Center for Biomedicine & Genetics and the Irell & Manella Graduate School of Biomedical Sciences. The Center for Biomedicine & Genetics serves as a manufacturing facility for the City of Hope. Specializing in the production of pharmaceutical-grade materials for use in experiments and patient treatment, the Center for Biomedicine & Genetics provides support to clinical researchers with regard to clinical trials and other translational medicine needs. The Irell & Manella Graduate School of Biomedical Sciences provides graduate-level study in cellular, chemical, and molecular biology. Seen as a way to train physicians and others to become research scientists with special expertise, the Irell & Manella Graduate School of Biomedical Sciences has gained a stellar reputation over its existence, and its graduates take positions in higher education, at research hospitals, and in private industry.

Stephen T. Schroth
*Towson University*

---

See Also: American Cancer Society; National Cancer Institute; St. Jude Children’s Research Hospital; University of Texas MD Anderson Cancer Center.

Further Readings

Clinical Trials
Cancer clinical trials are trials, or tests, designed to rigorously test the efficacy and safety of a procedure, treatment, screening, or preventive measure designed for a specific type of cancer. Cancer clinical trials are essential to the discovery of new technologies useful for the prevention and treatment of cancer through gene therapy, pharmaceuticals, radiation therapy, and surgical procedures.

The cancer clinical trial is a research study involving individuals as human subjects. In most cases, patients are randomly assigned to either a control (i.e., those receiving traditional cancer care) or an experimental group (i.e., those receiving a new or altered treatment or intervention). Patients participate in cancer clinical trials voluntarily and the results of these trials, or studies, is published in peer-reviewed publications. In this chapter, the key players, types, phases, execution of, and special considerations surrounding cancer clinical trials will be discussed. The cancer clinical trial is a necessity for the continuance of the improvement of cancer control.

Key Players in the Cancer Clinical Trial
Cancer clinical trials function with the assistance and leadership of many parties. To take a cancer clinical trial from start to finish, principal investigators (PIs), coinvestigators (Co-Is), physicians, pharmacists, research nurses, research coordinators, as well as a number of other allied and research professionals must collaborate effectively. Interdisciplinary care is now considered a necessity in the cancer clinical trial.
The patient is the key focus of any cancer clinical trial. Patient participation in a cancer clinical trial is completely voluntary; however, individuals must meet very specific inclusion and exclusion criteria to ensure they are eligible to participate in the study. The location of the patient’s cancer in or on the body, cancer stage, her or his age (pediatric vs. adult), and overall health generally determine study eligibility. Pediatric patients, compared to adult cancer patients, are more likely to participate in a cancer clinical trial. According to the National Cancer Institute (NCI), about 90 percent of pediatric cancer patients under age five and about 60 percent of pediatric patients under age 15 diagnosed with cancer participate in clinical trials. Two percent of cancer patients between 20 and 39 years of age participate in cancer clinical trials. The most cancer treatment success has occurred for pediatric cancer patients, likely because of high participation rates.

PIs and Co-Is are responsible for the design, submission, execution, management, and analysis of the cancer clinical trial. PIs and Co-Is typically possess either or both a PhD or an MD (or equivalent) and have extensive prior research experience. PIs and Co-Is are familiar with the landscape of applying for, managing, and receiving monetary grants to conduct cancer clinical trials. PIs are responsible for working with the institutional review board (IRB), the committee charged with adjudicating the beneficence and fairness associated with a research trial, and must respond to any internal or Food and Drug Administration (FDA) audits. At any point in time, a cancer clinical trial can be audited by an internal (i.e., the IRB) or external agency (e.g., the funding agency, FDA, Cancer Therapy Evaluation Program [CTEP] via the NCI, etc.). PIs are also charged with training and supervising members of their research teams and ensuring patients in their studies are treated with the highest-quality health care.

Pharmacists play vital roles in cancer clinical trials requiring pharmaceutical treatments. Research pharmacists maintain drug and study protocol procedures and store and manage pharmaceuticals. They provide expert advice through the length of the trial. Clinical research coordinators (CRCs) are responsible for organizing the day-to-day operations associated with executing the clinical trial. Some CRCs may be registered nurses (RNs). CRCs recruit patients, gain patient consent, schedule patient visits, collect data, manage data or specimens, and ensure the study is completed according to protocol. Some CRCs assist in developing research trial protocols. The CRC grasps not only the design of the cancer clinical trial but is an expert in carrying out procedural details. CRCs typically work hand in hand with the nurses staffing the research team.

Other research staff will likely be involved in the cancer clinical trial, as well, and often play more behind-the-scenes roles. Other staff aiding in the cancer clinical trial process may include biostatisticians, research specialists, compliance specialists, dieticians, social workers, and grants managers. These allied health science professionals provide additional expertise to the team and may help the team analyze and publish results (e.g., research specialists or associates and biostatisticians) on various types of clinical trials in different phases.

**Types of Cancer Clinical Trials and Trial Phases**

There are five primary types of cancer clinical trials (prevention, treatment, screening, diagnostic, and quality of life or supportive care), each performed for a variety of reasons. Unlike in most cancer clinical trials, prevention trials may include healthy participants in order to test interventions aimed at precluding cancer cell development. Other cancer prevention clinical trials include cancer survivors that participate in interventions aimed at preventing cancer recurrence. In treatment trials, investigators test new procedures, techniques, drugs, or combinations of drugs. The goal of the treatment trial is to discover the treatment’s efficacy. In screening trials, investigators test the safest way to detect cancer, even in early stages. Participants in screening trials may be healthy patients, as well, but generally have a higher-than-average risk of cancer. The goal of the diagnostic trial is to identify, or diagnose, cancer with more precision; therefore participants in diagnostic trials have cancer signs and symptoms. Finally, investigators examine how different types of care can best improve the lives and well-being of cancer patients at various cancer stages in quality-of-life or supportive care cancer clinical trials.

Cancer clinical trial phases are the stages of a cancer clinical trial nested inside a given cancer clinical trial. The NCI describes the four phases (I through IV) of the cancer clinical trial and denotes a pre-phase. The pre-phase occurs prior to the cancer
clinical trial and is also known as a pre-phase I trial, Phase 0, pilot study, or exploratory new investigational drug (IND) study. The purpose of the Phase 0 study is to test an IND on a small number of human participants. Generally, between 10 and 15 patients are provided a drug with a limited dosing duration (often only one course is given), wherein no therapeutic benefit is intended. The goal of Phase 0 is to provide information about how the IND works and increase treatment success rates.

The goal of Phase I of the cancer clinical trial is to determine whether or not the drug is safe and a therapeutic dose of the pharmaceutical being tested. At this stage, investigators seek to examine the side effects of a trial drug. Participation in Phase I trials is limited to a small number of patients (near 20). These patients generally have advanced cancer not responding well to standard treatment (if a treatment does exist).

During Phase II, investigators measure the efficacy of the intervention (generally an anticancer drug) and continue to examine the safety of the intervention. Traditionally, Phase II includes somewhere between 50 and 100 patients, but occasionally, as many as 300 individuals will participate in the trial. Randomization is an important research design feature of Phase II. If a treatment is demonstrated to be ineffective in Phase II, investigators will discontinue the line of research, but if they demonstrate efficacy, a trial moves to Phase III.

The goal of Phase III cancer clinical trials is to examine the efficacy of the new interventional treatment compared to the standard treatment traditionally given for a given cancer type. Clinical trial investigators compare the side effects of the new intervention with those associated with the current treatment standard. Phase III of the cancer clinical trial involves several hundred patient participants—up to several thousands of patients—randomly divided into the control or experimental group. The randomization process, or randomization, ensures patients assigned to each group are essentially equivalent. Finally, in Phase IV, patients undergo cancer treatment approved by the FDA. Phase IV is often referred to the post-marketing surveillance trial and is sponsored by a pharmaceutical company. Hundreds to thousands of patients participate in the fourth phase, and generalizability (i.e., measuring and reporting efficacy of an intervention in the general population) is the goal of Phase IV cancer clinical trials. In some occasions, investigators will examine the efficacy and safety of pharmaceutical treatment for a condition beyond the drug’s intended purpose during Phase IV.

**Designing and Executing the Clinical Trial**

The key players of the cancer clinical trials team must design and execute the cancer clinical trial per strict guidelines and follow the protocol written by the PI and Co-Is. The cancer clinical trial begins with the investigators leading the efforts in writing a study protocol. The study protocol outlines all the steps, from start to finish, that the research team will follow to complete the cancer clinical trial. The protocol includes prior research relating to the cancer study in question; goals to be achieved and methods for achieving those goals; recruitment inclusion and exclusion criteria for participants; plans for treatment and managing adverse events; strategies for data analysis; and ensuring the proper protection of human subjects and human subjects’ personal health information. Protocols will vary slightly depending on the type of cancer and trial phase to be examined or conducted.

Research teams must complete research training and receive IRB approval to begin the study. Patients must be informed of their health information privacy rights (HIPAA), and research team members ensure their information is kept secure. Patients must be recruited to participate in the clinical trial. Recruitment is a difficult process that will last most of the clinical trial. The NCI outlines five steps PIs must enact to recruit patients: (1) determine the number of patients needed to complete the trial, (2) outline strategies the research team will employ to ensure just and safe recruitment, (3) screen potential participants for eligibility, (4) enroll and inform eligible participants, and (5) monitor enrollment procedures and results for quality. Some cancer clinical trials are recruited in an outpatient setting, wherein their provider refers them to the study, and other patients search online or government resources to find and enroll in an applicable trial.

Some physicians are very encouraging of cancer clinical trial participation and make appropriate referrals knowing the trial may help a patient and further scientific advancement. Unfortunately, some providers inadvertently serve as a barrier to
clinical trial participation because they are unaware of existing trials to recommend to patients. Some physicians may be hesitant to recommend clinical trials as they assume participation will lead to an increased administrative burden on their practice, which generally is not the case.

The decision-making process in choosing to enroll in a cancer clinical trial can be quite involved for most patients. Patients should consider (1) how the trial may benefit them (if at all); (2) their goals, values, and preferences surrounding treatment, healing, and mental health; (3) their current health status; (4) their life stage goal; and (5) their family's needs or desires. Socioeconomic status, age, racial or minority status, and comorbidity factors (i.e., other health concerns) predict whether or not an individual will enroll in a cancer clinical trial. Many PIs work especially hard to recruit minorities (e.g., Latinos and African Americans), adolescents, adults over age 65, and individuals of lower socioeconomic status. These groups are underrepresented in cancer clinical trials and often face barriers to entry into the health care system in general.

Once recruited for a clinical trial, participants are assigned to either a control or treatment group and subsequently receive standard cancer treatment or investigational treatments, procedures, screenings, and so on. The types of pharmaceuticals or interventions a patient receives is dependent upon the trial type and phase. Not all cancer clinical trials involve drugs, and some may involve alternative medicine or radiation. Importantly, placebos are rarely used in the cancer clinical trial; ethically, patients assigned to the control group must receive standard treatment as they are not given the experimental drug.

Throughout the length of the study, research coordinators or research nurses do continuous monitoring and care of patients. Health care providers assess the patient’s experience of side effects and record them in health record files. Patients may be asked to follow strict procedures regarding self-care should they participate in a clinical trial wherein periods of a treatment or intervention do not occur in hospital or clinical settings. No matter the trial, the research team must (1) keep participants informed of their health status in general and with regard to treatment or intervention, (2) make themselves available to participants to answer any questions, and (3) join patients in the clinical trial journey. Often, members of the clinical research team will follow up with participants regarding their overall health after the completion of a trial.

During the cancer clinical trial, and especially at the conclusion, the investigative team measures and writes about the results of the trial. These results, in manuscript form, are released, and standards of care are changed for the better. A cancer clinical trial—from start to finish—can last for several years, as bringing a pharmaceutical even to Phase I can take months up to a couple years.

Clinical Trial Sites

Cancer clinical trials are typically conducted at inpatient hospital facilities (e.g., academic hospitals, medical centers, or clinics) depending on the nature of the trial or treatment required. Trials can be conducted at one location (single site) or multiple locations (multicenter trial).

The NCI currently designates 41 cancer clinical trial locations as comprehensive cancer centers (CCCs), and another 27 are NCI-designated cancer centers. CCCs are generally located inside academic medical centers and are given the distinction of CCC due to research and treatment excellence. CCCs provide physicians and researchers with expert training, deliver the superior treatment and care to patients (minus seven centers not providing cancer care), focus on community outreach and education, and house interdisciplinary scholars. CCCs are typically located in areas including special and minority populations. NCI-designated cancer centers are not considered the pinnacle in cancer research but are nevertheless quite prestigious.

The National Health Institute (NIH), via NCI, funds and provides support to the Community Clinical Oncology Program (CCOP) Network. The CCOP Network allows physicians at community hospitals and facilities to participate in cancer clinical trials. Thus, patients do not necessarily have to participate in a cancer clinical trial at a CCC or other large research institution. Rather, patients can enroll in a trial wherein care is provided by a physician at a community hospital using the same treatment or intervention protocol as is used at a CCC. This is especially helpful for patients living in underserved regions, like rural areas.
Funding and Sponsoring the Clinical Trial

While participating in a cancer clinical trial, patients may be responsible to pay for standard or routine cancer treatment and care, including provider visits, laboratory tests, hospital stays, or imaging tests. However, patients are not responsible to pay for investigational treatments, examinations, or procedures not traditionally considered cancer standard of care. In the latter case, PIs use funds from various sources to pay for these treatments and for the personnel required to complete a cancer clinical trial. PIs often apply for and receive grant funds to conduct cancer clinical trials from the NCI, the Department of Veterans Affairs, and the Department of Defense. The federal government appropriates billions of dollars to cancer clinical trial research each year (e.g., $4.8 billion for fiscal year 2013).

Along with receiving funds from government agencies, PIs may conduct cancer clinical trials through monies received from volunteer organizations, foundations (e.g., Damon Runyon Cancer Research Foundation), or biotechnology or pharmaceutical groups (e.g., AstraZeneca or Pfizer). Biotechnology or pharmaceutical groups work with PIs, physicians, and pharmacists to conduct industry-sponsored cancer clinical trials. The biotechnology or pharmaceutical group generally pays for the study drug, manages the testing and handling of biological specimens, offers to cover all or some of IRB processing fees, and reimburses study staff for their time.

Benefits and Drawbacks to Cancer Clinical Trials

A number of benefits and drawbacks to conducting and participating in cancer clinical trials are worth noting. First, experts especially encourage patients to consider the benefits and potential drawbacks associated with cancer clinical trial participation. Patients choosing to participate in any trial phase still will obtain the minimum standard of care per their cancer type. Many patients choose to enroll in a cancer clinical trial after exhausting unsuccessful treatment options. Some find success in the cancer clinical trial treatment, but others do not. No matter the outcome, however, many patients do choose to participate in the trial to advance science and help others. Additionally, cancer clinical trial participation can provide patients with additional health services (e.g., diagnostics, devices, etc.) not generally covered by insurance plans. Those managing the cancer clinical trial must make patients fully aware of any potential known drawbacks to trial participation.

Cancer patients do face risks when enrolling in a clinical trial—the efficacy of a cancer clinical trial treatment or intervention is never guaranteed. Furthermore, at times, the side effects of an experimental treatment could be worse than those of the standard treatment. Some research demonstrates the risk of a treatment not working deters some patients. Negative attitudes toward trials or the medical community, perceived travel time and cost, as well as concerns over health insurance coverage can also discourage trial participation.

Albeit of lesser importance, clinical trial participation also benefits and presents risks to PIs and the research team. Through carrying out the cancer clinical trial, PIs gain even more scientific expertise and can help future or current cancer patients. Similarly, PIs and members of the research team can develop advanced research skills and train others to conduct the next generation of cancer clinical trials. As mentioned, not all trials are successful,
Clothing intersects with cancer in numerous ways. Cancer treatment reduces body movement, so loose-fitting clothing is needed for cancer patients and survivors. Breast cancer survivors benefit from clothing that projects a normal appearance. Chemicals, airborne fibers, and dust created in the manufacture of clothing can be carcinogenic.
and an occupational hazard for clothing workers. For some time, it was thought that men's tight-fitting clothes were a cause of testicular cancer, although there is no current evidence to support this concern. This entry presents the positive side of clothing as a protector of the body against cancer. But to protect, clothing must be comfortable, affordable, and stylish, or it will find resistance in being used. This resistance can be countered with educational campaigns and through supervision at workplaces, schools, and public outdoor venues. Protective clothing in factories and foundries, such as safety helmets, gloves, and boots, is also resisted but becomes habitually used through a combination of safety campaigns and supervision.

The skin is the largest organ of the body and a major site of cancer. In the United States, there are a million cases of skin cancer each year. The world’s highest skin cancer morbidity is reported in Australia, where 400,000 cases are treated annually. The main cause of skin cancer is from exposure to the sun’s ultraviolet rays, which are highly energetic and damage the skin cells’ DNA. Fortunately, skin cancer can be treated, and the patient can fully recover if the cancer is treated early enough. However, cancer prevention rather than treatment is the most recommended approach.

In recent decades, the concern has substantially increased that sun exposure is a major source of skin cancer and a drain on health resources. The main countries experiencing this concern are Australia and the United States. The reduction in the Earth’s atmosphere’s protection against ultraviolet rays was first noticed in Australia, where light-skinned people of European stock were found to be at risk. The ozone hole noticed over Australia was the apparent cause of that increased risk. Atmospheric ozone provides a shield against damaging ultraviolet rays. The loss of ozone removed that protection and led Australia to become the world’s leading advocate for reducing skin cancer through seeking solutions for excessive sun exposure and its carcinogenic effects.

There are four ways to reduce skin cancer from the sun: (1) avoid exposure to the sun by remaining indoors; (2) cover the skin with lotion that blocks the passage of ultraviolet rays; (3) cover the body with protective clothing and the face with a broad-brimmed hat; and (4) restrict sun exposure to hours when the sun is low in the sky and the distance the sunlight must travel through the atmosphere increases its filtering of harmful rays. While sunscreen is more recognized, Australia has led in promoting protective clothing as a method against sun damage.

The advantages of using clothing for skin protection in principle include ease of use, permanence (it doesn’t wash off), and preventing much harmful ultraviolet rays from reaching the skin. Socially, completely covering the body may be seen as an act of modesty. The disadvantages would include limitation of movement, retaining heat on hot days, cost, and social issues of style.

While it would seem clear that covering the skin with cloth would protect against the sun, there are unseen issues with different types of cloth and how they are worn. Light fabrics may not shield the skin in the way anticipated. In studies, one-third of summer fabrics were found to provide an ultraviolet protection factor (UPF) of less than 15. Fabrics with loose weaves can admit the sun. Stretching fabric over the skin can reduce its coverage. Questions about how a fabric responds to perspiration or immersion in water have arisen, with most fabrics losing a majority of their protection when wet. Tight weaves and dark dyes protect more but are uncomfortable in heat. The result has been the development of standardized tests to measure the protective factor of cloth that are the equivalent of the UPF ratings for sun lotion. This has been of particular concern for clothes used for beachwear and outdoor recreation active wear. Parents have been concerned about their children's protection as well. Clothing is now marketed with its protective rating. In addition, chemicals that increase a fabric’s protective strength have been developed and are on the market. They too are rated according to the UPF standard system as well as the number of washing cycles the chemical effects are measured to withstand.

The disadvantages of wearing protective clothing vary with the age of the wearer. Children's skin has been found to be the most vulnerable to sun exposure and resulting skin cancer later in life. So parents have been responsive to public health messages to cover up their children's skin. Schools in Australia have found the parents to be effective advocates for policies to reduce the time at play outdoors, keep the children covered with proper clothes and hats, and provide shade sails.
against playground sun. Children may resist being covered with clothing on hot, summer days and, unless supervised, are likely to remove them. But if parents and teachers are consistent in supervising young children and demanding that they use protective clothing, the habits that they establish will be long lasting. Safety campaigns with protective clothing used in industry have found that consistent supervision will establish those safe habits, along with messages that attempt to change the workers’ orientation to safety. A safety culture will promote the value of preventive actions.

Young adults value their bodies and also resist the use of clothing that cover those parts of themselves they perceive as attractive and want to display. The literature that has appeal to young people is both a reflection of their values and a leader in setting trends and styles. A study of women’s photographs in Australian magazines found that messages contrary to those of public health campaigns were prevalent. The measures of the inherent messages in these photographs included the tanning of the model’s skin, the amount of bodily exposure, whether the model was in the sun or shade, and whether a hat was worn. However, there was no way to discern whether the model had used sunscreen lotion. The messages appeared to be that tanning, bodily exposure, and sunning were socially acceptable and even desirable. Another concern was the finding that the older models were more likely to be shown with less tanning and greater skin covering. So it appeared that the values of young people, who are most vulnerable to skin damage, are the least supportive of prevention. One way that the protection message can communicate with young people substitutes premature skin aging and wrinkles for the risk of skin cancer. By portraying tanning and burning as a precursor to looking old, the risk communicates directly to the target population.

Among the older population, skin damage is likely to be already apparent in skin aging. Covering the skin with clothing is still important for this age, and public health campaigns are needed to directly confront the skin cancer risk these people face from repeated sun exposure. Studies can be done of the effectiveness of public health campaigns to cover up by observing people’s behavior. Australian research work has found some evidence that these campaigns are effective, but after they are over, the public tends to revert to their former behavior. The problem appears to be a disconnect between what people know is good in the long term for cancer prevention and short-term advantages of style and conformity to youthful social values.

There are ways to address this problem. Public health campaigns to cover up can be measured for their effectiveness, and the more-successful messages can be identified and perfected. Locations where attention is needed can be identified for a public health response. Australian studies have found two venues where people are most likely to admit experiencing sunburn, an indicator of excessive exposure. Beaches and sports venues each had a 22 percent admission of sunburn. Prevention messages are needed at both venues and can be targeted to their audiences. With concerted efforts at public health education and supervision where appropriate, the public can learn necessary protective clothing habits.

Keith R. Johnson
Oakton Community College

See Also: Skin Cancer, Melanoma; Skin Cancer, Non-Melanoma; Solar Radiation; Sun Exposure (Australia).

Further Readings

Coal Industry

Coal is a brownish-black sedimentary rock that is the most abundant fossil fuel on earth. Coal is composed of carbon, oxygen, hydrogen, nitrogen, sulfur, and a mixture of minerals. The carbon
and hydrocarbon content of the coal rock make it combustible and an accessible source of energy. Statistics from the World Coal Association indicate that, globally, coal provides around 30 percent of the world’s primary energy needs and provides approximately 40 percent of the world’s electricity.

Coal is found on every continent, with recoverable reserves that are economically extractable in about 70 countries. The largest coal reserves are found in the United States, Russia, China, India, and Australia. Approximately 25 percent of the world’s coal content can be found in the United States. The majority of coal mined in the eastern United States is located in an area of largely rural and mountainous terrain that extends from southern New York to Mississippi, known as Appalachia. Specifically, eight states are considered the Appalachian coal mining region: Alabama, Kentucky, Maryland, Ohio, Pennsylvania, Tennessee, Virginia, and West Virginia. The majority of coal mined in the western United States is found in the Powder River Basin, which includes the states of Montana and Wyoming. However, several other states have active coal mines that perform underground and surface operations.

Estimates indicate that, at the current rates of production, there is up to 200 years of coal in reserves worldwide. However, with improvements in mining techniques and technology, reserves that are currently inaccessible may be able to be reached and extracted more easily in the future. Due to the abundance of recoverable coal reserves and the longevity of the coal mining industry, it is important to remain cognizant and responsive to the health and environmental impacts of coal mining and what risk-reduction methods can help minimize the occurrence of these associated health consequences. Therefore, after discussing types of coal and coal mining, this entry focuses on environmental and societal concerns of mining coal and control methods in place to alleviate these concerns.

**Types and Uses of Coal**

Coal forms from years of intense physical and chemical pressures that act to transform the Earth's vegetation into peat and eventually coal, a process known as coalification. Coalification is classified by rank, the degree of transformation of the original plant material to carbon. There are four types of coal: lignite, subbituminous, bituminous, and anthracite. These four types of coal vary in rank from lowest percentage of carbon to the highest percentage of carbon, with the lower-rank coal having more hydrogen and oxygen.

Lignite coal is the least mature and softest of the coal types, having been exposed to the extreme temperature and pressure for the shortest amount of time. Lignite coal is more accessible because it is closer to the surface. However, lignite coal also has the highest sulfur content of all the coal ranks. So, when combusted, it results in the release of elevated amounts of pollutants such as sulfur dioxide (SO₂). According to the Lignite Energy Council, about 79 percent of lignite coal is used to generate electricity, 13.5 percent to generate synthetic natural gas, and 7.5 percent to produce fertilizer.

Subbituminous coal, like lignite, is found closer to the surface and thus is cheaper to mine than higher-ranking coal. Similar to lignite, the main use of subbituminous coal is power generation. Both lignite and subbituminous coal are softer coals but subbituminous has been exposed to the extreme conditions for a longer period of time. Subbituminous coal generally has lower sulfur content and, as a result, burns cleaner than lignite. Further transformation, resulting from longer exposure to extreme temperature and pressure causes the lower-ranking coal rock to harden and become darker. As a result, the last two coal ranks are known as the hard coals.

Bituminous coal is the most plentiful type of coal, making up approximately 50 percent of the world’s coal reserves. Bituminous coal consists of two different types: thermal and metallurgical. While thermal coal is used in power generation, metallurgical coal primarily is used in steel and iron production.

Anthracite coal is the hardest, has the highest rank, and contains the highest carbon content of the four coal types. This type of coal is mostly associated with domestic and industrial heating. The World Coal Association indicates that there is less than 1 percent of anthracite reserves in the world.

Although coal is primarily used for power generation, several industries benefit from coal, including alumina refineries, paper manufacturers, and chemical and pharmaceutical industries. For example, coal is necessary to produce cement and steel. In addition, thousands of products have coal or coal by-products included in their component makeups, such as soap, plastic, nylon, aspirin, and dye.
Types of Coal Mining

The coal industry utilizes two methods to mine coal: surface mining and underground mining. Surface mining, also called opencast or open-pit mining, is used when the coal seam is near the surface and the coal can be recovered after the overlying soil and rock, referred to as overburden, is removed. Once the overburden is removed, large pieces of equipment including draglines, power shovels, and excavators are used to retrieve the coal. Large haul trucks and conveyors are then used to transport the coal to where it can be processed or used. Once all of the recoverable coal is removed, the area can be backfilled to promote land reclamation. In surface mining, lignite and subbituminous coal are most often mined.

Underground, or deep mining, is used when the coal is hundreds of feet below the ground. Two methods for underground coal mining include continuous or room and pillar mining and longwall mining. Longwall mining is the most productive underground mining method. In longwall mining, coal mine workers extract coal from a long section of the coal seam using mechanical shearers. Continuous mining machines are also used during development of the longwall sections. Underground mining requires detailed geological exploration and mapping to ensure that the geology is satisfactory to run shafts underground and that the roof can be securely supported to avoid collapsing while the mine is active. Common types of ground and roof support include steel ribs, concrete segments, steel and cable bolts, and wire mesh.

Both surface and underground coal mining result in the production of emissions that can pollute both the air and water. These environmental concerns are discussed next.

Environmental Concerns

Coal mining consists of several phases from mining the coal to processing, storing, and transporting it for eventual use. Throughout these phases, environmental concerns are always present, including harmful emissions into the air and water, potential impacts on global warming, and changes in land surface characteristics.

Air emissions from coal mining mainly consist of fugitive dust, diesel emissions, and methane. Fugitive dust, including coal dust, rock dust, and crystalline silica, is generated during the mining process by breaking the rock and also results from piles of uncovered coal and overburden when wind action suspends the dust into the air. Diesel emissions, including diesel particulate matter and oxides of nitrogen, from the large diesel engines used in mining, are also emitted into the atmosphere. Finally, methane is a greenhouse gas created during the coalification process. The mining of a coal seam with entrapped methane results in methane release. The deeper the coal seam, the greater the methane content of the coal. The World Coal Association estimates that underground coal mining accounts for 90 percent of methane emissions from the coal mining industry. Although the air emissions already discussed are generally associated with occupational exposures, due to the rural and isolated locations of coal mines, once in the air, there is potential for these emissions to reach nearby populated areas, resulting in public exposure to these emissions.

Water emissions from coal mining mainly consist of sediment and acid mine drainage. Sediment can be created during the mining process as water runs through the mine or when rainwater washes over uncovered piles of coal or overburden. Acid mine drainage results from water reacting with minerals released from the rock during the mining process. It is common for water released from mine sites to contain a higher concentration of sulfates, calcium, magnesium, selenium, arsenic, and other metals than their nonaffect counter bodies of water. Additional water contamination occurs as a result of coal washing, a process that applies chemical formulas containing surfactants, flocculants, and other agents to prepare coal for use in combustion. The result of this process is the formation of slurry that is stored in surface ponds that can leach into groundwater or is injected underground into old mining spaces.

In addition to air and water emissions, mining can also change the landscape of mined environments by a mining technique known as mountaintop mining or by land subsidence. Mountaintop mining is a surface mining technique where mountaintops are removed to expose coal. Not only does removing mountaintops change the topographical terrain and destroy forests, but the overburden, once removed, may be placed in valleys or streams, creating additional sediment pollution and further disturbing the natural biodiversity in the environment. Subsidence, although rare, is the readjustment of
the ground surface resulting from the collapse of underground mine workings. Subsidence results in the formation of a sinkhole or trough, which may result in major impacts on surface waterways and structures.

Health and Safety Concerns
In addition to their environmental impacts, emissions resulting from both the mining and the combustion of coal have been linked to adverse health consequences on the human population, including certain types of cancer. Several pollutants released into the environment from coal mining are of particular concern including coal mine dust, crystalline silica, diesel particulate matter, and arsenic.

Arsenic in drinking water can increase risks for lung, bladder, or kidney cancer. Crystalline silica has been associated with increased risks of lung cancer and silicosis, a debilitating respiratory disease. Several U.S. studies conducted by Michael Hendryx and colleagues concluded that living in coal-mining locations, such as the Appalachian region, is an independent risk factor for developing lung cancer and other health-related problems including colon, bladder, leukemia, and kidney cancer. Specifically, studies conducted with adults in two West Virginia communities, one in a mining area and the other in a nonmining area, found significantly higher self-reported cancer rates in the mining area after controlling for age, sex, smoking, occupational history, and family cancer history. Also, in June 2012, diesel particulate matter was classified by the International Agency for Cancer Research as a known human carcinogen.

Coal mine workers are an especially vulnerable population who experience greater risks because they are exposed to occupational pollutants, including respirable coal mine dust, crystalline silica, and diesel emissions, daily and over an extended period of time. Globally, hundreds of thousands of individuals have careers as coal mine workers, indicating a large population being directly and consistently exposed to coal mine-related pollutants. The American Cancer Society noted that occupational exposure to cancer-causing substances, or carcinogens, accounts for about 4 percent of all cancers in the United States. Coal mine workers are thought to be at increased risk for diseases such as heart disease, chronic obstructive pulmonary disease, and lung cancer.

More specifically, Coal Workers’ Pneumoconiosis (CWP), or black lung disease, is the leading cause of death due to occupational illness among underground coal mine workers. Silicosis, resulting from continued exposure to respirable crystalline silica, is more common for those who work on the surface of mine sites, although silica can be inhaled when coal seams are cut as well. With diagnoses of CWP or silicosis also come associated health problems such as lung cancer, autoimmune disorders, pulmonary tuberculosis, and chronic renal disease.

From the early 1980s to 2006, the underground coal mining industry experienced little change in levels of exposure to respirable coal mine dust. However, a chest X-ray surveillance program initiated by the National Institute for Occupational Safety and Health, which conducts preventative and diagnostic screenings of participating coal mine workers, found that, after many years of decline in the incidence of CWP, the prevalence of the disease is on the rise again. For example, between 2000 and 2005, data from the U.S. Department of Health and Human Services (HHS) indicated that CWP contributed to the deaths of close to 3,900 coal mine workers. This recent increase supports the need for additional risk reduction mechanisms to maintain the health of coal mine workers, specifically.

Because of the importance of coal energy to the world economy, it is necessary to continuously evaluate and create methods to help mitigate the exposure of coal miners and the public to hazardous emissions associated with coal mining as well as reducing the impact of coal mining on the environment.

Risk Reduction Efforts for Environmental and Societal Health
The coal industry and pertinent regulatory agencies remain vigilant in researching and adopting methods to help reduce and control respirable dust and pollution levels to help protect the environment and the public. In response, emissions of many of the pollutants that put individual and environmental health at risk are regulated and controlled to some degree.

The Environmental Protection Agency (EPA) proposes and modifies regulations to minimize risks generated from coal power plants and producers. Under the Surface Mining Control and Reclamation Act of 1977, it is required for land impacted by mining
Coal provides around 30 percent of the world’s primary energy needs and provides approximately 40 percent of the world’s electricity. Emissions resulting from both the mining and the combustion of coal have been linked to adverse health consequences on the human population, including certain types of cancer. (MorgueFile)

to be reclaimed for other uses. This act requires that mine companies reclaim land where coal has been extracted already. Closed mines can become housing units, farmlands, forests, or even public parks. For instance, in the European Union, more than half of mining lands are reclaimed as forests or grasslands, whereas in China, a majority of reclaimed mining lands are used for agriculture purposes.

Another environmental regulation is the 1976 Resource Conservation and Recovery Act (RCRA). This regulation indicates that any hazardous waste that results from mining be treated and stored properly and then disposed in a way that protects the environment and surrounding individuals. For example, in 2010, the EPA proposed to regulate coal combustion residuals under the RCRA. Further, in 2012, under the Clean Air Act, the EPA proposed a new source performance standard to limit emissions of carbon dioxide from new, fossil fuel-fired, utility-generating units, which includes coal and natural-gas-fired units. Limiting these emissions is expected to reduce greenhouse gas pollution.

Although regulations require an increase in accurate environmental assessment and rigorous planning, these strategies ensure that mining companies remain in compliance regarding protecting the environment from air, water, and gas pollution, thus providing more protection for individuals who reside in mining areas as well.

Absent of regulations, however, the coal industry makes several efforts to minimize harmful environmental consequences of mining coal. New technology at power plants helps keep air clean during the cleaning and processing of coal. One example of such technology includes an integrated gasification combined cycle (IGCC), which is a coal gasification process that turns coal into a gas before burning it, resulting in cleaner air. In addition, the coal industry has been actively involved in researching methods to extract the methane from coal and preventing its release into the environment. The capture of methane before it is released both reduces emissions of greenhouse gases as well as improves the safety of underground coal mines. Explosions in
underground mines result in loss of lives worldwide, and while any loss of life is too high, the number of explosions has been steadily declining as methane recovery technologies have been improved and deployed on a wider scale.

Due to the nature of their occupation, the environmental-based regulations and research do not fully protect coal mine workers, who are exposed to more respirable dust than the rest of the public. As a result, coal mine workers have a greater risk for various types of cancer and respiratory diseases than the general public. However, there are specific risk reduction efforts that target this at-risk group of individuals.

**Risk Reduction Efforts for Mine Worker Health**

Because the process of mining coal results in the potential for increased occupational exposures to coal dust and other pollutants, risk reduction efforts are needed on regulatory, organizational, and individual levels to best protect coal mine workers. For instance, in the United States, the Mine Safety and Health Administration (MSHA) promulgated regulations that limit the exposure to respirable coal mine dust to an average of 2.0 milligrams of respirable dust per cubic meter of air (mg/m³) over a standard work shift. Mine operators are responsible for regularly collecting respirable dust samples in active, working mines. If the results exceed the allowable average dust level, the mine must take corrective action to reduce the average concentration of respirable dust to below the permissible concentration. In addition, the mine operators must continue sampling until they measure dust concentrations below the allowable limit on five sequential samples.

Internationally, respirable dust regulations vary. In Australia, different mining areas such as New South Wales, Queensland, and Western Australia have separate health and safety regulations. In New South Wales, mine operators at each mine must ensure that no mine worker is exposed to more than 3.0 mg/m³ of respirable dust or 10.0 mg/m³ of inhalable dust over an eight-hour sampling period.

In addition to regulating allowable airborne dust concentrations, new advances in mining technology can help to (1) minimize the creation of dust and (2) allow individuals to more accurately monitor their dust exposure on the job. The National Institute for Occupational Safety and Health (NIOSH) has completed numerous studies to recommend the best methods to control exposure to airborne dust in coal mining. These researchers have found that technology controls, water spray systems, and ventilation systems function as protective devices to help prevent the formation of dust, suppression of dust to prevent it from becoming airborne, and removal or dilution of the dust once it is airborne. For example, water spray systems can help suppress or redirect dust away from mine workers and walkways. In addition, scrubbers can be mounted on existing mining machines to help move air and capture dust while mining coal. Improved ventilation systems can also dilute dust concentrations after becoming airborne.

The control methods already discussed are applied to help reduce the concentrations of airborne dust that reach the inhalable breathing zones of coal mine workers. However, personal protective equipment (PPE), such as an airstream helmet or respirator, can be worn by coal mine workers to reduce the amount of dust actually inhaled. This PPE functions as a barrier between coal mine workers and respirable mine dust. Other equipment can be used to help mine workers monitor their exposure to dust throughout the workday. Specifically, a continuous personal dust monitor (CPDM) is available to the coal mining industry that can provide mine workers with near real-time feedback on their exposure to respirable coal mine dust. If mine workers and mine site safety personnel know how to properly use and communicate about the information provided by CPDMs, they may be able to make adjustments to the workplace and work procedures to try to reduce their exposure to respirable coal mine dust as they complete work tasks.

Even though risk reduction methods are in place, exposure can still occur through breaches in these regulations, accidents, or inability of individuals to recognize and mitigate these hazards in their surrounding environment. Therefore, a final area of prevention includes education that empowers mines and respective mine employees to take action to reduce their exposure to respirable coal mine dust on the job. Educational interventions that seek to motivate and persuade changes in mine workers’ behaviors to lower their exposure to respirable coal mine dust can enhance methods used by mine
workers to reduce personal dust exposure and, consequently, the incidence of CWP. For example, if mine workers are aware of the areas that produce more dust and can stand in different positions, or are trained in the use of technology to reduce the concentrations of dust, they immediately have more control over their dust intake on the job. These changes in work behaviors can ultimately lead to improvements in coal miners’ longevity and quality of life.

Conclusion
This entry discussed the positive uses of coal while acknowledging the negative impact coal mining can have on the environment and individual health. Because of the pros and cons that exist due to coal mining, a systematic approach is needed to address some of the drawbacks, so the nation can continue to benefit from coal and coal by-products. Risk reduction efforts were discussed on a policy, organizational, and individual level that are used to protect the environment, general public, and coal mine workers as much as possible. Specifically, participating in strategic planning before mining, including ways the land can be reclaimed, enforcing health and safety policies, leadership engaging in surveillance of mine worker behaviors, and mine worker education and empowerment are crucial to preventing the onset of cancer and other adverse health effects for individuals who experience consistent exposure to carcinogens emitted from coal.

Emily Joy Haas
Steven E. Mischler
National Institute for Occupational Safety and Health

See Also: Lung Cancer, Small Cell; Pollution, Air; Pollution, Water.

Further Readings

Cold Spring Harbor Laboratory
Founded in 1890, Cold Spring Harbor Laboratory is a private, not-for-profit research institution that has more than 52 laboratories. Known for its prowess in research related to cancer, genomics, neuroscience, plant genetics, and quantitative biology, Cold Spring Harbor Laboratory also has a strong educational component to its work. The home to many notable researchers, including a group of Nobel Prize winners, the Cold Spring Harbor Laboratory conducts
cancer research that touches upon a variety of cancer genomics, drug resistance, gene regulation, and other topics. Scientists at the Cold Spring Harbor Laboratory collaborate with researchers at a variety of other institutions.

Originally sponsored by the Brooklyn Institute of Arts and Sciences, Cold Spring Harbor Laboratory was initially known as the Biological Laboratory. In its first years, it served as a summer program where college and university students and high school teachers interested in botany, comparative anatomy, nature, and zoology could engage in fieldwork. In 1904, the Carnegie Institution for Science established the Station for Experimental Evolution at Cold Spring Harbor on a parcel adjacent to that of the Biological Laboratory. Through the late 1930s, the laboratory’s major emphasis was eugenics, a now largely discredited field that examined how to improve the human gene pool. During the 1920s, research began on how cancer affected mice, especially their susceptibility to certain types of sarcoma. After Milislav Demerec was named director of the Cold Spring Harbor Laboratory in 1941, however, the institution’s focus shifted to the genetics of the microbe, work which was to prove instrumental in later cancer studies.

Under Demerec’s leadership, the Cold Spring Harbor Laboratory developed what became known as the Phage Course, which played a key role in the development of molecular genetics. Many scientists who took the Phage Course went on to conduct studies that helped determine the physical basis of the gene. In 1953, James Watson first presented his findings on the structure of deoxyribonucleic acid (DNA) at a Cold Spring Harbor Laboratory symposium, a talk that radically changed the future of biological research. In 1968, Watson would return to Cold Spring Harbor Laboratory as its director. Watson changed the laboratory’s focus to concentrate upon the study of cancer. In 1969, Watson succeeded in hiring virologist Joe Sambrook, who began a tumor virus group.

Since this time, the Cold Spring Harbor Laboratory’s cancer studies have thrived, and there has been a large expansion and broadening of its research. The facilities at Cold Spring Harbor Laboratory are world-class and have benefited from expanded educational programs. Since 1998, Cold Spring Harbor Laboratory has been a PhD degree–granting institution, culminating in the founding of the Watson School of Biological Sciences in 1998 and the establishment of the Cancer Genome Research Center two years later.

Cancer Research
Cold Spring Harbor Laboratory has long been on the forefront of cancer research. In 1972, scientists Joseph Sambrook, Phillip Sharp, and William Sugden developed a technique for separating and visualizing DNA fragments that continues to be used throughout the discipline of molecular biology. Nine years later, Michael Wigler discovered the first cancer-causing gene in a human tumor, and in 1988, Edward Harlow and his associates established a functional link between oncogenes and tumor-suppressor genes, the two general classes of cancer-causing genes. In 2004, Scott Lowe and his colleagues established a promising combination therapy for treating many cancers that did not respond to traditional chemotherapy, an approach that has been widely emulated by practitioners worldwide. The same year, Wigler detected a degree of large-scale variation in the copy number of genes in otherwise normal human genomes by using a technique that was initially developed to detect differences between normal cells and cancer cells. In 2005, Gregory Hannon, Scott Lowe, and Scott Powers discovered microRNAs as new targets that helped improve the diagnosis and treatment of a variety of cancers, including lymphoma, colon cancer, and others.

Researcher Chris Vakoc in 2011 began using an unconventional approach to cancer drug discovery. Vakoc’s approach identified new potential treatments for acute myeloid leukemia (AML). AML is an aggressive blood cancer that is incurable in approximately 70 percent of patients. This approach is being developed for therapeutic use for cancer patients by a major pharmaceutical corporation. Working with researchers at five other institutions, Vakoc identified a protein called Brd4 as a novel drug target for AML. Using drugs that impede the activity of Brd4, Vakoc’s team was able to suppress the disease in experimental models. These works are part of Cold Spring Harbor Laboratory’s cancer therapeutics initiative, which seeks to identify new therapeutic targets and then to quickly validate them using mouse models that closely mimic the behavior of specific human cancers. This approach has two advantages. First, it offers insights into
cancers’ molecular mechanisms. Second, this pre-clinical testing approach permits researchers to evaluate a specific cancer’s response to new treatments and to discern information that can adjust and adapt treatment strategies so that the success rates of pharmaceuticals that eventually enter clinical trials are increased.

Through its PhD program, Cold Spring Harbor Laboratory strives to produce researchers who are able to become leading scholars in the fields of cancer research and other disciplines. In addition to its own program, Cold Spring Harbor Laboratory collaborates with the State University of New York at Stony Brook to offer a variety of shared graduate programs. These shared graduate programs include those in genetics, molecular and cellular biology, molecular genetics and microbiology, and neurobiology and behavior.

The Cold Spring Harbor Laboratory annually offers a variety of programs that draw more than 10,000 researchers. In addition, each summer approximately 25 undergraduate students from across the globe come to Cold Spring Harbor Laboratory to participate in a 10-week program that permits them to work with researchers on projects. Summer projects span a variety of disciplines and have included work in cancer biology, neuroscience, plant biology, cellular and molecular biology, genetics, and bioinformatics and genomics. This undergraduate research program has been highly successful as it permits college and university students the opportunity to conduct original research, allows interaction with graduate students and senior researchers, introduces them to the physical and intellectual tools used in biological research, and exposes them to the research process. The program has been widely emulated by other institutions of higher learning and is seen as a key avenue for recruiting future cancer researchers.

Stephen T. Schroth
Towson University

See Also: Drugs; Education; Future of Cancer; Hospitals; National Cancer Institute; Yale Cancer Center.

Further Readings


Colombia

Colombia, officially known as the Republic of Colombia, is a country situated in the northwestern corner of South America. It is bordered to the south by Ecuador, the northwest by Panama, and the east by Brazil and Venezuela. The country shares maritime limits with Haiti, Costa Rica, Honduras, Nicaragua, Jamaica, and the Dominican Republic. Despite the fact that the republic is comprised of more than 30 percent of the population living under the poverty line (according to the National Administrative Department of Statistics in 2013), it is known as one of Latin America’s main health tourism destinations. This is due to the fact that there are many quality health care professionals, an immense number of architectural and natural sites, and several institutions devoted to health.

The Columbian League Against Cancer
There are many Columbian organizations dedicated to the fight against cancer. One such organization is the Colombian League Against Cancer: a private, nonprofit, nationwide organization that was created in 1960 to take action to promote cancer education, early diagnosis, and prevention-utilizing volunteers.

Over the course of the organization’s life span, more than 30 subleagues and sectional chapters have been created to further its mission to improve the quality of life for cancer patients. The overall organization is committed to quality safe care actions that reduce the risk to the patient, the family, and his or her doctors.

National Cancer Institute
Another cancer-related organization is the National Cancer Institute of Colombia, which is well-known for its resources across the developing world. Some of the best doctors in Colombia work here. The organization has a special partnership (winning
program) with the World Child Cancer organization, which has led to valuable training and mentorship for its doctors.

The institution of the Colombian state works nationally for comprehensive care for cancer patients as well as promotes the training of talented doctors, research for new solutions, and development of public health actions. Some of its guiding principles include commitment, honesty, respect, loyalty, equity, solidarity, quality, comprehensiveness, efficiency, and social participation.

**Types of Cancer**
The leading types of cancer in Colombia are breast cancer (number one for women), stomach cancer (number one for men), lung cancer, prostate cancer, cervical cancer, colorectal cancer, and liver cancer. Many of these cancers have seen a slight decrease over the last decade, due to educational and early prevention efforts.

In terms of prostate cancer, one highlighted diagnosis belongs to none other than Colombia’s president, Juan Manuel Santos, who was diagnosed with the disease around the age of 61. He underwent surgery and was able to recover. Santos is the latest in a long line of Latin American leaders who have been diagnosed with cancer.

**Melanoma (Skin Cancer).** Melanoma is also of large concern to Colombians, as the country sits near the equator. The increased risk of developing skin cancer occurs due to unprotected exposure to harsh sunlight in the first 15 years of life. The disease is cumulative and manifests in adulthood. Colombian state organizations post warnings about the disease and warn citizens to wear long sleeves and dark glasses and use sunscreens. Those who have light skin tones, hair, and eyes are more likely to get skin cancer. Melanoma-based efforts are headed by the Colombian Skin Cancer Foundation.

**Breast Cancer.** Unlike some other cancers in Colombia, breast cancer is on the rise—especially in women. Currently, about 6,000 Colombian women receive a positive diagnosis for the disease each year, and about 2,500 die as a result of it, according to the Colombian League Against Cancer.

According to the World Health Organization (WHO), most of those killed by breast cancer are women from developing countries. This is due to late diagnosis and difficulties in receiving timely and accurate treatment. On a global level, 545,000 women die annually from the disease.

According to the Colombian League Against Cancer, the rate of breast cancer doubled in the country from 2002 to 2007, and the National Institute of Cancerology has pointed out that it may easily become the leading cause of death among Colombian women age 50 to 69 if the current rates of occurrence and mortality do not decrease. Some say the increases are due to chemical used in crops and beauty products, while others blame fast food for the rise. GLOBOCAN, the WHO’s body in charge of health statistics, reports that breast cancer makes up more than 20 percent of all cancers globally.

Unlike cervical cancer, breast cancer in Colombia is highest among wealthy women. Though the cause of this is unknown, risk factors may include late last menstruation, early menstruation, relatives who have suffered breast cancer, obesity, absence of breast-feeding, and frequent alcohol consumption. Women who have had breast cancer are 0.5 to 1 percent more likely to develop breast cancer in their other breast within 10 years of the first diagnosis. Women who are younger than 35 are thought to have a greater risk of a second breast cancer occurrence. Breast cancer is treatable with early detection using mammograms and self-examination to detect lumps that may be cancerous.

**Childhood Cancer.** Each year, more than 29,000 children under 15 are diagnosed with cancer across Latin America. About 9,000 of these children die. In Colombia, specifically, 300 cases develop, and 500 deaths occur, according to the Ten-Year Plan for Cancer Control in Colombia, 2012–2021.

Cancer care for children requires a large effort by families and institutions. Many cancer fatalities in children occur because they drop out of their treatments due to financial issues, treatment inaccessibility, or otherwise. According to the Ministry of Health, children who do not drop out of treatment have a 75 percent survival rate, while those who do drop out of treatment have a survival rate of only 25 percent.

**Conclusion**
Though Colombia is well-known for its resources across Latin America, there are many ways in which it still must strive to become a country that is known
for its dedication to early detection and prevention. New health initiatives and laws across the country should decrease the number of deaths occurring from cancer, though breast cancer, in particular, continues to rise regardless of these efforts.

Katie Moss
Independent Scholar

See Also: Breast Cancer; Childhood Cancers; Melanoma; Prostate Cancer.

Further Readings

Colon Cancer

Colon cancer (also known as colorectal cancer when inclusive of rectal cancer) refers to the uncontrolled, unchecked malignant growth that originates in the large intestine, generally as adenocarcinoma. In most occurrences prior to malignancy, an adenomatous polyp forms as the benign neoplastic precursor, of which only a fraction might progress to cancer. Colon cancer may also develop in the setting of inflammatory bowel diseases (ulcerative colitis or Crohn's disease) without an adenomatous polyp precursor. Risk factors include age, family history, race, and also high caloric intake, low-fiber diet, tobacco, alcohol, and low-serum selenium. Low-fat and high-fiber diets, supplementation with calcium or vitamin D, regular usage of nonsteroidal anti-inflammatory drugs, physical activity, and ingestion of fish oils are associated with lower risk. Within the colon, an interaction between colon stem cells and the local environment ultimately triggers genomic instability in a stem cell, which progresses through histological stages from aberrant crypt foci to adenoma to cancer, paralleled with genetic changes that involve the adenomatous polyposis coli (APC), KRAS, and TP53 genes for most sporadic cancers or epigenetic inactivation of the DNA mismatch repair gene hMLH1 to cause microsatellite instability (MSI), a genetic signature observed in 15 percent of sporadic cancers. Patients with adenomas and early colon cancers are generally asymptomatic, and to detect these requires a screening intervention and ultimately colonoscopy to biopsy or remove the lesion if amendable. Patients with advanced cancers may present with iron deficiency anemia, weight loss, stool pattern changes, hematochezia, or abdominal pain.

Hereditary Colon Cancer

A strong family history of colon cancer may indicate a hereditary or familial colon cancer syndrome. Often, cancer presents at young ages in these families and affects more than one generation. There are two groups based on the type of polyps that form: adenomatous and hamartomatous syndromes. Among the adenomatous syndromes, Lynch syndrome is the most common, and families may present with colon cancer, cancers of the female reproductive tract, cancers of the urinary tract, and other gastrointestinal tract cancers. Lynch patients are found with germline mutations in DNA mismatch repair genes, such as hMLH1 or hMSH2, transmitted autosomally. Familial adenomatous polyposis (FAP) families demonstrate multiple to thousands of adenomatous polyps in their colon, with near 100 percent certainty of developing colon cancer without any intervention. FAP families carry a germline mutation in the APC gene that is transmitted in an autosomal dominant fashion. MYH-associated polyposis (MAP) is transmitted in an autosomal recessive pattern through biallelic mutations (one from each parent) of the MYH gene. MAP patients have few to hundreds of polyps in
their colons and present in a similar fashion as FAP patients. The hamartomatous syndromes include juvenile polyposis, Peutz–Jeghers syndrome, and PTEN hamartoma syndrome. These syndromes are rarer than the adenomatous syndromes and require a high index of suspicion for recognition. Most of these syndromes can be determined by genetic testing, with subsequent appropriate surveillance for cancers to reduce morbidity and mortality at young ages.

Screening and Prevention
Because of the asymptomatic nature of precursor adenomatous polyps and early colon cancers, and their curability when found early as compared to symptomatic colon cancer, screening asymptomatic men and women over the age of 50 years for colorectal neoplasia has become the standard and can detect cancers at an earlier stage compared to those not screened, and with some modalities, improve survival. Approved screening tests include fecal occult blood tests or fecal immunohistochemical tests, flexible sigmoidoscopy, colonoscopy, barium enema, computed tomography (CT) colonography, and fecal DNA tests. Each test has differing sensitivity and specificity in detecting cancers or adenomatous polyps, with ultimately colonoscopy being the preferred tool to detect and sample colorectal cancer and remove adenomatous polyps and early cancers. There is variation on sensitivity of detection for right colon cancers versus left colon cancers, and reduction in mortality from colonoscopy is greater for left-sided cancers.

Chemoprevention has not become standard practice except with forms of hereditary colon cancers and in high-risk patients with recurrent polyps or cancer. Epidemiological evidence suggests that nonsteroidal anti-inflammatory agents are beneficial in reducing future risk for colon cancer, but this must be balanced with the risk of side effects of these medications, and usage should be carefully considered in appropriate patients.

Prognosis, Treatment, and Precision Medicine
The prognosis of colorectal cancer is principally based on the stage of the disease at presentation. Staging may be performed using imaging techniques, such as CT or magnetic resonance imaging, or determined at surgery. Rectal cancer is best staged with rectal endoscopic ultrasound. Patients whose tumors demonstrate MSI may have improved survival when compared to patients without MSI tumors.

Therapy for colorectal cancer can be divided into colon and rectal cancer components. The main treatment for colon cancer is surgery. Surgery with wide resection margins is the only therapy needed for stage I and II disease, although some high-risk stage II patients receive chemotherapy. For stage III disease, adjuvant 5-fluorouracil-leukovorin (or FOLFOX: 5-fluorouracil, leukovorin, and oxaliplatin), six months is standard and has been shown to improve survival. For stage IV, surgery may be curative in highly selected patients with resectable bowel disease and resectable isolated hepatic or pulmonary metastases.

Unresectable liver lesions may also be managed locally with transarterial chemoembolization or radio frequency ablation if symptomatic. In many patients with stage IV disease, surgery is often palliative to prevent bowel obstruction. Chemotherapy is offered but may not improve overall survival. Palliative chemotherapy regimens for stage IV colon cancer include 5-fluorouracil-leukovorin, FOLFOX, and FOLFIRI (folic acid, 5-fluorouracil, and irinotecan), and IFL (irinotecan, 5-fluorouracil, leukovorin). Specific growth factor
inhibitors, such as bevacizumab (antibody to vascular endothelial growth factor) and cetuximab (antibody to epidermal growth factor receptor) added to the 5-fluorouracil-based regimens improve tumor shrinkage and add about five months to the survival of stage IV patients.

Rectal cancers are treated surgically by low anterior resection or abdominal perineal resection, often in combination with 5-fluorouracil-based chemoradiation. Stage I disease is approached with wide surgical resection with or without chemoradiation. Stage II and III disease is treated by wide surgical resection in combination with adjuvant or neoadjuvant (with an attempt at anal sphincter preservation) chemoradiation. The approach to stage IV disease is generally palliative with surgical bypass of local bowel obstruction and chemoradiation for local management.

Biologically driven decision making, or precision medicine, is becoming increasingly adopted for optimal care and outcome for colon cancer patients. The assessment of DNA (for direct mutation or epigenetic alterations without a change in sequence), RNA, or protein from normal tissue (blood or buccal swab), feces, or tumor is becoming more commonplace to help screen, diagnose, prognosticate, and perform personalized and precise care and treatment plans for patients at risk or with colorectal cancer.

Molecular screening, and in particular DNA testing, can assess the genetic background of a patient (passed through the germline from either parent) or characterize the genetic makeup of a tumor and, based on knowledge gained from the published human tumor literature for specific DNA changes, inform the physician regarding patient outcome and recurrence as well as inform an optimal approach to surveillance or treatment that will afford the patient the best outcome.

John M. Carethers  
*University of Michigan*

**See Also:** Colorectal Cancer, Childhood; Screening.

**Further Readings**


Carethers, J. M. “Secondary Prevention of Colorectal Cancer: Is There an Optimal Follow-Up for Patients With Colorectal Cancer?” *Current Colorectal Cancer Reports*, v.6 (2010).


**Colorectal Cancer, Childhood**

Cancers of the large intestines occur rarely in the pediatric patient. Whereas colorectal cancer accounts for one in four cancers diagnosed in the United States, the incidence is one in 1 million under age 20 years. In children, more cancers arise on the right side of the colon compared to adults and are usually associated with a hereditary colorectal cancer syndrome. The finding of one adenomatous polyp in a child should alert the clinician to the possibility of familial adenomatous polyposis (FAP), the most common polyposis syndrome in children. FAP is the result of a mutation in the adenomatous polyposis coli gene (APC) and is characterized by the progressive development of hundreds to thousands of adenomatous polyps in the large intestine, with presentation of adenomatous polyps by the early teen years. The number of polyps increases progressively, and the lifetime risk for colorectal cancer is 100 percent. One large study noted that
FAP patients presented with a colonic adenoma as early as eight months of age with a mean age of presentation of age 13. Polyp burden may also vary within families and are amenable to endoscopic therapy if the burden is limited (less than or equal to 30 polyps). Pediatric patients at risk (by having a family history) should be evaluated with a colonoscopy as early as two years before the youngest, earliest affected member. Plans for colectomy (surgical removal of the large intestine and rectum) should be discussed when the tumor burden becomes great or if high-grade dysplasia, a feature that indicates progression toward cancer, is noted on histopathology. Notable since the widespread practice of early colectomy for FAP are secondary causes of morbidity from FAP, primarily due to duodenal adenocarcinoma, with presentation as early as age 17. As such, new criteria for upper endoscopic surveillance have been recommended to closely follow colonoscopic surveillance.

Colon cancer can also be seen as a primary presentation in children with Lynch syndrome (LS), with presentation as early as nine years of age. LS is caused by a mutation in one of the DNA mismatch repair (MMR) genes. Unlike FAP, patients with LS may only develop one or few adenomatous polyps, thus making early diagnosis more difficult. A thorough family history for cancers involving the large intestines, and the uterus in female family members, is crucial in early detection of the at-risk child. Patients with a positive family history and symptoms should be screened with a colonoscopy (10 years earlier than the earliest index case in the family) and polyps removed as needed. The lifetime risk for colorectal cancer approaches 80 percent in these children, so discussions about timing for colectomy need to be addressed. A newer recognized form of colon cancer known as constitutional MMR deficiency syndrome (CMMR-D) occurs when both alleles of the same MMR gene are mutated. This results in a syndrome that is clinically distinct from LS with features of neurofibromatosis type 1 and a high risk of gastrointestinal cancers along with childhood malignancies to include brain, lymphoma, and leukemia.

Hamartomatous polyposis syndromes comprise a group of rare syndromes with intestinal polyposis along with other extraintestinal manifestations, often with presentation in early childhood. These hamartomatous polyposis syndromes occur at approximately one-tenth the frequency of the adenomatous polyposis syndromes and thus account for less than 1 percent of all colorectal cancers. Thus, the value and the importance of surveillance becomes complex. Recent molecular understanding of germline mutations in genes associated with hamartomatous polyposis syndromes (PTEN, BMPR1A, STK11, ENG) in patients with five or more polyps have helped improve management and surveillance of these patients. Juvenile Polyposis Coli (JPC) is one such syndrome, and patients may have multiple colonic juvenile polyps (greater than 3) that are nondysplastic.

However, JPC patients have a 12-fold increased risk for colorectal cancer and need to be closely monitored with regular colonoscopies. Colectomy is indicated if the tumor burden is great. Peutz–Jeghers Syndrome (PJS) is another hamartomatous polyposis syndrome with associated cancer risk both to the gastrointestinal tracts as well as extraintestinal sites. The relative risk for developing colon cancer in PJS was estimated at 98-fold higher when compared with the general population. Strict surveillance guidelines for PJS have been established for all cancer types in PJS with colonoscopies to commence at age 10. Recently, hamartomatous polyposis syndromes have been linked to various mutations in several different tumor suppressor genes and provide an additional avenue for diagnosis for the clinician through genetic testing.

Pediatric colon cancers usually present with symptoms associated with the site of the tumor. Hematochezia, weight loss, pain, finding of an abdominal mass, and intestinal obstruction can be a common presentation. Treatment involves surgical resection of the tumor and chemotherapy using the drugs 5-fluorouracil and leucovorin along with radiation if the tumor is in the lower pelvis.

See Also: Childhood Cancers; Colon Cancer; Unusual Cancers of Childhood.

Further Readings


Comprehensive Cancer Center of Wake Forest University

The Comprehensive Cancer Center at Wake Forest University is the first hospital focused on cancer in the Winston-Salem area of North Carolina. The center combines the medical curriculum and research parts of the Wake Forest School of Medicine. The center has 148 beds and includes an inpatient oncology intensive care unit (ICU).

As a comprehensive cancer center, this facility is credited as one of the national drivers in the battle against cancer. A comprehensive designation comes from the access patients at this facility have to advanced technology, treatment, and research.

At other medical centers, it may be weeks before a patient sees his or her physician. At the Comprehensive Cancer Center of Wake Forest University, the process has been streamlined so that the diagnosis, treatment, and after care of cancer patients is led by surgical, medical, and radiation oncologists as well as other allied health care personnel.

The center has made achievements since its foundation. It has been awarded full accreditation by the National Accreditation Program for Breast Centers, which is the first such accreditation awarded in the area. In addition to this, the institute is one of only 41 such facilities to be designated by the National Cancer Institute (NCI) as a comprehensive cancer center.

The center has more than 120 clinicians with focuses on every facet of cancer. This allows the institute to offer the best treatment for patients. The institute was also acknowledged as one of the top national leaders in the battle against cancer.

At the center, specialists in medical, radiation, surgical, and other treatments work collaboratively to ensure that patients receive treatments that are optimal for their maladies. Because patients see these experts who are able to cover every area of treatment, the process of investigation is streamlined and care can be given to the individuals more rapidly. In a single day, patients can see a team of professionals who specialize in the types of cancer ailing them.

The center treats many different types of cancer including breast, gastrointestinal, gynecologic, brain tumors, neck and head, oncology and hematology, melanoma, pediatric, orthopedic, prostate, thoracic, sarcoma, and urologic. The treatments offered by the center are multidisciplinary; specialists work in teams to ensure that the best answer for the patient is found as quickly as possible. The treatments available at the center include chemotherapy, radiation, and blood and marrow transplants.

While treatment for cancer is certainly part of treatment, there are other quality-of-life factors for which the center provides support. As cancer is a very stressful diagnosis for both patients and their families, the center offers support services so that patients and their families have experienced counselors to talk to. Counseling support programs offered include cancer patient support programs, psychosocial oncology, survivorship, massage, pastoral, and palliative. Some support programs are run by volunteers. The center accepts donations to help fund these aspects of patient care.

The center helps set up patients with clinical trials, and it has access to more trials than any other facilities in the area. These trials provide innovative treatment options for patients and have tremendous promise for future advances in cancer treatment and survivability. All of the current clinical trials may be viewed on the Wake Forest Baptist Health Web site.

In addition to offering treatment and care services to patients, the center also conducts research into advancing cancer therapies and patient treatments.
This is done by forming teams of professionals across disciplines and departments. Some of the research subjects include the development of pharmaceuticals, cancer imaging, all-natural products, genomics, nanotechnology, tumor microenvironment, survivorship, and disparities.

The center is composed of four different programs that make it easier for experts to interact and collaborate on issues. These programs aim to further acknowledge unity in working toward cancer prevention and cures. The divisions include cell growth and survival, clinical research, cancer prevention and control, and cellular damage and defense. The center also has three centers devoted to research brain, breast, and prostate cancers.

The four divisions of programs have differing goals. The goal of the cell growth and survival program is to explore the biological mechanisms present in proliferative and cell-death signals and to learn how to utilize this understanding to improve therapy and survival rates. Some of the contributions made to the cancer-fighting effort include modulation of cancer using all natural products, the tumor microenvironment, and decisions of cell fate in cancer.

The second division is the cellular damage and defense program. This program, as the name implies, aims to ascertain what role cellular defense and metabolic pathways play in tumor growth and to exploit these roles for therapeutic intervention. Within these research themes are projects with DNA damage, redox signaling, and metabolism on the cellular level.

The third division is the clinical research program. The center provides more clinical trials than every other hospital and medical facility in western North Carolina. There are nearly 250 research studies orchestrated by oncologists from the center or led by other organizations with which the center collaborates.

The final division is the cancer prevention and control program. The aim of this program is to utilize knowledge for the prevention and detection of cancer as well as to improve the quality of living for cancer survivors. The program’s goals are to reduce the occurrence of cancer, slow its progression, lessen morbidity, and increase the chances and rates of survival. The program has four main themes to achieve its objective: studying the effects of natural products, investigating carcinogens and other environmental risks, improving symptom management and survivorship, and elucidating the genetic predisposition to prostate cancer.

In addition to the previously mentioned four program divisions, the center also hosts centers of excellence. The comprehensive cancer center, as the name implies, involves all types of cancer. The centers of excellence have a narrower focus: brain tumors, prostate cancer, and breast cancer.

The Brain Tumor Center of Excellence was founded in 2003 in order to develop a thorough academic program at the center. This center of excellence was born of clinical care and research in patients with tumors as well as growing research interest in the field. The Breast Cancer Center of Excellence has a focus on four specific subjects: biology of carcinogenesis and malignant progression, analysis of data sets to identify predictive markers, survivorship and quality of life support, and novel imaging and therapeutics.

The Prostate Cancer Center of Excellence, founded in January of 1999, facilitates multidisciplinary research related to prostate cancer.

Michael Fox
Independent Scholar

See Also: Brain Tumor, Adult; Breast Cancer; National Cancer Institute.

Further Readings

Congo, Democratic Republic of

The central African nation officially termed the Democratic Republic of Congo has had a long
and tumultuous history. In the late 19th century, Belgium made the territory of the Congo into a Belgian colony, and the citizens of the Congo suffered greatly as a result of colonial mistreatment during this time. The Congolese people were granted their independence from colonial rule in 1960, and a series of wars ensued for control of the nation’s governance. Stability still lacks in the Democratic Republic of Congo, as election results as recent as 2011 were lauded as fraudulent.

In the Congo, the lack of access to treatment for cancer patients is an increasingly problematic national dilemma. According to recent studies, it is estimated that less than one out of every two cancer patients in the Congo have access to even the most rudimentary cancer care. Moreover, those who can afford their cancer care are forced to pay fees in excess of $600 every month that care is needed, which is largely unaffordable to the citizens of the Congo; the average monthly wage in the country amounts to just over $150, making it difficult for its citizens to meet even basic health care needs.

Another large problem in the Congo’s fight against cancer is that the country is failing to adequately track information about cancer within the country. As of 2014, the nation has yet to establish a national cancer registry, which would be a vital tool in tracking domestic trends in the disease. Because the Congo has a population of more than 60 million citizens and is quickly growing, it is now more important than ever for the country to begin instituting a nationwide cancer registry in the interest of its cancer patients, physicians, and researchers. Certain groups, like the African Organization for Research and Education on Cancer, are currently lobbying the Congolese government in an attempt to bring cancer registries to the nation.

The Congo is a unique country with a unique cancer situation; there are large obstacles in the way of cancer care in the nation, though with sustained national efforts, these obstacles can be overcome. Diseases like acquired immunodeficiency syndrome, cholera, and malaria are currently huge problems in the Congo, and thus, in light of the nation’s attempt to tackle these other diseases, cancer has not received enough attention over the past few years with regard to research and funding. To compound the problem further, physicians like Judith Nsondé Malanda, who is a cancer specialist at the University Teaching Hospital in the Congo’s capital of Brazzaville, estimate that there might not be even 40 specialists operating within the whole of the African continent, much less the Democratic Republic of Congo. If the Congo is to adequately meet its cancer treatment challenges, the nation will need to bring in more cancer specialists, increase funding and research on the disease, and begin public health campaigns in order raise awareness.

In light of the nation’s lack of a national cancer registry, it is difficult to ascertain with precision the exact nature of cancer incidences in the Congo. However, inferences can be made from the little information that is available on cancer in the country. Presently, it appears that the most prevalent forms of cancer in the Congo are breast, liver, prostate, and uterus cancer. Liver cancer is the most common form of cancer in males in the country, while uterus cancer is the most common incidence of cancer in females here. Data also suggest that certain cancers such as breast and cervical cancer are quickly increasing in prevalence in the nation’s female population, while lung cancer is increasing in prevalence in the male population of the country as a result of increased tobacco consumption.

As mentioned earlier, the Democratic Republic has a serious shortage of cancer specialists, cancer research, and cancer treatment centers. Advocates like Jean-Marie Kasongo Mpolesha of the African Organization for Research and Education on Cancer are currently trying their best to bring nationwide cancer registries to the Congo, and specialists like Judith Nsondé Malanda are providing the full extent of their desperately needed medical expertise in the fight against the disease. In the next several years, cancer researchers hope to see a more centralized and efficient effort in the domestic struggle against cancer.

William M. Peaster
Independent Scholar

See Also: Breast Cancer; Developing Countries; Lung Cancer, Non–Small Cell; Lung Cancer, Small Cell.

Further Readings
Cosmetics

According to the definition of cosmetics offered by the American Cancer Society, the majority of women and men in U.S. culture use some kind of personal care product that can be categorized as such. Products may include everything from traditional makeup such as eye shadow, lipstick, and face powder to perfume, cologne, shampoo, and hair colors—even toothpaste and deodorant. Although much current research is not conclusive, significant concerns have been raised that question the presence of possible cancer-causing agents in these products.

To the extent that most Americans use cosmetics on a daily basis that may potentially compromise health, it is important to understand the connections between the use of cosmetics and health concerns. Furthermore, the composition of these products and the regulation of that composition, or lack thereof, have created a number of significant controversies regarding the cosmetics industry.

Cosmetics and Health Risks

The American Cancer Society reports that some cosmetics may result in skin or eye irritation or allergic reactions for some consumers, although these types of problems are usually short term and go away if use of the product is stopped. It is difficult to determine to what extent cosmetic products contain ingredients that may have more serious or long-term consequences, as according to the American Cancer Society, testing has not been adequate to understand effects of many cosmetic brands. The Breast Cancer Fund notes that synthetic chemicals are components in cosmetics and points out that some of these same products are used to clean heavy-duty equipment, implying that health concerns may be an issue for further consideration.

Because the skin is a permeable surface, chemicals are absorbed through the skin, and when products are used regularly and remain on individuals for most of the day or evening, they saturate the body with untested ingredients. Some researchers argue that it is difficult to assess the long-term health effects of saturating the skin with chemicals due to the many variables that affect the speed (or probability) of penetration and absorption. Therefore, the long-term health effects of chemicals in cosmetic products are difficult to assess. The large number of ingredients contained in many cosmetics makes research difficult in understanding the possible impacts of specific ingredients on health. Some ingredients in cosmetic products are hormone disruptors, which can affect how estrogen and other hormones act in the body, by blocking them or mimicking them, which throws off the body’s hormonal balance and may cause hormone-receptor-positive breast cancer to develop and grow. Therefore, it is the recommendation of the Cancer Prevention Coalition to choose cosmetics...
that contain the fewest ingredients to achieve the consumers’ goals. More ingredients in personal care products increase the prospect that a product will cause adverse reactions, including allergy, irritation, and cancer. There are concerns that particular chemicals may lead to an increased risk of cancer in some consumers.

**Commonly Found Chemicals in Cosmetics**

A number of chemicals, commonly found in cosmetics, have been linked to potential health concerns. These chemicals include: phthalates, triclosan, 1, 4-dioxane, parabens, ethylene oxide, 1, 3-butadiene, polycyclic aromatic hydrocarbons (PAHs), placental extract, lead, and aluminum. Chemicals in cosmetic products are linked to a number of health issues that can include early puberty or delayed puberty, hormonal disruption, miscarriage, and fertility problems.

Studies show that, when cosmetics are absorbed through the skin, chemicals are found throughout the body, in, for example, blood and urine samples, and are suspected of interfering with the body’s natural processes. Although, as noted earlier, these connections are very difficult to prove with current scientific methods.

**Links to Breast Cancer**

While a number of common ingredients in cosmetics have been linked to cancer, the greatest number of studies appears to focus on links to breast cancer in particular. For example, some researchers are concerned that underarm cosmetics might be a cause of breast cancer due to the application of deodorants and antiperspirant products directly under or on breast tissues. Researchers argue that the strongest supporting evidence comes from unexplained clinical observations showing a disproportionately high incidence of breast cancer in the upper outer quadrant of the breast, just the local area to which these cosmetics are applied. A biological basis for breast carcinogenesis could result from the ability of the various constituent chemicals to bind to DNA and to promote growth of the damaged cells, describes P. D. Darbre.

Research in this area is especially critical because, if links do exist between chemicals and breast cancer, preventative action might easily be undertaken, though most researchers point out that more research is needed to learn about possible long-term health effects. Parabens are used as preservatives in many products, including a wide range of beauty products and are a group of chemicals that have been widely studied because of their links to breast cancer. Because they have the ability to pass through the skin, they are then able to have an estrogen-like influence on the body’s chemistry. They are found throughout the body due to their expansive presence in products including, but not restricted to, beauty aids. Phthalates, another commonly studied group of chemicals in breast cancer research, are found in nail polish, hair spray, and many other products in which scent is a component of the process. They function as hormone disruptors and disturb the body’s hormones, in particular those that influence estrogen production.

**Controversies**

There are several recent controversies regarding the use of unregulated products containing possible cancer-causing agents in the cosmetics industry. In particular, major companies such as Revlon and Avon have been challenged by consumer groups to reformulate products that contain possible cancer-causing agents. Revlon was alleged to use more than seven controversial chemicals in their products. Avon, Johnson & Johnson, and Procter & Gamble...
all have taken steps to eliminate the use of questionable chemicals in their makeup lines. For example, Avon has agreed ultimately to remove triclosan, a commonly used antibacterial compound, from its product line. Both Johnson & Johnson in 2012 and Procter & Gamble in 2013 have agreed to voluntarily adopt standards that are higher than governmental mandates, eliminating triclosan, parabens, phthalates, preservatives that release formaldehyde, and the phthalate DEP.

Catherine A. Dobris  
Indiana University–Purdue University  
Rachel Diana Davidson  
University of Wisconsin–Milwaukee

See Also: Breast Cancer; Chemical Industry; Daily Life; Hair Dye; Johnson & Johnson (United States).

Further Readings


Cost of Therapy

Health care costs continue to climb not only in the United States but across the world. As we become more aware of the etiology of disease, complex procedures for more accurate diagnoses, the complexity of treatments, and even the addition of preventative measures have become popular among the masses to maintain overall health. One of the most prominent and rising causes of death in the United States is cancer. Although advances in the oncologic conceptualization and disease have increased over the past years, cancer continues to represent a significant portion of health suffering and substantial financial cost to patients, their families, and their community. The Centers for Disease Control and Prevention reported that cancer was the second-leading cause of death in the United States, regrettably ending more than 500,000 lives in 2011.

In 2014, the American Cancer Society reported that approximately 585,720 residents in the United States alone will likely expire secondary to cancer, representing the second-leading cause of death. Cancer is expected to account for almost one-quarter of all chronic illness-related mortality, and the cost associated with treatment, including end-of-life care, is astronomical.

As the numbers of newly diagnosed cases increases, in the context of more effective but often costly treatments, the number of cancer survivors consequently rises. In 2010, the National Cancer Institute reported more than 13,700,000 cancer survivors living in the United States alone and projected more than 18 million survivors by 2020. On a worldwide spectrum, deaths due to cancer fall only behind cardiovascular and infectious diseases. The cost of cancer prevention and treatment programs continue to rise.

According to National Institutes of Health estimates, $89 billion were spent on cancer care in 2007, with the economic burden totaling
$219.2 billion when including indirect costs associated with lost productivity and death. As the incidence of cancer increases in the aged, and survivors live longer, the cost of care increases. In 2010, the cost of cancer care in the United States grew to $157 billion. The National Cancer Institute noted that the initial cost of cancer therapy increased more than 7 percent from approximately $40,000 dollars to $43,000, while continued care costs increased more than 10 percent, from approximately $46,000 to $52,000. Predictions of cancer therapy costs are astonishing, as the institute assumes that initial and continued care costs in 2020 will rise 19 and 31 percent, respectively. The National Cancer Institute also specified that brain cancer produces the highest cost of care, while melanomas represent the lowest cost of therapy, independent of gender.

Although costs differ on an individual basis, some of the major factors that contribute to costs of cancer therapy include specific cancer treatments, medications, surgeries, lab tests, the number and location of doctor’s appointments, travel, support costs, mental health care, and employment. Therapies can last from a few days to months and, in some cases, into years depending on a variety of factors. Typical cancer therapies include chemotherapy, radiation, and surgery. Oral chemotherapy drugs are expensive, and depending on an individual’s insurance plan, the co-payment may be extremely high, even into the thousands of dollars per treatment. Radiation therapy is usually deployed to arrest the growth of cancer cells. But like surgery, the costs of radiation can vary substantially as a function of individual status, insurance, and provider-related factors. Cancer therapy costs vary widely across modalities of treatment ranging from $1,700 for a single treatment with conventional radiation techniques to more than an average of $16,000 for four treatments using Cyberknife, according to N. Fawcett. Other overt and hidden therapy costs include traveling to appointments, the use of specialized facilities, and even home health assistance. In addition, work productivity can be reduced, employment may be stalled or terminated for the patient or caregiver, and a range of psychological factors and assets may be compromised. This includes the loss of primary and secondary support systems, the cost of depression and anxiety, and a compromised sense of self, explains L. C. Campbell and colleagues. These hidden costs of cancer and cancer therapy are sometimes greater for minority and historically disenfranchised populations.

Christopher L. Edwards
Jay Trambadia
Duke University Medical Center

See Also: Biologic Therapy; Cancer Therapy Evaluation Program; Chemotherapy; Gene Therapy; Proton Therapy; Radiation Therapy.

Further Readings

Costa Rica

Across the world, cancer is the second-leading cause of death and disability. It has moved beyond high-income countries to low-income, developing countries. In developing countries, there is a silence that surrounds the disease that results from
a lack of knowledge and meaningful information on causes and treatment. Many cultures never use the word cancer and rarely discuss the illness. The prevalence of cancer is on the rise in Costa Rica, claiming on average 2,559 deaths among men and 2,035 deaths among women per year. In 2009, there were 7,163 new cases of cancer in Costa Rica, and there is expected growth of 10,627 by 2020. There are many risk factors that contribute to the high rates of cancer. These include tobacco use, fruit and vegetable intake, alcohol consumption, obesity, and low physical activity. However, there are environmental and occupational risk factors that also lead to high incidents of cancer among Costa Ricans. Risk factors include agriculture occupations and the use of pesticides.

There are 14 regions in Costa Rica, and geographically, there are differences in the occurrence of cancer and types of cancers among Costa Ricans. The cancer registry was developed to help keep track of newly diagnosed cancer cases regionally as well as persisting cancer cases. The functioning and quality of the information in these registries is unknown. The cancer registry has catalogued many forms of cancer visible in Costa Ricans. In urban areas of the country, lung, colorectal, breast, uterus, ovary, prostate, testis, kidney, and bladder cancers were more visible. In rural regions, gastric, cervical, penile, and skin cancer were more prevalent. In excessive coffee-growing areas, skin cancer was diagnosed at a higher rate.

The growth of cancer in Costa Rica has been contributed to geographical and environmental differences such as the use of pesticides and occupational exposure to pesticides. Agriculture is the principal economic activity, and it has been this way for decades. In urban areas of Costa Rica, such as the Central Valley, Southern Central Valley, and Northern Central Valley, coffee is the main crop. In these areas, there is a high usage of pesticides, paraquat, lead arsenate, and copper. In rural areas of Costa Rica, noted as the northern mountain chain of Central Valley, Western Central Valley, southern mountain chain of Central Valley, Eastern Central Valley, east mountain chain, mid-north Costa Rica, Northern Central Pacific Region, Southern Central Pacific and South Pacific Region, northwest Costa Rica, mid-south Costa Rica, and east Costa Rica, the main crops are coffee, sugarcane, corn, beans, rice and bananas.

The use of pesticides is high in these areas, with many utilizing more than three or more combinations of pesticides. In these areas, pyrethroids, phenoxyacids, propanil, and fungicides are used, and formaldehyde is frequently used in addition to paraquat, lead arsenate, and copper. In fact, the excessive use of paraquat and lead arsenate in coffee-growing areas has been linked to skin cancer. Lung cancer and female hormone-related cancers have been linked to heavy pesticide use in rural areas among Costa Ricans. Cancer has also been linked to banana plantation workers, where there is use of formaldehyde and fungicides along with the more common pesticides.

High cancer risk has been declared among agricultural workers in Costa Rica. Skin and lip malignancies have been associated with ultraviolet radiation exposure during farming. Leukemia also has been linked to agriculture workers’ exposure to viral zoonosis. Additionally, leukemia in children has been linked to mothers’ occupational exposure to pesticides a year before conception and during the first and second trimesters. It was also found to link with fathers’ exposure to pesticides during the first year of conception and the first trimester. Paraquat, benomyl, and picloram have been noted specifically as pesticides that contribute to childhood leukemia by parental exposure.

Researchers also have found that there were elevated risk estimates among banana plantation workers. Banana production, considered to be labor, and related work has been linked to excessive pesticide use for decades. Researchers have found that, among male banana plantation workers, there was an increase in melanoma and penile cancer. Among female banana plantation workers, there was an increase in cervix cancer and leukemia. Additionally, men’s risk for lung cancer was elevated among those with longer lengths of employment.

Breast cancer has also become an increasing concern among women in Costa Rica. There has been an increase in occurrences between 1995 and 2003 from 32.3 to 40.07 percent per 100,000 women. In 2006, there were 13.14 per 100,000 women breast cancer-related deaths in Costa Rica, the highest occurring in malignant neoplasm. Self-exams and mammography have been the primary intervention focus for decades in Costa Rica, yielding really low coverage. Most are diagnosed at the hospital with
advanced stages of breast cancer. Research has identified a need for early interventions, which includes screening that extends beyond mammography and self-exams to combat diagnosis in advance stages.

The lack of control over work conditions and the lack of attention to environmental emissions from traffic, industry, and agriculture have led to the advancement of cancer regionally in Costa Rica. In fact, attention to the issues recently has become a concern in the country, causing Costa Rica to be behind in addressing these work and environmental issues. Furthermore, this country's developing status and reliability on agriculture to sustain the economy puts the country in a difficult position in addressing the use of pesticides. The new cases of cancer are expected to grow, and researchers offer the country limited alternatives in addressing the issues of cancer while maintaining its position in the agriculture production. Furthermore, there is a need for improvement in early detection of cancers, which include comprehensive advance screenings of breast cancer and cancers prevalent in areas of high pesticide usage as well as a need for cost-effective interventions for all types of cancer.

Narketta Sparkman
Hope Comer
Old Dominion University

See Also: Developing Countries; Pesticides; Screening, Access to.

Further Readings


Côte d’Ivoire

Côte d’Ivoire is situated in West Africa. It is bordered on the north by Mali and Burkina Faso, on the east by Ghana, on the south by the Atlantic Ocean, and on the west by Guinea and Liberia. It is the 15th-most populous country in Africa and 59th in the world, with a population of more than 16.9 million. French is the official national language, and there are 79 living indigenous languages still spoken by respective ethnic groups. The most widely spoken ethnic languages in Côte d’Ivoire include Anyin, Baoule, Dan, Jula, and Senufo. Each ethnic group has its own rich traditions of ethnomedicine. For example, a traditional healer who uses medicinal plants for treating ailments is known as komian in Agni as well as in Baoule and as fil-cha in Jula. Traditional medicine continues to play a very dominant role in health practices for much of the population, particularly those living in rural areas.

There are many traditional medicinal preparations used in Côte d’Ivoire for treating cancers and other associated conditions. Most of these traditional medicines incorporate the use of myriad local plant materials, many of which have shown medicinal properties in laboratory studies. For example, extracts of the inner bark of Kigelia pinnata have demonstrated significant antitumor activities. Research suggests that use of certain plants may actually help protect against cancer by reducing oxidative stress and stimulating enzymes and other processes that help the body to fight against carcinogens. For example, an extract from Bidens pilosa, a plant used by traditional healers, has demonstrated substantial antioxidant potential, as has an extract of Cleome gynandra.

Medicinal plants are used traditionally in Côte d’Ivoire to treat many health problems associated with cancers and associated conditions. For example, the plant juice of Mikania cordata, which the Abe call ndckpacha, the Ebrie call kokotobanji or kuagbo, the Guere call don, and the Shien call bazeru, is drunk traditionally for treating abdominal pain. A stem bark extract of Tetrapleura tetraptera,
which the Agni call *plakasse*, the Ebre call *mberekrechia*, and the Guere call *kussa*, is used traditionally for treating hemorrhoids. A root decoction of *Strophanthus hispidus*, which the Agni call *makwa*, the Baoule call *akueyama*, the Ebre call *salobego*, and the Guere call *bidu* or *zrebudu*, is drunk traditionally for relief of stomach pain. Leaves of *Leptoderris fasciculata* are widely used traditionally in cases of menorrhagia.

There are serious deficiencies of modern pharmaceutical supplies, as opposed to traditional preparations, and in modern medical services for cancer and similar conditions in Côte d’Ivoire. According to the World Health Organization’s (WHO’s) Health System Response and Capacity, as of 2010, there was no general availability of either chemotherapy or radiotherapy in the public health system in Côte d’Ivoire.

Côte d’Ivoire is a signatory to the Single Convention on Narcotic Drugs, Convention on Psychotropic Substances, and UN Convention against the Illicit Traffic in Narcotic Drugs and Psychotropic Substances; consequently, laws exist to control narcotic and psychotropic substances and precursors. The annual consumption of controlled substances is highly regulated to curtail abuse. Accordingly, the annual consumption of morphine in 2010 was 0.00277 milligrams per capita (mg/capita), fentanyl was 0.000365 mg/capita, and phenobarbital was 10.3475 mg/capita. This creates a serious lack of access to basic palliative care for cancer and other conditions.

Cancers account for a substantial amount of disability and suffering among impacted populations. According to the WHO’s Disease and Injury Country Estimates, the age-standardized disability adjusted life-year estimates for 2004, the 10 most prevalent cancers in Côte d’Ivoire were led by liver cancer at 241 per 100,000 population; breast cancer at 208 per 100,000 population; prostate cancer at 206 per 100,000 population; lymphomas at 201 per 100,000 population; cervical and uterine cancers at 177 per 100,000 population; stomach cancer at 99 per 100,000 population; leukemia at 71 per 100,000 population; colon and rectal cancers at 70 per 100,000 population; and bladder cancer at 40 per 100,000 population.

Modern pharmacological supplies, as opposed to traditional preparations, are generally, if available at all, in short supply in Côte d’Ivoire, as are modern medical services. Both prescription and over-the-counter products are often unavailable. Consequently, health problems are endemic and limit development. For example, an estimated 570,000 people live with human immunodeficiency virus (HIV) in Côte d’Ivoire, which ranks the country 12th highest in Africa and 17th-highest in the world. The mortality rate for HIV/acquired immune deficiency syndrome (AIDS) in 2010 was 7,700. Debate continues on the relative risks in Africa for respective cancer types for those infected with HIV. The mortality rate for tuberculosis in 2001 was 75 per 100,000 population and that for malaria was 103 per 100,000 population, while the mortality rate for cancers in 2009 was 170 per 100,000 population.

Nine cancers are among the 50 leading causes of death in Côte d’Ivoire. Prostate cancer is the 22nd-leading cause of death; the age-standardized death rate is 18.65 per 100,000 population, which ranks Côte d’Ivoire as the 12th-highest country in the world for prostate cancer deaths. Breast cancer is the 26th-leading cause of death; the age-standardized death rate is 14.49 per 100,000 population, which ranks 118th globally. The remaining seven cancers that are in the 50 leading causes of death, along with their age-standardized death rates, are cervical (9.53), liver (7.42), lymphomas (5.07), stomach (4.46), lung (3.63), colon and rectal (2.55), and leukemia (2.17). Furthermore, according to the WHO’s Global Health Observatory Data Repository, in 2008, the age-standardized estimates of deaths from all cancers was 80 per 100,000 population for males and 79 per 100,000 population for females. As a consequence, life expectancy is only 48.42 years, which ranks Côte d’Ivoire 28th in Africa, 199th in the world. There is a clear and urgent need for improved cancer awareness, early detection programs, and health services infrastructure in Côte d’Ivoire.

Victor B. Stolberg
Essex County College

See Also: Burkina Faso; Developing Countries; Ghana; Guinea; Mali.

Further Readings
COX-2 Inhibitors

Nonsteroidal anti-inflammatory drugs (NSAIDs) have been a staple of modern medicine ever since the mass production of aspirin began in 1899. Although aspirin and similar early-generation NSAIDs were immensely successful in treating various inflammatory and noninflammatory conditions such as fever, arthritis, and headache, their use was often limited due to adverse effects related to the gastrointestinal (GI) system. Chronic NSAID use is still associated with GI damage that leads to bleeding, ulcers, and perforation. Although most of the therapeutic and adverse effects of NSAIDs were known shortly after the introduction of aspirin to the market, it was not until several decades later that the mechanism of NSAIDs was discovered. NSAIDs inhibit the enzyme cyclooxygenase (COX), which is normally responsible for the synthesis of prostaglandins. Prostaglandins play important roles in both physiologic and pathologic processes including pain, fever, inflammation, cancer, and asthma.

In the early 1990s Needleman, Simmons, and Herschman discovered an inducible isoform of COX, known as COX-2. COX-1 is an isoform that is constitutively expressed in several tissue types, including endothelium, platelets and monocytes, while COX-2 is expressed during inflammation by tissues such as vascular endothelium, macrophages, monocytes, and osteoclasts. COX-2 is also constitutively expressed during reproduction, bone resorption, and renal physiology. COX-1 is constitutively expressed in the GI tract, where it produces prostaglandins that increase mucous release and decrease gastric acid secretion. Thus, the inhibition of COX-1 by traditional NSAIDs such as aspirin contributes to gastric erosion.

The discovery of an isoform that is induced by inflammation made it possible to design drugs that specifically inhibit that isoform without inhibiting the constitutively active COX-1 isoform that protects the gastric mucosa. Therefore, the first COX-2 inhibitors were designed with the intention of sparing users from the GI toxicity of traditional NSAIDs while still treating similar inflammatory conditions. Shortly after their release, the first COX-2 inhibitors (celecoxib and rofecoxib) became blockbuster drugs. However, it was not long before the COX-2 inhibitors were discovered to have their own unique adverse effects. Constitutive COX-2 present in the vascular endothelium is responsible for producing anti-aggregative prostaglandins that counter the pro-aggregative thromboxane A2 produced by COX-1 in platelets. Disinhibiting COX-2 alone disrupts this balance and significantly increases the risk of life-threatening cardiovascular thromboembolic events. It was not long before several COX-2 inhibitors, such as rofecoxib, were withdrawn from the market, and others, such as celecoxib, were marked with black box labels warning about their cardiovascular toxicity.

Although the risk of cardiovascular adverse effects has prevented COX-2 inhibitors from replacing traditional NSAIDs as the standard treatment for most inflammatory conditions, they have novel effects that still make them valuable therapeutic options for some conditions. Along with inflammation, COX-2 has been implicated in carcinogenesis, apoptosis, and angiogenesis, making it a viable target for preventative cancer therapies. COX-2 is overexpressed in most cancers, including colorectal, gastric, lung, breast, ovarian, skin, and esophageal cancer, and COX-2 inhibitors have been proven to significantly reduce the risk of many types
COX-2 and Malignancy
Chronic inflammation has long been considered a leading cause in the development of cancer, and recent evidence suggests that COX-2 may directly link chronic inflammation to cancer. COX-2 expression is directly induced by inflammation, and the overexpression of COX-2 alone is capable of stimulating all of the processes that eventually lead to carcinogenesis. These processes include mutagenesis, apoptosis inhibition, angiogenesis, metastasis, and immune system evasion. COX-2 can be found in all tissues involved in the progression of carcinogenesis, including premalignant lesions, carcinoma in situ, invasive cancer, and metastases. Furthermore, various molecular studies have identified COX-2 overexpression in all types of cancer. Overexpression of COX-2 contributes to the development of malignancy in many ways. COX-2 increases the production of reactive oxygen species that contribute to mutagenesis, increases the production of prostaglandins that promote cell proliferation, stimulates vascular endothelial growth factor (VEGF) release to promote angiogenesis, and increases matrix metalloproteinase production, which augments metastasis. It also leads to up regulation of the BAX gene (anti-apoptotic) and down regulation of the Bcl-2 gene (pro-apoptotic). New evidence continues to arise that suggests that the overexpression of COX-2 directly contributes to the cellular and molecular changes that precede and prolong malignancy. Therefore, there is interest in research studying the use of COX-2 inhibitors as effective agents of chemoprevention.

There is also evidence that there are COX-independent mechanisms by which traditional NSAIDs and COX-2 inhibitors prevent the progression of malignancy. Even in in vivo models with significantly decreased expression of COX-2, celecoxib still inhibited the development and progression of several cancer cell lines. Celecoxib has also been shown to be more efficacious in preventing certain cancers than rofecoxib, a much more potent COX-2 inhibitor. Studies show that COX-2 inhibitors have COX-independent pro-apoptotic properties by inhibiting NF-kB at the level of nuclear translocation, increasing p53 activity and inducing NSAID-activated gene-1 (NAG-1) activity. By another mechanism, β-Catenin, a protein that is appreciably elevated in both familial adenomatous polyposis (FAP) and most colorectal carcinoma tissue, was extensively degraded only two hours after celecoxib treatment was administered to human colon carcinoma cells. The existence of COX-2-independent mechanisms in celecoxib has incited interest in the development of a celecoxib analog that retains its antitumorigenic properties without inhibiting COX-2. Such a drug would be void of many of the adverse cardiovascular effects that currently limit the use of celecoxib in many potential patients.

As research continues to implicate COX-2 in contributing directly to carcinogenesis, there is an increasing interest in research studying the use of COX-2 inhibitors as effective agents of chemoprevention and adjuncts to standard chemotherapy. The next several sections review the usefulness of COX-2 inhibitors as chemopreventative agents in a variety of different cancers. Most of this focuses specifically on celecoxib as both valdecoxib and rofecoxib were removed from the market.

Colorectal Cancer
Human colorectal cancer is an ideal model for the study of carcinogenesis for a variety of reasons. For example, it develops in a step-wise fashion from premalignant lesions to malignancy over a long period of time (10 or more years from premalignant polyp to invasive cancer). This provides researchers with a long period of time to observe and intervene at various stages in carcinogenesis and a wide window to provide chemopreventative therapy. There are also conditions, such as FAP, in which an inherent mutation of a gene involved in carcinogenesis leads to a significantly increased number of precancerous polyps that overexpress COX-2. The step-wise development of CRC in people with and without FAP essentially remains the same, except that one of the steps is skipped in FAP. This shortens the time required for carcinogenesis and increases the number of precancerous polyps that arise. The similarity in the development of malignancy in FAP and spontaneous CRC makes FAP an ideal model for studying the carcinogenesis of CRC in normal subjects, albeit with a much higher incidence of cancerous and precancerous lesions in FAP. COX-2 plays an important role in initiating...
and maintaining the step-wise process that leads to the development of both CRC and the vast number of precancerous and cancerous lesions in patients with FAP. A major discussion point concerning the effect of COX-2 inhibition on the development of polyps in FAP is that it translates into similar results regarding the development of uncomplicated CRC.

A 2000 study by Steinbach's group was one of the earliest studies to investigate the effect of celecoxib in patients with FAP. Patients were given either celecoxib, 100 milligrams (mg), celecoxib 400 mg, or a placebo twice a day for six months and underwent an endoscopy before and after the trial. Changes in the size and number of polyps in the test subjects during the six-month period were then analyzed. Subjects receiving the high dose of celecoxib had a 28.0 percent reduction in the number of polyps and a 30.7 percent reduction in the total sum of polyp diameter, while those receiving placebo had 4.5 and 4.9 percent reductions in size and diameter, respectively. Subjects receiving the lower 100 mg dose twice a day had an 11.9 percent reduction in polyp size and 14.6 percent reduction in total polyp diameter, which was not statistically significant. A separate study confirmed these results with similar findings, and as a result, the Food and Drug Administration approved celecoxib as an oral adjunct to the standard care (endoscopic surveillance and surgery) of FAP.

There also have been studies to evaluate the potential use of celecoxib to prevent recurrent adenomatous polyps in subjects with recently removed adenomatous polyps. The Adenoma Prevention with Celecoxib trial studied more than 2,000 patients with high risk of adenoma recurrence. Patients were given a placebo—200 mg twice a day or 400 mg twice a day—for an average span of 33 months. Follow-up at that time revealed a significant reduction in polyp recurrence, particularly in the recurrence of more high-risk polyps. Thus, the patients taking celecoxib who did have recurrences presented with polyps that were far less likely to develop into adenocarcinoma.

Although the benefits of COX-2 inhibitors in the chemoprevention of patients with baseline risk for CRC are questionable due to the risk of cardiovascular events, the benefits of therapy far outweigh potential adverse effects in patients already at an elevated risk for developing CRC. Future therapies will focus on retaining the benefits of COX-2 inhibitors in the prevention of CRC while reducing the potential for catastrophic cardiovascular events. Nonetheless, COX-2 inhibitors, particularly celecoxib, are important agents in the chemoprevention of high-risk polyps and CRC.

More recent studies have examined the role of celecoxib as an adjunct to traditional chemotherapy, hoping to augment the effects of the chemotherapy on cancer cells without increasing toxicity. The combination of celecoxib with a regimen of folinic acid, fluorouracil, and oxaliplatin improved the quality of life and three-year survival rate in patients with advanced colorectal cancer. Celecoxib has also been established to decrease the risk of hand-foot syndrome, a common side effect in patients undergoing capecitabine treatment (an oral prodrug to fluorouracil).

Gastric Cancer
Although there is less existing literature regarding the use of COX-2 inhibitors to prevent gastric carcinoma than colorectal carcinoma, there is still a widely recognized progression in the carcinogenesis of gastric cancer that provides a foundation for the study of chemoprevention. A recent study revealed that two years of celecoxib treatment resulted in a significant regression of high-grade gastric lesions that was comparable to Helicobacter pylori (H. pylori) eradication, but there was no combined benefit of H. pylori eradication and celecoxib treatment. However, there have been recent studies that link celecoxib treatment in adjunct with traditional chemotherapy to decreased levels of VEGF, an indicator of tumor angiogenesis and progression.

Esophageal Cancer
Similar to gastric and colon carcinoma, both types of esophageal carcinoma have recognizable progressions from benign to malignant lesions. Esophageal squamous cell carcinoma is preceded by squamous dysplasia just as esophageal adenocarcinoma is preceded by Barrett’s esophagus (intestinal metaplasia in the esophagus). Both precursor lesions provide a basis for the study of COX-2 inhibitors in the chemoprevention of esophageal cancer. There is not a large body of evidence to support or negate the effectiveness of COX-2 inhibitors in the prevention of esophageal squamous cell carcinoma, but a phase IIb multicenter randomized placebo-controlled trial of celecoxib for patients with Barrett’s esophagus did
not significantly prevent progression of Barrett’s esophagus to esophageal adenocarcinoma. However, studies of celecoxib as a chemopreventative agent in both Barrett’s esophagus and squamous dysplasia warrant further consideration.

Breast Cancer
Breast cancer is the most common cause of cancer in women and the second-leading cause of cancer death in women. There is continuous intensive effort by the research community to novel therapies for the detection, prevention, and treatment of breast cancer. Among these novel therapies is the use of celecoxib as both a chemopreventative agent and adjunct in chemotherapy. Studies have shown that there is a significant risk reduction in the incidence of breast cancer in high-risk patients who have taken celecoxib for two or more years. There are also more recent studies that support celecoxib therapy in adjunct with cyclophosphamide for patients suffering from high-grade breast carcinoma. Dual therapy of celecoxib with aromatase inhibitors has also shown promise in high-grade cancer.

Lung Cancer
Lung cancer is the most common cause of cancer death in men and women, on average causing more deaths a year than breast, prostate, and colon cancer combined. Studies have estimated that COX-2 activity is increased in 70 to 90 percent of lung cancers. Lung carcinogenesis also has been associated with the alterations of the arachidonic acid cascade, which is inactivated by NSAIDs and COX-2 inhibitors. A key reason for the lethality of lung cancer is that there is no effective, noninvasive method of detecting precancerous and early malignant lesions. Therefore, lung cancer is often not diagnosed until it has progressed to late-stage disease. This also makes it difficult to develop a model with an appropriate end point to test the chemopreventative efficacy of various therapies, such as COX-2 inhibitors. Before the true potential of celecoxib in the chemoprevention of lung cancer can be exploited, an effective method of early detection must be developed. There has been at least one case-control study that has observed a significant risk reduction in high-risk patients (several pack a year history of smoking) taking NSAIDS and celecoxib, but two phase III trials regarding the effect of celecoxib on overall survival in non–small cell lung cancer showed no significant improvement. These results, however, do not negate the potential use of celecoxib in treating certain subpopulations. A recent study found an inverse relationship between the plasma level of VEGF and the impact of celecoxib (compared to placebo) on survival. Low plasma levels of VEGF were present in patients with cancer more likely to respond to celecoxib and improve survival. One possible explanation for this is that VEGF directly blocks the antitumor effects of celecoxib.

Non-Melanoma Skin Cancer
The use of celecoxib in the prevention of nonmelanoma skin cancers (NMSCs) has been studied in a limited context. NMSCs have an increased risk of developing in easily identifiable precancerous lesions, such as actinic keratosis, making patients with actinic keratosis (AK) viable candidates for preventative celecoxib treatment. One double-blinded, placebo-controlled, randomized, multicenter trial revealed that, although celecoxib did not reduce the risk of developing actinic keratosis, it did reduce the incidence of new NMSCs in patients with AK. However, due to the good prognosis of NMSCs and the possible risk of thrombotic cardiovascular events while on celecoxib, the study was stopped prematurely. Although the mortality from NMSCs is low, there are certain conditions where the mortality from NMSCs is significant enough to warrant further consideration of celecoxib chemoprevention. Patients with basal cell nevus syndrome (BCNS) often develop hundreds to thousands of basal cell carcinomas that may lead to significant functional disability and aesthetic disfigurement at an early age. A study of 60 patients with BCNS showed a promising but nonsignificant decrease in the tumor burden of patients taking celecoxib. A similar condition in which patients may benefit from celecoxib therapy is Xeroderma Pigmentosum (XP). In XP, patients have nearly 10,000 times the risk of developing NMSCs compared to the general population. No known trials have been performed involving XP patients and celecoxib, but they are a population of interest.

Bladder Cancer
Bladder cancer is the most common malignancy of the genitourinary tract, with more than 60,000 new cases and almost 13,000 deaths suffered annually.
The majority of these new cases (less than 80 percent) are transitional cell carcinomas that do not invade the bladder muscle. Nonmuscle invasive bladder cancer (NMIBC) is generally treated with surgical resection and postoperative Bacillus Calmette–Guérin (BCG) therapy to prevent recurrence. Nonetheless, recurrence is estimated to occur in anywhere from 30 to 80 percent of treated patients. The implication of COX-2 in the carcinogenesis of NMIBC and the efficacy of COX-2 inhibitors in the chemoprevention of various malignancies have garnered interest for celecoxib therapy to prevent NMIBC recurrence. Although a clinical trial revealed no significant prolongation of the time to recurrence (TTR) in patients with resected NMIBC receiving celecoxib, there was still a trend toward an increase TTR compared with placebo. BOXIT (Bladder COX-2 Inhibition Trial), an ongoing phase III trial that will report the recurrence of NMIBC over three years, will provide physicians with further insight regarding the potential of celecoxib in NMIBC chemoprevention.

Ovarian Cancer
Although most ovarian cancer is initially treatable with platinum-based combination therapy, most patient experience disease recurrence within two years of treatment. Overexpression of COX-2 plays a large role in the carcinogenesis of ovarian cancer and is directly related to poor prognosis. A recent trial found that the addition of celecoxib to first-line treatment plus docetaxel did not significantly improve progression-free survival or overall survival. Platinum-based treatment, generally used as first-line treatment, is often repeated in recurrent ovarian cancer that has already received first-line treatment and additional nonplatinum-based chemotherapy. The response rates for platinum-based retreatment are low, ranging from 6 to 23 percent. COX-2, which plays a role in platinum resistance in ovarian cancer, is suspected as a viable target to improve retreatment response. A separate phase 2 trial evaluated the effect of combined celecoxib and cisplatin treatment on heavily treated recurrent ovarian cancer. Patients receiving the combination therapy experienced an overall response rate of 28.9 percent with a median progression-free survival of five months. This compared favorably to response rates to platinum-based treatment alone and are particularly promising because many of the patients in the study had already demonstrated primary or secondary resistance to platinum-based treatment. Furthermore, the response rates showed no relation to the degree of prior platinum resistance, suggesting that celecoxib disrupts platinum resistance. Future treatments with adjunct celecoxib may be tailored to individual patients based on their cancer’s expression of COX-2 and related markers.

Conclusion
COX-2 overexpression is widely accepted as pathologic in all types of cancer and plays a significant role in both the carcinogenesis and malignancy of cancer. The potential of celecoxib and related COX-2 inhibitors as cancer therapies is based generally on two uses: as a chemopreventative agent or as an adjunct to traditional chemotherapy. Numerous studies reveal that celecoxib is effective at reducing the risk of various types of cancers, particularly if an identifiable precancerous state exists for that cancer. Celecoxib has also proven effective as an adjunct to chemotherapy by increasing tumor response to treatment and decreasing tumor recurrence rate. Future utilization of the drug will be dependent on controlling adverse effects and developing a further understanding of the COX-2-independent mechanisms of action of celecoxib.

Krishna Subhash Vyas
Kelsey W. Snapp
University of Kentucky College of Medicine

See Also: Bladder Cancer; Breast Cancer; Chemoprevention; Lung Cancer, Non-Small Cell.

Further Readings
Liebman, T. N., J. A. Stein, and D. Polsky. “Cyclooxygenase-2 Inhibitors for Chemoprevention of Nonmelanoma Skin Cancer: Is There a Role for
Croatia

Croatia, officially known as the Republic of Croatia, is a unitary democratic parliamentary republic known for its large tourism market and is situated at the crossroads of central and southeastern Europe and the Mediterranean. The population of Croatia is more than 4 million people across 20 countries, with most of these inhabitants being Croats (who have their own Croatian language).

Like the rest of the world, Croatian citizens are affected by all of the various forms of cancer, though lung cancer is a particularly large threat in this country.

Lung Cancer

Lung cancer has been a threat to many Croatians over the last several years due to the popularity of cigarette smoking. According to the Croatian Medical Journal, lung cancer incidence and mortality rates in Croatian men under 70 saw a sharp decline between 1998 and 2008; however, the same is not true of Croatian women. According to the journal, lung cancer prevalence and mortality rates in women increased significantly in all age groups older than 40 years and decreased in women between 30 and 39 years old.

Though lung cancer is decreasing overall in Croatia, the republic is still among the highest in number of deaths and incidences for men across European countries. And, though women's rates may be increasing for the younger population, the female age-standardized incidence rates are still fivefold lower than in men. The trends can be explained by the fact that more older women are taking up smoking in Croatia, while men are slowly beginning to quit. This denotes the need for additional cessation and prevention policies across the republic.

Today, lung cancer is the most common cancer in Croatian men and the fifth-most common cancer in Croatian women, and more than one-fourth of all Croatian adults smoke every day. Unfortunately, there are many barriers to creating smoking prevention programs, including limited resources, the social acceptability of smoking, and the transnational tobacco industry’s interest in the republic.

Prostate Cancer

Incidences in prostate cancer are rapidly increasing for Croatian men. Mortalities from this cancer are also on the rise, contrary to trends in countries with higher incomes. To improve this situation, prostate cancer units and different treatment methods should be established across the republic. Increases are likely due to an aging population. In addition to age, risk factors for prostate cancer include ethnic origin and heredity. Other possible factors include exposure to UV radiation, alcohol consumption, sexual behavior patterns, and nutrition.

Leukemia

Leukemia trends in Croatia have stayed relatively the same over the past decade or so, though mortality rates are significantly more unfavorable in Croatia when compared to other countries in western Europe. The lack of improvement in these numbers stems from a late introduction of optimal therapies, though health insurance companies are beginning to cover these needs more efficiently throughout the republic. There are several different forms of leukemia, and it is difficult to determine what may cause the disease, but some breakthroughs have been made over the past several years to address it. We expect that this, combined with greater insurance coverage, will cause mortality rates in Croatia to decline in regard to this disease.

Melanoma

Melanoma occurrences are on a shocking rise in Croatia, with similar trends to countries with intermediate and lower incidence. According to the Croatian Medical Journal, over the span of
20 years, from 1988 to 2008, the overall melanoma incidence increase between the first and the last five-year period was 149 percent for men and 130 percent for women. With numbers this shocking, there is a desperate need for targeted public policies to curb these issues. Sun exposure is a major risk factor for melanoma, and the Croatian coast and islands have more than 2,600 hours of sunshine every year.

Breast Cancer
According to the Canadian Medical Journal, breast cancer rates for women of all ages are increasing in Croatia, though mortality rates remained stable from 1998 to 2008. This increase could be due to lifestyle factors such as alcohol consumption and the use of hormonal replacement therapies and oral contraceptives. According to GLOBOCAN estimates, in 2008, Croatia is among the European countries with an intermediate breast cancer frequency. In 2006, Croatia introduced its national breast cancer screening program, called Mamma, which urges women age 50 to 69 to obtain regular mammograms.

Organizations and Famous Faces
There are a number of cancer-related organizations across Croatia. One such organization is the Croatian League Against Cancer, which was founded in the capital of Zagreb in 1966. The organization specifically focuses on breast and cervical cancer treatment and prevention, and it hosts several symposiums annually to discuss these topics. The Croatian League Against Cancer has been an associate member of the International Union Against Cancer (UICC) since 1967.

Famous Croatians who have been afflicted with various forms of cancer include Vanja Drac (lung cancer), a theater and film actor; Emil Glad, a film actor; Vida Jerman (lung cancer), a film, theater, and television actress; Josip Kuže (leukemia), a football coach and player; Tomislav Ladan, an essayist, critic, and novelist; Antun Gustav Matoš (throat cancer), a poet, short story writer, journalist, travelogue writer, and essayist; Krsto Papić, a Croatian screenwriter and film director; Mate Parlov (lung cancer), a Croatian boxer and Olympic gold medalist; Vjekoslav Šutej (leukemia), a prominent Croatian orchestral conductor; and Franjo Tuđman, the country’s first president.

Conclusion
Despite the fact that new and comprehensive data about cancer incidences and mortality rates in Croatia is now available, more educational investment is needed to ensure early detection and prevention. In terms of lung cancer, more education is needed about the hazards of smoking tobacco, especially among young women. Men should be educated about the dangers of prostate cancer, which is widely spread across the country. Finally, all Croatians should be alerted to the dangers of melanoma resulting from sun exposure.

Katie Moss
Independent Scholar

See Also: Breast Cancer; Leukemia, Chronic Myelogenous; Lung Cancer, Non–Small Cell; Lung Cancer, Small Cell; Melanoma; Prostate Cancer.

Further Readings

Cuba
Cuba is the largest island in the Caribbean Sea, the Pearl of the Caribbean. Its rich soil has been the basis
of its economy since the Spanish conquest, leading to the production for export of sugar and tobacco and the import of African slaves for this labor-intensive work. The Spanish colony established there was supplanted by the United States in the Spanish–American War of 1898, with Cuba under North American influence for the next half century. Another abrupt change came when a physician, Dr. Fidel Castro, led a revolutionary movement to oust the ruling dictator and turn the country toward a socialistic state, with the support of the Soviet Union. Since that time (1959), the country’s situation has been dominated by an embargo imposed by the United States and the eventual fall of the Soviet Union in 1989. These events have pressured Cubans to become independent, improvise from their limited resources, and adopt prevention and innovate new treatments as their way to address public health.

In recent decades, Cuba has achieved the same life expectancy (79 years) for its citizens as has the United States, with a far less costly health system. Thus, the Cuban experience is a natural experiment in how different health systems work. The importance for cancer lies in the study of preventive actions, compared with a costly treatment approach. Cuba does not have the resources to provide advanced cancer treatment to many of its citizens, but it does provide them access to medical doctors.

Medical education in Cuba has been successful enough to produce a surplus of tens of thousands of doctors and dentists. These professionals have provided a national outreach for Cuban influence. Acting as volunteers or part of economic exchange outside the economic embargo of the United States, medical professionals have spread the Cuban medical approach. In Venezuela, a major petroleum producer, there are 31,000 Cuban doctors and dentists serving the people of Venezuela, and in exchange, the Venezuelan government has provided Cuba with an estimated 100,000 barrels of oil a day. Other arrangements for Cuban medical professionals have been made in 80 countries. It is fair to say that this outreach has created the basis for an evaluation of many preventive and treatment outcomes, but this potential has hardly been realized. Due to the political conflict that has characterized Cuban—United States relations over the decades, Cuban successes are ignored on one side, while their limitations are buried in politicized claims of success on the other. This is troublesome, for the experience with diverse cancer prevention studied on a large scale would be a great advance due to the foreseeable demographic changes that the world’s developing nations will experience. Cancer has not been a major health problem in countries with relatively low life expectancy. But the World Health Organization forecasts that cancer will become a leading cause of mortality as these developing countries experience modernization and its accompanying demographic changes. We see these changes in Cuba today.

According to the Pan American Health Organization (PAHO), Cuba’s demographic profile is an aging population of 11,253,700 with a median age of 39.5 years. The country is facing a growing number of cancer cases along with pressure to add treatment and palliative care to its emphasis on preventive health strategies.

As the population of Cuba ages, it joins industrialized countries with their increasing concerns about cancer diagnosis and treatment. Currently, Cuba has 12 percent of its population at 65 years of age and above, while half of its cases of malignant cancer appear in this older population. The rate of cancer increases markedly with advancing age. Thanks to a national cancer registry, created in 1964 and fully operating since 1986, the details of mortality from every type of cancer in Cuba are known. The result is that, since 2012, cancer has become recognized as the primary cause of mortality.

The national health services have responded to increased cancer mortality, for a third of cancers are preventable and others can be treated successfully if diagnosed early. The limits of the Cuban health system and its preventive medicine are apparent in the problem of lung cancer. This is the leading cause of cancer mortality in Cuba. However, due to the historic place of tobacco in Cuban society, efforts to reduce tobacco use in Cuba have been resisted. The nation lacks a ban on tobacco advertising, while bans on smoking in public places are widely ignored. Nonetheless, there has been a two-thirds reduction in tobacco use over 20 years. The number of people admitting smoking also has declined, from 53 to 36 percent. Adolescent use of tobacco has declined among males but not among females.

Prostate cancer is the second-leading cause of cancer mortality in Cuba. Among women, breast cancer is the greatest cause of mortality, from a Westernized life style of few children and greater levels of education and income (about half the
Czech Republic

The central European nation officially termed the Czech Republic is a relatively new country on the world stage, having been formed in 1993 out of the peaceful dissolution of the state of Czechoslovakia. In recent years, the economy of the Czech Republic has been excelling, and the nation is regarded internationally as having one of the most effective and reliable democratic governments in the world. The Czech Republic is presently home to nearly 11 million citizens, one-tenth of which live in the nation's capital, Prague.

The national cancer registry of the Czech Republic was first established in 1977. In recent years, it is regarded internationally as one of the most robust and effective cancer registry systems in place in the entire world. All of the nation's hospitals and universities are mandated to report every domestic cancer incidence that is observed, so the coverage of the registry is comprehensive. Researchers who utilize the database have access to well-kept domestic records that have proven invaluable in the country's fight against cancer as the records accurately indicate mortality, diagnosis, and treatment rates with the nation.

Data from the cancer registries of the Czech Republic suggest that mortalities from cancer are decreasing in the nation at one of the most distinctive rates of all central Europe. Generally, cancer incidences are down in both the male and female populations of the country, but there is much still to be done. The Czech Republic's elderly population has some of the highest rates of cancer incidence in all of Europe, so more effective preventative measures and screening methods will need to be utilized in the country. Also, the government of the Czech Republic will need to better campaign against certain cancer risk behaviors such as the above-average usage of alcohol in the country. The population of the Czech Republic has been shown statistically to have some of the heaviest drinkers in all of Europe, and researchers believe that such behavior is most likely the cause of the nation's high rates of stomach cancer. To reign in stomach cancer incidences in the country, the government will need to take a more active role in making the Czech public aware of the risk factors of certain behaviors.

As of late, the most prevalent forms of cancer in the Czech Republic are breast, bowel, lung, prostate, and stomach cancer. Lung, bowel, and stomach cancers are the most dominant forms of cancer incidences in males in the nation, while breast, bowel, and stomach cancers are the most common

See Also: Bolivia; Developing Countries; Venezuela.

Further Readings
incidences of cancer in females there. Nationwide, incidences of bowel, breast, prostate, and stomach cancers have been consistently increasing over the past two decades, while occurrences of cervical, liver, and gastric cancers have been steadily decreasing.

Unfortunately, many citizens of the Czech Republic have experienced cancer throughout the nation’s history. The popular Czech politician and social advocate Pavel Dostal died in 2005 as a result of struggling with pancreatic cancer for over a year. Arnost Lustig, the critically acclaimed Czech fiction writer and Holocaust survivor, passed away in 2010 after suffering from non-Hodgkin’s lymphoma for several years. Furthermore, the beloved Czech hockey player Miroslav Dvořák died in 2008 at the age of 56 as a result of his bout with throat cancer.

Presently, the Czech Republic is well prepared to deal with the nation’s domestic cancer incidences, and the situation is improving every year. There are currently 19 regional cancer centers, one national cancer institute, two pediatric cancer facilities, six hemato-oncological centers as well as numerous outpatient care locations. Moreover, the National Cancer Control Program of the Czech Republic is currently hard at work educating all age groups of the Czech population regarding cancer prevention behaviors. The institute is also set to begin initiating a new system of audits within the hospitals of the country in order to better screen for domestic cancer incidences. Nationwide, new hospices, palliative treatment facilities, and outpatient care centers are being constructed every month in a sustained effort by the Czech government to effectively combat the disease. International researchers are optimistic that the Czech Republic is taking all the proper steps it needs to meet the domestic challenges of cancer in the decades to come.

See Also: Breast Cancer; Lung Cancer, Non–Small Cell; Prostate Cancer; Stomach (Gastric) Cancer.

Further Readings
Masaryk University. “Cancer Screening Programmes in the Czech Republic and Importance of Personalised Invitation,” Institute of Biostatistics and Analyses (January 2013).
Daiichi Sankyo (Japan)

Daiichi Sankyo is a corporation created from the merger between Sankyo Company, Limited and Daiichi Pharmaceutical Company, Limited in 2005. As of early 2014, the corporation has 17,256 employees worldwide, including subsidiaries, but excluding the 15,535 employees within the Indian Ranbaxy group from which Daiichi Sankyo disinvested its majority share in April 2014. Daiichi Sankyo ended up as number four in Japan and as number 20 on a global basis in the Medical Care & the Pharmaceutical Industry 2013 overview of 2011 pharmaceutical corporations’ sales.

Overall turnover for fiscal year (FY) April 2013 to March 2014 was approximately 87 percent domestic pharmaceuticals, 4.5 percent pharmaceutical sales abroad, and 8.5 percent health care products. There is as of 2014 a distinct domination of drugs related to remedying high blood pressure and antihypertension. The most-selling pharmaceutical products in FY 2013 to 2014 were the antihypertensive agent olmertasan and related products marketed as Olmetec and as Rezaltas in Japan; as Benicar, Benicar HCT, Azor, or Tribenzor in the United States; and as Olmetec, Olmetec Plus, Sevikar, or Sevikar HCT in Europe. In FY 2013 to 2014 the products Benicar, Azor, and Tribenzor held the number one ($857 million), number three ($174 million), and number five ($90 million) positions of the corporation’s U.S. turnover.

Sankyo was first founded as Sankyo Shoten in 1899. It was established by three businessmen as a joint investment, with the main product takadiastase, which was a digestive enzyme discovered by the chemist Jokichi Takamine (1854–1922) in 1894. The company subsequently launched the adrenal cortex hormone agent adrenalin in 1902. In 1913, the corporation changed its name from Sankyo Shoten to Sankyo Co., Ltd. As for internationalization, subsidiaries were established in 1985 in the United States and Germany. Daiichi was established in 1915 as Arsemin Shokai, based on the launch of the antisyphilitic agent arsemin. It attained the name Daiichi Pharmaceutical Co., Ltd. in 1918.

After having established a joint holding company in 2005, the new fully merged corporation began operations on April 1, 2007. Apart from the main Daiichi Sankyo, there is a group of subsidiaries including Daiichi Sankyo Healthcare Co., Ltd. (est. 2006), generic products specialist Daiichi Sankyo Espha Co., Ltd. (est. 2010), and Kitasato Daiichi Sankyo Vaccine Co., Ltd. (est. 2011). Moreover, Japan Vaccine Co., Ltd. is a joint venture with GlaxoSmithKline K. K. (est. 2012). Asubio Pharma Co., Ltd. was originally Suntory Institute for Biomedical Research, founded in 1979 and reorganized as a fully owned subsidiary in 2010 focusing on pharmaceutical research and development (R&D). Internationally, Daiichi Sankyo acquired during 2008 through 2011 a number of companies including U3 Pharma GmbH of Germany, based mainly
on antibody drugs (2008); Ranbaxy Laboratories Ltd. of India (2008, but disinvested in large parts in 2014); and oncology-focused Plexxikon Inc. based in Berkeley, California (2011). Zepharma, which had been an Astellas Pharma over-the-counter drugs subsidiary, was acquired in 2006 and later integrated within Daiichi Sankyo Healthcare.

Corporate Philosophy and Recent Strategy
The corporation’s global slogan is Passion for Innovation, Compassion for Patients, and was implemented in 2012 along with its cornerstone business management plan for fiscal years 2013 to 2017, focusing on becoming a global pharma innovator. The first business plan (2007–2009) after the merger had been focused on maximizing synergies from integration and accelerating global expansion, whereas the second plan (2010–2012) was focused on the development of a hybrid business model, which meant being present within both prescription and generic drugs.

The R&D expenditures are relatively high; 18.3 percent in relation to sales as of FY 2011 to 2012. Daiichi Sankyo maintains what they call an R&D culture, including a willingness to change working and behavioral patterns. The corporation states as key words for such a culture taking challenges in a respectful way, empowerment of employees, proactive engagement of stakeholders, and taking calculated risks. Daiichi Sankyo focuses on cardiovascular metabolics when it comes to R&D, as evidenced by its current high-selling products but also on oncology together with subsidiaries Plexxikon (United States) and U3 Pharma (Germany). Plexxikon uses a special scaffold-like screening library trademarked as Scaffold-Based Drug Discovery Platform early in the drug lead-generation process together with compound and target structural data in order to attempt the design of new drug candidates. One inherent aim is to leverage target-specific chemistry investments for multiple targets within a given family. Plexxikon had already before the acquisition by Daiichi Sankyo discovered and subsequently developed in conjunction with Roche the mutation-specific medicine Zelboraf (vemurafenib), its first oncology drug to have reached the market. Plexxikon has, as of mid-2014, a number of compounds in clinical trial processes, including for melanoma, pancreatic cancer, colorectal cancer, and hairy cell leukemia. U3 Pharma has several projects, including two that concern interfering or inhibiting tumor growth.

A new biologics oversight function was established in 2013 and integrates the previously dispersed biopharmaceutical function. Biologics Pharmacology Research Laboratories was created within this function. In addition Venture Science Laboratories, which is comprised of a small number of scientists challenging new approaches, was established in April 2013. Daiichi Sankyo started a collaborative drug discovery project called TaNeDS (Take a New challenge for Drug diScovery) in 2011, consisting of receiving funding applications from Japanese universities and public research centers. The program was expanded to Germany, Austria, and Switzerland in 2013. In April 2014, Astellas Pharma and Daiichi Sankyo announced that they planned to form a joint compound library sharing partnership for approximately 400,000 selected compounds to enable them to promote their R&D efforts.

Terje Grønning

University of Oslo

See Also: Astellas Pharma (Japan); Eisai (Japan); Ono Pharmaceutical (Japan); Takeda Pharmaceutical (Japan).

Further Readings
Several aspects of daily life can contribute to the cause or prevention of cancer. However, once diagnosed with the disease, life often changes drastically in many aspects, and patients and caregivers need to be educated on how to deal with them. Equally important is to counsel cancer survivors when they are ready to return to their daily lives after finishing treatment. Even after diagnosis, lifestyle changes improve outcomes; for example, smoking cessation prolongs life among survivors.

**Causes of Cancer Encountered in Daily Life**

The evolution of cancer is considered to be a multistep process where external insults to underlying defects in the body keep accumulating until cells start behaving and growing abnormally, leading to tumor formation. Such insults are generally in the form of carcinogens—substances that are implicated as causative agents of cancer. We encounter many such carcinogens in our everyday lives. These may be a part of our habits, diet, work, or environment.

The most important carcinogen identified thus far is tobacco. The carcinogenic effects of tobacco have been associated with cancers of the lung, stomach, liver, pancreas, cervix, bladder and kidney, and (in combination with alcohol) the larynx, mouth, pharynx (except nasopharynx), and esophagus. Although tar levels in cigarettes are steadily decreasing, smoking-related cancers are still on the rise globally. Certain dietary habits also contribute toward cancer causation, and risk in old age may depend as much on diet in early life as on current habits. Heavy alcohol intake, consumption of foods contaminated with aflatoxin, and a few local customs (such as feeding Chinese-style salted fish to infants, which causes nasopharyngeal cancer) have been consistently associated with increased risk of cancer. Obesity, a major problem in developed countries, has also been linked to postmenopausal breast cancer and tumors of the endometrium, gall bladder, and kidney.

Reproductive and hormonal factors also contribute to carcinogenesis. Changes in hormonal levels due to endogenous dysregulations or exogenous hormone administration can lead to breast and ovarian cancers. Breast cancer incidence is increased transiently by pregnancy and estrogen administration as oral contraceptives or hormone therapy (HT) and is lowered by late menarche, early menopause, early first childbirth, and a high number of pregnancies. Western diet is associated with earlier age at menarche and postmenopausal obesity, which increase endogenous estrogen production and hence breast cancer risk. Endometrial cancer incidence is also increased by HT. Ovarian cancer incidence declines with increasing number of pregnancies, and endometrial and ovarian cancers are less common among oral contraceptive users.

Daily exposure to carcinogens at the workplace has been an important cause of many cancers. Exposure to the combustion products of coal can increase the risk of lung cancer. Uncontrolled asbestos use in the construction industry was common from the 1940s to the 1970s, which can result in development of mesothelioma among workers exposed to it at that time. Individuals exposed to certain aromatic amines in the dye industry have an increased risk of developing cancer of the urinary bladder, especially if they harbor genetic traits that cause them to eliminate the compounds slowly.

Chronic infections with certain pathogens can also have carcinogenic effects. These include human papillomaviruses causing cervical cancer, hepatitis B and C viruses causing liver cancer, and *Helicobacter pylori* causing stomach cancer. Other pathogens that contribute to substantial cancer risk in certain populations include Epstein–Barr virus (associated with various B-cell malignancies and nasopharyngeal cancer), human T-cell lymphotropic virus type 1 (some T-cell leukemias and lymphomas), human herpesvirus 8 (Kaposi’s sarcoma with human immunodeficiency virus [HIV]), schistosomiasis (bladder and colon cancer), and liver flukes (cholangiosarcoma).

Apart from skin cancers due to exposure to ultraviolet rays from sunlight, the only substantial and widespread cancer risk known to be caused by an avoidable environmental factor in developed countries is the higher risk of lung cancer among smokers caused by indoor radon escaping from the ground or building materials, although both indoor and outdoor air pollution from fossil fuels may also contribute to the risk.

**Everyday Measures to Prevent Cancer**

Cancer prevention aims to reduce mortality by lowering the incidence of the disease. This can be
accomplished by avoiding a carcinogen or altering its metabolism, pursuing lifestyle or dietary practices that modify cancer-causing factors or genetic predispositions, and medical intervention (chemoprevention) to successfully reverse preneoplastic changes.

Much of the promise for cancer prevention comes from studies that show associations between modifiable lifestyle or environmental factors and specific cancers. Examples of modifiable risk factors include tobacco and alcohol consumption, physical inactivity, and obesity. Studies have shown decreased incidence of cancers associated with smoking and alcohol when the respective habits were ceased. Dietary modifications, intake of a balanced diet, exercise, and dietary supplements and micronutrients can also modify cancer risk. Aspirin and folate supplements can potentially reduce colorectal cancer incidence in the long term. Risk of various cancers is also likely reduced by intake of foods containing carotenoids, vitamins C and E, and selenium.

HT and other hormonal therapies are usually administered after considering all possible benefits and side effects to decrease the risk of hormone-associated cancers. Screening for precancerous lesions and immunizations against and treatment of infections that can cause cancer may be important in preventing neoplastic growths.

Use of sunscreens and other agents that protect against the harmful effects of ultraviolet radiation can help prevent development of skin cancers. Several countries now have regulatory bodies that monitor carcinogen levels in the workplace. Rules generally require workers to use protective equipment and work in shifts and necessitate industrial processes to meet standards that limit exposure. Stringent measures and legislations are required to limit or ban the use of proven or suspected carcinogens in industry, provide adequate health benefits and examinations to workers exposed to such hazards, and compensate those affected.

Living With Cancer

Facing each day after a diagnosis of cancer can be stressful for many patients. A multitude of challenges including treatment side effects, reduced income, inability to perform routine tasks, and psychosocial effects can impact daily tasks.

Patients need to cope with changes in appearance including hair loss and weight loss. Chemotherapy tends to drain the body of energy, leaving patients feeling relatively weak to perform even everyday chores. For some, in-home care is unavoidable, and access to social services in such cases becomes essential. In-home hospice services may also be needed for those in the final stages of their disease, especially when family members are unable to shoulder the burden.

Dealing with the financial implications of treating cancer can also be a serious concern, especially if the patient is a major earning member for the home. Many patients are able to sustain a regular schedule, but others will need to stop working or take some time off. Here, a dialogue with the employer on health benefits, sick pay, leave of absence, or disability is essential. Involvement of a financial or investment planner and a lawyer may also be required. Social workers and organizations may be able to assist in cases where debts need to be repaid and income is low or absent due to disease. Depending on a patient’s age and insurance coverage, treatment for cancer and other related costs
can be expensive. Additionally, knowledge of what the insurance policies cover and what, if any, out-of-pocket expenses are involved, is important. Financial counseling or social work intervention may be necessary and should be discussed with the health care provider. Local service organizations may have grants available to cover some costs of transportation or treatment.

Most cancer survivors look forward to resuming normal life after treatment, but for many, the experience does not end with their last oncology visit. Survivors often deal with psychosocial issues that affect their work performance, finances, sexual health, and self-identity. The range and severity of these issues can vary based on the type of cancer, disease management, patient age, and personality traits.

Returning to work represents a return to the routine that survivors were used to before they had cancer. Survivors should be educated to pace themselves when returning to work and that they may require a workplace accommodation to manage long-term effects. Suffering emotional fallout from their disease is a common problem among survivors. This may include worrying about recurrence or new cancers, thereby leading to depression. Positive attitude and self-identification can help them cope with these aftereffects. Sexual problems may include loss of desire for sex, impaired fertility, erectile dysfunction in men, and painful intercourse in women. Interventions including cryopreservation of sperm, eggs, and embryos; conservative surgical and hormone treatments may also help in these cases.

After being diagnosed with cancer, patients may face different challenges related to physical health, support systems, financial status, and access to health care that may influence their daily lives in many ways. While government and health care services need to address those issues thoroughly, they also need to promote public awareness of the different causes of cancer and educate everyone on steps that can be taken each day to minimize risks of acquiring the disease.

Anirban P. Mitra
University of Southern California

See Also: Alcohol; Asbestos; Diet and Nutrition; Smoking and Society; Solar Radiation.

Further Readings


Dana-Farber Cancer Institute

Dana-Farber Cancer Institute (DFCI) was formed in 1947 by Sidney Farber, M.D., as the Children’s Cancer Research Foundation. Farber’s goal was to provide a facility that would not only advance the development of childhood cancer treatments but also provide a place for young cancer patients to receive cutting-edge care. In 1969, the foundation expanded its reach to welcome patients of any age.

In 1974, the organization’s name was changed to the Sidney Farber Cancer Center as a tribute to its founding father. The name was modified to its present incarnation in 1983 to recognize the enduring support of the Charles A. Dana Foundation, a private philanthropic organization that supports brain research through funding and educational programs. DFCI also is supported by the National Cancer Institute, the National Institute of Allergy and Infectious Diseases, numerous foundations, and individuals who contribute to specific clinical or research programs or to DFCI’s charity, the Jimmy Fund.

As of 2014, DFCI was supporting more than 300,000 patient visits annually and actively participating in approximately 700 clinical trials. It is a principal teaching affiliate of Harvard Medical School, a federally designated center for acquired immune deficiency syndrome (AIDS) research, and a founding member of the Dana-Farber/Harvard Cancer Center. DFCI also conducts community-based programs in cancer prevention, detection,
and control throughout New England and maintains joint programs with other leading health care institutions in Boston, including Boston Children's Hospital, Brigham and Women's Hospital, and Massachusetts General Hospital.

Dr. Sidney Farber

Sidney Farber, M.D., was a pathologist at Boston Children's Hospital when World War II ended. At that time, a boom in medical research was helping to revolutionize treatments for a number of diseases. Leukemia, however, was not one of them. The deadly disease, which originates in the bone marrow and affects white blood cells, was aggressive and painful. Farber wanted to find a way to treat it.

He reviewed studies made during the war that had shown how some types of anemia, which are also caused by immature cells in the bone marrow, could be cured with vitamin B12 and folic acid. Farber felt that he could achieve similar results with leukemia using the same idea. Folic acid was known to stimulate the growth and maturation of bone marrow, so Farber felt that, if a drug could be created that chemically blocks folic acid, it would shut down the production of abnormal marrow associated with leukemia. A U.S. pharmaceutical manufacturer called Lederle was actually testing a folic acid inhibitor at about the same time. In November of 1947, Farber was ready to try the drug Aminopterin on a group of 16 children who were suffering from acute lymphocytic leukemia. Ten of the recipients achieved temporary remission of the cancer, marking the first clinical remission ever reported using chemotherapy for childhood leukemia.

Shortly after, Dr. Farber and his colleagues at what is now DFCI also achieved the first remissions in a common form of childhood kidney cancer known as Wilms's tumor. The application of research that moves scientific knowledge from the laboratory floor to the hospital bed became the model for DFCI's approach to cancer treatment.

The Jimmy Fund

The Variety Club of New England, a charitable organization made up of members from the entertainment community, organized a national radio broadcast in May 1948 from the bedside of a young leukemia patient who was being treated by Dr. Farber as part of his work with the Children's Cancer Research Foundation. During the broadcast, the boy—who Farber insisted be called Jimmy rather than by his real name as a way to protect the child's privacy—was visited by members of his beloved Boston Braves baseball team.

After the airing, contributions flooded in from all over to help buy Jimmy a television set so that he could watch the Braves play their games from his hospital bed. The financial gifts resulting from the broadcast totaled approximately $250,000, with the funds going to support Dr. Farber's groundbreaking work in the fight against childhood cancer. The donations became the starting point for the Jimmy Fund, which has raised millions of dollars for DFCI throughout the years and helped support cancer advances that have become the standard of cancer care and research across the globe.

One of the first substantial uses of Jimmy Fund donations was the construction in 1952 of a dedicated Jimmy Fund Building, which would later become the Sidney Farber Cancer Institute, to house state-of-the-art laboratories, business offices, and a patient care clinic.

Research Philosophy

Dr. Farber envisioned a facility where scientists in upper-floor laboratories would make discoveries that could be applied in the treatment of cancer patients in ground-floor clinic rooms. He wanted there to be a close proximity between research and patient care, not only in terms of philosophical approach but also in respect to physical distance. In particular, he wanted scientists to routinely encounter the beneficiaries of their efforts—patients and their families—as a way to inspire scientific creativity and human compassion. DFCI has continued to follow the same agenda since its founding, dividing its facilities, funding, and focus just about equally between research endeavors and provision of patient care.

Research at DFCI always has been based on the principle that scientific and clinical investigations are complementary activities that strengthen each other. The insights from research inform and invigorate patient care and vice versa, according to the institute's underlying belief and modus operandi. From the start, DFCI has followed an organizational framework that promotes inquiry, free-flowing information exchange, and unbridled collaboration among professionals from all disciplines. The unfettered environment has helped
DFCI create one of the largest cancer clinical trials programs in the United States, which has fostered a significant number of advances in the understanding of cellular and systemic processes in the battle against cancer.

A distinguishing factor of DFCI is the quality and extent of the organization’s scientific collaborations, which include nationally recognized leaders from nearly all fields of cancer research, affiliations with Harvard Medical School and other leading teaching and health care institutions, and significant grant awards from the National Cancer Institute and National Institutes of Health programs, among others.

Shari Parsons Miller  
Independent Scholar

See Also: AIDS-Related Cancers; Chemotherapy; Childhood Cancers; History of Cancer; Hospitals; Jimmy Fund; Leukemia, Acute Lymphoblastic, Childhood.

Further Readings  

Danish Cancer Society  
A cancer society’s work involves all matters of cancer prevention, education, and support to cancer patients or interested parties and cancer research. The Danish Cancer Society (DCS) remains in line with other cancer society’s roles and responsibilities.

The beginning of the DCS can be traced back to 1904, when leading Danish physicians came together to fight against cancer. The discovery of radium to treat cancer motivated the Danish physicians to combine their efforts in the fight against cancer.

Denmark ranks the DCS as the largest cancer-fighting organization in their country; it is located in Copenhagen. Their membership comprises 455,000 members. The goals of the DCS consist of (1) prevention of cancer, (2) support of cancer patients and significant others, and (3) cancer research.

The DCS aspires to the goals of preventing the development of cancer, to enhance patients’ abilities to recover effectively, and to reduce the physical, emotional, and social adverse effects of cancer. The DCS uses multiple ways to accomplish these goals. The DCS belongs to the Union for International Cancer Control (UICC). The UICC, established in 1933 and based in Geneva, Switzerland, involves more than 800 organizations covering 155 countries. Membership in UICC consists of leading cancer societies, ministries of health, research facilities, and patient groups. A convergence of the members, major partners, the World Health Organization, and World Economic Forum take on the challenge of the growing cancer crisis on a worldwide degree. The UICC brings together the cancer community to decrease the worldwide cancer burden, to encourage profound justice, and to assimilate cancer control into the global health and advancement strategy.

The DCS supports two research institutes: the Institute of Cancer Biology and the Institute of Cancer Epidemiology. In 2008, the members of the two research institutes put out more than 200 articles in prominent scientific journals. The majority of funds raised by the DCS function to support the research activities of the two institutes.

The Institute of Cancer Biology aims to produce research to expand the understanding of the molecular mechanisms causing cancer and to link the chasm between basic and clinical research for progress in the care of cancer patients. This institute contains six divisions composed of (1) cell cycle and cancer, (2) proteomics in cancer, (3) molecular cancer biology, (4) apoptosis, (5) breast cancer, and (6) laboratory of cancer genomics. Two other research centers are associated with this institute, the Danish Centre for Translational Breast Cancer Research and the Centre for Genotoxic Stress Research.

The Institute of Cancer Epidemiology aspires to achieve two primary goals. The first goal aims to determine yet unidentified causes of cancer in the environment and in our genes. This goal helps
health care practitioners more efficiently preclude the existence of new cases of cancer in the Danish population. The second goal intends to examine and explain critical adverse consequences of therapy for cancer among cancer survivors. This goal assists physicians to alter and individualize the treatment for cancer and improve the quality of life of the cancer patients.

The Institute of Cancer Epidemiology contains seven research sections: (1) genetics, (2) diet and lifestyle, (3) psychosocial cancer research, (4) virus and hormones, (5) occupational cancer, (6) environmental exposures, and (7) statistics. This institute works to achieve the publication of new and original research findings into peer-reviewed international journals of high distinction. The researchers in this institute published 151 articles in 2009.

The research institutes contribute to the advancement of scientific knowledge by publishing innumerable articles every year. S. O. Dalton, T. M. Laursen, L. Ross, P. B. Mortensen, and C. Johansen published a stellar article on depression and cancer in 2009; likewise, L. Groth-Pedersen and colleagues put in print their article on novel research on lysosomal activity and targets for drug therapy in cancer. These types of articles provide impetus for further research to benefit people with cancer.

In keeping with the vision of life without cancer, the society plays host to international symposiums to present the latest study results in all lines of research on cancer from molecular to epidemiological. The Cancer Society Symposium on the Immunotherapy of Cancer—Present Status and Future Promise represents an example of a state-of-art meeting sponsored by DCS. This symposium, held in September 2013, concentrated on subject matters about adoptive cell therapy, therapeutic vaccination, cellular regulators in the tumor microenvironment, and immune-regulatory pathways to attack cancer cells. These subjects embody the latest lines of immunotherapy research on cancer. Other symposiums cover the multiple lines of research under study at the DCS, like epidemiological, other molecular subjects, and breast cancer research, to name a few.

The DCS carries out an annual nationwide campaign to assemble capital to support their mission. The organization collects money from lotteries, membership fees, and donations. Another 5 percent comes from the public system. The DCS’s income rose to 87.6 million euros in 2009. The society distributes costs of 37.5 million euros for research, 16.6 million euros for patient support, 11.3 million euros for prevention and information, and 4.2 million euros for administrative cost to manage the business of DCS.

In summary, the description of the DCS indicates a prominent, national organization based in Copenhagen, Denmark, with the mission of conquering the scourge of cancer. As evidenced by the publications and symposiums, the society truly supports its mission.

Sharon A. Takiguchi
Nurse Consultant

See Also: Denmark.

Further Readings


DDT

Dichlorodiphenyltrichloroethane (DDT) is a pesticide once widely used to control insects in agriculture and insects that carry diseases such as malaria. It is a white, crystalline solid with no odor or taste. DDT was used with great success in World War II to control malaria and typhus among civilians and troops. After the war, it was made available for use as an agricultural insecticide. American biologist Rachel Carson published the book *Silent Spring* in
In 1962, which explained the environmental impacts of indiscriminate DDT spraying in the United States. After publication of this book and public outcry, its use in the United States was banned in 1972 because of damage to wildlife and concern over carcinogenicity, bioaccumulation, and health effects on wildlife. However, it is still used in some countries to control mosquitoes that carry and spread malaria. Also, it has been used as an insecticide for crops because DDT is effective and relatively inexpensive to manufacture.

DDT is a persistent organic pollutant that is readily adsorbed by soils and sediments. It entered the air, water, and soil during its production and use as an insecticide before its ban in the United States in 1972. DDT is present at many waste sites, and releases from these sites still continue to contaminate the environment. Large amounts of DDT were released into the air, soil, and water when it was used on crops as an insecticide and to control malaria. It also evaporates from the contaminated water and soil, and while in the air, it may get deposited on land or surface water. This cycle of evaporation and deposition may be repeated many times. For example, atmospheric deposition continues as a current source of DDT contamination in the Great Lakes. Some soil particles with attached DDT, DDE (dichlorodiphenyldichloroethylene), and DDD (dichlorodiphenyldichloroethane) may get into rivers and lakes in runoff. It accumulates to high levels in fish and marine mammals in their adipose tissue.

These chemicals can be carried long distances and have been found in bogs, snow, and animals in the Arctic regions. DDT enters the environment by improper use and disposal, soil and sediment runoff, and atmospheric deposition. It can be absorbed by some growing plants from soil and by animals. DDT remains in the environment for long periods of time and degrades into DDE, with further degradation into DDD. DDT and its degraded byproducts DDE and DDD are persistent and toxic. These pesticides strongly adhere to soil and generally remain on the surface of soil for long periods of time.

People are exposed to DDT via consumption of contaminated fish, shellfish, and food and via breastfeeding to infants. Fish consumption advisories are in effect for DDT in many waterways, including the Great Lakes ecosystem. The amount of DDT might have decreased since its ban, but the largest fraction of DDT in a person’s diet comes from meat, poultry, dairy products, and fish, including the consumption of leafy vegetables. Today, in the United States, DDT, DDE or DDD enters the body mainly when a person eats contaminated food. The actual amounts of this pesticide absorbed from food intake depend on both the concentration in the food and the amount eaten. DDT metabolites leave the body mostly in urine but may also leave by breast milk and pass directly to nursing infants. DDT from the mother can enter her unborn baby through the placenta. DDT has been found in amniotic fluid, human placentas, and umbilical cord blood.

Research has shown that DDT and its metabolites have harmful effects on humans. Eating food containing a large amount of DDT over a short period of time would most likely affect the nervous system. People excessively exposed to DDT, while working with the chemical or through accidental exposure, report a prickling sensation of the mouth, nausea, dizziness, confusion, headache, lethargy, incoordination, vomiting, fatigue, tremors in extremities, anorexia, anemia, muscular weakness, hyperexcitability, anxiety, and nervous tension. Many studies have found that DDT can induce adverse effects on the liver, nervous system, and reproductive system.

DDT is a probable human carcinogen. The Department of Health and Human Services has determined that DDT is reasonably anticipated to be a human carcinogen. Similarly, the International Agency for Research on Cancer (IARC) has determined that DDT is probably carcinogenic to humans. The Environmental Protection Agency (EPA) has determined that DDT, DDE, and DDD are probable human carcinogens. Theoretically, DDT could contribute to breast cancer either by being a complete carcinogen, an initiator, or a promoter. However, evidence from epidemiological studies have not been consistent and may support the hypothesis that exposure to DDT or DDE increases the risk of cancer in humans. Previous studies of DDT and breast cancer assessed exposure later in life when the breast may not have been vulnerable, after most DDT had been eliminated and after DDT had been banned. B. Cohn and colleagues investigated whether DDT exposure in young women during the period of peak DDT use predicts breast cancer. They conducted a prospective, nested, case-control study with a median time to diagnosis of 17 years using samples obtained.
from young women during 1959 to 1967, which was the peak time of DDT pollution and exposure. After the research, they proposed that exposure to DDT early in life may increase breast cancer risk. Many U.S. women heavily exposed to DDT in childhood have not reached 50 years of age. The public health significance of DDT exposure in early life may be large. Research studies have proposed that women with the highest exposure to the pesticide DDT had four times the breast cancer risk of women with the least exposure. Some scientists reported in the April 29 issue of the *Journal of the National Cancer Institute* that men with the highest blood levels of DDE were 1.7 times more likely to develop testicular germ cell tumors than those who had the lowest levels. Studies suggest that genetic differences in metabolism may interact with body burden to predict breast cancer risk. Direct toxicity of DDT and induction of enzymes that produce other genotoxic intermediates and DNA adducts are possible mechanisms in causing cancer.

Limited studies have examined the association between exposure to DDT and increased risk of liver cancer, lymphoma, endometrial cancer, and prostate and testicular cancer. However, outcomes have been inconclusive or do not support an association. Recently, risk of both seminomatous and nonseminomatous testicular germ cell tumors (TGCTs) has been reported to be associated with increased exposure to \( p,p' \)-DDE.

At this time, most people are exposed to DDT and its metabolites products as a result of eating foods or drinking liquids that may be contaminated with small amounts of DDT. The Food and Drug Administration (FDA) analyzes a wide variety of imported food items as well as domestic products to ensure that pesticides residues are below FDA guidelines. Adults and children might get exposed to this harmful pesticide by eating certain types of fish or wildlife caught from certain locations. Many states have fish advisories to warn people about DDT contamination and to educate the public about bodies of water that have restrictions. In 1972, the EPA issued a cancellation order for DDT based on adverse environmental effects of its use, such as those to wildlife and potential human health risks. Since 1996, the EPA has been participating in international negotiations to control the use of DDT around the world. In September 2006, the World Health Organization (WHO) declared its support for the indoor use of DDT in African countries where malaria remains a major health problem, citing benefits of the pesticide, which outweigh the health and environmental risks. This is consistent with the Stockholm Convention on persistent organic pollutants, which bans DDT for uses except for malaria control.

DDT can remain in the environment for persistently long periods of time and can still be found in air, water, and on land, even in places where it has been banned. People are exposed to DDT when they eat food grown in soil contaminated with DDT or they eat fish from water polluted with DDT. Many studies have supported the fact that DDT is harmful to humans, wildlife, and the environment. The EPA banned DDT in 1972 in the United States due its harmful effects and probable risk of causing different types of cancers, such as liver and breast. DDT still is used in many countries for agriculture, although that goes against the Stockholm Convention. The WHO only supports
limited indoor use of DDT in the countries where malaria poses a great risk for human populations. Many studies have supported banning its use in agriculture all over the world because spraying DDT on plants exposes the land, air, and water to dangerous contamination. People may put themselves at great risk in consuming DDT exposed fish, wildlife and plant products, depending on the warnings and advisories issued for specific lakes, ponds, and other places.

Hueiwang Anna Jeng
Vint K. Jha
Old Dominion University

See Also: Breast Cancer; Diet and Nutrition; Food and Drug Administration; Insecticides; Pollution, Air; Pollution, Water.

Further Readings

Denmark

The northern European nation officially termed the Kingdom of Denmark is one of the oldest states in all of Europe, and the royal lineage of its current ruler, Queen Margrethe II, can be traced back all the way to the 10th century C.E. The nation of Denmark has a long history of being a dominant player on the world stage, acting as a European superpower between the 13th and 17th centuries. After a series of lost conflicts in the 19th century, Denmark lost much of its territory, though its economy blossomed during this period. The modern political rendition of Denmark was instituted in 1918, when constitutional and governmental reorganizations were achieved.

Denmark instituted one of the earliest national cancer registries in all of Europe when it created the Danish Cancer Registry in early 1942. Now, every single individual case of cancer within the Kingdom of Denmark is accounted for by the registry. The Danish Cancer Society, the Danish Medical Association, and the National Board of Health all work closely together to maintain and analyze the registry archives. Such efficiently maintained data has allowed the relevant domestic and international specialists the ability to closely track mortality statistics and incidence trends in the nation. Unfortunately, the detailed information provided by the Danish Cancer Registry has led to the revelation that Denmark has the highest rate of cancer incidences in the entire world.

To further compound the fact that the Danes experience the highest levels of cancer in the entire world, contemporary data suggests that the average Danish citizen who suffers from cancer is diagnosed with the disease when the cancer is at a much more advanced stage than his or her European peers. Cancer incidences in Denmark are believed to be as high as they are because a large proportion of the Danish population is smokers and consumers of alcohol, though proactive diagnosing practices used in the country also contribute to the higher levels of incidences. Currently, an average of 321 out of every 100,000 Danish citizens will be diagnosed with some type of cancer in their lifetime.

Presently, the most prevalent forms of cancer in Denmark are bowel, breast, lung, prostate, and uterus cancer. Prostate, bowel, and lung cancers are the most dominant forms of cancer incidences in males in Denmark, while breast, bowel, and uterus cancers make up the most common forms of cancer incidences in females there. In fact, Denmark has the highest incidences of lung and uterus cancers in all of northern Europe. Also, as tanning beds have become
Deodorizers

Deodorizers include various substances and products to mask, absorb, or neutralize odor for both consumer and industrial use. This includes substances added to virtually all bar and liquid soaps, including shampoos and conditioners, as well as deodorants, laundry products, dishwashing and household cleaning products, baby wipes, some toilet paper and tissues, body sprays, air fresheners, mothballs, pet odor removers, and so on. Most of them include a number of ingredients that are bad for human health. A National Resources Defense Council study found that most of the household air fresheners they studied (drawn from the most popular brands) included dangerous chemicals that included carcinogenic phthalates, toxins that could aggravate asthma, and various compounds that impact reproductive development. Many hormone-disrupting chemicals are especially dangerous to young children and babies. In the case of plug-in air fresheners, this is especially concerning of Population Based Cancer Registry Data.” London School of Hygiene and Tropical Medicine (November 2010).


Storm, H. H. “Appendix 3 (a) The Danish Cancer Registry, a Self-Reporting National Cancer Registration System With Elements of Active Date Collection.” Danish Cancer Society (February 1991).

See Also: Breast Cancer; Lung Cancer, Non–Small Cell; Prostate Cancer; Uterine Sarcoma.

Further Readings


given the 24-hour release of these chemicals, if the product is used as directed. It is also important to note that many of these chemicals were found even in products labeled organic or green, or promoting their usage of essential oils. (In many such cases, the essential oils do provide the fragrance itself, but more dangerous chemicals are used as dispersants to make the air freshener easier to spray or to affect the thickness or viscosity of the liquid or gel. Thus, while the essential oils are being used instead of synthetic fragrance chemicals, the chemicals they replace are a small part of the larger picture.) One plug-in air freshener included in the study contained more than 20 different volatile organic compounds, eight of which were classified by federal law as toxic or hazardous.

Deodorizing products have become almost ubiquitous since the mid-20th century. In 2007, the market for air fresheners alone was $1.72 billion, and a *Time* article found that plug-in, spray, liquid, and gel air fresheners were used in 75 percent of American households.

Many deodorizing products contain significant amounts of phthalates, a group of chemicals used in plastics, which pose a number of health concerns, including carcinogenicity. A Centers for Disease Control (CDC) study in the Fourth National Report on Human Exposure to Environmental Chemicals, conducted 2003 and 2004, found that phthalate exposure is widespread in the American population and that adult women have significantly higher levels of exposure than men because of greater use of phthalate-containing products like soaps, body washes, shampoos, cosmetics, and personal care items. Banned from use in personal-care and beauty products in many countries, they are much less regulated in the United States.

Phthalates are esters of phthalic acid (produced by oxidizing napthalene). In addition to being used in plastics like polyvinyl chlorides (PVCs), in which form they may be found in the containers of many beauty products, they are used as gelling agents, stabilizers, dispersants, suspending agents, and emulsifying agents and so are found in the majority of beauty products that come in the form of any kind of liquid, spray, or certain nonpowder solids (like soaps, lipsticks, and underarm deodorant blocks). Their ill effects result both from direct contact and from the release of phthalates into the environment, though, in the latter case plastics, PVC, linoleum, and various coatings are the larger culprits. The major concern with phthalates is not single incidences of exposure but the cumulative effects of exposure. Phthalates are suspected to be endocrine disruptors, for instance, which can lead to birth defects, changes in hormone levels, and cancers, especially breast cancer in women, and there are multiple studies finding correlations between phthalate exposure and female breast cancer. Phthalates may also be implicated in the obesity epidemic, especially in men, and in the increase in type 2 diabetes. Phthalates also have been shown to cause damage to the liver and testes.

One suspected reason for phthalates’ correlation with male obesity is because phthalates are xenoestrogens—chemical compounds that imitate estrogen. Xenoestrogens pose a significant human health risk in the environment and have been tied with increases in precocious puberty (and consequently early menarche, a breast cancer risk factor). Studies have confirmed a positive correlation between early thelarche (breast development in girls) and phthalate exposure, with phthalates’ functionality as xenoestrogen presumed as the responsible mechanism. In men, xenoestrogens can result in elevated estrogen levels, causing weight gain and breast development and decreasing testosterone and libido.

There are different mechanisms by which deodorizers work, depending on the purpose for which they are meant. Mothballs, for instance, which both repel clothes moths and prevent the stale smell associated with long-term storage of clothing, accomplish both with para-dichlorobenzene, replacing the older use of naphthalene, which has been discontinued largely because of its flammability. Both substances sublimate (evaporate directly from a solid to a gas without passing through a liquid phase first) at room temperature and do so slowly, thus gradually producing a gas.

That gas is toxic enough to moths to repel them and kills off moth larvae that may already be present. It also produces a sweet odor that displaces the aforementioned stale smell. Para-dichlorobenzene is a likely carcinogen, as listed by the National Toxicology Program, the International Agency for Research on Cancer, and the state standards of California; research on humans have not been conducted at full scale, and this classification is based on animal studies.
Similar chemicals are found in urinal cakes, the solid sublimating blocks used to reduce the smell of urine in public urinals. Like mothballs, such cakes or pucks were originally made with naphthalene; though flammability is not really a concern in this application, para-dichlorobenzene nevertheless phased naphthalene out, though in some jurisdictions, usage of para-dichlorobenzene for this purpose has been banned. Newer formulations use water-soluble surfactants that keep the interior of the urinal reasonably clean so that deodorizing is less necessary. Still newer, greener formulations use blocks of bacteria selected for their ability to neutralize key components of the urine that passes through them, which can be used in waterless, no-flush urinals.

Para-dichlorobenzene is used in many air fresheners, including unscented or fresh-air air fresheners for a simple reason: When dispersed in the air, it coats the nostrils in a film that deadens the sense of smell, not freshening the air but rather impairing your ability to smell it. This also helps cloak the chemical smell of some of the additives.

Benzene, an organic chemical compound, is found in many detergents as well as being used in rubbers, explosives, pesticides, and as a gasoline additive. It is widely known to contribute significantly to acute leukemia, bone marrow abnormalities, acute myeloid leukemia, aplastic anemia, myelodysplastic syndrome, chronic myeloid leukemia, and acute lymphoblastic leukemia and is a Group 1 carcinogen. Benzene exposure also can result in birth defects, male infertility, chromosomal problems leading to birth defects regardless of which parent is exposed, and damage to the liver, kidney, lungs, heart, and brain.

Acetaldehyde, an organic compound that occurs naturally, is also included in many beauty and deodorizing products. An irritant in large concentrations, it is also a toxin and carcinogen. Large concentrations in the air result in irritation to the respiratory tract, throat, eyes, mucous membranes, and sometimes the skin within a few minutes. In some workplaces where acetaldehyde concentrations are over the safe threshold but not dense enough to cause immediate obvious health problems, workers may notice respiratory troubles, dry or irritated eyes, or irritated skin, similar to allergy attacks or the effects of dry winter air and plausibly mistaken for same. This can happen as the result of heavy use of acetaldehyde-containing cleaning agents, especially with poor ventilation. Acetaldehyde also builds up in indoor spaces for reasons that are not entirely understood, possibly as a result of off-gassing from flooring, laminate, linoleum, and building materials, so the use of deodorizers can be just enough to push the concentration over the limit. Acetaldehyde is also one of the carcinogens in cigarette smoke and linked to lung, liver, and gastrointestinal cancers.

Dioxane is found in shampoos, deodorants, toothpastes, mouthwashes, and cosmetics and, in a 2008 study, was found to be present in almost half of the organic personal-care products surveyed. It is classified as a Group 2B carcinogen, known to be carcinogenic in other mammals and suspected to be carcinogenic to humans but not yet proven to be one by epidemiological studies.

Underarm deodorant usually contains aluminum chlorohydrate if it is also an antiperspirant. However, while a small amount of aluminum is absorbed into the skin, aluminum chlorohydrate is not the same as the neurotoxin aluminum chloride. It is a common urban legend that underarm deodorant is a cause of breast cancer, but there is no apparent link, at least not through aluminum; though it is theoretically possible that underarm antiperspirant use could lead to dangerously high levels of absorbed aluminum, this would require numerous applications of antiperspirant every day, for many days.

Air fresheners and other deodorizers also contain terpenes, chemicals derived from citrus oils. On their own they pose no health risk. In the air, they react with ozone and form formaldehyde, which is highly toxic and classified as a known human carcinogen with specific links to nasal sinus cancer and nasopharyngeal cancer and has suggested links with leukemia.

A number of harmful substances that may not be carcinogenic also are found in deodorizing products. Chloromethane, for instance, is a common ingredient. Though it is not believed to be carcinogenic, chronic exposure is linked to birth defects, and short-term exposure can result in seizures or central nervous system depression.

Bill Kte’pi
Independent Scholar

See Also: Chemical Industry; Cosmetics; Detergents; Paranasal Sinus and Nasal Cavity Cancer; Perfume.
Detergents

Detergents, whether in liquid, cake, or powder form, are perceived as being largely safe household products. Scientific research, however, has shown that many common detergents contain substances that can adversely affect human health. These include several cancer-causing substances.

Detergents are substances that help remove dirt, both in the home and in industry. Around the middle of the 19th century, the first experimental synthetic detergents were produced. These experimental detergents were developed further in Germany during World War I. Advances in various chemical processes in the 1930s finally made it feasible to produce synthetic detergents in large quantities, leading to the first commercial use of such detergents in the 1950s. Detergents are found in many products, including dry-cleaning solutions, toothpastes, mouthwashes, antiseptics, laundry soap, dishwashing soap, and antiseptics.

Over the years, most complaints about detergents were associated with polluting the environment because many of the chemicals they contain were not easily biodegradable. In terms of human health, skin and eye irritations were the most common problems associated with detergent use. Some research has also determined a link between detergents and the risk of allergies, asthma, and various other health dangers.

Most of the research focusing on links between detergents and some forms of cancer is in the preliminary stages. Nevertheless, ongoing research of detergents has revealed that some of the ingredients used or produced as by-products of the production process are associated with increased risk of various toxicological problems. For example, liquid detergents emit benzene vapors.

Benzene

Benzene is a colorless, flammable liquid that evaporates almost immediately when exposed to the air. Both animal and human studies have shown that benzene can cause cancer. Most of the research has focused on leukemia and other blood-cell cancers, such as multiple myeloma and non-Hodgkin’s lymphoma. In addition, animal studies have shown that benzene can cause chromosome changes in bone marrow cells.

Agencies that have evaluated the cancer-causing risks associated with benzene include the International Agency for Research on Cancer (part of the World Health Organization), the National Toxicology Program, and the U.S. Environmental Protection Agency (EPA). All have classified benzene as a known carcinogen for humans. Linear alkyl benzene sulfonates (LASs) are typically listed as anionic surfactants on detergent labels and are often major cleaning agents in granular, tablet, and powdered detergents.

Although no definitive link has been established between cancer in humans and benzene in laundry and dishwashing detergent, it is known that the benzene in LAS gets into clothes. As a result, benzene can then be absorbed by the wearer via the skin when a person sweats and via the underarms into the lymphatic glands. Benzene exposure can also occur in some workplaces, including the manufacturing facilities for detergents.

1,4 Dioxane and Acetalehyde

Classified as an ether, 1,4 dioxane is an organic compound and colorless liquid. According to the EPA, dioxane is a probable human carcinogen. Studies have revealed increased incidence of cancer in animal studies. However, no relationship has been definitively observed between dioxane and workers who use the compound or at concentrations found in products such as detergents. According to the EPA, animal studies have found that the greatest risk is likely to be due to dioxane vapors that are inhaled.

Further Readings


Detergents

Dioxane is found in numerous laundry detergents. Dioxane is not an additive to cleaning products but rather is a contaminant left behind by the use of ethoxylated ingredients found in many cleaning products. A 2011 study conducted by the nonprofit Women’s Voices for the Earth (WVE) found that Tide Free & Gentle laundry detergent and the company's regularly formulated detergent both contained dioxanes at levels of 89 parts per million (ppm) and 63 ppm, respectively. Some animal studies have estimated that daily exposure at levels above 50 ppm for two years can cause liver damage. Other laundry detergents were also found to contain the substance, but Tide had the highest levels.

In 2013, Procter & Gamble, the company that manufactures Tide, announced that it was reducing the amount of the chemical in its Free & Gentle and regular detergents. This announcement came after the company ignored initial calls from WVE and then faced a lawsuit brought by a group called As You Sow, which claimed the company was unnecessarily exposing customers to high levels of 1,4 dioxane without notifying them via the products' labels. Although this lack of notification did not violate any federal law, it did violate California's Proposition 65 labeling law concerning toxic chemicals. After losing the suit, Procter & Gamble stated it would reduce levels of the chemical in these products nationwide to below 25 ppm.

Acetaldehyde is another compound found in some detergents. Although it occurs naturally in the environment and also during normal metabolism in the body, extensive exposure can cause acetaldehyde to become a neurotoxin leading to depression, headaches, irritability, lethargy, and poor memory. Animal research has shown that acetaldehyde can increase the risk for nasal and throat cancer. However, data gathered from humans on its carcinogenic effects are inadequate. The EPA has classified acetaldehyde as a probable human carcinogen.

Scented Detergents
Manufacturers do not have to disclose all the ingredients in laundry products, including substances used to scent the product. In 2011, a study noted a potential health risk due to scented detergents and dryer sheets. In a small study in the August 2011 issue of *Air Quality, Atmosphere and Health*, research looked at the effluent from dryer vents in two households. Comparing scented laundry cycles with unscented laundry cycles, researchers found that scented cycles contained 25 volatile air pollutants, including the carcinogens benzene and acetaldehyde.

The researchers estimated that, in the Seattle, Washington, area, where they conducted the study, acetaldehyde emissions from scented detergents would be approximately 3 percent to all acetaldehyde emissions from cars. They also noted that they determined that emissions from the top five brands of laundry detergents would be equal to about 6 percent of acetaldehyde emissions from cars. Other research has indicated that possibly one-third of all scented detergents have at least one chemical ingredient that the EPA considers carcinogenic.

In another study conducted in Seattle, researchers examined what chemicals classified as being
hazardous to human health were in scented detergents and other fragrance products. The study, however, did not examine any links between exposures to these chemicals and health problems. Nevertheless, researchers examined the air in an isolated space for volatile organic compounds (VOCs), which are small molecules released into the air from the surface of the products. The study found almost 100 VOCs at levels in the air considered to have potential health concerns due to exposure to them. Three of them were classified as hazardous air pollutants, including acetaldehyde and 1,4 dioxane.

The study pointed out that none of the product labels listed these substances on the ingredients label. For example, in the case of 1,4-dioxane, the carcinogen is created when detergents are processed using ethoxylation. Because 1,4-dioxange is a by-product of ethylene oxide reacting with other substances, it is considered a contaminate and not required to be listed on the label. Industry spokespeople noted that the amount of potentially carcinogenic ingredients in the various products have not been shown to be hazardous to human health. They also point out that people sensitive to fragrances can simply avoid using them.

**Cancer Patients and Detergents**

Because of the many substances used to manufacture most popular laundry detergents, cancer patients undergoing chemotherapy are warned to avoid detergent residue on their clothes and other articles in the house, such as bedsheets. According to the National Cancer Institute (NCI), pruritus, or dry skin and itching, often occurs in cancer patients, and one of the causes could be detergents. NCI notes that traces of laundry detergents and fabric softeners can help make pruritus worse in cancer patients.

NCI recommends using one teaspoon of vinegar per quart of water in the laundry rinse cycle to help prevent trace residues. NCI also suggests using milder detergents, such as detergents specifically made to wash baby clothes. In addition, mild bath soaps have less detergent in them to irritate the skin.

**Drinking Water**

A 2010 study published in *Environmental Science & Technology* implicated detergents, along with shampoos and fabric softeners, as potential precursors to the formation of carcinogenic contaminants in treated wastewater. The contaminants are nitrosamines, which are found in numerous products, including detergents. Treating wastewater with chlorine or ozone does not reduce the formation or nitrosamines, resulting in their presence in drinking water and recreational water.

The primary concern is over a nitrosamine called N-nitrosodimethamphetamine (NDMA), which is a toxic organic chemical and has undergone studies indicating it may be a human carcinogen. Researchers stress that the study results are preliminary. Furthermore, it is unlikely that any one compound or product, such as a detergent, would cause most of the NDMA formation. Detergents also varied widely in their formation of nitrosamines.

Consumer advocates have noted that people may want to consider going with “green cleaners” that, as far as it is known, do not contain or produce potential carcinogens. In addition, they recommend carefully reading detergent labels. For example, signs that the detergent may contain dioxane, which is not listed, include ingredients such as polyethylene, polyethylene glycol, PEG, polyoxymethylene, and words containing “oxynol” or “eth.”

David Petechuk

*Independent Scholar*

**See Also:** Chlorine; International Agency for Research on Cancer; Water Treatment; World Health Organization.

**Further Readings**


Developing Countries

The prevention, detection, treatment, and palliation of cancer can be an economically daunting task for the poorer nations of the world. Combined with an increasing prevalence of cancers, many of which have an infectious etiology, lack of economic stability, a burgeoning population, the acquired immune deficiency syndrome (AIDS) pandemic, and inadequate health care services, these countries are on the verge of a crisis. However, the shift in paradigm from cancer treatment to prevention and early detection may possibly avert a major catastrophe.

Cancer in Developing Countries

Estimates of global cancer incidence and progression indicate that there will be approximately 17 million cases detected by 2020 and 27 million by 2050. Approximately two-thirds of cancer cases by 2050 will occur in the developing countries of the world. Compounded with problems of increasing population and life expectancy, greater influence of Western lifestyles, and lower cure rates, a higher incidence of cancer in the future will translate into increased mortality rates due to the disease in this part of the world.

The typical epidemiology of cancer in developing countries differs from that of the developed world in certain major aspects. Developed countries have higher rates of lung, breast, colorectal, prostate, and bladder cancer, possibly due to the earlier onset of the tobacco epidemic, exposure to occupational carcinogens, influence of the Western diet, and a relatively sedentary lifestyle. In contrast, developing countries have higher rates of stomach, cervical, and liver cancers due to the prevalence of infections that are strongly implicated as causative agents in these types of tumors. Incidences of lung and breast cancer, however, are comparable between developed and developing nations.

The causes of cancer vary worldwide. In developed nations, tobacco is a major causative agent, causing a third of all cancer deaths. It has been calculated that a quarter of all tumors are smoking related. Tobacco consumption is becoming a growing cause of concern in developing countries as well. Smoking has been primarily implicated for the high incidence of lung cancer, which in turn currently accounts for the highest numbers of new cancer cases and cancer-associated deaths among males in developing countries. Oral tobacco consumption is also an important carcinogen for oropharyngeal and laryngeal carcinomas.

Nearly one in four cancer deaths in developing countries are associated with chronic infections. These particularly include the human papillomavirus (HPV) that is associated with cervical cancer, Helicobacter pylori that causes stomach cancer, and hepatitis B and C viruses (HBV and HCV) that are major causes of liver cancer. Together, these agents account for more than 90 percent of cancers due to an infectious agent. Dietary ingestion of substances produced by the mold Aspergillus flavus, specifically aflatoxin B1, is associated with development of liver cancer. Improper storage of grains and similar foods after harvesting, especially in humid, developing countries, is a major cause of contamination of this mold. Superimposed exposure to aflatoxins in a person infected with HBV increases his or her chances of developing liver cancer.

Kaposi’s sarcoma, a formerly rare and indolent cancer, has emerged as a new cancer problem in sub-Saharan Africa. For many years, Kaposi’s sarcoma was the most common cancer observed in AIDS patients, and indeed this, in part, initially defined the AIDS epidemic. However, this is no longer the case since the advent of highly active antiretroviral therapies for human immunodeficiency virus (HIV) in the 1990s. Where these therapies are available to those infected with HIV, Kaposi’s sarcoma has again become a rare diagnosis. However, due to the limited availability of antiretroviral therapies in sub-Saharan Africa, Kaposi’s sarcoma is now one of the most common cancers and can also affect young children.

Health services in developing countries are currently struggling with a growing population, lack of funds, wars, natural disasters, cultural biases, and the HIV pandemic. However, in the midst of evaluating the logistical and natural differences between
the developed and developing world, the disparities in experiences of patients diagnosed with life-limiting illnesses are generally ignored. Studies have shown that, while cancer patients from developed countries describe unmet psychosocial needs, the problem among patients from developing nations is more acute where physical needs are often unmet. Unaffordable and inaccessible health care services mean that not all cancer patients can obtain treatment or painkillers. The main issue in these cases, therefore, is the physical suffering associated with cancer. This is notably absent in developed countries where patients have direct and affordable access to health care. A diagnosis of terminal cancer in developing countries is often met with acceptance and a long wait for death that can be especially discomfiting in the absence of adequate medical support.

**Interventions for Cancer Control**

When developing national strategies to control cancer, the World Health Organization recommends that countries follow four broad approaches: primary prevention, early detection and secondary prevention, diagnosis and treatment, and palliative care. In addition, health care providers in developing countries also examine the cost-benefit ratios of such interventions before their mass implementation.

The goal of primary prevention is to minimize or eliminate exposure to cancer-causing agents, including environmental carcinogens and lifestyle factors related to nutrition and physical activity. With infectious agents being a major and preventable cause of cancer deaths in the developing world, primary prevention of cancer in these countries needs to focus on immunization and treatment of infectious, cancer-causing agents. The HBV vaccine was designed to prevent liver cancer and is now widely used in several developing countries. Efforts are also underway to develop vaccines to prevent *H. pylori* infection. Cervical cancers are strongly associated with HPV. Use of barrier contraception can protect against this infection, but many developing countries do not have health and family planning programs in place to impart education regarding use of such contraceptives. An HPV vaccine is now available that protects against two viral subtypes that are responsible for approximately 75 percent of all cervical cancer cases.

Tobacco consumption is the most important cause of lung and esophageal cancers. Effective national tobacco control programs need to encompass health promotion, education, and health service interventions with tobacco control policies, including regulation of tobacco advertising, increased taxation, and smoking bans in public places. This also can reduce secondhand smoking, which is a major factor for development of many cancers and other diseases of the respiratory tract. Excessive alcohol use also can be a major contributor for liver and esophageal cancers, and control of alcohol consumption can tackle this problem too. Prevention of food-grain contamination along with dietary supplementation of food rich in chlorophylls can reduce the carcinogenic potential of aflatoxins. For those infected with *H. pylori*, reduced consumption of salted, pickled, and smoked food that is otherwise typical of cuisines in some developing countries can avoid the formation of gastritis and ulcers, which are common precursors to stomach cancer.

Screening for cancers, especially among susceptible population subgroups or geographic locations, remains the mainstay of early detection and effective intervention in developing countries. Screening for liver cancers includes ultrasound examination and blood tests to detect specific proteins that can be elevated in cancer. Screening for colorectal and stomach cancers includes fecal examination, routine radiology including contrast studies, and endoscopic examinations. Urea breath test is a specific screening test to detect presence of *H. pylori* infection and is gaining popularity in mass screening programs. Methods of early detection of breast cancer include screening by mammography, clinical breast examination, and breast self-examination.

Cytology-based examination using the Papanicolaou (Pap) smear has been the main screening method for secondary prevention of cervical cancer worldwide. However, this is often difficult to sustain in developing countries due to lack of expertise and infrastructure. An effective alternative approach is by visual inspection of cervix after application of acetic acid, which can be performed by trained health workers. Studies have shown that this may be as effective as a Pap smear and is being increasingly employed by developing countries with a see-and-treat approach. This involves detection of suspicious cervical lesions followed by immediate
Diesel Exhaust treatment using electrosurgical excision or cryo-therapy as an outpatient procedure so that patients are not lost to follow-up.

Developing countries often face a multitude of problems with respect to diagnosis and treatment of cancer due to poor infrastructure and laboratory support, lack of adequate hospitals and clinics, low physician-to-patient ratios, absence of insurance and social security policies, lack of government funding, superimposed political crises, and social misconceptions. In addition to the traditional therapeutic interventions for cancer therapy, developing nations need to focus on the treatment and eradication of infections that are major causes of cancer. Important examples include treatment of *H. pylori* infection using various antibiotic regimens, use of sterile needles (to avoid HBV infection), and safe blood for transfusions (to avoid HCV infection) to prevent liver cancer. In addition, the high morbidity and mortality rates of cancer in the developing world imply a greater need for access to palliative drugs and painkillers that can help relieve the pain associated with cancer therapy and the natural course of the disease.

Anirban P. Mitra
*University of Southern California*

See Also: Asian Diet; Kenya; Poverty; Vaccines; Western Diet.

Further Readings

Ngoma, Twalib. “World Health Organization Cancer Priorities in Developing Countries.” *Annals of Oncology*, v.17


**Diesel Exhaust**

Diesel exhaust is the product of combusted diesel fuel used to power many larger vehicles and machinery. The first diesel engines emitted high amounts of soot, or diesel particulate matter, which has now been shown to be a cause of lung cancer. Although technologies have decreased the amount of particulate matter released by these diesel engines, there is still a measurable link between its inhalation and increased risk of cancer. Exposures still occur today on a wide scale in occupational and public settings from diesel industries from mining and professional driving to residential metropolitan areas.

Exposure to diesel exhaust is a known occupational hazard to truckers, railroad workers, and miners using diesel-powered equipment in underground mines. Adverse health effects have also been observed in the general population at ambient atmospheric particle concentrations well below the concentrations in occupational settings. The first diesel engines started to be used more frequently in the early 20th century; the engine was patented by the German scientist, Rudolph Diesel. Not until the mid to late 20th century did the diesel engine really become commonplace. These trucks, cars, and machines emitted large amounts of particulate matter and other gaseous products from the combustion of diesel fuel, which at the time was not known to be hazardous. In the 1960s through the late 1980s and even today, government regulation on diesel exhaust standards has dramatically reduced the amount of particulate matter and other components released; however, there is still reason to be concerned about this carcinogen.

**Constituents of Diesel Fuel and Exposure**

Diesel fuel is burned to extract the energy it withholds to power an engine. The exhaust released by this process is a source of atmospheric soot, fine particles, and gaseous chemicals with unique characteristics. Diesel engine exhaust depends on many factors including size, temperature, lubrications, and fuel composition ratios. These factors may affect the composition of the exhaust, although significant particulate matter is associated with all diesel engines. Diesel engines produce 50 to 200 times more particulate matter than catalyst-gasoline engines. The rough surfaces of these fine particles make it easy for them to bind with other toxins in the ambient air, thus increasing the health hazards of particle inhalation.

Fine particles from diesel exhaust are a group of air pollution hazards linked to cancer and heart and lung damage. Fine particles less than 2.5 microns in
size can penetrate deep into the lung issues, where gas transfer occurs between red blood cells, lodging themselves in the tissues permanently. Because these particles cannot be removed, they often cause irreversible damage. This particulate matter is one of the most-recognized harmful components of diesel exhaust and may account for many of the lung-related illnesses associated with diesel exhaust.

Accompanied by soot, there are other harmful chemical compounds. Some of these components include acrolein, benzene, carbon dioxide, carbon monoxide, formaldehyde, nitrogen dioxide, and sulfur dioxide. Nitrogen dioxide is used as a marker for traffic-related pollution such as in a city and can be a good tool in measuring the public’s estimated exposure. Exposure to trace amounts of nitrogen dioxide is almost constant due to the combustion of fuel in all populated places. Most of the components of diesel exhaust are either irritants, asphyxiants, or suspected or confirmed carcinogens. Some of the components are released in such small quantities, however, that they are not above allowable occupational exposure levels.

Types of Exposures
Occupational exposures can happen to a wide variety of workers in many different diesel-related industries. Public exposure can occur indirectly from occupational sources or simply living near high-volume traffic. Industries that see high exposures to diesel exhaust, in particular diesel exhaust particulate matter, include professional driving (e.g., trucks and buses), railroads, construction, agriculture, and maritime fields as well as specific jobs, such as: traffic police, garage mechanics, taxi drivers, tunnel workers, and gas station attendants. Because the public is usually woven into all of these jobs, it is not uncommon for the general public to receive small exposures also. The extent to which these small exposures affect the general public are still unclear, although there are clearer trends between occupationally exposed individuals and health effects.

Mining is one of the most commonly studied diesel exhaust exposure industries. Vehicles are used in underground mines to assist tunneling and removal of debris. These vehicles are powered by diesel fuel and release diesel exhaust into underground mines that may not be well ventilated. Studies have shown a relationship between underground miners and increased risk of lung and esophageal cancer as well as pneumoconiosis. The evidence, however, may be complicated by the synergistic effects of other hazards associated with mining, including coal dust, silica particulate matter, and smoking. Professional driving, or operation of large diesel vehicles, is another industry that may pose a measurable, elevated risk of cancer due to the close proximity of the worker to exhaust release.

Public exposures can occur from daily life, travel, as well as nondiesel related occupations (i.e., office adjacent to a busy highway); however, exposures are usually much less than that of an individual working near or with diesel machines (i.e., miners and professional drivers). Workers exposed to diesel exhaust on the job also commute and spend free time where significantly smaller, but prevalent, exposures can occur. The adding relationship that some exposure reports are urging is that normal exposures to nitrogen dioxide (a traffic exhaust marker) are added upon when working in a diesel industry. These researchers are basically urging that the exposure never stops; it merely decreases. This relationship may be a concerning factor in certain metropolitan situations where traffic exhaust pollution and diesel industry are large issues.

Carcinogenicity and Health
Short-term or acute exposures to diesel exhaust have been linked with symptoms such as headache, dizziness, nausea, coughing, and irritation of the eyes, nose, and throat. Research has shown an inflammatory response in respiratory epithelial cells that line the airways, causing some of these acute exposure signs and symptoms. Acute exposures usually cause no further long-term damage to the body, although continued exposure has this potential.

Long-term exposures can lead to chronic, more-serious health problems such as cardiovascular disease and respiratory cancers. The reason diesel exhaust is thought to be a carcinogen is that it is made from many components that are proven carcinogens. These components, combined together, may result in an increased negative health effect or synergistic effect. Chemical components of diesel exhaust have the ability to enter directly into the bloodstream due to the systemic nature of inhalation. Similar to how oxygen is transferred from the alveoli chambers of the lungs to the red blood cells in the bloodstream, inhaled chemicals can diffuse into the bloodstream in the same manner.
Additionally, each constituent of diesel exhaust has separate carcinogenic effects, and not all fuels are the same. For example, benzene, a chemical component of diesel exhaust, is thought to cause leukemia, and carbon monoxide is an asphyxiant. There are some fuels richer in certain components, making them possibly more or less hazardous than others. Chronic exposure can lead to an increased risk of developing cancer due to repeated exposure contact with possible carcinogens and human cells (i.e., lung tissue cells). The exhaust’s fine particles can come in contact with lung tissue and cause cells to mutate. Diesel exhaust particulate matter has been shown to be a mutagen in the way it can affect human DNA, causing usually long-term health problems and possibly death. There is clear evidence of this mutation in occupational exposure studies, many of which lead to lung-related cancers and illnesses.

Studies have shown associations between diesel exhaust exposure and increased incidence of lung cancer, even in nonsmokers. While smoking increases the risk of cancer by itself, smoking while exposed to other carcinogens, like diesel exhaust, can create a multiplying or synergistic effect, dramatically increasing the risk of developing cancer. As both of these exposures are respiratory, the lungs are usually a target site for cancer when exposed to both.

The means associated with development of cancer concerning diesel exhaust are source, exposure, and the mutation site, creating a potential for cancer. First, there must be a source of diesel exhaust, usually motor vehicles or machines that use diesel fuel. The exhaust these machines create is released into the surrounding air and, depending on weather conditions and wind, may be quickly dispersed or linger around the machine or inside of a vehicle’s cab in varying concentrations. Once the source is established, the exposure occurs through an individual’s respiration. As the exhaust enters the lungs, the particulate matter sticks to the moist tissues in the respiratory system, some of which make it into the smallest segments of the lungs. The chemicals in the exhaust may be exhaled or enter into the bloodstream to be removed and excreted or deposited in an organ or tissue within the body. The particulate matter still in the lung tissues has the potential to mutate the cells that it comes in contact with, possibly resulting in a tumor or scarring of tissues. Mutation occurs when the particulate matter changes the DNA of the targeted cell in the lung.

That cell can become a cancer cell, able to replicate and reproduce more cancer cells, which leads to a tumor and lung cancer.

**Conclusion**

Diesel exhaust is a conglomerate of many carcinogens and hazardous substances that pose a threat to both occupational and public settings. There is considerable evidence that diesel exhaust exposure, especially chronic exposure, increases the risk of lung cancer and possibly a host of other health problems. Exposure can occur in both occupational and public settings and wherever diesel-powered machines are used. Diesel exhaust is thought to be a carcinogen due to its components, including diesel exhaust particulate matter as well as many chemical compounds. Synergistic effects of diesel exhaust and other carcinogenic inhalation hazards may create compounding factors that have the potential to increase cancer rates among many occupationally exposed workers. It is hard to measure the public’s exposure and cancer response to diesel exhaust due to its nature of components and other confounding factors that affect each individual’s susceptibility.
Diet and Nutrition

The importance of diet in maintaining health and preventing disease, including cancers of many anatomic sites, has been recognized for millennia. Despite contradictory results from prospective cohort studies, most but by no means all of the tens of thousands of scientific papers on the subject support the role of diet and nutrition in causing cancer or affecting survival. After tobacco use, diet and diet-related factors (such as body weight) appear to be the most important determinants of cancer risk.

More than 30 years ago, Drs. Richard Doll and Richard Peto estimated that 35 percent of all human cancers are caused by diet. Despite the large degree of uncertainty around this estimate, it still is considered widely to be a reasonable, well-informed guess. The uncertainty accompanying any global estimate of the effect of diet and nutrition on cancer results from: the complexity of dietary exposures; the wide variety of the kinds of evidence that exist; methodological difficulties involved in conducting studies that assess diet and cancer risk in humans; reductionist approaches that, in their attempts to simplify research questions, are at high risk of providing erroneous inferences about human cancers; the desire for researchers and the public to sensationalize results from individual studies; and the fact that cancer represents a wide variety of diseases that vary in terms of anatomic site, histology, molecular biology, morphology, and a variety of other characteristics.

**Total Caloric Intake**

Some of the earliest studies linking diet and cancer were laboratory experiments showing that animals on calorie-restricted diets were less likely to get cancer than animals that ate freely. Those animals that did get cancer on such calorie-restricted diets (e.g., ones that were given a known carcinogen or cancer-causing agent) were often found to have fewer or less-aggressive tumors. Corroborative evidence comes from international comparisons showing that countries with high rates of estimated energy consumption and in which individuals tend to be sedentary have very high rates of certain cancers such as breast, prostate, and colon. Findings from a number of “natural experiments” in which humans who were deprived of sufficient food for short periods of time—the World War II–induced Dutch Famine of the winter of 1944 and 1945 have yielded conflicting results, indicating the complexity of diet–cancer relationships in terms of timing, recall bias, and mechanisms of carcinogenesis. Recent work showing that caloric excess can be pro-inflammatory, which in turn may increase cancer risk, underlines the importance of regulating total intake. As with work conducted in the 1970s on cardiovascular disease, it appears that increasing physical activity with a concomitant need for additional energy appears to reduce cancer risk.

**Specific Nutrients and Other Dietary Constituents**

Early on in the scientific study of diet and cancer, it was shown that dietary fat increases risk in certain animal models of cancer. Subsequent work in humans, especially focusing on breast cancer, has led to equivocal results. Population-level comparison studies (usually comparing countries with very different cancer death rates) have supported the
laboratory animal trials. Studies that are thought to be methodologically stronger, that is, cohort or prospective studies of free-living humans, tend not to support the fat–cancer hypothesis. There are a variety of methodological issues that may explain these discrepancies, including the limited range of exposures within specific populations in comparison to both the cross-national comparisons and many of the laboratory animal experiments. As for total caloric intake, most categories of fatty acids are pro-inflammatory.

The study of other macronutrients (nutrients that contribute calories to the diet, i.e., protein, carbohydrate, and alcohol in addition to fat), facing similar methodological barriers and challenges, have come to similar conclusions. One striking exception is alcohol: In the presence of tobacco, it is a strong cocarcinogen for most of the sites of the upper aerodigestive tract, including the oral cavity, larynx, and esophagus. In addition, there is evidence that alcohol increases breast cancer risk.

Over the past several decades, there has been greatly increased focus on specific micronutrients (nutrients such as minerals and vitamins that do not contribute calories to the diet) and other constituents of the diet, including compounds in spices and categories of fiber (e.g., some nondigestible components). On balance, patterns of nutrient consumption associated with vegetarian diets and certain traditional foodways (e.g., East Asian, South Asian, and Mediterranean cuisines) are associated with lower overall cancer rates. In the past several years, intensive research has shown that most of these micronutrients and other constituents such as flavonoids are anti-inflammatory. There is a complementary body of evidence showing that meat (especially processed and red meat) intake is both pro-inflammatory and is associated with increased cancer risk.

Whole Diets: Special Populations
Despite heavy use of dietary supplements among a small minority of individuals, the vast majority of nutrients are consumed as part of individuals’ diets. Nutrients and other components of diet are therefore rarely eaten as separate components. They occur together within foods and usually are eaten as part of complex sets of rules and social behaviors. There is therefore an organic connection between individual dietary components, both in terms of how people relate socially and psychologically around food and how individual food constituents interact with one another in the body.

For example, membership in a group can reinforce a pattern of food intake that is high in dietary fiber and will include many antioxidant vitamins (e.g., of which beta-carotene is but one of many hundreds of carotenoids). The diet will be generally low in fat and very rich in many other micronutrients besides the carotenoids. It also will tend to be anti-inflammatory and antioxidant, factors that are known to be associated with lower risk of many cancers. Based on encouraging evidence from epidemiologic studies, intervention trials that have given research subjects high doses of specific micronutrients have generally met with failure. Notable examples include two large randomized trials begun in the late 1980s in which beta-carotene was associated with increased risk of lung cancer. The International Agency for Research in Cancer (IARC) concludes that greater consumption of vegetables and fruits is associated with decreased risk of lung, esophageal, stomach, and colorectal cancer. The connections with other cancers are considered probable. In contrast to studies that have attempted to reduce the dietary prescription to a few nutrients, there is a substantial body of evidence showing that special groups within high-risk populations and members of cultures eating whole food, predominantly vegetarian or near-vegetarian diets, have low rates of cancer and other chronic diseases. These include vegetarian Seventh-Day Adventists in the United States and certain major population groups in east and south Asia. Some of these groups, in particular Indians, eat relatively large quantities of spices and natural flavorings that have been found to be protective against cancers in laboratory animal experiments. Some of these, including garlic, ginger, cumin, and onion, are common to many cuisines.

Studying Diet and Cancer
In general, the strongest evidence for diet and cancer comes from free-living populations that choose to eat diets that diverge from the Western norm. Cross-cultural studies designed to measure and test the effect of diets of individuals who differ from one another to as great a degree as countries represented in cross-national comparisons have not been undertaken.
Besides the complex mix of nutrients, individuals adhering to vegetable-based, whole-food diets may avoid exposures known to increase cancer risk such as tobacco and alcohol. They also usually engage in a range of other healthy behaviors related to stress and physical activity. Often, these other behaviors and the social support they entail reinforce the commitment to healthy eating. It is widely known that individuals’ attempts at dietary change almost always fail. The kind of randomized clinical trials the biomedical community considers definitive require removing the specific dietary component from the larger dietary regimen in which it can react with many other components of diet. Additionally, such studies rarely provide the durable social support structures that make it possible for individuals to maintain a long-term commitment to consume such whole-food diets (and the many nutrients they contain).

One notable exception to the natural tendency of people to avoid making dramatic dietary changes is cancer patients who may be highly motivated by having had a life-threatening illness diagnosed. There are some small studies that have shown that vegetable-based, whole-food diets may decrease the recurrence of breast and prostate cancer and colon polyps.

Clearly, any study of cancer in humans will have to face the complexity of diet, including food preferences, preparation techniques (e.g., charring of food is related to cancer), serving size estimation, consumption of foods outside of meals and away from home, natural and intentional food contaminants and additives, and a host of problems with recall. Any attempt to simplify the study system will need to account for eliminating the other aspects of diet and lifestyle that appear to interact to reduce risk.

Conclusion
Whole food, vegetarian, or near-vegetarian diets are associated with lower rates of cancer. Supportive findings derive mainly from studies outside the nutritional mainstream in countries such as the United States. Many of the components of these diets appear to be protective. Attempts to study specific dietary components, especially in humans, generally have not met with much success.

James R. Hebert
University of South Carolina

See Also: Beta-Carotene; Exercise; Food Additives; Obesity; Selenium; Stress; Vitamins.

Further Readings

Disability

People with cancer can have a complex relationship with the word disability. Some see it as a very negative word, focusing on what they cannot do, and they do not want to see themselves that way. On the other hand, when people have severe symptoms, they may need to get some welfare assistance, such as Social Security Disability Assistance.

People with cancer also may experience health-related prejudice and discrimination. In such circumstances, they are protected by the Americans With Disabilities Act (ADA). This act has recently been broadened to include a much wider range of people and conditions than originally thought.
Attitudes Toward Disability
Disability is traditionally considered a very negative category—where people are seen as the tragic victims of various health-related conditions. Additionally, people tend to focus on the negative things about someone identified as disabled as opposed to what they can do. For this reason, many people with cancer are reluctant to identify as disabled. However, others feel that they have no option: Their health has deteriorated to the point where they are unable to work, or they need employment or income assistance. In such circumstances, they often rethink their attitudes toward people with disabilities and disability in general.

Protections Under Legislation
On January 1, 2009, the Americans With Disabilities Act Amendments Act came into effect. This act was follow-up legislation to the original 1990 ADA and aimed to restore its original intent of providing a broad-scale means to reduce discrimination. The ADA and this subsequent piece of legislation aim to make it unlawful to discriminate against a person because of his or her disability status. This new disability definition includes people with cancer.

In the 2008 act, Congress clarified the definition of “disability” by identifying a number of major life activities that may be affected by a person with a disability. The act specified activities such as caring for oneself and performing motor tasks, including walking, standing, lifting, speaking, breathing, hearing, and eating as well as cognitive tasks, including learning, reading, concentrating, and thinking. The phrase major life activities was also expanded to include routine operation of major bodily functions, such as normal cell growth; immune system activity; digestion; bowel activity; bladder operation; neurological activity; and respiratory, circulatory, endocrine, and reproductive functioning. All of these major life activities can be affected by various forms of cancer.

The ADA and the subsequent Amendment Act also demand that employers provide reasonable accommodations to people with disabilities, which includes things such as making existing facilities accessible to individuals with disabilities, changing employment to duties, and providing equipment, devices, or interpreters to afford a person with a disability the opportunity to perform his or her occupational role. The act stipulated that employers must provide these accommodations unless providing them would impose extreme hardship on the employer, which was determined on account of the size of the firm and the nature and cost of the accommodation.

Disabling Barriers
While many services afforded to individuals with disabilities are helpful and make a difference in disabled persons’ lives, there remain a number of barriers disabled persons continue to face. Major disabling barriers experienced by people with cancer include barriers in employment, transport, the built environment, insurance, and vocational and educational areas. People with cancer can also experience stigma. People with disabilities have civil rights protections that recognize they are entitled to engage in regular activities, and employers, educational institutions, and businesses need to make their services accessible.

Stigma is a major issue for people with disabilities, including those with cancer. Unfortunately, in everyday interactions, some people are misinformed and prejudicial toward those with cancer. This leads many people with disabilities to be sad or angry about being misunderstood and mistreated. There are many ways of dealing with such prejudice, from ignoring it to challenging it by being assertive. Responding to such problematic behavior is always an individual decision, and it is important to try not to become depressed because depression can have secondary health effects for those with cancer.

Employment barriers, including prejudicial attitudes and failure to provide reasonable accommodations are sometimes reported by people with cancer. An example of a reasonable accommodation for someone with cancer might include needing a different type of chair in an office, needing regular breaks during the day, or needing to switch some duties with another employee. If an employer refuses to provide such reasonable accommodations, individuals may be entitled to take legal action.

Transportation barriers are another common experience for people with disabilities, including people with cancer. For instance, some people will develop mobility problems as a result of cancer. They may not be able to drive or move freely and may use wheelchairs. Accessible transport
therefore becomes a major priority. While some people are able to afford to purchase or rent accessible vehicles, many more become reliant on public transportation. The supply of accessible transportation varies from city to city. In some places, there are a lot of buses, taxis, and trains that are accessible, whereas in other locations (particularly small towns and rural locations), getting around is much harder for those with mobility impairments.

Problems With the Health System and Insurance
A number of financial resources are available to people with cancer. Individuals may be afforded access to government-funded insurance plans, private health plans, health insurance risk pools, and other options. Some government-funded options include Medicare, Medicaid, state-sponsored plans, as well as veteran and military benefits. Private options include both individual and group plans as well as access through government-maintained marketplace plans such as those available through the Affordable Care Act. For those individuals who are uninsured, insurance help may be found at some hospitals.

Nonetheless, a number of people with cancer face obstacles finding, receiving, and enjoying the benefits of health insurance. As a result of their health problem experiences, people with cancer may find themselves needing to access disability assistance programs. They are usually entitled to such programs and to the legal protections offered to people with disabilities under relevant legislation because of their health problems. However, like many people with disabilities, they may face many gaps and barriers in service provision and problems with the affordability of necessary procedures.

Mark D. Sherry
Walter Scott Stepanenko
University of Toledo

See Also: Government; Hospitals; Insurance.

Further Readings
(Accessed July 2014)


Disinfectants and Antiseptics

Antiseptics and disinfectants are commonly used in hospitals and other health care settings as the primary method to control infection and prevent nosocomial infection. Antiseptics are biocides that destroy or inhibit growth of microorganisms in or on living tissue. Disinfectants are similar but are used on inanimate objects or surfaces. Biocides have been used for hundreds of years for antisepsis, disinfection, and preservation, displaying wide activity that inactivates various microorganisms. To communicate the wide variety of action carried out by biocides, suffixes are attached including “–static,” referring to agents that inhibit growth (e.g., bacteriostatic, fungistatic, and sporistatic), and “–cidal,” referring to agents that kill the target organism (e.g., sporicidal, virucidal, and bactericidal). Antiseptic and disinfectant activity on microorganisms can be influenced by the presence of an organic load, synergy, temperature, dilution, and test method.

Types of Antiseptics and Disinfectants
Acetic acid (vinegar 8 percent) has shown substantial activity against two gram-negative bacilli, P. aeruginosa and S. choleraesuis. Acids deactivate many microorganisms, but because concentrated solutions can be casuistic, cause chemical burns, and are toxic at high levels in the air, they have been limited as disinfectants. Acidic-electrolyzed water is made from the electrolysis of ordinary water and measured amounts of salt such as sodium chloride (table salt). When combined with chlorine, the water solution possesses bactericidal activity against mycobacteria and spores of Bacillus subtilis.

Alcohols produce rapid, broad-spectrum antimicrobial activity against vegetative bacteria (including mycobacteria), viruses, and fungi, with an optimal level in the 60 to 90 percent range. It is fast acting with most bacteria killed within five minutes of exposure. Alcohols are used for
Disinfectants and Antiseptics

Surface disinfection, topical antiseptic, and in hand-sanitizing lotions. They are highly flammable, can cause damage to rubber and plastic, and can be very irritating to injured skin. Ethyl alcohol (ethanol and alcohol), isopropyl alcohol (isopropanol and propan-2-ol) and n-propanol are widely used for both hard-surface disinfection and skin antiseptics. Generally, isopropyl alcohol is considered slightly more efficacious against bacteria, and ethyl alcohol is more potent against viruses. They are not considered sporicidal and are not recommended for sterilization.

Alkalis, such as sodium hydroxide (lye, caustic soda, and soda ash), are highly caustic and are used to disinfect buildings. Protective clothing should be worn when mixing and applying the chemical. Water should not be poured directly into lye as violent reactions will occur and produce high heat that can melt plastic containers. Sodium hydroxide is corrosive for metals. It is considered an effective foot-and-mouth disease (FMD) disinfectant.

Aldehydes are effective against bacteria, fungi, viruses, mycobacteria, and spores. They are non-corrosive to metals, rubber, plastic, and cement. Glutaraldehyde is a dialdehyde used primarily in low-temperature disinfection, in sterilization of endoscopes and surgical equipment, and as a fixative in electron microscopy. It has broad-spectrum activity against bacteria as well as spores, fungi, and viruses. However, it is caustic, producing mucous membrane-irritating effects, bronchial asthma, and contact dermatitis. O-Phthalaldehyde (OPA) has been suggested as a replacement for glutaraldehyde in endoscope disinfection as it is less volatile and irritating while maintaining potent bactericidal and sporicidal activity. Formaldehyde is bactericidal, sporicidal, and virucidal, generally used as a disinfectant and sterilant in liquid or in combination with low-temperature steam. When formaldehyde is used as a fumigant, it is done in an air-tight building, which must remain closed for at least 24 hours after treatment. The carcinogenicity of formaldehyde in rats and mice after long-term inhalation exposure has led to reduced use.

Anilides are antiseptics commonly found in cosmetic soaps and deodorants and rarely used in clinics. Triclocarban is active against gram-positive bacteria and does not stay on skin well.

Chlorhexidine is a biguanide with broad activity substantively for the skin, with low irritation, making it one of the most widely used biocides in antiseptic products. It is found in hand-washing and oral products and also used as a disinfectant. Mycobacteria are generally highly resistant to chlorhexidine; it is not sporicidal, and the antiviral activity of chlorhexidine is variable.

The bis-phenols are hydroxy-halogenated derivatives. They exhibit broad-spectrum efficacy but have little activity against \( P. \) aeruginosa and molds and are sporostatic toward bacterial spores. Triclosan and hexachlorophene are the most widely used biocides in this group, especially in antiseptic soaps and hand rinses, and have persistent effects on the skin. Concern over the toxicity of hexachlorophene has limited its use as an antiseptic.

Halogen-releasing agents and halogen compounds are popular as they are considered to have low toxicity and low cost and are easy to use. They lose potency over time in the presence of organic debris, sunlight, and some metals. To be effective, they must be applied to thoroughly cleaned surfaces. Chlorine- and iodine-based mixes are the most prevalent microbicidal halogens used in clinics and have both antiseptic and disinfectant applications. Chlorine-releasing agents (CRAs) are typically used as hard-surface disinfectants. Sodium hypochlorite solutions (household bleach) can be used for disinfecting spillages of blood containing human immunodeficiency virus or hepatitis B virus (HBV). CRAs at higher concentrations are sporicidal; CRAs also possess virucidal activity. Iodine is rapidly bactericidal, fungicidal, tuberculocidal, virucidal, and sporicidal, though less so than chlorine. Aqueous or alcoholic (tincture) solutions of iodine have been used for 150 years as antiseptics; however, they are associated with irritation and excessive staining.

Hydrogen peroxide \( (H_2O_2) \) is a widely used biocide for disinfection, sterilization, and antisepsis with broad-spectrum efficacy against viruses, bacteria, yeasts, and bacterial spores. At higher concentrations and longer contact, hydrogen peroxide has sporicidal activity. Hydrogen peroxide is available in a variety of concentrations, from 3 to 90 percent in many stores, and is considered environmentally friendly because it degrades into oxygen and water. Peracetic acid is more potent than hydrogen peroxide, being sporicidal, bactericidal, virucidal, and fungicidal at low concentrations. It remains active in the presence of organic loads and
is also environmentally friendly, breaking up into acetic acid and oxygen. Peracetic acid has applications as a low-temperature liquid sterilant for medical devices and as an environmental surface sterilant.

Physical disinfection, such as the use of heat, is one of the oldest methods to control against microorganisms and somewhat reliable for sterilization. Heat can inactivate microorganisms in moist form (autoclave and steam) and dry (flame and baking), but moist heat is more effective and requires less time. Sunlight and ultraviolet (UV) radiation inactivate viruses, mycoplasma, bacteria, and fungi. Light may be also be particularly useful against airborne microorganisms. UV light sterilizing is limited on surfaces because it cannot readily penetrate obstructions. Gamma radiation and microwaves are also used.

Polymeric biguanides including Vantocil are active against gram-positive and gram-negative bacteria and not sporicidal. Polymeric biguanides are used as disinfecting agents in the food industry and for disinfecting swimming pools.

Phenolic-type antimicrobial agents are antibacterial, antifungal, and antiviral and traditionally have been used for their antiseptic and disinfectant properties. They can be found in mouthwashes, disinfectant soaps, hand washes, and other forms of household disinfectants.

Silver compounds have a long history of antimicrobial applications and have been used to prevent infection of burns and some eye infections and to destroy warts. The most relevant silver compound used is silver sulfadiazine (AgSD). Silver metal, silver acetate, silver nitrate, and silver protein, all of which have antimicrobial properties, have also been used.

Vapor-phase sterilants, including ethylene oxide, are broad-spectrum alkylating agents. They are used to sterilize heat-sensitive medical devices and surgical supplies. Their main advantages over other vapor-phase systems include low toxicity, rapid action, and activity at lower temperature; the disadvantages include limited penetrability and applications. In 1994, ethylene oxide (ETO) was upgraded in the overall evaluation from being probably carcinogenic to humans to be a human carcinogen.

Disinfection by-products (DBPs) are formed when disinfectants (chlorine, ozone, chlorine dioxide, or chloramines) react with organic matter, anthropogenic contaminants, bromide, and iodide in water. Trihalomethanes (THMs) and haloacetic acids (HAAs) are the most common DBPs formed in chlorinated drinking water, of which the THM chloroform has been linked to cancer in laboratory animals. Many DBPs are bioaccumulative and stored in body tissues. A person can receive exposure to THMs through showering, bathing, or swimming in addition to drinking water. Chloroform and bromodichloromethane have been classified by International Agency for Research on Cancer (IARC) as 2B, possibly carcinogenic to humans. The U.S. Environmental Protection Agency (EPA) Integrated Risk Information System (IRIS) describes bromodichloromethane as B2, probable human carcinogen. The EPA concludes that, as long as exposure to chloroform remains under a given threshold, the risk for cancer is very low and that standards set for chloroform in drinking water are far below these values. The health effects of THMs in humans remain controversial in the scientific community.

Malik Muhammad
Synthesis Behavioral Medicine PLLC

Christopher Edwards
Duke University Medical Center

Ashland Thompson
Synthesis Behavioral Medicine

See Also: Broad-Spectrum Ultraviolet (UV) Radiation; Chemical Industry; Detergents.

Further Readings


Mohamadshadafae, M. R. and L. Taghavi. “Health Effects of Trihalomethanes as Chlorinated...
Disparities Within Nations (Elimination of Cancer)

Disparities are defined as the dissimilarities or inequalities between groups. Disparities may exist in the distribution of known cancer-related risk factors or simply may be evident in cancer rates. The distinction between establishing cause and that to which cause cannot be attributed is extraordinarily important. Epidemiologic studies have long focused on disentangling the underlying intrinsic factors that determine cancer from those that are within individuals' control to modify or remediate. Understanding what individuals can do to reduce risk is absolutely essential to making progress in moving toward eliminating disparities.

 Observable differences in cancer rates between groups may arise because of inequities that concern the nature of underlying factors that affect health and the quality of accessible health care. Underlying factors may vary according to place, time, and a wide variety of socioeconomic factors ranging from access to financial and educational resources to racism. These factors condition virtually everything to which individuals are exposed in the environment—from industrial contaminants that may have leaked into the water supply or ambient air to access to educational resources, food, and recreational facilities.

 Health equity refers to the absence of disparities in factors known to be the causes of cancers or that determine their clinical course. Inequities can be traced to some kind of economic, social, environmental, or health care-related injustice. It is conceivable that these underlying factors could be eliminated and that there still may be differences in cancer rates between populations because of some intrinsic (e.g., genetic) factors. However, it is generally assumed that the vast majority of factors that condition the probability of having a cancer diagnosis and the outcomes associated with that diagnosis are determined by factors within our power to change—individually or in the aggregate via public policy.

Data Requirements: How We Know What We Know

Understanding disparities requires access to high-quality data. Population-based cancer registries collect data from entities (often hospitals, but also including pathology laboratories) within defined geographical areas in order to produce statistics on cancer incidence and the severity of the disease (e.g., grade and stage) that are expressed as rates per unit population per year (usually newly incident cases per 100,000 persons per year). These registries
collect additional data on sociodemographic factors, including race, sex, age, place of residence, and ethnicity. Usually, they also include additional data on characteristics of specific cancers (e.g., anatomic subsite and morphologic characteristics) and treatments provided. Without access to this kind of information, it can be only conjecture as to whether or not a disparity, or inequity, exists.

The presence, and even quality, of cancer registries is associated with an array of socioeconomic factors that condition the probability of ever getting diagnosed with a cancer. A very enlightening example is provided by comparing two common cancers, breast and prostate, in India versus the United States. While India has a number of hospital-based cancer registries, less than 10 percent of the country has coverage by population-based cancer registries. By contrast, virtually the entire United States is covered by high-quality cancer registries that are based within the states, regions, and territories. Overall incidence rates of breast and prostate cancer are much higher in the United States than they are in India; by factors of about four and 10, respectively. By contrast to the situation in India, where mortality per unit incidence is much higher, both prostate and breast cancer are relatively indolent diseases in the United States; only 17 and 19 percent of individuals, respectively, diagnosed with these diseases actually die of them. Also, while prostate cancer incidence is much lower than breast cancer in India, the rates are roughly equal in the United States, with slightly higher rates of prostate cancer, which spiked with the advent of prostate specific antigen-screening in the early 1990s and then leveled off.

Analysis of population-based registry data from the United States and India showed very clearly that stage of disease (which is an indicator of the size of the primary tumor and its spread to other organ sites) was inversely associated with incidence. These analyses revealed other, very interesting, differences. For example, while the stage distributions of breast and prostate cancer are very similar within the United States—that is, about 85 percent of both are diagnosed at local, early stages—in India, early-stage diagnosis accounts for about 40 percent of all breast cancers but only 12 percent of all prostate cancers. This is clearly observed in the aggregate data reported by all registries within the United States but appears to be more much more extreme in areas such as the Deep South, where there are large numbers of African Americans. For example, mortality-to-incidence ratios are much higher for virtually all cancers among African Americans in South Carolina and Georgia in comparison to their European American counterparts. These contrasts provide very interesting insights into the geographic distribution of cancer. For example, the distribution of mortality-to-incidence ratios in South Carolina, which is primarily a rural state, look very similar to those in Georgia, after excluding the metropolitan Atlanta area. Indeed, ecological-level data analyses in Georgia indicate that some of the differences may be related to disparities or inequities in

**Existing Disparities**

Underserved and racial and ethnic minority subgroups within populations often have unusually high cancer rates. While incidence often is higher than the observed population-average rates, mortality rates and factors related to survival and quality of life are typically much worse. This is clearly observed in the aggregate data reported by all registries within the United States but appears to be more much more extreme in areas such as the Deep South, where there are large numbers of African Americans. For example, mortality-to-incidence ratios are much higher for virtually all cancers among African Americans in South Carolina and Georgia in comparison to their European American counterparts. These contrasts provide very interesting insights into the geographic distribution of cancer. For example, the distribution of mortality-to-incidence ratios in South Carolina, which is primarily a rural state, look very similar to those in Georgia, after excluding the metropolitan Atlanta area. Indeed, ecological-level data analyses in Georgia indicate that some of the differences may be related to disparities or inequities in
the availability of health care facilities and related access. In South Carolina, analyses of environmental data indicate that differences may be related to varying concentrations of minerals (e.g., zinc, selenium, and uranium) in soils and groundwater supplies. Some of these exposures may, in turn, be related to historical factors associated with agricultural practices that were prevalent in these regions. Unlike the rest of the United States, there is very high African American representation in rural areas in the South. This calls into question historical factors related to slavery, which was an important part of the economy of the South through the Civil War. Vestiges of these social injustices continued in the form of Jim Crow laws through much of the 20th century, and some still exist in more subtle forms today.

Data on African American cancer rates make for the most stable and compelling contrasts due to the fact that African Americans traditionally have been the largest well-defined population subgroup represented in the registry data. However, there is emerging interest in looking at rates among Hispanic subgroups as they are currently growing at the highest rate within the United States. Although the data are not as robust, other groups that appear to have disparate cancer rates include Asian Americans, Hawaiians and Pacific Islanders, Alaskan Natives and American Indians, and underserved populations such as those located within Appalachia. All of these populations share common features including economic and social stress. Disproportionately, they reside in rural and impoverished urban communities that are unsafe, offer limited access to healthy foods, and provide little opportunity for physical activity. They tend to have low rates of education and health literacy and occupy insecure service-sector jobs that typically entail little physical activity and frequently require working odd and long hours. Given that it is estimated that diet, physical activity, tobacco use, and appropriate screening account for 90 percent of all cancer incidence and mortality, it is easy to see how factors related to socioeconomic stress could explain a large portion of the disparities within populations.

Although cancer rates have gone down in the United States and other developed countries, relative disparities have often gotten worse. For example, within the United States, incidence and mortality rates of breast cancer have fallen in nearly every group over the past 40 years. However, the relative difference between blacks and whites has grown over this period. Incidence, as mentioned previously, is at least partly an artifact of screening. However, overall screening rates in places where high-risk subgroups reside (e.g., in South Carolina) do not differ much by race. Mortality differences also may be ascribed to intrinsic, genetic differences. While the effect of highly penetrant genes do not account for much of the overall cancer burden, genetic factors appear to be particularly important in highly virulent cancers that present at younger ages (often well below standard age cut points for general population screening). This is certainly true for hormone-sensitive cancers such as breast and prostate, for which incidence at very young ages is much more common in blacks than whites.

Owing to its large size, diverse population, and availability of excellent cancer registry data, the United States presents the best examples of cancer disparities within a particular nation. However, there are many instances of documented disparities in other populations, most notably those considering stage at diagnosis. The United Kingdom provides an interesting case study in that it also documents clear disparities by race or ethnicity as well as excellent information on social class. As in the United States, it appears that a sizable portion of racial and ethnic disparities can be attributed to social justice issues related to socioeconomic status.

Future Directions
The debate that has raged about the relative contributions of social, environmental, and biological factors as determinants of cancer is crucially important to understanding how we can prevent the disease and ameliorate its effects. In order to understand how to intervene effectively in order to reduce disparities, it will be important to link registry-derived information to data on other factors, including those associated with residence and place of work. With the advent of statistical methods associated with geographical information systems, it will become much more feasible to relate putative risk factors that are distributed in space in order to disentangle modifiable risk factors (i.e., those related to socioeconomic conditions) from intrinsic factors that are not within the control of individuals to modify. While the problem of
population heterogeneity in relation to data quality has been pretty well solved within the United States and other developed countries, it will be important to maintain vigilance in terms of data quality and to extend knowledge and techniques to other populations where it is very likely that the same factors that underlie differences in cancer rates also affect data quality.

Addressing cancer-related health disparities in effective and comprehensive ways will require confronting the nexus between social justice and health outcomes. For example, there is a well-established literature on environmental justice that links exposure to known or suspected carcinogens to a variety of socioeconomic factors, including racism. There are vested interests that would prefer that these issues not be addressed. However, the evidence over the last many decades indicates that simply ignoring them is associated with increased relative disparities.

James R. Hebert
University of South Carolina

See Also: Breast Cancer; Prostate Cancer; Screening, Access to; United Kingdom; United States.

Further Readings


Dominican Republic

The Dominican Republic is a developing country that makes up the Greater Antilles Islands located in the Caribbean Sea. This nation occupies the eastern end of the Hispaniola Island. The island was a Spanish Colony until it gained its independence in 1844 and was officially named Dominican Republic.

In December of 1492, Christopher Columbus disembarked on the Samaná peninsula at the north coast. At that time, the island was inhabited by the Taino people and called Quisqueya. One of the earliest measures Spain undertook was building hospitals. The first known European settlement in the New World, reports say that, in January 1494, at Hispaniola was where Columbus constructed a building to keep supplies and ammunition for the soldiers, a church, and a hospital. Afterward, the capital of Hispaniola was founded during August of 1496 on the eastern bank of the mouth of the Ozama River. The location for the capital was chosen because it was believed that the winds that came to the island from the north produced diseases. The capital was originally called Villa Nueva Isabela. This name in turn was later changed to Santo Domingo de Guzman.

In 1503, Nicolás de Ovando, governor of Hispaniola, built what would be considered a hospital and
named it Hospital San Nicolás de Bari. The hospital was a hut situated in the same place as the Chapel of Our Lady of the High Grace. It is believed that, originally, it belonged to a pious black woman who gathered all the poor people she could and treated them according to her skill.

De Ovando followed the instructions received from King Ferdinand and Queen Isabella to build hospitals in towns where he saw greater need and where the Christian poor and the Indians could receive care. In 1590, brothers and officials of the Brotherhood of the Conception laid the first stone of what was at that time known as the old hospital. The aim of the hospital was to treat the poor and care for no more than six patients at a time. Although historical primary sources of evidence cannot be identified, it is proper to infer that the established medical model at Hospital San Nicolás de Bari, such as in Spain and its colonial possessions during the XVI century, was guided by the Hippocratic and Galenian humoral theory. The four humors were considered to be the basic units and fundamental building blocks of all nature. Good health was believed to be the result of the harmonious balance of those four humors throughout the body. Illness was thought to be the manifestation of the disturbance of that balance. As such, a malignant tumor treated from this medical perspective was the direct result of the aforementioned imbalance.

In Spain, as in many western European countries, experimental medicine models started to develop at the beginning of the 17th century. Cancer began to be understood as a local or regional disease, related to the tumor nodes. Medical doctors advocated for breast cancer surgery, which included the removal of the tumor, nodes, and pectoralis major. During the 19th century, pathology and cancer surgery advanced. During the 18th century, the Hospital San Nicolás de Bari adopted the experimental medical model and mainly cared for ill soldiers. As result, its name was changed to Hospital Militar.

Contemporary Context

Presently, the country is politically and administratively organized into 31 provinces and a national district, with a total of 117 municipalities and 56 municipal districts. From 1994 to 2000, the country occupied the top places in leadership in economic growth in Latin America and the Caribbean. As of 2012, Dominican Republic has an estimated total population of 10,135,105. Its residents can expect an average of 12.3 years of schooling, and a gross national income per capita of $5,762. The estimated life expectancy at birth in 2012 was 72.04.

The age-standardized adult mortality rate by cancer at ages 30 to 70 per 100,000 population in 2008 was 270. In 2010, there were 8,433 estimated cancer-reported deaths. Despite Dominican Republic’s sustained economic growth, public health research shows that it has not corresponded with a sustainable human and social scale strengthening. That is, the rise in the production of wealth has not been met by a similar rise in the promotion of an environment that provides viability for the exercise of full human capabilities. In 2012, the density of physicians per 10,000 population was 8.1. Based on official estimated data, as of 2012, the five most common cancers in Dominican Republic are (1) urological (bladder, kidney, prostate, and testis), (2) gynecological (cervix uteri, corpus uteri, and ovary), (3) breast, (4) lung, and (5) head and neck (lip and oral cavity, nasopharynx, other pharynx larynx, and thyroid). The number of oncologists needed for the 2010 population estimated, and based on 2008 research data on new cancer cases at Dominican Republic’s two most populous cities (Santo Domingo: 3,389 cases and Santiago: 723) are Santo Domingo—at least two hematologist oncologists, four surgical oncologists, 17 radiation or clinical oncologists, two urologic oncologists, and seven pathologists and in Santiago—at least two hematologist oncologists, two surgical oncologists, four radiation or clinical oncologists, two urologic oncologists, and two pathologists.

Dominican Republic approved an extensive health financial reform in 2001, which began full implementation at the end of 2007. Prior to the reform, cancer lacked financial protection. Most specialized services were provided by two nonprofit oncological hospitals as well as private facilities primarily serving high-income groups. The public hospitals offered only basic services to low-income patients in the early stages of their disease. Most insurance plans provided limited coverage for cancer; further, only minor support and subsidized care were available from civil society organizations and not-for-profit hospitals, respectively. Thus, patients were forced to finance treatments out of pocket.

The Liga Dominicana contra el Cancer Inc. (Dominican League Against Cancer Inc. [DLAC]) is a pioneer in the management of cancer in the
Dominican Republic. It was founded on September 13, 1942, and incorporated in 1947, by decree No. 4134 of the Executive. At its inception, the institution was called Cuerpo de Voluntarias del Instituto de Oncología Milagro de la Caridad (Miracle of Charity Voluntary Institute of Oncology). The institution was later named after Dr. Heriberto Pieter, a Dominican hospital benefactor. One of this nonprofit private institution’s main objectives was to engage in social and health issues such as education, detection, prevention, treatment, and cure of cancer. The institution also provides assistance to low-income patients who need medical services such as hospitalization, chemotherapy, radiation therapy, and diagnostic studies, among others. DLAC has 70 years of work in the prevention, detection, and treatment of cancer attending daily an estimated 1,200 to 1,600 patients, which represents around 327,000 a year.

Founded in 1982, the Dominican Society of Hematology and Oncology (DSHO) is a group of Dominican medical doctors specialized in diverse branches of oncology. Originally, DSHO was organized under the name of the Dominican Society of Hematology and Oncology, attached to the Dominican Association Medical College. It is also a private nonprofit organization that aims to promote the development of oncology in the Dominican Republic through communication and integration of all its stakeholders whose objective is also to improve the life quality of cancer patients.

Other establishments in the private, nonprofit sector offering treatment are: the General Maternal and Child Hospital—Plaza de la Salud, the Nordestano Cancer Center, the Marcelino Vélez Santana Hospital, and the Oncology Institute of Cibao. Also, the Ministry of Health provides partial services (diagnosis and surgical treatment) in 16 of its hospitals; these services also are offered in four centers in the Armed Forces and National Police Institute and, for teachers of the public segment, the SEMMA Medical Center. Most recently, the government created the National Cancer Institute Rosa Emilia Tavares, which will run a hospital with 120 beds and new medical technology, with large capital spending in infrastructure and equipment. Partial services (diagnosis, chemotherapy, and surgical treatment) are offered in about 87 private, for-profit health institutions.

Héctor E. López-Sierra
*Inter American University of Puerto Rico*

**See Also:** Chemotherapy; Hospitals; Radiation Therapy; Surgery.

**Further Readings**

International Agency for Research on Cancer.


Drugs

Human life has been tremendously improved through the significant benefits of drugs and modern medicines. This entry examines drugs and their implications for cancer in society. A drug is any substance (solid, liquid, or gas) that changes the functions or structures of the body in some way. This excludes food and water, which are required to maintain normal body functioning. The drugs of most concern are those that affect an individual's central nervous system. These are the psychoactive drugs. They act on the brain and can change the way a person thinks, feels, or behaves. Drugs have achieved some of the millennium development goals in terms of longevity, life span, and decreases in morbidity and mortality. Drugs play major roles in cancer control and management. In other words, drugs have significant influence in preserving, protecting, maintaining, and restoring the health of individual members of society. Broadly, a drug is a medicine or other chemical substance that has a physiological effect when injected or otherwise introduced into an individual's body.

In pharmacology, a drug is a chemical substance used in the treatment, cure, prevention, or diagnosis of disease or used to otherwise enhance physical or mental well-being. Drugs may be used for a limited duration or on a regular basis for chronic disorders. Furthermore, the World Health Organization (WHO) defines drugs to be any substance or product that is used or intended to be used to modify or explore physiological systems or pathological systems for the benefit of the recipient.

In terms of sources, drugs come from three natural channels. The first is naturally from plants. They are used to prepare herbal medicines, and some have been produced into tablets and capsules. Second is through animals, such as honey from bees, oils of certain fish, and others. The third source is from microorganisms. For example, penicillins are drugs from fungi. Synthetically, there are various chemical reactions that can be carried out in the laboratory to obtain potent or active drugs. The drugs from synthetic sources are usually larger in quantity than those from natural sources. Put differently, drugs come from a range of sources. Many are found in plants, for example, nicotine in tobacco, caffeine in coffee beans, and cocaine from the coca plant. Morphine and codeine are derived from the opium poppy, while heroin is produced by the chemical modification of morphine. Marijuana is the leaf, buds, and seed heads of the cannabis plant, while hashish and hash oil are the plant's resin. Alcohol is produced by the natural process of fermentation that happens when fruit, grain, or vegetables decompose. Certain fungi, such as mushrooms and cactus plants, are considered drugs in Nigeria because of their hallucinogenic properties. Medicines can be manufactured from both natural and artificial chemicals.

Names, Uses, and Sources of Drugs

Most drugs have at least three names: (1) full chemical names usually too long and complicated to use regularly, for instance, para-amino acetamido phenol (paracetamol) or acetyl salicylic acid (aspirin); (2) generic or nonproprietary names, that is, accepted internationally as common names that are shorter and easy to pronounce or say, for example, chloroquine or paracetamol (more acceptable for prescriptions); (3) brand or trade or proprietary names given by pharmaceutical manufacturers or companies for their own particular brands, for instance, Seprin and Maloxine.

There are three major uses of drugs. One is to cure diseases, and another is to control or eliminate symptoms and, last, to prevent diseases. In all, drugs exist for the purpose of legally prohibiting certain substances (natural or synthetic) that affect the body's functioning or structure and are used in the diagnosis, mitigation, treatment, or prevention of a disease or relief of discomfort. They are also called legal drugs or medicine. A legal or medicinal drug, however, can be harmful and addictive if misused.

In terms of sources, drugs come from three natural channels. The first is naturally from plants. They are used to prepare herbal medicines, and some have been produced into tablets and capsules. Second is through animals, such as honey from bees, oils of certain fish, and others. The third source is from microorganisms. For example, penicillins are drugs from fungi. Synthetically, there are various chemical reactions that can be carried out in the laboratory to obtain potent or active drugs. The drugs from synthetic sources are usually larger in quantity than those from natural sources. Put differently, drugs come from a range of sources. Many are found in plants, for example, nicotine in tobacco, caffeine in coffee beans, and cocaine from the coca plant. Morphine and codeine are derived from the opium poppy, while heroin is produced by the chemical modification of morphine. Marijuana is the leaf, buds, and seed heads of the cannabis plant, while hashish and hash oil are the plant's resin. Alcohol is produced by the natural process of fermentation that happens when fruit, grain, or vegetables decompose. Certain fungi, such as mushrooms and cactus plants, are considered drugs in Nigeria because of their hallucinogenic properties. Medicines can be manufactured from both natural and artificial chemicals.

Cancer-Related Drugs

There are some cancer-related drugs such as Alimta (pemetrexed disodium), Avastin (bevacizumab), Erbitux (cetuximab), Gleevec (imatinib mesylate), Herceptin (trastuzumab), Nexavar (sorafenib tosylate), Revlimid (lenalidomide), Sprycel (dasatinib), Sutent (sunitinib malate), Tarceva (erlotinib) and Xeloda (capecitabine). These cancer drugs such as chemotherapy, hormone therapy, and other biological or genetic treatments, are used to destroy cancer cells. Most times, the goal of cancer drugs is to cure. When cure is not possible, cancer drugs can often prolong life or improve quality of life. Many
Drugs Can Work in a Number of Ways to Kill Cancer Cells

Chemotherapy drugs can slow down cancer cells from growing or multiplying. They can also encourage these cells to die naturally (apoptosis). In general, chemotherapy drugs can harm some of the healthy cells in the same way, causing side effects. Hormone drugs usually stop the body’s hormones from helping some cancers to continue to grow. Biological therapy involves drugs that help the immune system in the body to fight against cancer. Targeted drug therapy includes drugs that are designed to attack only certain areas found mainly in cancer cells. These drugs tend to cause less harm to healthy cells, which means fewer side effects.

Chemotherapy uses drugs to treat cancers of the blood and bone marrow as well as for cancers of the lymphatic system (lymphomas). Chemotherapy is also used to treat cancer when it has spread, when it has come back, or when there is a strong chance it could come back (recur). Hormone therapy uses drugs to interfere with hormone production or hormone action to kill cancer cells or slow their growth. Surgery is also used to remove hormone-producing glands to slow or kill cancer cells.

Chemotherapy is recommended to patients as an option based on the following:

1. Does the specific cancer react to chemotherapy? Only certain types of cancers (the ones with large proportions of dividing cells) are responsive to drugs. These are usually small tumors (either because they are detected early or because most of the tumor has been removed by...
surgery or radiation) or are systemic cancers like leukemias and lymphomas (systemic means they are everywhere in the body).

2. Even if the tumor can respond to cancer drugs, its actual location will affect the choice of treatment. In some cases, tumor location will make cancer drugs, perhaps combined with radiation therapy, the only treatment option. For example, certain brain tumors cannot be removed surgically, so cancer drugs or radiation therapy are the only choices.

3. The body has to be otherwise healthy in order to tolerate some chemotherapy drugs. Cancer patients are often shocked when they hear medical personnel refer to them as healthy. How can someone with cancer be healthy? When doctors term a cancer patient healthy, they are referring to how well the body is functioning, except for the site of the cancer. When they speak about a cancer patient being sick, they are talking about a serious breakdown in the functioning of vital organs and systems.

Pain Control

Pain control is a significant issue in cancer care, particularly in end of life care. The World Health Organization (WHO) has developed a three-step “ladder” to help guide the provision of relief from cancer pain. The general principle is that pain should be treated promptly, with drugs provided until the patient is free of pain. Drugs should be administered in three steps, with the second and third steps used only if necessary to provide pain relief: first non-opioids such as aspirin, then mild opioids such as codeine, then strong opioids such as morphine. In addition, adjuvant drugs should be provided as necessary to deal with related issues such as fear and anxiety. Drugs should be provided on schedule (e.g., every 3–6 hours) rather than on demand. According to the WHO, following this laddered approach provides effective pain relief in 80 to 90 percent of cases.

The WHO Essential Medicines list has included palliative care medicines since 2013, but sufficient pain relief is often not provided to patients, particularly in low- and middle-income countries. An estimated 80 percent of cancer patients suffer moderate or severe pain at the end of their lives. One reason for the lack of adequate pain control for many patients is that few countries have integrated palliative care with their medical system. A second is that opioid drugs, which can provide relief from severe pain, are subject to additional scrutiny in most countries due to their high potential for diversion and abuse.

Types of Drugs

The three main types of drugs, classified by their effects on the central nervous system, are namely depressants, stimulants, and hallucinogens.

Depressant drugs slow down, or depress, the functions of the central nervous system (however, they do not necessarily make a patient feel depressed). Depressant drugs include: alcohol; opiates and opioids, including heroin (also known as H, hammer, smack, and gear), morphine, codeine, methadone, and buprenorphine; and cannabis (also known as green, smoke, weed, pot, dope, cone, and mull), including marijuana, hashish, and hash oil. In stronger concentrations, such as in hashish and resin, cannabis can also act as an hallucinogen in addition to being a central nervous system depressant as can minor tranquillizers and benzodiazepines (benzos), including diazepam (Valium), oxazepam (Serepax), nitrazepam (Mogadon), temazepam (Normison and Euhypnos), and some solvents and inhalants, including vapors from petrol, glue, chrome paint, and lighter fluid. In moderate doses, depressants can make people feel relaxed. Some depressants cause euphoria and a sense of calm and well-being. They may be used to wind down or to reduce anxiety, stress, or inhibition. Because they slow a person down, depressants affect coordination, concentration, and judgment. This makes driving and operating machinery hazardous. In larger doses, depressants can cause unconsciousness by reducing breathing and heart rate. A person’s speech may become slurred and his or her movements sluggish and uncoordinated. Other effects of larger doses include nausea, vomiting, and in extreme cases, death. When taken in combination, depressants increase their effects and increase the danger of overdose.

In contrast to depressant drugs, stimulant drugs speed up the functions of the central nervous system. People use the following stimulants every
Drugs

369
day: caffeine (most coffee, tea, and cola drinks contain caffeine, which is a mild stimulant), nicotine (the nicotine in tobacco is a stimulant, despite many smokers using it to relax), and ephedrine (used in medicines for bronchitis, hay fever, and asthma). Stronger stimulant drugs include amphetamines and methamphetamines, also known as speed, ice, and crystal meth; cocaine, also known as coke and snow; slimming tablets, for example, Duromine and Tenuate; and dexamphetamine, prescribed to treat attention deficit disorder in children and narcolepsy, which is an uncontrollable urge to fall asleep. Stimulants speed up or stimulate the central nervous system and can make the users feel more awake, alert, or confident. Stimulants increase heart rate, body temperature, and blood pressure. Other physical effects include reduced appetite, dilated pupils, talkativeness, agitation, and sleep disturbance. Higher doses of stimulants can overstimulate the users, causing anxiety, panic, seizures, headaches, stomach cramps, aggression, and paranoia. They can also cause heart problems such as arrhythmia. Prolonged or sustained use of strong stimulants can also cause these effects. Strong stimulants can mask the effects of depressant drugs, such as alcohol. This can increase the potential for aggression and poses an obvious hazard if the person is driving.

Hallucinogenic drugs distort the user's perceptions of reality. These drugs include lysergic acid diethylamide (LSD), also known as trips, acid, and microdots; magic mushrooms (psilocybin), also known as mushies; mescaline (peyote cactus); and ecstasy (methylene dioxyamphetamine [MDMA]), also known as E, XTC, and Eccies and produces a combination of hallucinogenic and stimulant effects; and ketamine, also known as K and Special K.

The main physical effects of hallucinogenic drugs are dilation of pupils, loss of appetite, increased activity, talking or laughing, jaw clenching, sweating, and sometimes stomach cramps or nausea. Drug effects can include a sense of emotional and psychological euphoria and well-being. Visual, auditory, and tactile hallucinations may occur, causing users to see or hear things that do not actually exist. The effects of hallucinogens are not easy to predict, and the person may behave in ways that appear irrational or bizarre. Psychological effects often depend on the mood of the users and the context of use. Negative effects of hallucinogens can include panic, paranoia, and loss of contact with reality. In extreme cases, this can result in dangerous behavior that can put the user and others at great risk. Driving while under the influence of hallucinogens is extremely hazardous. It is common for users to take minor tranquilizers or marijuana to help them come down from a hallucinogenic drug.

Drug Abuse or Drug Misuse
Drug abuse is the act of taking a drug that harms or has the ability to harm the physical or mental health or social well-being of an individual or other individuals or society at large or that is illegal, for instance, taking any drugs such as heroin, cocaine, hallucinogens, cannabis, ecstasy, ketamine, injectable drugs, and methamphetamines. There is confusion about the following terms on drug abuse or misuse.

Drug addiction is having an overwhelming desire or need to continue taking a drug and to obtain it by any means. It is psychic and has psychological influence with detrimental effect on the individual and on the society.

Drug dependence is a psychic or psychological and sometimes a physical state resulting from the interaction between a person and a drug, characterized by behavioral and other responses that always include a compulsion to take the drug on a continuous or periodic basis in order to experience its psychic effect and sometimes to avoid the discomfort of its absence. Tolerance may or may not be present. An individual may be dependent on more than one drug.

Drug tolerance is an adaptive state characterized by diminished response to the same quantity of drug or by the fact that a large dose is required to produce the same degree of pharmacodynamic effect or response. Dependence drugs include opioids, sedatives, cannabis, stimulants, hallucinogens, and volatile inhalants.

Rational Drug Use
This implies that an appropriate drug is prescribed, that it is available at the right time at an affordable price, that it is dispensed correctly, and that it is taken in the right dose at the right interval and for the right length of time. “Rational” stands for accordance with reason or principle or understanding and not upon simple experience. Its elements include appropriate diagnosis, appropriate drugs,
appropriate dose or dosage, appropriate usage and
duration of usage, and appropriate cost. There are
three major targets for rational drug use, and they
include the prescribers or physicians, the pharma-
cists, and the patients or recipients.

Irrational Use of Drugs
This is the use of nonessential pharmaceuticals,
drugs with doubtful efficacy, wrong or unsafe drugs,
correct dosages and routes of administration,
self-medication, over-prescribing, and other wrong
practices with drugs. Examples of irrational use
of drugs include over-prescribing, self-medication,
overuse and underuse of antibiotics, use of wrong
drugs, and overuse of injections. These are factors
contributing to irrational use of drugs: deregula-
tion and expansion of the private sector as source
of drugs, de-scheduling of drugs, widespread avail-
ability of prescription drugs from unqualified drug
sellers, increases in advertising of drugs and new
forms of market promotions, lack of political will to
implement programs of rational drug use, and lack
of research into the extent and impact of irrational
drug use.

Impact of Drugs on Society
The negative consequences of drug abuse affect
not only individuals who abuse drugs but also their
families, friends and colleagues, various businesses,
and government resources. Many of these effects
cannot be quantified. The most devastating drug-
related harm to the community is the death toll fol-
lowed by morbidity. Drug use causes around one
in 15 of all deaths all over the world. It is a factor
in about one in seven of all deaths of men between
25 and 54 years old. Recent figures indicate that
approximately 3,000 to 4,500 of all deaths in Nige-
ria, for example, in 2011 were attributable to drug
use or alcohol use. On top of this, many more people
died from diseases or causes associated with drugs
or alcohol. The majority of these costs relate to lost
productivity, crime, and health care. There are a
range of other harms that can result from excessive
or inappropriate use of psychoactive substances.
Loss of life is one extreme and tragic possibility.

Negative health effects, family and social prob-
lems, psychological and emotional difficulties, and
legal and financial problems are more common
experiences. It should be stated that many people
start and then continue to use drugs to find relief or
escape from these types of problems. There is a pre-
vailing community fear that, if a person uses drugs,
he or she will become dependent or addicted. No
drug leads to an immediate physical or psychological
dependence. However, drug-related harm can hap-
pen at all levels of use, including experimental, recre-
ational, and dependent use. The most obvious effects
of drug abuse—which are manifested in the individ-
uals who abuse drugs—include ill health, sickness,
and ultimately, death. Particularly devastating to an
abuser’s health is the contraction of needle-borne ill-
nesses including hepatitis and human immunodefi-
ciency virus/acquired immune deficiency syndrome
(HIV/AIDS) through injection drug use.

Children of individuals who abuse drugs often
are abused or neglected as a result of the individu-
als’ preoccupation with drugs. It is also shown that
parents who abuse drugs often put their need to
obtain and abuse drugs before the health and welfare
of their children. Children whose parents and other
family members abuse drugs often are physically or
emotionally abused and often lack proper immuni-
zations, medical care, dental care, and necessities
such as food, water, and shelter. The risk to children
is even greater when their parents or guardians manu-
facture illicit drugs such as methamphetamine.
Methamphetamine abusers often produce the drug
in their own homes and apartments, using hazard-
ous chemicals such as hydriodic acid, iodine, and
anhydrous ammonia. Children who inhabit such
homes often inhale dangerous chemical fumes and
gases or ingest toxic chemicals or illicit drugs. These
children commonly test positive for methamphet-
amine and suffer from both short- and long-term
health consequences. Moreover, because many
methamphetamine producers also abuse the drug,
children commonly suffer from neglect that leads to
psychological and developmental problems.

The economic impact of drug abuse on businesses
whose employees abuse drugs can be significant.
While many drug abusers are unable to attain or hold
full-time employment, those who do work put oth-
ers at risk, particularly when employed in positions
where even a minor degree of impairment could be
catastrophic; airline pilots, air traffic controllers,
train operators, and bus drivers are just a few exam-
pies. Economically, businesses often are affected
because employees who abuse drugs sometimes
steal cash or supplies, equipment, and products that
can be sold to get money to buy drugs. Moreover,
absenteeism, lost productivity, and increased use of medical and insurance benefits by employees who abuse drugs affect a business financially.

The economic consequences of drug abuse severely burden federal, state, and local government resources and, ultimately, the taxpayer. This effect is most evident with methamphetamine. Clandestine methamphetamine laboratories jeopardize the safety of citizens and adversely affect the environment. Children, law enforcement personnel, emergency responders, and those who live at or near methamphetamine production sites have been seriously injured or killed as a result of methamphetamine production.

Methamphetamine users often require extensive medical treatment; some abuse, neglect, and abandon their children, adding to social services costs; some also commit a host of other crimes including domestic violence, assault, burglary, and identity theft. Methamphetamine producers tax strained law enforcement resources and budgets as a result of the staggering costs associated with the remediation of laboratory sites. For instance, the average cost to clean up a methamphetamine production laboratory is $1,900.

**Drug Regulatory Authorities**
Regulatory authorities continually deal with issues such as drug administration and control, increased responsibilities from expansion of the market, and the improvement and sophistication of products. Each country regulates and controls the import, export, manufacture, advertisement, distribution, sale and use of food, drugs, cosmetics, medical devices, packaged water, and use of chemicals. For instance, in Nigeria, there are the National Agency for Food and Drug Administration and Control (NAFDAC), the Pharmacist Council of Nigeria (PCN), and the National Drug Law Enforcement Agency (NDLEA). These drug agencies adopt measures to identify, trace, freeze, confiscate, or seize goods from drug-related offences. They also eradicate illicit cultivation of narcotic plants and use of narcotic and psychotropic substances such as cocaine, morphine, and others.

**Recommendations**
Governments should invest in policies and programs designed to reduce drug abuse and misuse, cancer risks associated with environmental factors, and unhealthy behaviors. Regardless of socioeconomic status, individuals from racial and ethnic minority populations experience a myriad of stressors in the context of their social locations. The effects of social location are mediated by lifetime exposure to social and environment factors as well as individually modifiable drug behavioral risks. Such social and individual-level exposures translate into differential health care quality and access.

Public and private-based organizations should address drug behavioral risk factors such as physical inactivity, obesity, heavy alcohol consumption, a diet high in red or processed meats, a diet that lacks fruits and vegetables, a diet high in animal fat, smoking, and environmental hazards such as radon, asbestos, air pollution, and certain metals (chromium, cadmium, and arsenic). Community-level interventions are also warranted. At the community level, such interventions might address community norms and lifestyles that promote adverse drug-related health outcomes.

There is also need for better research data. Drug registries should collect socioeconomic data (income, education, and health insurance status). To make use of existing registry data to compute survival and mortality rates, drug registries should be linked to social security records. This will permit the computation of trends in incidence, survival, and mortality.

Olusegun Moses Temilola
*University of Lagos*

**See Also:** Cancer Drugs, Cost and Benefits of; Chemothrapy; Marketing, Drug.

**Further Readings**
Duke Cancer Institute

The Duke Cancer Institute (DCI), formerly the Duke Comprehensive Cancer Center, is located on the Duke University campus in Durham, North Carolina. The DCI is one of 41 centers in the country designated by the National Cancer Institute as a comprehensive cancer center. It serves nearly 6,000 new cancer patients each year and is ranked as the top cancer hospital in the south by U.S. News & World Report. The DCI treats patients from a range of ages, ethnic and racial backgrounds, socioeconomic statuses, and from rural and urban settings in North Carolina and the larger region as well as from across the country. While the DCI offers care for patients with every form of cancer, it is nationally recognized for its brain tumor and blood and marrow transplantation programs. Patients at the DCI receive care across the cancer continuum, from prevention and diagnosis to treatment and survivorship.

Duke has made a $400 million investment in the DCI, including construction of a new 267,000-square-foot DCI building that opened in early 2012, expansion of clinical services, and investment in state-of-the-art technologies. The DCI includes more than 300 researchers and physicians and 500 clinical staff dedicated to a broad spectrum of cancer research and the translation of that research into the latest in patient care. It offers hundreds of clinical trials for the treatment and prevention of many forms of cancer.

The DCI also supports numerous shared resources that provide access to technologies, services, and scientific consultation that enhance scientific interaction and productivity. These shared resources include, but are not limited to, bioinformatics, biospecimen repository and processing core, biostatistics, flow cytometry, high-resolution nuclear magnetic resonance spectroscopy, integrative cancer genomics, pharmaceutical research, and proteomics. The DCI is also home to a variety of research programs and groups, including 10 disease-site groups and nine NCI-designated programs. Each disease-site group has leaders representing clinical care, clinical research, and basic research who work collaboratively to address the various needs of cancer patients. The nine NCI-designated programs at the DCI, supported by the shared resources, are multidisciplinary in nature and designed to address research opportunities impacting cancer care through basic, clinical, and translational research. Researchers at the DCI are also involved in quality and outcomes research. Specifically, the Duke Cancer Care Research Program is a team of clinical scientists whose research efforts focus on improving health-related, emotional, and psychosocial outcomes for cancer patients.

The DCI has demonstrated a consistent record of state-of-the-art patient care and positive patient outcomes. In 2011, the DCI served more than 45,000 individuals with cancer and was recognized by the Joint Commission as an exemplar in performance on key quality measures. The DCI provides treatment for several types of cancer, including breast, genitourinary, gastrointestinal, and gynecologic cancer in addition to leukemia and lymphoma, brain tumors and neuro-oncology, thoracic cancer, adult bone marrow cancer and stem cell transplant, sarcomas, and melanomas. However, the most commonly treated cancers at the DCI are uncommon types of cancer. The treatment capacity of the DCI is largely attributable to the numerous clinical trials that are housed with the institute. Approximately 900 open trials at the DCI provide patients with access to the most innovative treatments, many of which are not widely available at other hospitals.

For example, pioneering research led by the Preston Robert Tisch Brain Tumor Center continues to demonstrate the utility of bevacizumab and temozolomide for the treatment of brain tumors. This ongoing research contributed to the accelerated approval by the Food and Drug Administration of
bevacizumab for glioblastoma multiforme. As a result of this research, patients with brain tumors at the DCI are provided with this innovative and effective treatment, despite its relative scarcity in other cancer treatment centers. Similarly, breast cancer patients at the DCI are experiencing substantial improvements in survival rates based on research examining the effectiveness of a new treatment protocol: lapatinib and trastuzumab. The DCI also offers cutting-edge treatment options for other forms of cancer, such as stem cell transplants from mismatched family or unrelated donors for central nervous system (CNS) tumors, rotationplasty for sarcoma patients, and endocrine therapy for breast cancer patients.

The DCI offers an array of comprehensive and multidisciplinary resources for patients and their families in the areas of: individual and family counseling, support groups, self-image resources, cancer patient education resources, physical and occupational therapy, pharmaceutical counseling, social work, and nutrition counseling. One such support service is the Duke Cancer Patient Support Program (DCPSP). The DCPSP is an established psychosocial support program with providers specializing in psychology, psychiatry, and medical family therapy. The DCPSP provides services and resources, at no charge, to help support patients and their loved ones throughout their experience with cancer. Also housed within the DCI is the multidisciplinary psychosocial oncology team, which includes psychology, psychiatry, medical family therapy, oncology recreation therapy, occupational therapy, social work, and child life specialists. The recently founded Duke Center for Cancer Survivorship is another multidisciplinary resource that coordinates resources for support, care, education, and research for men and women surviving cancer. Finally, Duke’s Cancer Patient Education Program, which includes a resource center and a variety of education classes, uses a multimedia approach to assist DCI patients and their families with obtaining disease and treatment-related information, gaining resources for health decision making, managing the effects of cancer and its treatment, and advocating for themselves. Through providing an array of multidisciplinary support services and survivorship resources, the DCI aims to improve patient outcomes and decrease cancer burden.

The DCI is one of the first comprehensive cancer centers in the United States. Since 1973, it has continued to lead the nation in cancer prevention, treatment, education, and research. Currently, the DCI provides multidisciplinary, individualized care to more than 45,000 local, national, and international patients. The DCI also leads the field of oncology in the development of new techniques, treatments, and approaches to cancer treatment through numerous clinical trials and research protocols. Thus, the DCI serves as a model for the provision of innovative, comprehensive cancer treatment through both clinical and research activities.

Christopher Edwards
Sarah Kelleher
Duke University Medical Center

See Also: Comprehensive Cancer Center of Wake Forest University; Herbert Irving Comprehensive Cancer Center; Holden Comprehensive Cancer Center at the University of Iowa.

Further Readings

Dyes and Pigments

Dyes and pigments are ubiquitous in modern society, from food and clothing to magazines, tattoo ink, hair colorants and other beauty products, and host of other consumer goods. Research has shown...
that some dyes and pigments are associated with an increased risk for cancer. Among the cancers related to dyes and pigments are bladder cancer, lymphocytic leukemia, breast cancer, and Hodgkin's lymphoma.

Dyes and pigments are both colorants but differ in several ways. Their classification is related to a variety of factors, including their composition, method of application, dyeing properties, and origin, such as organic and synthetic dyes. Most dyes dissolve in water and create color through chemical or physical reactions. They are used to dye a variety of materials, including cloth and other porous material, such as hair.

Pigments are particles of color that can leave residues. They usually come in the form of an insoluble powder mixed into other materials, such as water, oil, and resins. They are used to make paint, tattoo inks, and other products.

At least 13 common chemicals in dye and pigments have been related to increased cancer risk. These include the azo dyes (benzidine and benzidine congener-based dyes, including the benzidine derivative o-diansisidine) and the aromatic azines originating from azo dyes, such as (analine, o-tulidine, and n-methylaniline). Both the Occupational Safety and Health Administration (OSHA) and the National Institute for Occupational Safety and Health (NIOSH) have concluded that benzidine-based dyes increase risk for cancer, and the National Cancer Institute (NCI) has noted several azo dyes in general as being carcinogenic. Azo dyes are synthetic dyes known for their bright colors. They are used for a variety of goods, including cosmetics, foods, carpets, clothes, leather and textiles.

Many azo dyes are safe to eat, while others have been associated, primarily with bladder cancer. Some azo dyes can form aromatic amines when broken down. In European Union countries, aromatic amines are banned from both the manufacture and sale of consumer goods.

OSHA banned the production of benzidine dyes in the United States in 1973. Although importing the dyes is banned now also, products containing benzidine-based dyes can still be imported to the United States. Epidemiologic studies show an increased risk of bladder cancer due to occupational exposure, and animal studies have found tumors in various sites due to benzidine exposure, including oral and inhalation exposure. The Environmental Protection Agency (EPA) classifies benzidine as a Group A, a known human carcinogen. The risk for cancer associated with benzidine was substantially increased when dosages occurred in early life.

Aromatic amines exposure from various sources has been linked to cancer, from occupational settings to smoking. Aromatic amines are typically found in the plastic and chemical industries and also as by-products during the manufacturing of a wide variety of products, including dyes, pharmaceuticals, and polyurethane foams. Studies have found that various classes of the aromatic amines are connected with an increased risk for cancer.

For example, female rubber-factory workers have been shown to have an increased risk of breast cancer due to exposure to aromatic amines; and a lifetime consumption of grilled meats and fish, which contain these amines, was connected with an increased risk of postmenopausal breast cancer. Aromatic amines in hair dyes have been associated with bladder cancer.

Food

Food dyes were at one time synthesized from coal tar but are now produced from petroleum products. Many food dyes have been banned due to animal studies. The U.S. Food and Drug Administration (FDA) has established limits for dye contaminants that may be carcinogenic. Banned food dyes that studies have shown to be carcinogenic include Green 1, Red 1, Red 2, Sudan 1, and Violet 1. FDA limits are calculated to limit the lifetime risk of getting cancer to no greater than one cancer per 1 million people.

Controversy continues concerning food dyes. An estimated 15 million pounds of dyes are used in the food supply each year, including three that carry known carcinogens. Studies have shown that seven food dyes have been associated with cancer in animal studies, including colon cancer and brain and testicular tumors as well as DNA mutations. It was estimated that Americans consumed 17.8 million pounds of these dyes in 2005. These dyes are found in food products such as some sodas, popsicles, candy, baked goods, ice cream, maraschino cherries, and snack foods, as well as most pet food.

Overall, since 1955, food dye consumption per person has increased fivefold in the United States. Furthermore, artificial dyes derived from petroleum
are in numerous other foods aimed at children, including breakfast cereals and even vitamins. The dyes Red 40, Yellow 5, and Yellow 6 make up 90 percent of the dyes used in foods.

Groups concerned about food dyes and their toxicities have noted that these dyes are not necessary from a nutrition standpoint. They are only used to enhance a food's appearance and do nothing to improve the nutritional quality or safety of foods. Some contend that dyes still used have been inadequately tested for cancer and other toxicities. Thus, they are an unnecessary risk, especially for young children.

One such group, the Center for Science in the Public Interest (CSPI), petitioned the FDA in 2008 to ban artificial food dyes. This request was made primarily on studies showing a relationship between food dyes and childhood behavioral problems. In 2010, CSPI published “Food Dyes: A Rainbow of Risks,” which pointed to nine artificial dyes approved in the United States that are likely to be carcinogenic or have other serious health consequences.

The report pointed out that benzidine is found in Red 40, Yellow 5, and Yellow 6 food dyes. The FDA has calculated that the ingestion of free benzidine does not raise cancer risk to the threshold of concern. Nevertheless, bound benzidine has been found in greater amounts than those in free benzidine, which is the only type of benzidine the FDA has traditionally tested for in food products. Concerns also focus on higher exposure rates from benzidine in food because intestinal enzymes release bound benzidine.

Hair Dye and Cosmetics

Scientists first noted health risks associated with hair dyes in the late 1970s, focusing initially on a link to breast cancer. For example, a 1976 study found that 87 of 100 breast cancer patients studied had used hair dye for many years. A 1979 study provided further evidence of a relationship between breast cancer and the frequency and duration of hair dye use. The greatest risk was found in women 50 to 79 years of age who had used hair dye for decades. Other links between hair dye and breast cancer included a greater risk of developing breast cancer in women with a history of benign breast disease who also dyed their hair and a greater risk for breast cancer in women dying their hair to change color rather than to remove gray hair only.

Japanese and Scandinavian studies in the 1990s found a correlation between hair dye use and leukemia and ovarian cancer. Another study conducted at Harvard University in the 1990s found a link between hair dyes used one to four times a year with a 70 percent increase in the risk for ovarian cancer. In addition, twice the risk of developing ovarian cancer was found in women who dyed their hair four times a year or more than in women who never dyed their hair.

The FDA is charged with regulating cosmetic product safety. In 1976, the Cosmetic, Toiletry, and Fragrance Association (CTFA) established the Cosmetic Ingredient Review (CIR) program, now known as the Personal Care Products Council. The council is charged with assessing personal care product safety.

Many colorants used in cosmetics are coal tar dyes. Coal tar is made from petroleum-based chemicals and is considered a human carcinogen. These dyes may also have low levels of heavy metal contamination. In addition some are mixed with an aluminum substrate. Both heavy metals and aluminum metals are associated with neurotoxicity.

Permanent synthetic hair dyes and intermediates contain a wide range of substances, including ammonia, diaminobenzenes, phenylenediamines, resorcinol, and phenols. Phenylenediamines are the most common ingredient found in hair dyes today. P-phenylenediamine is a coal-tar-based colorant used in many hair dyes. Generally, darker, permanent hair dyes have more phenylenediamine than lighter hair dyes. Animal studies conducted by the NCI have linked p-phenylenediamine to tumors. Another study found that hair dyes containing p-phenylenediamine and used over a long period of time increased the risk for non-Hodgkin's lymphoma (NHL).

It should be noted that toxic dye ingredients such as diaminotoulene and diaminotoluene were banned in the early 1990s. These ingredients have been linked to breast cancer, and scientists believe it is likely that the past use of these dyes may have led to some modern-day cases of breast cancer. Although modern-day hair dye ingredients have been found to cause mutation in DNA and fetal abnormalities in some animal studies, they are not required to appear on warning labels. In the United States, dyes containing 4-methoxy-m-phenylenediamine are required to include a warning about irritant effects.
and studies showing a relationship to cancer in animal studies.

A 2013 epidemiological review study found what it called "alarming data." It showed that the evidence linking hair dye with most human cancers was inconclusive because of mixed results. The study found that the strongest evidence pointed to an increased risk for NHL, leading the researchers to caution people with a family history of NHL in using hair dyes because of a possible cumulative risk. The study also found evidence of link between pregnant women's use of hair dye and the development of several childhood malignancies in their children, including neuroblastoma and brain tumors. Researchers have noted that the development of these cancers suggest that the harm may occur in utero. As a result, the researchers noted that concerned women might want to avoid using hair dye.

Although the use of hair dyes has been associated with an increased risk for several types of cancer, studies have yet to conclusively confirm that these dyes directly cause cancer. Nevertheless, some precautions are recommended. Because the carcinogenic components of many hair dyes penetrate human skin, one is to rub a petroleum-based ointment onto the scalp to reduce cutaneous exposure to the dye. In addition, people who dye their hair can reduce application time by 25 percent. Nevertheless, these are anecdotal practices that have not been studied for effectiveness.

Some dyes not approved as food additives are still used in cosmetics, such as lipstick and moisturizers, both of which can seep into the skin. Several natural colors used in lipstick include trace amounts of lead, which according to the National Institutes of Health (NIH) is a likely human carcinogen. The FDA, however, has stated that lipstick containing lead is not a human health safety problem because it is only ingested in small quantities.

**Tattoos**

Tattoo inks are made with various pigments, some of which contain toxic substances associated with cancer. Red inks can contain mercury, which has been found to cause cancer in rats. Cobalt can be found in green and blue inks and has been connected with cancer in animals. Black ink includes the polycyclic aromatic hydrocarbon called benzo(a)pyrene, which is found in coal tar and has been connected to skin cancers in petroleum workers.

Some pigments used in tattoo ink also contain nanoparticles (ultramicroscopic particles), which can enter the bloodstream and accumulate in organs, including the kidneys and spleen, which filter impurities. In a preliminary study conducted in Great Britain, researchers studied tattoos at the nano-level have shown that tattoos are reactive histologically. They found that the process of tattooing remodels the body’s main connective tissue (collagen), which helps dye constituents enter other parts of the body.

Scientists have found evidence that some nanoparticles can have toxic effects on the brain and may be carcinogenic in nature. A 2011 study found nanoparticles in tattoo ink. Except for white inks, researchers found that most tattoo inks included nanoparticles. Black ink is most associated with potential dangerous toxicity due to nanoparticles.

There is some concern that black inks are potentially carcinogenic and may cause DNA damage. They may also contain the known carcinogen benzo(a)pyrene. Significant amounts of nanoparticles in black ink may lead to easier and greater absorption of benzo(a)pyrene. In addition, research has uncovered a potential relationship between tattoos and skin cancer, although such a relationship has yet to be substantiated.

Research into tattoo inks and cancer is still in the early stages, and there is no definitive evidence that they cause cancer. Concerns about tattoo inks and cancer are based primarily on evidence linking certain carcinogenic substances found in pigments and other substances used to make the ink. One concern is that pigments from tattoos may reach the body’s lymph nodes. In addition, alcohol is used to disinfect the skin before a tattoo. Alcohol is known to make the skin more permeable, which could lead to more pigments entering the body.

Although the FDA has the power to regulate the contents of pigments, the agency has noted that a lack of strong evidence has led them to create few regulations for these colorants. However, the National Center for Toxicological Research is conducting studies of tattoo pigments. In addition to the safety of tattoo inks and pigments, these studies focus on the chemical composition of the inks, their breakdown in the human body, and their reaction in humans when exposed to light and magnetism. Such studies are pertinent considering the tremendous increase in getting tattoos among the general population.
Occupational Exposure
Studies have found that hairdressers are at a higher risk for cancer. A 2001 study showed that hairdressers who worked for 10 more years in the field had a fivefold higher risk of bladder cancer than the general population. In addition to bladder cancer, evidence has been found that they may also suffer from an increased risk for ovarian cancer.

The NCI notes that permanent hair dyes are the most dangerous to hairdressers. In addition, these dyes work with the aid of hydrogen peroxide, which can cause chemical reactions between aromatic amines and dye couplers used in chromatic photography film. The result is the formation of pigment molecules. Another study found that hairdressers were exposed to the confirmed carcinogen o-toulidine. Higher concentrations of carcinogens were also found in hairdressers who performed higher numbers of hair-dyeing or hair-waving treatments.

Various studies have produced significant medical evidence that working with dyes and pigments in the printing industry is associated with an increased risk of bladder cancer, including a 1.5 percent increased risk of this cancer among typographers. Studies have also consistently showed a higher risk for ovarian cancer in female workers in the printing industries. Another study garnered data showing that the highest risk for cancer due to ink exposure occurs in people exposed before they are 20 years old.

Several studies have found an increase in bladder cancer incidence in workers in dye-manufacturing facilities. A 1985 occupational analysis of chemical dye workers in England found that these workers had a twofold to threefold increased risk for bladder cancer, even after accounting for work age and factors such as smoking. The study also found an association between increased risk and the number of years people worked in the facilities.

A NIOSH study of employees working in dye-manufacturing plants between 1940 and 1972 found that these workers had a significant increase in the risk for bladder cancers. The risk was higher for those employed for 10 years or more in these plants. Workers also had an increased risk for esophagus cancer, and deaths from lung cancer and prostate cancer increased. Dyehouse workers, such as those who work in yarn-dyeing plants, have also been shown to have twice the expected mortality rate for esophageal cancer.

The FDA has acknowledged a growing body of evidence indicating that dyes and pigments used in consumer products and manufacturing may be related to numerous health risks, including cancer. As more studies are focusing on the health effects of dyes and pigments, future restrictions on dye use and manufacturing are likely. For example, a study published in 2014 discovered that yellow dye found in clothing and paper contains PCB-11, which can be found in yellow dyes and pigments.

Polychlorinated biphenyls (PCBs) were banned in the United States in the 1970s because of their environmental impact and their link to cancer. They can build up in the human body and have been linked to cancer. Although PCB-11 is not known to build up in the body, there is still concern, especially when PCB-11 is found in children’s clothing. PCB-11 is an unintentional by-product of pigment manufacturing. As a result, PCB-11 found in consumer products is exempt from U.S. laws regulating compounds in consumer products. The EPA has begun a study to review potential risks of PCB-11’s presence in clothing and other consumer goods.

David Petechuk
Independent Scholar

See Also: Bladder Cancer; Breast Cancer; Lymphoma, Hodgkin’s, Adult; Lymphoma, Hodgkin’s, Childhood; Lymphoma, Non-Hodgkin’s, Adult; Lymphoma, Non-Hodgkin’s, Childhood; National Cancer Institute.

Further Readings


Ecuador

The northwestern South American nation officially termed the Republic of Ecuador has been the historical site of several empires, conquests, and peoples. In antiquity, the country was the home of the Inca civilization. The modern state of Ecuador was formed in 1811, when Ecuadoran citizens in the capital of Quito declared their independence from Spain. The nation is home to more than 15 million citizens and has the highest diversity of flora and fauna in the world.

In the past 20 years, Ecuador has some of the lowest rates of male cancer incidences in all of South America. However, incidence rates have been relatively stable in both the nation’s male and female populations over the same period of time. Also, researchers have observed the unique trend of Ecuadoran females having higher levels of the alcohol- and tobacco-instigated bowel and lung cancers, whereas in the vast majority of the world, the opposite trend is true. Furthermore, the country is noted to have some of the most incidences of cervical cancer in all of South America.

Ecuador has a regional cancer dilemma in the Amazonian portion of the country. The situation was apparently caused over the past 40 years as a result of environmental pollution produced by Texaco during its operational tenure in the nation. From 1967 to 1992, Texaco operated numerous oil-drilling operations in the nation’s Amazonian region. During this period and beyond, researchers have documented how cancer incidences in the regions in which Texaco worked have skyrocketed, and the affected residents claim this is a result of the pollutants that Texaco procured and disseminated during their operations. In the area in which Texaco worked, researchers have observed the rates of cancer incidences of the Ecuadorans living there to be 150 percent greater than in the nonaffected parts of the country. Also, leukemia incidences in adolescents also skyrocketed in the affected portion of the nation. Since 1992, numerous studies have appeared in respectable medical journals detailing the scope and trends of the remarkable increase of cancers in the Ecuadoran Amazon. The situation appears to be a domestic medical crisis that the country will continue to deal with in the coming decades.

Though Ecuador has only one active cancer treatment facility in the country, the nation is the location of promising new research that could provide a revolutionary breakthrough in modern cancer treatment. For an unrelated medical project, a researcher named Arlen Rosenbloom was visiting Ecuador to offer temporary treatment services to patients. During his time there, he observed a region of the country that was home to an unusually large portion of citizens who suffered from a rare type of extreme dwarfism called Laron syndrome. Arlen Rosebloom teamed up with fellow peer Jaime
Guevarra-Aguirre to study this unique group of Ecuadoran dwarfs. After a great deal of study, the two researchers deduced that this population of Laron dwarfs seemed to have no cancer incidences whatsoever as a result of a unique aspect of their Laron syndrome: a complete lack of the hormone IGF-1 in their bodies. In various studies, an over- abundance of IGF-1 hormones within the human body has been tangibly correlated to higher levels of bowel, breast, prostate, and other cancer incidences. Scientists are now studying these Ecuadoran Laron dwarfs in an attempt to replicate the anticancerous mechanism of their syndrome.

In recent years, the most dominant forms of cancer in Ecuador have been breast, bladder, blood, cervical, and stomach cancer. Bladder, blood, and stomach cancers have been the most common forms of cancer incidences in males in the nation, while breast, cervical, and stomach cancers are the most prevalent incidences of cancer in females there. Over the past decade, incidences of the most-prevalent cancers in Ecuador have generally stayed level, though certain cancers like cervical cancer have steadily increased in incidences.

Presently, Ecuador is regarded as needing to do more to ascertain effective pathways to treatment for domestic cancer patients. Cancer incidences in the rural portions of the country usually go untreated, and even in urban parts of the nation, there are few facilities capable of advanced cancer care. If Ecuador is to deal with its domestic cancer burden in the coming decades, the nation will need to invest in the creation of more cancer treatment facilities and in the training of more domestic oncologists.

William M. Peaster
Independent Scholar

See Also: Bladder Cancer; Breast Cancer; Cervical Cancer; Stomach (Gastric) Cancer.

Further Readings
Kruckewitt, J. “Oil and Cancer in Ecuador: Ecuadoran Villagers Believe High Rates of Disease Are Tied to Petroleum Pollution, a Contention Chevron Disputes.” SFGate (December 2005).

Education

Cancer education is an important component of efforts associated with prevention, detection, and management of the disease. Whereas individuals may be impacted physically, emotionally, and economically, the costs to society are substantial.
In the United States, the cost of cancer to the economy exceeded $200 billion in 2009, thus timely and effective education can have a positive impact on individuals and society. Although cancer may be caused by genetic, environmental, and lifestyle factors, or certain types of infections, an estimated two-thirds of all cases may have been prevented by lifestyle choices. Cancer education is therefore a vital component in efforts to reduce morbidity, mortality, and disability burdens. The main lifestyle factors that are addressed through cancer education include tobacco use, exposure to sun, physical activity, and diet.

**Purposes and Importance of Cancer Education**

Cancer education may be specifically geared toward prevention, early detection, treatment, and management of symptoms, side effects, comorbidities, and rehabilitation. Each of these areas may be targeted toward the general public, cancer patients, and health professionals. Prevention education is primarily focused around lifestyle choices, including tobacco use, sun exposure, diet, and physical activity.

**Tobacco Use**

Besides general advertising and smoking cessation promotional campaigns, the surgeon general’s reports have consistently highlighted the effects of tobacco use and exposure to secondhand smoke on cancer risk. These reports have sought to educate the public about the importance of not being exposed to secondhand smoke in cars, at work or home, or in enclosed public places. Evidence is building about the effect of what is now termed thirdhand smoke—residual particles from tobacco that is smoked indoors. This is an area of cancer education that is expected to develop further in the near future. Agencies such as the American Cancer Society (ACS), the Environmental Protection Agency (EPA), and the American Chemical Society are currently involved in thirdhand smoke education.

**Sun Exposure**

Skin cancer education is imperative. There are more cases of skin cancer diagnosis per year than diagnoses of all other cancers combined. Educating the public about the simple preventative steps that can be taken to avoid overexposure to UV rays from either the sun or tanning beds is the primary method used for education of skin cancer. Educational information on sun exposure and skin cancer may be obtained from the American Academy of Dermatology (AAD), the EPA, and the Melanoma Research Foundation. Educational campaigns from agencies such as the Skin Cancer Foundation are targeted to medical professionals and the public and focus on prevention, early detection, and treatment. Information is provided on sun-protective products, steps in skin protection, and the visible warning signs of skin cancer. Audiovisual material, manuals, newsletters, brochures, posters, and books are distributed via the Internet, health fairs, screening clinics, wellness programs, and grassroots educational campaigns.

**Physical Activity and Diet**

Various institutions have focused on increasing awareness of the roles of physical activity, diet, and body weight in the prevention and treatment of cancer. For example, the American Institute for Cancer Research (AICR) provides peer-reviewed materials that help medical professionals to advise patients on weight, physical activity, and diet issues. AICR also helps to keep the public well-advised by providing facts for journalists and by putting journalists in touch with researchers, clinicians, dietitians, and other experts. As another example, the National Cancer Institute (NCI) hosts Web sites that include nutritional and physical activity facts and recommendations, such as types, frequency, and duration of exercise. NCI Web sites also present information on the relationships among physical activity, nutrition, and risk for various types of cancer, prognosis, and survivorship.

**Cancer Education Challenges: Patient-Centered Education**

Recent work in the area of patient-centered education has led to the development of patient-centered communication in cancer care. The domains include: information exchange, fostering of healing relationships, recognizing and responding to emotions, managing uncertainty, making decisions, and enabling patient self-management. These domains underscored the importance of collaboration and interaction between physician and patient (inclusive of family members), support systems, trusting and culturally sensitive partnerships among all members of the health care team, along with
Education

involvement of the patient in decision making regarding managing day-to-day aspects of cancer illness and patient well-being. Other work on holistic, patient-centered cancer education also has included the concept of care communities, which include the patient, family, oncologists, surgeons, nurses, therapists, radiologists, and clergy. Providers must become competent in framing the information in light of what the patient has already received from other sources. This is necessary to achieve the goal of patient-centered education—making it easier for patients to understand how all information about cancer fits together.

Cancer Disparities
Morbidity, mortality, and disability-related education are influenced by factors associated with populations, medical practitioners, and cancer-reduction advocates. Educating the general population about the importance of early detection, for example, has the potential to positively impact cancer prognosis. This is even more crucial for ethnic or racial minority groups and for those who are considered lacking in health literacy and are therefore unable to adequately source, process, and understand information about screening, risk, and symptoms associated with cancer. They may therefore be unable to make prudent health-related decisions. These groups may live within medically underserved communities, where cancer is disproportionately distributed. To help reduce the impact of literacy disparities, health care providers should adapt their communication to the level of patients; this is easier than for patients to adapt to the level of providers. Customized videos and community-based collaborations and outreach programs that provide culturally and linguistically competent education and access to early detection services have been found to be particularly successful in these communities.

Practitioners and Advocates
Patient-provider communication is a key source of information about the association between early diagnosis of cancer and prognosis or survival. What, and how much, information is provided, however, has become a question of much debate. The passage of the Affordable Care Act (ACA), which now allows for some routine screenings to be covered by health insurance, has fueled dialogues pertaining to early detection and patient education. There have been concerns about what messages are disseminated to the public regarding routine screening for breast cancer. One reason behind the concerns is the claim that increased screening and the attendant increased incidence of early detection have not been accompanied by the expected decrease in late stage presentations and overall mortality. One recommendation that has been proposed to address this issue is that physicians inform patients about both sides of the screening controversy. This provides opportunities for practitioners to have case-by-case discussions with their patients, helping them to arrive at the best decision for each case rather than making screening decisions based on routine policy recommendations.

The Future of Cancer Education
Continued immigration from various cultures around the world has further diversified the U.S. population. To continue providing meaningful information to members of the entire population, providers will need to account for the differences that exist among immigrant residents in designing culturally appropriate educational material.

Finally, the pace of technological advancement presents both opportunities and challenges for cancer education. Computer technology is well poised to facilitate creative educational sources. For example, computer games, such as the Cancer Game (http://cancergame.org) and HopeLab (http://hopelab.org) have been developed to help in cancer-related medication adherence and living with cancer. Those who, because of socioeconomic or other disadvantages, are not able to keep pace with technological development may have less and less access to cancer education. Cancer education professionals must therefore be mindful to consider the disadvantaged as educational programs are developed in a fast-changing technological environment.

Cancer education sources include the following:

- American Cancer Society (http://www.cancer.org), where education focuses on prevention, and screening
- American Association for Cancer Education (AACE), which provides education on treatment guidelines, training, and information to those who educate groups
concerned with the early detection of cancer, early multimodality therapy, rehabilitation, and support for cancer patients

- National Cancer Institute’s (NCI) Cancer Information Service (CIS), which provides information to professionals and the public and is also involved in the development of research programs—timely information is provided to the public through various channels, including telephone (1-800-4-CANCER) and online (http://www.cancer.gov); the NCI also provides counseling services the cessation of smoking (1-877-44U-QUIT)
- The Agency for Healthcare Research and Quality’s Web site called the National Guideline Clearinghouse (http://www.guideline.gov), which is a database of cancer-related abstracts and guidelines, listed as neoplasms
- The National Comprehensive Cancer Network (http://www.nccn.org) Web site, which contains practice guidelines for clinic practices relating to most of the oncological tumors
- Center for Advancement in Cancer Education, a U.S. federally approved, not-for-profit information, counseling, and referral agency providing education on cancer prevention and support during and after treatment to individuals and health professionals worldwide (http://www.naturallifestyle.net/profiles/The-Center-for-Advancement-in-Cancer-Education-135)

Anthony F. Lemieux
Melany Chambers
Georgia State University

See Also: American Association for Cancer Research; American Cancer Society; National Cancer Institute.

Further Readings


Egypt

The Arab Republic of Egypt is a lower middle-income country with a population of approximately 80 million. Most of the population lives in the Nile Valley, with a roughly even division between those living in densely populated urban centers and rural areas. Urban life in Egypt is associated with a higher risk for cancer, perhaps due to greater exposure to environmental pollutants and more sedentary, urban lifestyles. Urban diets consist of a higher proportion of meat and fat as opposed to vegetables, and over a third of Egyptian adults are obese, which is a risk factor for some cancers.

For all cancers common to both genders, Egyptian men show a higher prevalence of cancer than women. In 2010, 35 percent of men used tobacco on a daily basis, while the comparable figure for women was only 0.2 percent, largely because of social stigma. However, the 2005 Global Youth Tobacco Smoking Survey indicated that smoking rates among 13- to 15-year-olds was closer: 16 percent for boys and 7.6 percent for girls. This indicates that smoking among women may increase in coming decades.

Smoking is permitted in most workplaces, restaurants, and private homes, so secondhand smoke represents a threat to nonsmokers and youth. Public advertising of tobacco products is not permitted, but other forms of marketing are allowed. Consumption taxes are approximately 65 percent of retail cost, but tobacco prices remain low, ranging between $0.50 per pack for domestic brands to $1.50 per pack for imported brands. In recent years, there has been a trend toward water pipe smoking, which is perceived as culturally authentic, natural, and less damaging to health than cigarette smoking.

Bladder cancer is the most prevalent cancer among Egyptian males, with a mortality rate (16.3 per
100,000 population, or around 8,000 deaths annually) that is twice as high as the highest European rates and more than four times as high as in the United States.

Bladder cancer in Egypt has typically been squamous cell carcinoma, associated with a history of *Schistosoma haematobium* parasite infection from unclean water. Several decades of interventions aimed at reducing schistosomiasis have reduced the occurrence of squamous cell carcinoma. However, prevalence of transitional cell carcinoma bladder cancer has increased. The cause of this increase is unclear but may be due to exposure to environmental pollutants and tobacco use. Despite the prevalence of bladder cancer in Egypt, there is no comprehensive screening program in place.

Breast cancer is the most common cancer among Egyptian women, representing 18.9 percent of total reported cancer cases (35.1 percent in women and 2.2 percent in men), occurring at a rate of 49.6 cases per 100,000 individuals. After the first symptoms appear, patients often wait more than 3.5 years before seeking treatment, and total mastectomy is the most common treatment for locally advanced malignancy. Small-scale efforts at screening have been promising in terms of early diagnosis and treatment, but population based screening programs do not exist. Mortality from the disease is significantly higher among women with lower socioeconomic profiles, including education, occupation, and income. This difference is likely a result of reduced health awareness and agency in seeking treatment. Women in rural areas have a higher mortality compared to women in urban areas, perhaps due to access to screening and treatment facilities.

Colorectal cancer is typically less prevalent in developing countries compared to Western countries, and though it is the third-most common cancer among Egyptian men, it is also relatively rare, representing only 3 percent of malignancies. There are troubling indications, however, that colorectal cancer may become a more significant health threat in the future. Since the 1990s, one-third of colorectal cancer cases have been in patients under the age of 40, though there is no indication of a hereditary predisposition. Adoption of a Westernized diet may contribute to this unusual age distribution, but exposure to agricultural and industrial chemicals and a history of eating food directly from farms has also been shown to be associated with an increased risk for colorectal cancer in Egypt.

Sheila Peuchaud

*American University in Cairo*

See Also: Bladder Cancer; Breast Cancer; Colorectal Cancer, Childhood; Diet and Nutrition.

Further Readings


**Eisai (Japan)**

Eisai is a Japanese corporation with 10,419 employees worldwide including subsidiaries as of early 2014. Eisai ended up as number five in Japan and as number 25 in on a global basis in the Medical Care & the Pharmaceutical Industry 2013 overview of pharmaceutical corporations’ sales. Eisai integrates a whole range of pharmaceuticals and health care products within its portfolio, except for veterinary medicines. A majority of the products are sold overseas. One main product for a number of years was Aricept (donepezil) for Alzheimer’s disease, approved by the U.S. Food and Drug Administration (FDA) in 1996. It was developed by Eisai but subsequently co-marketed with Pfizer. The product lost U.S. market exclusivity in 2012, and there is currently competition from a generic version. More recent products include the breast cancer treatment Halaven (eribulin mesylate), approved by the FDA in 2010, and the receptor antagonist Fycompa for epilepsy, approved by the FDA in 2012. These were both developed in-house and are considered to be two of Eisai’s future core products. The anti-obesity agent Belviq was in addition launched in the United States in 2013.

**Eisai’s Oncology Segment**

Eisai has increased its presence within the oncology field, with oncology-related products increasing from 10 to 18 percent during 2010 to 2012. As of 2013, the plan was to increase oncology to 22 percent by 2015. Halaven’s eribulin is a synthetic derivative of halichondrin B, which is a natural marine product derived from a sea sponge. It is a new anticancer treatment in the sense that it acts against tumors by suppressing the growth of microtubules. Halaven was, as of 2013, also in a phase III study investigating the potential for use in non–small cell lung cancer treatment, and phase II studies are underway in Japan in order to investigate the agent as a potential treatment for sarcoma. Another drug, Lenatinib, has been designated an orphan drug for thyroid cancer in Japan (2012) and Europe (2013), and there are several other projects underway.

The increased ratio of oncology is partly due to acquisitions as well as new research and development (R&D) efforts. Eisai acquired Morphotek, Pennsylvania (2008), MGI Pharma, Minnesota (2007), and AkaRx, New Jersey (2010). Morphotek had been established in 2000, based on the invention of the company’s legacy technology called morphogenics, which is a platform technology regulating the ability of a host organism to repair mutations that occur during DNA replication.

Morphotek has got several monoclonal antibodies for cancer and inflammatory disease in clinical development. Morphotek, Inc. continues to exist as a subsidiary. MGI Pharma had been founded in 1979, focusing on products for oncology and acute care applications. AkaRx had been developing a therapeutic agent for thrombocytopenia (relative decrease of platelets in blood), a condition that may be a side effect of chemotherapy. In addition, H3 Biomedicine Inc. was established as a research subsidiary in Cambridge, Massachusetts, in 2010 and aims at discovering drugs based on using genetic information from cancer patients. If successful, this can shorten the R&D process and reduce the scale of clinical trials. The genetic information can help identifying what types of drugs could be most effective, thereby allowing fewer trial subjects in the clinical R&D process.

**History of Eisai**

Eisai was founded as Nihon Eisai Co. Ltd. in 1941 by Toyoji Naito, a former employee of an existing pharmaceutical corporation. At 57 years of age, he started Eisai, which eventually merged with the company Sakuragaoka Research Laboratory in 1944 and was listed on the stock exchanges in 1961. Key products in the first years included Vitamin E and health care products. Then the corporation announced a much-publicized innovation declaration in 1988 and started a series of five-year development plans. From 1987 to 1991, the focus was to strengthen domestic marketing, from 1992 to 1996 to focus on globalization with a special emphasis on the U.S. market, from 1997 to 2001 to focus on expansion, and from 2001 to 2007 to focus on the implementation of a millennium plan. Then, due to certain imminent developments such as the expiration of market exclusivity of key products such as Aricept, the focus from 2007 to 2011 was on implementing a
dramatic replanning. These corporate developments have attracted the attention of renowned management theorists Nonaka, Peltokorpi, and Strebel. The veterinary business was divested in 2003, whereas, as mentioned, the Pennsylvania-based monoclonal antibodies company Morphotek as well as the Minnesota-based oncology-focused MGI Pharma were acquired in 2007, and AkaRx, based in New Jersey, was acquired in 2010.

Corporate Philosophy and Recent Strategy
Eisai’s R&D expenditures in relation to sales were 21 percent in fiscal year 2012, and the corporate slogan is Human Health Care (HHC). As of 2012, the corporation was present in a total of 73 countries, and the plan has been to reach 114 countries by 2015. After the founder’s death, the presidency has continued to be in the Naito family. The corporation has, however, implemented a broad structure where a majority of the members are external, including for example, university professors and lawyers. Eisai tries to operate according to a performing better with fewer resources concept, which means to enhance product creation capabilities, generate innovation, and fundamentally strengthen marketing capabilities. The corporation also strives to improve access to medicines in emerging and developing countries, for example, through a so-called 4P mix strategy, which consists of a differentiated pricing policy, utilizing the benefits of production also overseas, maintaining products that may ensure full-scale entry to markets in emerging countries and pursuit of differentiated partnerships. The corporation’s special incentive system allows awards to exceptional individual employees. After the development success of Aricept, for example, several employees received such awards.

Terje Grønning
University of Oslo

See Also: Astellas Pharma (Japan); Daiichi Sankyo (Japan); Ono Pharmaceutical (Japan); Takeda Pharmaceutical (Japan).

Further Readings


El Salvador

The central American nation officially termed the Republic of El Salvador was established in 1992 after the conclusion of a civil war in the nation. Since then, the nation has developed and industrialized quickly. El Salvador is now home to close to 6 million citizens, and it is currently one of the most compactly populated nations in all of the Americas.

El Salvador has a unique national cancer situation as its female population experiences more cancer incidences than its male population, which is the opposite of the global trend of males generally experiencing higher cancer rates. Fortunately, a study conducted by the Fifth Annual Cancer Control Congress in 2013 ascertained that El Salvador has a tangibly declining cancer mortality rate, even in the cancers that are large domestic problems such as breast, cervical, and stomach cancers. Researchers estimate that there are up to 7,000 new cases of cancer occurring in El Salvador every year, and they have also determined that cancer of the stomach is presently the leading cause of cancer mortalities in both the nation’s female and male populations.
In line with El Salvadoran females experiencing higher rates of cancer than their male counterparts, breast and cervical cancers are one of the most substantial health problems in the country. Unfortunately, these two diseases are largely preventable, and their high levels of incidence in El Salvador correlate with various obstacles to diagnosis. To start, many El Salvadorans do not have access to even basic health care facilities, much less cancer treatment centers. El Salvador is a developing country, and thus the distribution of health information in the nation’s rural areas is inadequate, and many El Salvadoran females are wholly unaware that early screening for breast and cervical cancers can provide an effective path to warding off the diseases. Culturally, and also due to the lack of regular physician visits in which trust is built, El Salvadoran women are averse to having their reproductive organs examined for cancer. Furthermore, and like numerous other developing nations around the world, the El Salvadoran population is not informed enough regarding what cancer is and how the disease is developed. Several organizations and governmental departments are working to overcome these treatment obstacles, but it may take a decade or two to substantially negate these impediments.

Currently, there is a crisis in El Salvador regarding the lack of effective management for pain derived from cancer. Researchers estimate that more than 80 percent of all terminal cancer patients will experience severe pain at some point during their affliction, and El Salvador has been observed to have astonishingly low amounts of painkillers available for palliative treatment. Medical experts believe that El Salvador needs to have up to 40 kilograms of morphine in its domestic medicine supply in order to sufficiently manage the severe pain of its terminal cancer patients, but in 2007, the nation had and used less than half a kilogram of morphine on all its medical patients. Even if such a small amount of morphine was used exclusively on the nation’s cancer patients, it would only account for 1 percent of the El Salvadoran terminal cancer patients. Access and availability to effective avenues of pain treatment will need to drastically improve in El Salvador in the coming years as the nation currently has the lowest rate of morphine availability out of all the countries of North, Central, and Latin Americas.

In the past several years, the most prevalent forms of cancer in El Salvador have been breast, bladder, blood, cervical, and stomach cancer. Bladder, blood, and stomach cancers are the most common forms of cancer incidences in males in the nation, while breast, cervical, and stomach cancers are the most common incidences of cancer in females there. Over the past decade, incidences of bladder, blood, and stomach cancers have been consistently increasing nationwide in both El Salvador’s male and female populations, while occurrences of cervical and breast cancer have been consistently declining.

Sadly, many citizens of El Salvador have suffered from cancer throughout the nation’s history. The El Salvadoran ex-president Jose Napoleon Duarte Fuentes died as a result of stomach cancer after having struggled with the disease for several years. Rafael Menjivar Ochoa, the critically acclaimed El Salvadoran writer and journalist, passed away in 2011 after succumbing to his fight with colon cancer. Moreover, Roberto D’Aubuisson, the infamous leader of Salvadoran death squads in the nation’s civil war during the 1980s, died from his bout with esophageal cancer in 1992.

William M. Peaster
Independent Scholar

See Also: Bladder Cancer; Breast Cancer; Cervical Cancer; Stomach (Gastric) Cancer.

Further Readings
Electrical Industry

Thomas Edison developed the light bulb in 1880 and electrical companies sprang up in urban areas by 1890. Regulation of utility companies began in 1907 and two-thirds of the urban areas in the United States possessed street and home lights by 1920. Since the beginning of commercial electricity, over a century of high-voltage electricity use transpired in the industrialized world. When mentioning the electrical industry, discussions about cancer often arise. The visible, health-associated problems to electricity initially consisted of fire, explosions, and electrocutions. Only toward the later part of the 20th century did research into biological effects of electricity appear.

Electric and Magnetic Fields

Some studies carried out in the 1960s found that invisible electromagnetic fields (EMF) created by high-voltage utility lines demonstrate a link to cancers in adults and children. Power lines generate both electric and magnetic fields. Because the body acts as an electrical conductor, the electric field goes down in magnitude within the human body and, in fact, the electric fields from power lines exist at a lower level than the electric field in the body.

A Swedish study by S. Tornqvist, S. Norell, A. Ahlbom, and B. Knave on 3,358 power lines workers and 6,703 power station operators between 1961 and 1979 showed no consistent risk of cancer, especially leukemia and brain tumors. The groups displayed no elevated risk of cancer of the urinary tract.

Magnetic fields remain as a possible source of deleterious health in the human body. Yet even magnetic fields from power lines remain very small. The Earth's magnetic field exists at between 300 to 500 milliGauss, compared to the power line source of 2 milliGauss. Initial studies in the 1970s and 1980s conducted by Nancy Wertheimer and Ed Leeper alleged that electric power lines generated an increased incidence of childhood leukemia, but the research turned out to be flawed. J. G. Davis and colleagues published a review in 1992 that discussed in detail the problems with the earlier research on power lines and cancer.

G. Zeman from the Health Physics Society reported no known health risks arise from living next to high-voltage power lines but stated that science cannot prove that low levels of electromagnetic fields remain risk free. Consequently, scientists continue research to ascertain any health risks, but most believe that, if risks are present, the risk represents a small contribution to developing cancer. Later research shows some effects.

C. Sermage-Faure and colleagues studied the association of living next to high-voltage overhead power lines (HVOLs) and childhood acute leukemia in France from 2002 to 2007. Children living within 50 meters of a HVOL showed a small elevated risk of developing acute leukemia. The study supports similar findings in other international sites.

A study by C. F. Robinson, M. Petersen, S. Palu, and J. P. Sestito calculated the mortality of a large cohort of electrical workers from the United States for the years 1982 to 1987. The research confirmed the presence of lung cancer from asbestos exposure in male workers but indicated the need for more research to relate leukemia and melanoma skin cancer to electrical work. The outside environment of electrical industry workers causes their skin to be overexposed to ultraviolet (UV) radiation. The overexposure can produce skin cancers and melanomas.

Wireless Telecommunication Technologies

M. Roosli and K. Hug performed a literature review on the association of radiofrequency electromagnetic field (RF-EMF) exposure and health problems. The authors found nine randomized trials that found no association between RF-EMF and health problems from 2007 to 2011. Two observation studies looked at the effect of RF-EMF on quality of life and found no adverse effects. The reviews stated
that the researchers followed the exposures for short periods of time, and longer-term studies are needed to accurately determine any associations to health problems.

S. Sadetzki and colleagues designed an international study to determine the possible health effects of exposure to radiofrequency (RF) and extremely low frequency (ELF) electromagnetic fields in children and adolescents using mobile phones. The multinational case-control study will investigate the exposure of EMF in 14 countries on children ages 10 to 24 years old.

Electricity Fields
J. Aoun, N. Saleh, M. Waked, J. Salame, and P. Salameh describe their study of lung cancer and a sample of Lebanese adults. The case control study on lung cancer found risk factors of cigarette smoking, living near an electricity generator, a family history of cancer, and consuming low quantities of fruits and vegetables. The authors advise further study to confirm these findings. This study did show an effect of an association between lung cancer and living near an electricity generator.

Polychlorinated Biphenyl
The electrical industry began using polychlorinated biphenyl (PCB) in 1929 as a cooling and insulating fluid for industrial transformers and capacitors as well as for stabilizing additives in the production of coating for electrical wiring and electronic components. As early as 1936, the toxicity associated with PCB came to light when family members developed pustules on the skin from exposure to the electrical workers’ clothing. By 1947, R. M. Brown published a report on PCBs being “objectionably toxic” and described a maximum permissible concentration of 1 microgram per meter cubed for an eight-hour day. However, the use of PCBs persisted with few restrictions until the 1970s.

When studies about the carcinogenic properties of PCBs arose in the 1970s, outcries to stop using PCBs arose. A ban on open sources of PCBs went into effect in the 1970s, but unfortunately, PCBs endure in the environment due to PCBs being allowed in totally enclosed uses like transformers and capacitors. If the enclosure fails, the PCB can leak, catch fire, or explode. When the substance leaks from the transformers on the electrical poles, it contaminates the soil below the utility pole.

PCBs generate mutagenic consequences by disturbing the hormones in the body. The PCB can both impede and mimic estradiol, the primary sex hormone in females. Mimicking estrogen can fuel breast cancer cells and possibly other cancers, like uterine or cervical.

Multiple routes of contact with PCBs exist. A person can breathe in air contaminated with PCB, consume PCB-tainted food, or absorb PCB though the skin via contact with old electrical equipment. Once a person becomes exposed, certain PCBs change in the body to other chemicals. So chemically changed and unchanged PCBs may be passed by way of feces or can stay in the body fat or other organs for months. PCBs, in milk fat, can be passed to infants during breast-feeding.

A. M. Ruder, M. J. Hein, N. B. Hopf, and M. A. Waters assessed the mortality of 24,865 electrical capacitor workers exposed to PCBs at plants in Indiana, Massachusetts, and New York over 10 years, ending in 2008. The study showed an association between cumulative PCB exposure and cancers of the stomach, uterine, and prostate as well as multiple myeloma. These results demonstrate cancer’s relationship to PCBs in this longitudinal study.

A study completed by A. C. Pesatori and colleagues in an Italian cohort present different cancers occurring in electrical capacitor production. The cancers suggested from exposure to PCB included the digestive system, brain, and lymphohemopoietic tissue. The authors stated the sample size limited the ability to make a definitive statement.

K. Mallin and colleagues studied 2,885 workers at an electrical capacitor plant between 1944 and 1977. The authors found females possessed significantly elevated rates of liver or biliary cancer and intestinal cancer, whereas males demonstrated significant elevations in stomach cancer and thyroid cancer.

Electrical Lighting and Breast Cancer Risk
Light during the night suppresses melatonin, and it disrupts circadian rhythms. R. G. Stevens describes a theory, proposed in 1987, purporting an increase in the use of electricity at night to light streets and inside homes accounts in part for the elevated risk of breast cancer worldwide. R. G. Stevens, G. Brainard, D. E. Blask, S. W. Lockley, and M. E. Motta reviewed the evidence for electric lighting disrupting circadian rhythm and causing breast cancer but found a paucity of data to link
this association. More research will be needed to determine the association of breast cancer and circadian disruption.

**Biologically Closed Electric Circuits**


The book on BCEC describes a new theory on carcinogenesis and a novel method of treatment against cancer. The innovative theory proposes using electric currents against inflammatory states, fractures, atheromas, and neurologic complications of disease. He basically proposes a new approach to electrophysiology, indicating that fluctuating electrical potentials arise from within cancers and could affect the extracellular fluid dynamics around a tumor. Unfortunately, this novel theory will require testing from other scientists before electrical currents can be used to treat human disease.

**Bioelectrical Impedance**

All living cells contain electrical capability and even create electric currents. E. Hondroulis, S. J. Melnick, X. Zhang, Z. Z. Wu, and C. Z. Li describe a laboratory study showing the electrical properties of cancer cells differ from the body's normal cells. The researchers used ovarian cancer cells in comparison to normal ovarian cells. By applying alternating electric fields to both cell groups, the scientists showed how the electric fields slowed the growth of the cancer cells. The study indicates the possible effects of alternating electric field therapy to future applications in clinical and drug treatments.

A group of researchers in Poland consisting of T. Malecka-Massalska, A. Smolen, and K. Smorshed used bioelectrical impedance analysis (an ImpediMed bioimpedance analysis machine) in a case-control study of breast cancer patients and health subjects. Significantly higher levels ($p = 0.0031$) of reactance and resistance at 50 kHz occurred in the breast cancer patients over healthy subjects. This preliminary observation appears to be in line with the research carried out by Nordenstrom, but further research is needed in larger patient groups to validate these initial findings.

Malecka-Massalska and colleagues further studied a group of patients with squamous cell carcinoma in head and neck tumors in a cross-sectional study using bioelectrical impedance analysis.

The results showed significantly higher levels ($p = 0.0002$) of resistance in the patients with the head and neck cancer than the control group. Further observations in head and neck cancer are needed to confirm results.

Previous results show a significant electrical property difference between malignant and benign prostate tissue. V. Mishra and colleagues evaluated an electric property-sensing biopsy needle to determine the effectiveness of the needle in biopsies of malignant and normal prostate tissue. The study found higher resistive and reactive electrical components in the malignant prostate tissue. By sensing the malignant prostate tissue in real time, the device improves the accuracy of cancer during biopsy procedures.

**Conclusion**

Despite the widespread existence of electricity since the 1920s, only a few characteristics of the electrical industry show a direct relationship to the development of cancer. Electric workers develop cancer from PCB used in capacitors and from asbestos used in the insulation. Due to the strong association of cancers and PCB, regulators banned open sources of PCB in 1979, but electric workers still come in contact with the closed sources. Research on high-voltage overhead power lines in the last decade confirmed an association to childhood acute leukemia. The electric lighting at night and breast cancer has yet to be confirmed.

More recently, the electrical activity of cells came under study from the original work of Nordenstrom. The last 10 years have demonstrated the need for more research on electrical currents present in cancer cells. This research shows that cancer cells show higher levels of electrical activity than normal cells. The future will surely demonstrate more use of measuring electric currents in cells to diagnose and treat cancer.

Sharon A. Takiguchi
Independent Scholar

See Also: Breast Cancer; Chemical Industry; Electronics; Head and Neck Cancer.
There are a wide variety of legitimate reasons for considering an association between electronics and cancer as a societal issue. There are ongoing debates in scientific communities, for example, on the extent to which electromagnetic energy is a risk factor or associated cause of cancer. There is no shortage of publications on technology use and suspected negative effects on human health. These discussions often focus on whether there is a link between magnetic field exposure and cancer in the home or at work. There is an interest in the risk of leukemia or breast cancer (for men and women) that may be associated with various levels of exposure to electromagnetic fields (EMFs). Some of these discussions have even made their way
into popular media, for example, the concern over mobile telephone use and cancer risk. Most recently, discussions have also focused on the increasing popularity and prevalence of electric cigarette use and the possible risk for cancer in high-risk individuals. However, despite these legitimate concerns, there are equally viable uses of electronics and electronic technology associated with health and healing.

Electronic communication and access to electronic media may increase health awareness and is associated with healthier lifestyle choices and reduced risk of cancer or other illnesses or disease. Another modern use of electronic technology that is indirectly related to health and healing includes electronic data sharing of health information. This includes access to medical records and patient information between physicians and possibly health systems. Some countries have developed electronic surveillance systems for use in the early detection of possible epidemics. It is conceivable that these systems might also be useful for tracking possible risk factors for certain types of cancer or monitoring the health conditions of individuals or communities at higher risk for some types of cancer. Finally, an essay on the association between electronics and cancer in society would be incomplete without mention of the many direct uses of electronics in cancer treatment.

**Does Electromagnetic Energy Cause Cancer?**

Research has looked into the electromagnetic radiation (EMR) produced by electricity in the home and from overhead power lines as a possible cause of cancer. EMR can be categorized into two types: ionizing (e.g., X-rays, radon, and cosmic rays) and nonionizing (e.g., radiofrequency and extremely low-frequency or power frequency). No conclusive link has been found so far between EMR and the incidence of cancer. The most recent research studies seem to show that low levels of electromagnetic energy do not increase the risk of cancer.

Studies have looked mainly at EMFs and the risk for leukemia and breast cancer. In 2001, the National
Radiation Protection Board (NRPB) reported that there might be a very slight increased risk for leukemia in children. The EMR exposure investigated in this report was mostly from domestic use of electricity. A study from England in 2005 found that children who lived within 200 meters from high-voltage power lines at birth had an increased risk for leukemia. In 2012, the Advisory Group on Non Ionising Radiation (AGNIR), within the Health Protection Agency in UK, reported on electromagnetic radiation and breast cancer risk. The belief was that exposure to EMFs could lower the levels of a hormone called melatonin and that this could increase the risk of breast cancer. After looking at the available evidence, the group reported that exposure to EMFs did not appear to increase the risk of breast cancer. They also reported that EMF exposure did not appear to influence melatonin levels.

A Danish review of studies published in 2008 reported that long-term exposure to EMFs among children does seem to be associated with an increased risk for leukemia. Yet, the explanation is not clear, and researchers suggested that the observed relationship could be due to chance. Studies from Australia in 1996, and from Italy in 2002, have reported childhood leukemia clusters close to high-power television and radio broadcast transmitters. However, large, systematic studies in South Korea and Germany show no association between exposure to radio frequency EMFs from broadcast towers and childhood leukemia. A report in February 2014 from the Childhood Cancer Research Group at the University of Oxford found that children who live near overhead power lines in early life do not have a greater risk of developing childhood leukemia. Therefore, research is likely to continue, but existing evidence suggests that it is unlikely that electromagnetic fields cause cancer.

What About Mobile Phones and Cancer?
Mobile phones transmit radiofrequency energy. Radiofrequency energy is a form of nonionizing electromagnetic radiation. Human skin and underlying tissues nearest to where the phone is held can absorb this energy. Currently, there is no consistent evidence that nonionizing radiation from mobile phones increases the risk of cancer. The World Health Organization (WHO) says that the EMFs produced by mobile phones are classified by the International Agency for Research on Cancer as possibly a carcinogen in humans. They also say that studies are ongoing to fully assess the potential long-term effects of mobile phone use.

The WHO reports that, over the past 20 years, no adverse health effects have been found across a large number of studies that have been done to assess whether mobile phones pose a potential health risk. Mobile phones were not used widely until the early 1990s, so longer-term effects are not yet known. However, animal studies of long-term exposure to electromagnetic fields have not shown any increased cancer risk.

**Technology Use and Human Health**
Some social media sites and other electronic sources that increase health awareness may include recommendations for physical exercise and prevention diets that may reduce the risk for certain types of cancer. Electronic access to readily available information also provides a level of insight into symptoms and possible treatment options that previous generations did not have. Likewise, the rise of social media and electronic social networks allows countless individuals to discuss health issues with other people around the world without leaving their homes. Originally, the Internet was mostly a large repository of information that could be tapped in increasingly clever ways, but the transfer of information was mostly unidirectional (from the World Wide Web to the end user). Since the beginning of the 21st century, though, the Internet has become a two-way information highway, where the uploading of personal information has become as common as the downloading of information. This behavior evolved into the formation of online social networks on Web sites like Myspace, Facebook, Twitter YouTube, and Tumblr as well as professional networking sites like LinkedIn. This nascent use of electronic communications by the common layperson, therefore, has the potential to improve general health conditions through public health awareness.

Another interesting development in the connection between electronics, technology use, and cancer risk is the increasing popularity of telework. Electronics technology enables companies to seek opportunities for employees to work from home or other remote locations—telework. Telecommuting, or telework, can reduce required transportation to work and any associated environmental pollution that may be linked to increased risks or incidence of cancer in society.
A more direct use of electronics and public health is the Electronic Surveillance System for the Early Notification of Community-Based Epidemics (ESSENCE). Public health surveillance can be defined as the systematic collection, analysis, interpretation, and dissemination of health-related data. The purpose of an electronic health surveillance system is to prevent or control disease or injury and to improve health or to improve a health program or service, including cancer registries.

Finally, there are many direct uses of electronics in cancer treatment. Cancer treatment research has demonstrated that low-intensity electric fields can disrupt the division of cancer cells and slow the growth of brain tumors with little danger to normal brain tissue. This noninvasive procedure uses a small device with alternating electrical fields to disrupt the rapid cell division exhibited by cancer cells in some malignant tumors. A similar technique called transcutaneous electrical nerve stimulation (TENS) has been shown effective as a method of relieving acute and chronic pain caused by cancer as well as other problems such as surgery, childbirth, migraine headaches, and so on. Some practitioners believe that the low-voltage electrical impulses stimulate the production of endorphins, the body’s natural painkillers.

Jody A. Worley  
University of Oklahoma

See Also: American Cancer Society; Canadian Cancer Society; European Association for Cancer Research; Radiation; Radiation Therapy.

Further Readings
American Institute of Physics. “Electric Fields Have Potential as a Cancer Treatment.”  


Swerdlow, A. J. “Epidemiology of Long-Term Health Effects of Radiofrequency (RF) Exposure.”  
Mutagenesis, v.27 (2012).

University of California, San Diego Health Sciences. “New Hope for Patients With Brain Tumors.”  

Eli Lilly & Company (United States)

Eli Lilly & Company (Lilly) researches, develops, manufactures, and sells pharmaceuticals. With products sold in approximately 130 countries, Lilly has manufacturing and distribution facilities in 17 other countries in addition to the United States. Lilly also includes the Lilly Oncology division, which focuses on innovative cancer drugs and on improving outcomes for patients.

Founded in 1876 by a pharmaceutical chemist and Civil War veteran Colonel Eli Lilly, the company remained under Lilly family management until 1953. Lilly began a concerted effort in the 1960s to find solutions for cancer. In the 1970s, it began marketing Eldisine (vindesine sulphate) for the treatment of leukemia. The drug’s use would eventually be expanded to include breast cancer, non–small cell lung cancer, and melanoma.

On September 13, 2007, following three clinical trials, the FDA approved Lilly’s raloxifene hydrochloride tablets (Evista) for reduction in the risk of invasive breast cancer in postmenopausal women with osteoporosis and in postmenopausal women at high risk for invasive breast cancer. Raloxifene is not prescribed to decrease the risk of developing non-invasive cancer. Raloxifene, which is also used to prevent and treat osteoporosis, reduces the risk of developing invasive breast cancer by preventing the female hormone estrogen from affecting breast tissue, thus reducing the chance of tumors developing that need estrogen to grow. Raloxifene does not completely prevent breast cancer, and women who take the drug are instructed to continue to receive regular breast examinations.

Lilly got approval from the U.S. Food and Drug Administration (FDA) in 1996 for Gemzar (gemcitabine) to treat pancreatic cancer. Gemzar is also used to treat non–small cell lung cancer. Other chemotherapies produced by Lilly include Alimta (pemetrexed) for pleural mesothelioma and non–small cell lung cancer and Erbitux (cetuximab) for metastatic colorectal cancer and head and neck cancer.
The cancer drug Cyramza (ramucirumab), which the company acquired via acquisition of ImClone Systems in 2008, became the first FDA-approved treatment for advanced gastric cancer after prior chemotherapy. The drug was also approved to treat gastroesophageal junction adenocarcinoma, a cancer located at the junction between the esophagus and stomach. However, in July 2014, phase 3 clinical trials of the drug for use as a secondary treatment for patients with liver cancer did not produce statistically significant data that these patients had longer survival rates.

The Lilly Oncology unit was formed in 2009 as part of a company restructuring designed to improve Lilly’s success of getting experimental drug therapies approved for marketing. A major focus of the effort was the idea of developing drugs tailored to specific strains of cancer. In the case of breast cancer, for example, it is actually a myriad of different diseases influenced by a woman’s genetic makeup.

The oncology unit is conducting research in several areas. Research on cancer signaling revolves around cancer cells’ ability to sustain chronic proliferation. Investigations revolve primarily around cell cycle regulation. The research is a genetics-based effort to develop drugs that could target aberrant cell-signaling pathways.

Another area of research is cancer angiogenesis (blood vessel sprouting). Lilly’s efforts focus on identifying and developing new antiangiogenic agents with an emphasis on discovering agents for specific tumor types or for cancers that do not respond to current chemotherapies. Other areas of research include cancer metabolism, tumor immunotherapy, and epigenetics.

The company also conducts research into supportive care. One research area focuses on toxicities often associated with cancer and cancer therapies, such as anemia and muscle wasting. Ongoing research focuses on using antibodies to target regulators of muscle metabolism and iron homeostasis.

The company is also conducting phase 1, 2, or 3 clinical trials on a number of cancer-fighting agents. These trials focus on agents for early development cancers and for breast, gastrointestinal, genitourinary, hematologic, lung, and neurologic cancers as well as soft tissue sarcoma and melanoma supportive care. In 2014, Lilly announced that it had formed an agreement with UK Biotech to develop new cancer drugs.

The Lilly Oncology division also runs several initiatives concerned with helping physicians better manage cancer cases and communication with patients. There are also several patient-based initiatives. PACE is a Lilly Oncology initiative and stands for Patient Access to Cancer Care Excellence. The Global initiative focuses on encouraging public polices and other health care decisions that foster the development of new medicines, enhanced learning from cancer cases, and better response to cancer treatment and care.

Lilly has also created mobile applications (apps) for oncologists to run via their mobile devices, such as smartphones and tablet computers. The Oncology Pipeline app provides health care professions access to the Lilly Oncology Clinical Development program. The app includes information on drug discovery platforms in development and molecules under research. The Lilly Oncology Clinical Trials Resource app includes free access to clinical trial information, including trials for various types of cancer.

Lilly has developed a number of programs and resources for clinicians and other health care professionals directly related to patient care. The company’s app called the Cancer Companion was developed for health care professionals to learn more about cancer treatment and care, especially in terms of information that they can then pass on to their patients. Other apps include the MDLinx Oncology app, which provides the latest oncology journal articles for review on mobile devices.

Lilly also provides online, interactive lung and colorectal staging galleries for use by health care professionals. These galleries help health care providers better discuss with their patients various issues concerning their cancer and its treatment. The IASLC Staging Atlas for Thoracic Oncology smartphone app provides updated staging information for non–small cell lung cancer. (IASLC stands for International Association for the Study of Lung Cancer.)

Lilly also has developed a number of programs that focus on better communication between health care professionals and patients. For example, the company has an interactive educational speaker program that helps providers improve patient care through better communication. It also has information on promoting health behavior for cancer survivors who are recovering.

Lilly’s Taking Back Control video targets patients and focuses on the difficulties they face after being diagnosed with cancer. The Lilly Oncology on Canvas art competition, cosponsored by the National Coalition for Cancer Survivorship, promotes anyone in the
United States and Puerto Rico to express through artwork or writing their experiences with cancer with a focus on life-affirming changes in their lives. The program is open not only to patients but also to caregivers, family members, friends, and health care professionals.

The Lilly Patient One program is for health care providers who have patients who may be experiencing financial and insurance coverage issues. For patients prescribed a Lilly Oncology product, their health care providers can find out information to help patients gain access to financial assistance or reimbursement assistance programs and services. In addition to offering information on insurance issues, such as payer policy information and payment methodologies, the program can help in the evaluation of other funding options, drug replacement options, possible reimbursement assistance, and appeals assistance when insurance claims are denied.

David Petechuk
Independent Scholar

See Also: Breast Cancer; Food and Drug Administration; Genetics; Lung Cancer, Non–Small Cell; Melanoma; Sarcoma Foundation of America.

Further Readings

Embalming Fluids

More than 5 million gallons of embalming fluid are used every year in the United States in order to sanitize, disinfect, and preserve human and animal cadavers, whether for funerals and burial or for scientific study. The main components of embalming fluid are formaldehyde and methanol in combination with other solvents and numerous additives. Embalming fluids have been linked to cancer rates and other health risks faced by embalmers.

Embalming is the practice of treating the remains of the deceased—especially humans, but animal remains are preserved for scientific study and to teach dissection and anatomy—in order to preserve or restore them. With human remains, the principal purpose is to display the remains, such as at a wake or viewing before the burial. As such, preventing the deterioration, putrefaction, and odor of dead tissues is paramount.

The following are the five stages of embalming:

1. In the pre-embalming preparations, the corpse is washed with antibacterial and germicidal solutions, and rigor mortis (a postmortem effect that stiffens the limbs beginning a few hours after death) is relieved by bending and massaging the arms and legs. The corpse is posed in a process called setting the features, consisting of arranging the face so that it appears to have a calm expression of being at rest. This is performed even if the corpse is going to be cremated or if there is no viewing planned as a gesture of respect for the deceased.
Setting the features involves using eye caps to keep the eyes shut, and using sutures, adhesives, or wires injected by needle in order to manipulate the mouth, lips, and jawbone. In some cases, some amount of facial reconstruction may be necessary. Specialized techniques and tools have been developed purely for the mortuary industry. Male corpses are also shaved of any visible stubble.

2. Embalming chemicals are injected into the body, traditionally through the right common carotid artery. Blood and other fluids are displaced and expelled from the body through a tube injected into the right jugular vein. The body is massaged in order to break up clots and distribute embalming fluids, and if circulation

Embalming Fluids

More than 5 million gallons of embalming fluid are used every year in the United States in order to
remains poor, multiple injection points at other arteries are used.

3. The internal fluids inside body cavities are similarly displaced during cavity embalming, in which an incision is made in the navel so that a trocar can be inserted into the chest and stomach cavities in order to aspirate the contents of hollow organs. A formaldehyde-heavy mixture is pumped in to fill the space.

4. In hypodermic embalming, tissues are injected with embalming fluids by syringe on an as-needed basis.

5. Surface embalming preserves the skin’s surface and deals with damage from accidents, decomposition, or cancerous growths.

Additional steps are needed for many organ donors because of the complications of preparing a body after a long-bone donation or skin donation. If an autopsy was performed, this also complicates the procedure. Embalming takes several hours at a minimum. After the embalming, the body is washed to remove the smell and appearance of embalming fluids, dried, moisturized, and cosmetics are applied to improve the color of the skin. (Warm-toned lighting is usually used during the viewing as well.)

Embalming chemicals include a wide variety for various purposes. Formaldehyde is usually the key ingredient because of its preservative properties. About three gallons of embalming fluid are used for an adult corpse.

Embalming fluids also include anti-edemic chemicals that draw excessive fluid from bodies, humectants that restore the tissues of dehydrated bodies, cell conditioners that help prepare cells to absorb fluid from the arteries, dyes to restore natural coloration, and disinfectants. The cavity embalming fluid is a separate mixture, usually an undiluted formaldehyde-heavy solution.

Formaldehyde is the most important carcinogen in embalming fluids, not only because it constitutes a large percentage of the fluid preparation but because, despite its classification as a class 1 carcinogen, the industry has resisted pressures to adopt an alternative. This is in part because a good alternative with the same properties has simply not presented itself. Similar chemicals tend to be disinfectants rather than actual preservatives that can maintain the body’s appearance postmortem—and prevent the smell of decay as perfectly as formaldehyde does. Instead, embalming facilities depend on adequate ventilation to protect their workers, along with gloves and masks. Ventilation ducts are ideally placed at table level rather than the older system of ceiling ducts, which caused fumes to be carried past workers’ faces before being removed from the room.

Formaldehyde is highly toxic. A single ounce—half a shot glass—of formaldehyde in the concentration used in the funeral industry is sufficient to kill an adult male. Even formaldehyde resins, used in construction materials, can result in chronic headaches, asthma-like symptoms, and respiratory problems among workers in workplaces where the resins decompose. Formaldehyde has been suspected as a carcinogen since 1978 and classified as such since the 1980s. In 2006, the International Agency for Research on Cancer (IARC) formally reclassified it as a known human carcinogen. Its links to nasal sinus cancer and nasopharyngeal cancer are known, especially through inhalation in the workplace. More recently, its link to leukemia has been established.

Though the industry as a whole has continued to embrace formaldehyde, individual embalmers have not always done so. In 2012, a New Jersey mortician diagnosed with acute promyelocytic leukemia filed a lawsuit against his employer and the manufacturers of the embalming fluids blamed for his illness. He also alleged that, after returning to his job after a nine-month disability leave, his employer denied his request to improve ventilation or transfer him to a second, newer, and better ventilated, facility.

According to a 2009 study of funeral industry professionals who died between 1960 and 1986, death from myeloid leukemia—associated with formaldehyde—was statistically significantly more likely than in the rest of the population, and that this risk was elevated for subjects who performed more than 500 embalmings in their lives, compared to those who performed fewer. The study concluded that membership in and duration of association with the embalming profession were positively correlated with risk of death from myeloid leukemia. No link to brain cancer could be established. Separate studies found increased risk among embalmers of death from brain tumors, colon cancer, cirrhosis of the liver, and arteriosclerotic heart disease, without
positively correlating these risks to formaldehyde exposure specifically.

Embalming fluids also contain methanol, which is not carcinogenic but is highly toxic in sufficient doses, both because it depresses the central nervous system and because it metabolizes to formic acid, which causes cellular hypoxia.

The practice of green burial or natural burial is interment of the body in soil without preserving it against decomposition in the long term. In some green burials, conventional embalming is actually still used—the primary difference is in the type of coffin used, moving away from the trend in recent decades toward using coffins that resist degrading longer. In other green burials, the body is either not embalmed or alternative, nonformaldehyde preparations are used. Sometimes, for this reason, there is no viewing of the body offered.

Bill Kte’pi
Independent Scholar

See Also: Chemical Industry; Colon Cancer; International Agency for Research on Cancer.

Further Readings


independent prognostic factor. However, although high endogenous levels of unopposed estrogen are related to increased risk of endometrial cancer, their independence from other risk factors is inconsistent with being a common underlying biologic pathway through which all risk factors for endometrial cancer operate. An increased incidence of endometrial cancer also has been associated with tamoxifen treatment of breast cancer, reports R. F. van Leeuwen and colleagues. Researchers studied 813 cases of endometrial cancer and concluded that there is an increased risk of the cancer associated with tamoxifen treatment extending beyond five years. Other risk factors include obesity, hypertension, and diabetes mellitus. Cardiovascular disease is the most common cause of death in patients diagnosed with endometrial cancer.

The pattern of endometrial cancer is partially dependent on the degree of cellular differentiation. Well-differentiated tumors usually limit their spread to the surface of the endometrium; myometrial extension is less common. In cases with poorly differentiated tumors, myometrial invasion occurs more frequently. Myometrial invasion is frequently associated with lymph node involvement and distant metastases and is often independent of the degree of differentiation.

Metastatic spread occurs in a characteristic pattern: to the pelvic and para-aortic nodes. When distant metastasis occurs, it most commonly involves the lungs, inguinal and supraclavicular nodes, liver, bones, brain, and vagina. M. Hanson and colleagues found another factor that correlates with extraterine and nodal spread to be involvement of the capillary-lymphatic space.

Three prognostic groupings of clinical stage I disease have been identified: Diagnoses with grade 1 tumors involving only endometrium and no evidence of intraperitoneal disease have a low risk (less than 5 percent) of nodal involvement. Cases with grade 2 or 3 tumors and invasion of less than 50 percent of the myometrium and no intraperitoneal disease have a 5 to 9 percent incidence of pelvic node involvement and a 4 percent incidence of positive para-aortic nodes. Cases with deep muscle invasion and high-grade tumors or intraperitoneal disease have a 20 to 60 percent risk of spread to pelvic nodes and a 10 to 30 percent risk of spread to para-aortic nodes. C. Tornos and colleagues identified four statistically significant risk factors: myometrial invasion, vascular invasion, eight or more mitoses per 10 high-power fields, and an absence of progesterone receptors.

In cases without extraterine spread, the greatest determinants of recurrence were grade 3 histology and deep myometrial invasion. In this study, the frequency of recurrence increased with positive pelvic nodes, adnexal metastasis, positive peritoneal cytology, capillary space involvement, and involvement of the isthmus.

At the cellular levels, endometrial cancers are classified in one of the following two categories: Type I tumors include tumors of endometrioid histology that are grade 1 or 2; these comprise approximately 80 percent of endometrial carcinomas. These tumors typically have a favorable prognosis, are estrogen responsive, may arise from complex atypical hyperplasia, and are pathogenetically linked to unopposed estrogenic stimulation. Type II tumors account for 10 to 20 percent of endometrial carcinomas. They include grade 3 endometrioid tumors as well as tumors of nonendometrioid histology: serous, clear cell, mucinous, squamous, transitional cell, mesonephric, and undifferentiated. These tumors are often high grade, have a poor prognosis, and are not associated clearly with estrogen stimulation. A precursor lesion is rarely identified.

Four subtypes have been identified that will refine classification and provide prognostic and therapeutic implications.
The most common endometrial cancer cell type is endometrioid adenocarcinoma, which is composed of malignant glandular epithelial elements that may include an admixture of squamous metaplasia. Adenosquamous tumors contain malignant elements of both glandular and squamous epithelium. Clear cell and papillary serous carcinoma of the endometrium are tumors that are histologically similar to those in the ovary and the fallopian tube, and the prognosis is worse for these tumors. Mucinous, squamous, and undifferentiated tumors are rarely encountered. Frequency of endometrial cancer cell types are as follows: endometrioid (75–80 percent); uterine papillary serous (less than 10 percent); mucinous (1 percent); clear cell (4 percent); squamous cell (less than 1 percent); mixed (10 percent), and undifferentiated.

Prognoses for cases with endometrial cancer that have localized disease are significantly good with hysterectomy or hysterectomy and adjuvant radiation therapy. Results of two randomized trials on the use of external-beam radiation therapy (EBRT) in patients with stage I disease did not show improved survival but did show reduced local-regional recurrence (3–4 percent vs. 12–14 percent after 5–6 years’ median follow-up, \( P < .001 \)) with an increase in side effects, reports the National Cancer Institute. Some patients have regional and distant metastases that, though occasionally responsive to standard hormone therapy, are rarely curable. For these patients, adjuvant chemotherapy is a consideration.

Uterine serous histologies have higher rates of recurrence than do other stage I endometrioid carcinomas. The outcomes in institutional case series utilize a policy of adjuvant carboplatin plus paclitaxel, occasionally including radiation therapy. If there is cervical involvement, options include radical hysterectomy, bilateral salpingo-oophorectomy, and pelvic and para-aortic lymph node dissection. If the cervix is not involved but extension to the cervix is documented on postoperative, radiation therapy should be considered.

Patients with stage III endometrial cancer are treated with surgery, followed by chemotherapy or radiation therapy, or both. For years, radiation therapy was the standard adjuvant treatment for patients with endometrial cancer. However, several randomized trials have confirmed improved survival when adjuvant chemotherapy is used instead of radiation therapy. In a trial conducted in a subset of patients with stage III or IV disease with residual tumors smaller than 2 centimeters and no parenchymal organ involvement, the use of the combination of cisplatin and doxorubicin resulted in improved overall survival (OS) compared with whole-abdominal radiation therapy (adjusted hazard ratio, 0.68; 95 percent confidence interval limits, 0.52–0.89; \( P = 0.02 \); five-year survival rates of 55 versus 42 percent). In some studies, cisplatin, doxorubicin, and paclitaxel may be a superior treatment, however, may result in peripheral neuropathy.

When possible, patients with stage IV endometrial cancer are treated with surgery, followed by chemotherapy or radiation therapy, or both. Treatment of patients with stage IV endometrial cancer is determined by the site of metastatic disease and site-specific symptoms. For bulky pelvic disease, radiation therapy consisting of a
combination of intracavitary and EBRT is used. When distant metastases, especially pulmonary metastases, are present, hormonal therapy is indicated and useful. Observational studies support maximal cytoreductive surgery for patients with stage IV disease, although these conclusions need to be interpreted with care because of the small number of cases and likely selection bias. Hormonal treatment of progestational agents, have produced good antitumor responses in as many as 15 to 30 percent of patients.

An inoperable disease caused by tumor that extends to the pelvic wall may be treated with a combination of chemotherapy and radiation therapy. The usual approach is to use a combination of intracavitary radiation therapy and EBRT. When patients are neither candidates for either surgery or radiation therapy, they may be treated with progestational agents. A high rate of failure for distant metastases in the upper abdominal and extra-abdominal sites have been found, and for this reason, patients with stage III disease may be considered for innovative clinical trials.

Progestational agents have been evaluated as adjuvant therapy in a randomized clinical trial of stage I disease and have been shown to be of no benefit. These studies, however, were not stratified according to level of progesterone receptor in the primary tumor. No trials of adjuvant progestins in more advanced disease have been reported. Determination of progesterone receptors in the primary tumor is encouraged, and entry onto an appropriate adjuvant trial (if receptor levels are high) should be considered. If no trial is available, data from receptors on the primary tumor may help guide therapy if disease recurs.

A recent review by F. Lin and colleagues compared laparoscopically assisted surgery (LAS) and open surgery in endometrial cancer patients. LAS had fewer intraoperative complications, lower incidence of transfusion, less blood loss, and shorter hospital stays, but longer surgical times. The conclusions regarding safety were cautious due to concerns in validity evaluation and the small number of studies analyzed, and they might not be reliable.

Christopher Edwards
Mary Wood
Duke University Medical Center

See Also: American Cancer Society; National Cancer Institute; Uterine Cancer, Endometrial.

Further References

Environmental Justice and Cancer

Even though cancer is caused by mutations in human genes, factors outside the human body, including environmental factors, cannot be ruled out. The relationship between environmental exposures and cancer has been established, giving proof to the argument that cancer is an environmental as
well as lifestyle disease. When considered broadly, environmental factors account for about 67 percent of all cancer cases; specifically, tobacco is known to cause about 29 to 31 percent of all cancer deaths, diet accounts for 20 to 50 percent of cancer deaths, bacterial and viral infections account for 10 to 20 percent, ionizing and ultraviolet (UV) lights account for 5 to 7 percent, occupation exposures account for 2 to 4 percent, while pollution in the air, water, and food account for 1 to 5 percent of all cancer deaths.

Environmental justice is a concept that addresses civil rights, antitoxicity, environmental sustainability, fair and just labor practices, and related issues of sustainable human and earth rights. Environmental justice also intersects with environmental racism in the commitment of fair treatment and meaningful involvement of all people regardless of ethnicity, national origin, or income to fair and just development, implementation, and enforcement of environmental laws, regulations, and policies. Persons in developing nations, and poorer regions in the United States, Europe, and other industrialized nations, are far more likely to live in proximity to industrial areas, nuclear plants, landfills, pollution from ground transportation, water-quality problems, and other related environmental concerns. All persons should have a fair and just level of protection from environmental and health hazards and equal access to the decision-making process to have a healthy environment in which to live, learn, and work. Goals of environmental justice include protecting health in communities overburdened by pollution; empowering communities to take action to improve their health and environment; establishing collaborative partnerships with local, state, tribal, federal, national, and international organizations to achieve healthy and sustainable communities.

Environmental Justice and Occupational Cancer Risks
One key commitment of environmental justice advocates is upholding the right of all workers to safe and healthy work environments without being forced to choose between an unsafe livelihood and unemployment. Chemical exposures may be responsible for the elevated incidences of cancer of workers in numerous industries including, but certainly not limited to, the chemical, plastics, and coal mining industries. For example, the plasticizer contamination of firefighters’ protective clothing has been found to increase health risks. Research has found that firefighters are exposed to high levels di-(2-ethylhexyl) phthalate (DEHP), a plasticizer and probable human carcinogen, which is added to polyvinyl chloride (PVC) to enhance the flexibility of firefighters’ protective clothing.

Environmental causes of cancer can be modified or prevented with changes in lifestyle choices or choices of type and location of employment. Approximately one-third of cancer cases can be prevented by a change in lifestyle. Cancer cases have depended on how long a person has been exposed to particular environmental factors in addition to the person’s genetic makeup, age, and other factors.

Environmental justice advocates aim to uphold the right of those who work at home to be free from environmental hazards in their domestic environments. Advocates and researchers are informed by the International Agency for Research
Environmental Justice and Cancer

403

on Cancer’s classification of environmental agents into groups of one to three depending whether they are carcinogenic (Group 1), probably carcinogenic (Group 2A), possible carcinogenic (Group 2B), or not classifiable (Group 3).

Occupational pollutants can contribute to cancer incidence. Cancer incidence as a result of occupation-related chemical exposures (occupational cancers) accounts for about 15 to 20 percent of cancer cases in men. Chemicals in products such as paints, dyes, and solvents and some petroleum products also have been linked to occupational cancer incidence. For instance, some phthalates, which are used in cosmetics and some medical devices, are noted to cause sterility in men. A unique set of occupational cancer risks is found in the textile and leather industries. For example, while ancient practices in the leather tanneries in such locations as Fez, Morocco, used natural dyes, more current practices tend to incorporate synthetic dyes. Environmental impact assessments have been made to evaluate the potentially carcinogenic metabolites of these synthetic dyes as well as chemicals that are known to be lethal, most notably Chromium 3.

Radiation can induce cancers such as leukemia and lymphoma, thyroid cancers, skin cancers, some sarcomas, and some lung and breast cancers; radiation can be ionizing or nonionizing. An example of nonionizing radiation is UV rays; exposure to UV rays could be artificial in the form use of sun beds or tanning beds and natural through depletion of the ozone layer. UV rays as a cancer risk factor depend on the amount of exposure (dose). Radiation could be in the form of occupational exposures such as chemicals radiation technologists, uranium miners, and workers in nuclear plants who are exposed in their workplaces; exposures to atomic bombs; and patients treated by radiotherapy or chemotherapy. Additionally, exposure to radon and radon decay products has been found to be responsible for about 10 percent of lung cancer causes. Exposure to very low frequency (VLF) and extremely low frequency (ELF) electromagnetic fields (EMFs), including power lines, transformers, and electric train engines, among others, also has been known to induce cancer. Indeed, recent studies have established an association between long-term use of cellular phones and brain tumors; however, this finding has been contested by other studies. Some X-ray imaging and magnetic resonance imagining (MRI) can also cause certain cancers.

Different environmental exposures are linked to different types of cancers. For instance, exposure to asbestos can lead to lung cancer, while exposure to benzidine has been shown to cause bladder cancer. In fact, in the United States, talcum products for use in the home have since the 1970s been required by law to be asbestos-free; this is based on the relationship between asbestos and certain types of cancer. Asbestos has also been banned in the United Kingdom. Incidence of leukemia was twice as likely in workers who have had both 10 or more years of exposure to formaldehyde and 20 years or more since their first exposure to formaldehyde. In addition, research has linked formaldehyde exposure with cancer of the nasal cavities, nasopharynx, prostate, lung, and pancreas among industrial workers.

Carcinogenic Ingredients in Domestic Products

There is a growing body of research in the area of toxic and carcinogenic ingredients in various products that most persons use on a daily basis. The documentary Plastic Planet (2008), written and directed by Werner Boote, an Austrian filmmaker and grandson of a plastics industry executive, draws attention to the nearly 1,000 scientific studies that have found carcinogenic, toxic, and other problematic causes of various plastics used in industry and consumer goods.

Numerous studies have found certain consumer products (including cosmetics and other health and beauty or personal care products) may be linked to various cancers, most notably breast cancer. The International Agency for Research for Cancer has classified numerous cosmetic ingredients including, but not limited to, ethylene oxide as carcinogenic and mutagenic to humans, with sufficient evidence of carcinogenicity for breast cancer. Of further concern, in the United States, major loopholes in federal law allow the cosmetics industry to put thousands of synthetic chemicals into personal care products, even if those chemicals are linked to cancer, infertility, or birth defects. For example, the U.S. Centers for Disease Control and Prevention reports male reproductive problems have doubled between 1970 and 1993. There is a correlation between reproductive problems and environmental chemicals and toxins.
As untested chemicals have been steadily introduced into the environment, breast cancer incidence has risen dramatically. In one study on teens’ exposures to cosmetic use, conducted by researchers with the Environmental Working Group, which includes researchers in environmental toxicology at Cornell University and in chemistry at Northwestern University, results revealed the presence of 16 chemicals in the bodies of U.S. teenage girls age 14 to 19. The 16 chemicals were from the phthalates, triclosan, musks, and parabens families, all commonly used in cosmetics and body care products. They have been determined as capable of disrupting the hormone system, according to laboratory tests. More biomonitoring research is needed, as is awareness-raising efforts about the environmental and health implications of many cosmetics and personal care products, particularly concerning their use by girls and young women. The European Cancer Registries reports incidence of breast cancer, the most common cancer among women, has increased not only in postmenopausal but also in very young women.

Research on compounds of toxicological concern in household exposures are particularly relevant as persons spend up to 90 percent of their time indoors, often at home, where household environments and household products have not been adequately assessed. More research is needed to inform public health efforts regarding exposure reduction of toxicological compounds. Of further concern is how parents’ exposure to occupational pollutants can increase the risk of cancer in their children. Outdoor pollution in the form of smoke, vehicle exhaust, and indoor pollution all contain chemicals such as polycyclic aromatic hydrocarbons (PAH), biocides, and formaldehyde, which are known to induce cancer. Pesticides and food additives also can cause cancer. Exposure to arsenic oxides and other metals such as lead, hexavalent, nickel, and mercury can induce cancers in the lung, bladder, liver, and kidney, among others.

Increasing collaboration among scientific researchers, community advocates, and activists is emerging. The experiences of patients, survivors of breast cancer, and their family help to inform research findings, for example, concerning breast cancer, for ethnic minority women in industrialized nations. Assessment initiatives, such as the U.S. National-Scale Air Toxics Assessment, have been utilized to evaluate correlations between environmental pollutants that have been linked to breast cancer and to health problems inherent in lower-income, minority communities in industrialized nations. For example, toxicological compounds that have been found to affect breast cancer are in the industrial category of oil combustion and refining. Such compounds from emissions from oil refineries are known to affect the lower-income communities situated within geographic proximity.

The U.S. National Institute of Environmental Health Sciences has established an environmental justice grant program to support community-based participatory research collaboration. Key partners include Communities for a Better Environment and the Silent Spring Institute, whose mission addresses women’s health, particularly breast cancer.

Similar collaborative efforts are emerging in developing nations. For example, l’Institut de Presse et des Sciences de l’Information (IPSI) at l’Université de la Manouba, in Tunisia, l’Institut de Communication et des Sciences de l’Information (ISIC) at the Faculty of Political and Information Sciences of the University of Algiers, and the School of Media and Communication at Bowling Green State University have established a partnership with North African civil society organizations including, but not limited to, le Centre International des Technologies de l’Environnement de Tunis (CITET), the Arid Lands Institute (IRA), in Sousse, Tunisia, le Centre d’Études Maghrébines en Algérie (CEMA), and l’Association pour la Recherche sur le Climat et l’Environnement (ARCE) both located in Oran, Algeria, with consultation by the Ministry of the Environment and Sustainable Development of the Republic of Tunisia. Such collaborative partnerships seek to bring together practitioners to assess environmental concerns and raise awareness among citizens, organizations, and governing bodies with oversight for public health efforts regarding exposure reduction of toxicological compounds in homes and communities.

More effort from collaborative partnerships and biomonitoring experts and activists is needed to assess environmental factors that can influence cancer rates and risks, particularly as they differ by region within nations, and regions of the world. It is important to note that environmental exposures...
alone do not cause cancer; they need to interact with certain gene mutations in the body, lifestyle choices, and proximity to sources of exposure, among other considerations. Such diverse combinations of factors often result in various people who are exposed to the same environmental factors being diagnosed with cancer. Unfortunately, this can make it very challenging to enact litigation against corporations that have been deemed to be emitting toxins into the environment.

Lara Lengel
Catherine Cassara
Bowling Green State University

See Also: Acrylic Rubber and Fibers; Alcohol; Asbestos; Automobiles; Battery Acid; Bicycles; Cell Phones; Chemical Industry; Chlorine; Chloroform; Coal Industry; Cosmetics; Daily Life; DDT; Deodorizers; Detergents; Diesel Exhaust; Dyes and Pigments; Electrical Industry; Electronics; Embalming Fluids; Environmental Tobacco Smoke; Explosives; Flame Retardant; Flavoring Agents; Food Additives; Freon; Glass Industry; Herbicide; Insecticides; Lead; Meat Processing; Nickel Compounds; Nuclear Industry; Paint; Paper Industry; Pesticides; Pollution, Air; Pollution, Water; Smokeless Tobacco; Smoking and Society; Solvents; Stainless Steel; Sunlamps or Sunbeds; Tobacco Smoking; Tobacco-Related Exposures; Toxic Mold; War Gases and Chemicals; Western Diet; Wood Dust; Wood Preserver.

Further Readings

Environmental Tobacco Smoke

The ill effects of smoking on a person’s health are well documented, dating back to 1964 and the first report of the U.S. Surgeon General’s Advisory Committee on Smoking and Health. The toxic and carcinogenic aspects of environmental tobacco smoke (ETS) would not be firmly established until much later. Nevertheless, substantial research has shown that ETS increases the risk of lung cancer, causing the disease in approximately 3,400
Environmental Tobacco Smoke

nonsmokers each year. Subsequent research has linked ETS with lymphoma, leukemia, and brain tumors in children and cancers of the larynx, pharynx, nasal sinuses, brain, bladder, rectum, stomach, and breast in adults who do not smoke.

ETS refers to exposure to tobacco smoke that originates from someone else smoking. Breathing in ETS is also called passive smoking, secondhand smoke, and involuntary smoking. According to the American Cancer Society, there are two sources of ETS: sidestream smoke coming from cigarette, pipe, or cigar smoke and mainstream smoke exhaled from the smoker.

Sidestream is considered more dangerous to people’s health because it has higher levels of carcinogens and is more toxic than mainstream smoke. Scientists have shown that sidestream smoke has smaller particles that enter more easily into the lung and cells of those exposed to it. Nonsmokers who are exposed to ETS inhale nicotine and toxic chemicals that reach higher levels the more they are exposed to ETS in terms of amount and duration. Overall, ETS contains more than 7,000 chemical compounds, 250 of which are known to adversely affect human health and 69 are known to be carcinogens.

Since the first 1964 surgeon general’s report on smoking, more than 30 subsequent reports from the surgeon general’s office have addressed in some manner the harmful effects of ETS. The surgeon general, who is the top public health official in the United States, first addressed the issue in a 1972. The report noted that tobacco smoke in the air often caused discomfort in nonsmokers and could possibly harm people with chronic heart or lung disease. Another report in 1975 also noted the annoyance smoking caused to some nonsmokers and included data that elevated nicotine levels in nonsmokers could be the cause of atherosclerotic disease.

Scientists and public health officials were not the only people raising the alarm about secondhand smoke. In the 1970s, nonsmokers began complaining more and more that they suffered headaches and found themselves coughing and gagging when exposed to ETS. Furthermore, people with respiratory illnesses began pointing out that they could not enter certain places of business because of ETS, from bars to trains and airplanes. Employees started to complain about workplace smoking as well. These complaints eventually led to the formation of community groups targeting public smoking, such as the Group Against Smoking Pollution (GASP) in California.

The U.S. surgeon general’s office continued to put out reports that contained warnings about ETS. A 1979 report recommended further studies about the issue due to the limited amount of scientific data available on ETS. Another report in 1982 discussed three studies that had noted a potential link between ETS and lung cancer in nonsmokers.

The first major report in the United States that ETS can increase definitively the risk of developing lung cancer in nonsmokers came in 1986, when the U.S. surgeon general published the first report dedicated entirely to the health effects of secondhand smoke, “The Health Consequences of Involuntary Smoking.” Among the findings reported was conclusive evidence that secondhand smoke can cause lung cancer in nonsmokers. Furthermore, it noted that it might not be enough to protect smokers merely by separating them from nonsmokers in the same room or area. That same year, the International Agency for Research on Cancer, part of the World Health Organization, noted that data was connecting ETS to increased risk of cancer in some nonsmokers, and the National Research Council estimated that a nonsmoker married to a smoker increases his or her risk of getting lung cancer by 25 percent.

In 1992, the U.S. Environmental Protection Agency (EPA) released its report on secondhand smoke, titled “The Respiratory Health Effects of Passive Smoking: Lung Cancer and Other Disorders.” The report concluded that ETS exposure in the United States was a serious public health problem that caused approximately 3,000 lung cancer deaths each year in U.S. nonsmokers. The report also cited ETS as being especially dangerous for children.

In 2005, the EPA released a report that updated scientific findings concerning ETS. The report noted that, among other health problems, ETS played a role in approximately 9,000 deaths in the United States each year due to lung cancer and other respiratory disorders. The following year, the 2006 surgeon general’s report, “Health Consequences of Involuntary Exposure to Tobacco Smoke,” definitively stated that the scientific community had reached a consensus on the dangers of ETS.

The 2006 surgeon general’s report stated that ETS has far-reaching health implications for nonsmokers. It noted conclusive biologic, epidemiologic,
behavioral, and pharmacologic evidence of its harmful effects, which include not only cancer but also coronary and lung disease and premature death in adults. The report also noted that ETS was likely associated with other cancers in adults and children as well as diseases such as chronic obstructive pulmonary disease (COPD) and asthma. The report concluded that there were no acceptable levels of exposure to ETS. The 2014 surgeon's report restated that secondhand smoke has been causally linked to cancer and other diseases.

**How ETS Causes Cancer**

Scientists have determined that, among the 7,000 chemicals that occur in secondhand tobacco smoke, approximately 250 are known to be harmful to human health. In addition, 69 of these chemicals are known to cause cancer, including arsenic, benzene, beryllium (a toxic metal), 1,3-butadiene (a gas), cadmium, chromium (a metallic element), ethylene oxide, nickel (a metallic element), polonium-210 (a radioactive chemical element), and vinyl chloride. Scientists are also concerned about the potential of other chemicals in the smoke to cause cancer, including formaldehyde, Benzo[α]pyrene, and toluene.

The various chemicals in ETS can adversely affect nonsmokers’ immune systems, weakening them to the point that they have difficulty fending off the spread of cancer cells. Some of these chemicals damage a nonsmoker’s DNA, which controls normal cell growth and function. Damaged DNA can lead to uncontrolled cell growth, resulting in the creation of a cancerous tumor.

Other biological pathways also contribute to carcinogenesis due to ETS. For example, chemical compounds called nitrosamines are specific to nicotine and tobacco and bind to various cellular receptors in the body, leading to activation of biologic pathways that can lead to cytogenetic changes, resulting in cell proliferation and transformation. Scientists also have produced evidence that even noncarcinogenic compounds in ETS enhance tobacco smoke’s carcinogenicity via the stimulation of cell proliferation.

**Tobacco Companies Respond**

The tobacco industry is a big business in the United States, with the U.S. market bringing in approximately $66 billion in 2013. The tobacco industry has sponsored various studies questioning the negative health effects of ETS. For example, a 2003 study sponsored by the industry and published in the *British Medical Journal* reported that data proving the harmful health effects of passive smoking were greatly exaggerated. The article also noted that many studies about ETS were not statistically significant to prove a definitive relationship between smoking and lung cancer. The American Cancer Institute responded by objecting that the study had numerous flaws in how it was conducted and data analyzed.

The industry also started a public relations campaign in the early 1990s to dispute the scientific evidence that ETS was harmful. The industry campaigns also have focused on issues such as personal rights and freedoms. As a part of its campaign efforts, the tobacco industry funded various think tanks, such as the Cato Institute, which criticized growing efforts in policy to restrict exposure to secondhand smoke. As early as 1994, the EPA...
stated that attacks on the scientific research were unfounded and that secondhand smoke was a preventable health risk. The EPA noted that its Science Advisory Board, made up of independent scientific experts, had reputed virtually every argument against ETS increasing the risk of lung cancer in nonsmokers.

Nevertheless, some rigorously conducted studies have questioned just how serious ETS is in causing lung cancer in nonsmokers. A 2013 study conducted at Stanford University and published in peer-reviewed *Journal of the National Cancer Institute* confirmed a strong link between lung cancer and people who smoke but found no statistically significant association between lung cancer and secondhand smoke.

Tracking more than 76,000 women for more than a decade, the Stanford study found that the only statistically significant relationship between ETS and lung cancer in nonsmokers occurred in women who had lived with a smoker for 30 years or more. Nevertheless, the researchers have noted that it was too early to conclude that passive smoking had absolutely no role in causing lung cancer in some nonsmokers. Furthermore, ETS also has other adverse effects on the lungs and circulatory system.

**ETS Laws and Society**

Substantial efforts to limit ETS exposure has taken place since the 1980s, including various laws on the state and local levels to prohibit smoking in public and workplaces. Employers and businesses also have taken voluntary actions to limit or eliminate exposure to ETS. On the federal level, smoking restrictions laws and regulations have been limited. They largely target airplanes, federally owned buildings and facilities, and facilities that provide services to children and receive federal funds.

The most comprehensive laws concerning ETS occur at the local level, from the state to city and town ordinances and laws. Initially, city and town governments played the most important role in restricting smoking in public as they responded to growing antismoking sentiments among the local citizens. The first state law to establish nonsmoking restrictions took place in 1993, when the Vermont state government enacted a law outlawing smoking in restaurants. Nevertheless, nonsmoking efforts still are strongest at the local level, where as of July 2014, there were 4,036 municipalities with laws restricting where people can smoke. On the international level, more than 90 countries have laws and ordinances restricting smoking in public and work environments.

David Petechuk

*Independent Scholar*

See Also: Passive Smoking; Smokeless Tobacco; Tobacco Smoking.

**Further Readings**


Peres, J. “No Clear Link Between Passive Smoking and Lung Cancer.” *Journal of the National Cancer Institute* (December 6, 2013).


---

**Ependymoma, Childhood**

Ependymoma comprises roughly 5 percent of brain tumors occurring in children and is often diagnosed at age 4 or younger. For a couple of decades, childhood ependymoma has been treated with the
total removal or gross resection of the affected brain tissue, followed by irradiation. Approximately 75 percent of cases that underwent this treatment approach showed a three-year disease-free survival rate. Despite the promising outcomes in terms of cancer recurrence in children, this technique has also resulted in other treatment-related outcomes, including damage to various epithelial and vascular tissues as well as disorders involving the endocrine system. However, the most significant impact of irradiation is on cognitive skills, such as lower intelligence quotients (IQs) and poor academic performance.

Several studies have thus been performed in order to identify specific approaches in reducing these treatment-related effects involving cognitive functions in pediatric patients. Previous reports have shown that children who underwent treatment for ependymoma such as surgery, irradiation, and chemotherapy are at an elevated risk for late-onset cognitive problems, including a general decline in intellectual capabilities and academic performance. These effects also could be further carried forward in the adult years, often resulting in poorer quality of life and difficulty in performing daily tasks without the assistance of a family member or caregiver.

The high incidence of cognitive side effects among pediatric ependymoma patients has thus prompted clinicians to conduct investigations that would identify the specific causative factors that were responsible for lower IQ scores and decline in functional abilities. These extensive studies have thus far identified various factors that influence the degree of cognitive decline among pediatric ependymoma patients. The information gathered from these studies may also help in designing personalized treatment schemes for patients.

A clinical study conducted by Kelli Netson and colleagues showed that one of the main causative factors responsible for cognitive decline after ependymoma treatment is the radiation dose applied to the brain. Their report described an inverse correlation between the radiation dose and the level of cognitive decline. Thus, a higher radiation dose applied to a pediatric ependymoma patient would result in a lower IQ postirradiation. However, pediatric ependymoma patients who received focal irradiation using modulated intensities showed a higher chance of maintaining their IQ scores compared to those who underwent irradiation of the entire craniospinal region. These patients also were spared from deterioration in verbal learning as well as in academic skills such as mathematics and spelling, thus suggesting that this specific treatment approach reduced the development of cognitive side effects in pediatric ependymoma patients.

In an attempt to determine the progress of cognitive skills in children who underwent focal irradiation using modulated intensities, the research team of Netson examined a total of 123 pediatric patients diagnosed with intracranial ependymoma. The mean age of the children at irradiation was approximately 4.6 years. A series of neurocognitive assessments such as age-appropriate measurements of IQ as well as Vineland Adaptive Behavior Scales (VABS) were employed at baseline (prior to irradiation), six months posttreatment, and annually for the next five years. The VABS tool allows the assessment of adaptive behaviors among children, including communication, socialization, skills required in daily living, and motor functions. These efforts generated approximately 579 neurocognitive assessments that were included in the analysis. The results of the study showed that the IQ and VABS scores of the pediatric patients at baseline and during the next five years were generally stable and within the normal range, except for the VABS score for communication, which significantly deteriorated. The results of their study indicated that focal irradiation using modulated intensities spared the children from a massive decline in IQ and cognitive skills, except for the ability to communicate.

In another study led by Karen Kuhlthau, the quality of life of 142 children diagnosed with brain tumors such as ependymoma, medulloblastoma, and glioma were assessed after treatment with proton radiation. The use of proton radiotherapy was based on earlier observations that this procedure utilizes a significantly lower amount of dose than the classical technique of using external-beam photons. This novel technique may thus serve as an alternative treatment scheme for brain tumors that would result in lower levels of toxicity and minimal reduction in cognitive functions. To determine the quality of life of the pediatric patients after proton radiotherapy, a self-report assessment was conducted. In cases wherein the pediatric patient was unable to respond to the questions in the assessment tool, the parents served as proxy in answering each item on the questionnaire. The results of
this investigation showed that proton radiotherapy resulted in a better quality of life compared to patients who underwent global craniospinal irradiation. Furthermore, the quality of life of pediatric patients after irradiation were strongly influenced by the type of brain tumor and the intensity of the proton treatment. Thus, pediatric patients with medulloblastoma experienced a worse quality of life after proton radiotherapy compared to those with ependymoma.

A research team led by Katja von Hoff also conducted an assessment of the quality of life of pediatric ependymoma patients who underwent surgery and irradiation of the posterior fossa. A total of 23 pediatric patients with an age range of 0.3 to 14 years at ependymoma diagnosis were subjected to neuropsychological assessment after irradiation using a dose of 54 Gy. The assessment of quality of life was conducted for an average of 4.5 years, with a monitoring range of one to 15.5 years after radiation treatment. The results of the study showed that all the pediatric patients showed difficulties in cognitive functions such as reading, memory, and attention span. However, the IQ levels of the pediatric patients remained the same. The study also identified a correlation between the detection of cerebellar deficits and a deterioration of IQ after irradiation therapy. Pediatric ependymoma patients who underwent surgery and chemotherapy before the age of four also showed a worse deterioration in IQ after treatment. Furthermore, pediatric ependymoma patients who did not develop a hydrocephalus prior to radiation treatment were more likely to undergo better cognitive functions after radiotherapy.

Rhea U. Vallente
PreventionGenetics, LLC

See Also: American Brain Tumor Association; Brain Tumor, Childhood.

Further Readings

Eritrea

Eritrea is a country located on the Horn of Africa on the eastern part of the African continent. It is bordered by the Red Sea, Ethiopia, Sudan, and Djibouti. Eritrea has a population of 6 million and is ethnically diverse. Like many African countries, cancer rates go underreported in Eritrea. Decades of war with neighboring Ethiopia depleted health care facilities and services during the second half of the 20th century. Subsequently, the Eritrean government has invested heavily in a primary health care infrastructure throughout the country, although specialized cancer treatment facilities remain limited.

Beginning in the 1st or 2nd centuries c.e., Eritrea and its neighbor Ethiopia both belonged to the kingdom of Aksum. The Eritrean people adopted the Christian religion during this period. In the medieval period, current-day Eritrea was divided into the Medri Bahri kingdom and the Hamasien republic. From 1890 to 1941, Eritrea was an Italian colony. The Federation of Ethiopia and Eritrea was formed in 1947, following a period of British occupation that began during World War II. The federation dissolved shortly thereafter, when Ethiopia annexed Eritrea, beginning several decades of war. Eritrea became an independent nation in 1991, although border disputes with Ethiopia are ongoing. Long-term military conflicts devastated the Eritrean economy and national infrastructure. Poverty is widespread in Eritrea, where the majority of the population is engaged in agricultural work, fishing, or mining.

European missionaries and Italian colonizers introduced modern health care services in Eritrea at the end of the 19th century. Italians established the first Eritrean hospital in Asmara during this period.
Prior to the creation of the Federation of Ethiopia and Eritrea, health services in the region were relatively advanced for the time. The Eritrean War of Independence effectively destroyed the health care infrastructure as well as the economy and the environment. Following independence in 1991, the Eritrean Ministry of Health (MOH) has worked to rebuild medical facilities, train health care professionals, and restore drug supplies and medical equipment.

The majority of health care facilities is owned by the Eritrean government and are available to everyone in the nation. The MOH oversees 23 hospitals in Eritrea as well as 52 health centers and 225 local health stations. Since 1991, the number of Eritrean hospitals has increased by 50 percent. The number of health centers and health stations has increased by 100 percent since independence. In addition, there are a small number of public–private partnership facilities available. Access to health care facilities is better in the central and south highlands of Eritrea than in the lowlands, constituting a geographical disparity. While Eritrean health care facilities are widespread through the country, most are devoted to primary care and basic health services.

In Eritrea, as in many African countries, malnutrition, infant mortality, and infectious diseases receive the most attention and funding support from governments and nongovernmental organizations. Although rates of cancer incidence in Eritrea are similar to those in more developed countries, these tend to go underreported and undertreated in Africa. Infectious diseases like human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) and malaria receive more support for treatment and prevention. This disparity can result not only in a lack of services for cancer patients but also can lead indirectly to higher rates of cancer incidence. For example, exposure to dichlorodiphenyltrichloroethane (DDT) and other pesticides used to control the mosquito populations that spread malaria in Eritrea can increase the risk of leukemia, pancreatic cancer, and breast cancer.

In Eritrean men, prostate and colorectal cancers are responsible for the majority of cancer deaths, followed by non-Hodgkin's lymphoma. Each year approximately 125 men are diagnosed with prostate cancer in Eritrea, although many cases go undiagnosed.

Breast cancer constitutes the highest rate of cancer mortality for women in Eritrea, followed by cervical cancer. Studies have shown that the majority of Eritrean women who present with breast cancer symptoms are under 50 years of age. Women do not tend to present until reaching the later stages of the disease, and there are no standard protocols for managing and treating breast cancer in Eritrea. There is no human papillomavirus (HPV) vaccine program in Eritrea. The ICO Information Centre on HPV and Cancer estimates that, every year, 265 Eritrean women are diagnosed with cervical cancer, and 189 women die of the disease. There is a lack of reliable information on cancer incidence, treatment, and mortality rates in Eritrea due to the absence of a cancer registry and other resources.

Many women are skeptical about Western medicine and choose traditional methods of healing instead. These traditional Eritrean health care practices include herbal remedies as well as spiritual healing techniques that involve the cutting and burning of the body. Although traditional medical treatments tend to have inconsistent results and can sometimes be counterproductive, they continue to be widely practiced in Eritrea.

Jessica A. Hutchins
Independent Scholar

See Also: Breast Cancer; Cervical Cancer; DDT; HPV Vaccination; Lymphoma, Non-Hodgkin’s, Adult; Pesticides; Poverty; Prostate Cancer.

Further Readings
Esophageal Cancer

Esophageal cancer is a malignancy in the muscular tube that connects the throat to the stomach. There are two common forms (histologic subtypes) of esophageal cancers; these include squamous cell carcinoma and adenocarcinoma. Squamous cell carcinoma forms in the squamous cells of the esophagus and mainly occurs in the upper two-thirds of the esophagus. Adenocarcinoma forms in the glandular cells of the esophagus and usually occurs in the lower third of the esophagus near the stomach. These histologic subtypes have differing global trends and their own sets of risk factors. However, signs and symptoms, diagnosis, and conventional treatment options are similar and are dependent on the stage of cancer at diagnosis rather than the histologic subtype.

Global Trends and Risk Factors

In 2012, Globocan estimates that esophageal cancer is the eighth-most common cancer worldwide and the sixth-most common cause of death from cancer. Its incidence varies greatly globally, with the highest rates found in eastern Asia, southern Africa, and eastern Africa and the lowest rates found in Central America and western Africa, consistently affecting males at a higher rate than females. The occurrence of esophageal cancer is uncommon before the age of 40, and most esophageal cancers that occur in the world are squamous cell carcinoma.

A region of the world with some of the highest rates of esophageal squamous cell carcinoma is known as the esophageal cancer belt. This geographical area spans eastward from Iran through Turkmenistan, northern Afghanistan, Uzbekistan, and Kazakhstan into northern China and Mongolia and extends southwest to Quetta, Balochistan, located in Pakistan. Within this high-risk region, males and females are affected at similar rates, and risk factors reported for esophageal squamous cell carcinoma are different from those reported in North America. Some of these risk factors include: poor nutritional intake, consumption of dietary carcinogens, and chronic irritation and inflammation of the esophagus (e.g., the result of consuming extremely hot mate tea, use of opium or opium dross, consumption of silica-contaminated flour, and exposure to polycyclic aromatic hydrocarbons).

Studies conducted within the United States show higher incidence of esophageal squamous cell carcinoma among black people and those of low socioeconomic status. These racial and social disparities likely act as surrogates for other underlying and documented risk factors for esophageal squamous cell carcinoma, such as those relating to lifestyle (e.g., alcohol and tobacco use) and environmental factors and workplace hazards (e.g., exposure to air pollutants via certain chemicals and dusts).

Esophageal cancer trends within North America and parts of Europe have changed over the past few decades. The incidence of adenocarcinoma has surpassed the once-higher incidence of squamous cell carcinoma. In North America, the United States and Canada have reported some of the highest rates of esophageal adenocarcinoma. The most common risk factors for esophageal adenocarcinoma include: high body mass index (obesity), severe and frequent gastroesophageal reflux disease (GERD, the backflow of stomach acid into the esophagus), esophagitis (an inflammation of the esophagus), an increase in the use of medication that contributes to reduced sphincter pressure, and Barrett’s esophagus (a metaplastic change of the lining of the esophagus and a precursor for esophageal adenocarcinoma).

There are other important documented risk factors for esophageal cancer that are also worth noting. These include but are not limited to: family history, poor oral health, chronic lye strictures, achalasia (an esophageal motility disorder), tylosis (a genetic disorder), Plummer–Vinson syndrome (a complex vitamin deficiency), caustic injury to the esophagus, exposure to radiation, history of gastric surgery, genetics, environmental and occupational factors (e.g., the use of certain dry-cleaning agents,
with workers exposed to combustion products) as well as various esophageal disorders and conditions and certain diseases and viruses. Some of these risk factors are applicable to only one histologic subtype, while others are linked to both.

**Signs and Symptoms**

Some of the most common signs and symptoms of esophageal cancer include: dysphagia (difficulty swallowing foods or liquids), significant weight loss, hoarseness and cough, indigestion and heartburn, and chest pain. When esophageal cancer is at a more-advanced stage, odynophagia (painful swallowing) and regurgitation are often the result of a large tumor obstructing the esophagus. Esophageal cancer is associated with a poor prognosis and a low five-year survival probability because symptoms are not usually apparent until the disease has progressed to a later stage.

**Diagnosis, Staging, and Treatment**

There are a number of different diagnostic tests that could be performed to detect esophageal cancer. The most common include some combination of: a medical history and physical exam, complete blood count, blood test, barium swallow (a special type of X-ray that outlines the upper gastrointestinal tract when barium is swallowed), endoscopy (the examination of the upper gastrointestinal tract via the use of a lighted, flexible instrument called an endoscope), and biopsy (the removal and examination of a sample of tissue).

Esophageal cancer can be classified from stage 0 (precancerous) to stage IV (invasive and inoperable). Prior to 2010, the TMN (tumor, node, metastases) system, whose rankings within each of these were grouped together, was used to determine the stage of esophageal cancer. In 2010, the American Joint Committee on Cancer refined and made specific changes to how esophageal and esophagogastric junction tumors are staged by pathologists. Esophageal squamous cell carcinoma and adenocarcinoma used to be staged according to the same principles, but this is no longer the case. Some categories within the TMN system have been redefined and extended, and a new category G has been added, which takes into account the grade of the tumor. Now, staging indicates the type of data used to inform the staging (i.e., clinical or pathological data). Also, esophagogastric junction tumors and proximal five centimeters of the stomach are now staged as esophageal adenocarcinoma rather than stomach cancer.

Understanding the stage of disease, alongside an individual’s overall health is important in determining a treatment plan. There are a number of treatment options for esophageal cancer. These range from any combination of surgery, chemotherapy, radiation, endoscopic treatments and procedures (i.e., endoscopic mucosal resection, photodynamic therapy, laser surgery, radiofrequency ablation, electrocoagulation or plasma coagulation, and palliative endoscopic procedures), and clinical trials. These conventional treatment options are often determined by a team of specialists.

**Conclusion**

Esophageal cancer has a poor prognosis given that, by the time symptoms appear, the disease is already at an advanced stage. Its global trends differ according to histological subtype as do its risk factors. The risk factors associated with developing esophageal squamous cell carcinoma vary depending on geographical location. Consideration to wider social and environmental dimensions can help shed light on why these differences exist. There are several diagnostic tests used to identify esophageal cancer. Once staged by a pathologist, treatment options are targeted as a means of palliative (to alleviate symptoms relating to the disease) or curative (to eliminate disease) treatment of disease.

Ann Del Bianco
York University

**See Also:** Alcohol; Chemotherapy; Diesel Exhaust; Diet and Nutrition; Obesity; Pollution, Air; Radiation; Radiation Therapy; Solvents; Stomach (Gastric) Cancer; Tobacco Smoking.

**Further Readings**


Esophageal Cancer, Childhood

Esophageal cancer is one of the 10 most common cancers worldwide, although it occurs at a less frequent incidence in the United States (3.2 per 100,000 in persons younger than 80 years of age). The two principal subtypes of esophageal cancer are esophageal squamous cell carcinoma (ESCC) and esophageal adenocarcinoma (EAC). In adults, these subtypes differ markedly in tumor development, risk factors, and outcomes. Alcohol and smoking, particularly when used concomitantly, are the greatest risk factors for ESCC, which is more prevalent in developing countries. EAC is associated with chronic reflux disease and intestinal metaplasia (Barrett’s Esophagus [BE]) and is more prevalent in developed countries such as the United States. Increased age (greater than 60) and male sex are risk factors for both subtypes. Because symptoms often do not present until the cancer has progressed to an advanced stage, both subtypes have a poor prognosis (10–25 percent five-year survival rates). Esophageal cancer in both adults and children most often presents as dysphagia and weight loss, although other symptoms may include hoarseness, voice changes, aspiration, nausea, and vomiting. Surgery is generally indicated if the cancer is resectable, and chemotherapy is often included as adjuvant therapy before or after surgery. If the tumor is not indicated, then platinum-based chemotherapy is the treatment of choice.

The carcinogenesis of both ESCC and EAC are related to the development of dysplastic and metaplastic lesions due to chronic irritation over a long period of time. Due to the chronic nature of the events that eventually lead to esophageal cancer, it is rarely diagnosed in childhood. Most of the literature on esophageal cancer in childhood is limited to case reports. Nonetheless, it is clear that esophageal cancer in childhood has a similar poor prognosis when compared to esophageal cancer in adults. In a study reviewing 10 case reports of children diagnosed with ESCC, two died within 14 months of diagnosis, four were alive after limited follow-up (less than 14 months), and four were lost to follow-up. The same study reviewed 14 case reports of children with EAC and, of the 14, only three were alive after case report follow-up (at 11, 12, and 36 months). Of the six cases of AEC that reported time from diagnosis until death, the average time was less than eight months. Research evaluating the efficacy of different treatment modalities in treating childhood esophageal cancer is almost nonexistent due to the rare nature of the cancer, a major obstacle in improving outcomes in pediatric patients with esophageal carcinoma.

Pediatric Risk Factors

Although there is a limited amount of cases of esophageal cancer available for study, there is a much greater population of pediatric patients with well-known risk factors and precancerous lesions that predispose patients to esophageal cancer at younger ages. This population provides researchers with a means of studying the progression of esophageal cancer in childhood and physicians with the opportunity to prevent cancer in high-risk patients. In a literature review of nine pediatric patients with esophageal carcinoma, seven of the patients had coexisting BE, and the other two’s BE statuses were unknown, although they had factors predisposing them to BE such as gastroesophageal reflux disease (GERD) and hiatal hernia. The prevalence of BE increases with the severity and chronicity of GERD in pediatric patients.

There are a number of conditions that predispose pediatric patients to GERD. These include neurologic impairment, congenital esophageal atresia, cystic fibrosis, family history, congenital syndromes,
obesity, and inflammatory disorders. In a study of children with chronic GERD, intestinal metaplasia of the esophagus was present in 10 percent of children, much higher than the baseline rate for children without GERD. Hiatal hernia is also a significant independent predictor of BE in children. In a study of institutionalized children, GERD was found to be much more frequent and severe in children with scoliosis, cerebral palsy, or a very low IQ. Of that subset, 18 percent of patients who underwent endoscopy were diagnosed with BE. Another subset of children at a higher risk of developing BE are those who suffered from congenital esophageal atresia (EA). A study that followed patients with EA for 36 years revealed that 11 percent of patients developed BE. Cystic fibrosis patients have also been shown to have higher incidences of GERD and BE. Obesity has also been implicated in the development of GERD in both adults and children. Moderately and extremely obese children are more likely to develop GERD than children with normal weight. Although there has been no direct genetic cause identified in GERD or BE, there are many studies that suggest familial clustering of hiatal hernia, GERD, BE, and esophageal adenocarcinoma incidence. Therefore, an unidentified genetic link may exist to the predisposition of esophageal cancer at a younger age.

Conclusion
Esophageal cancer in childhood is a very rare disease, affecting less than two in every million children. Because of its rarity, there are no ongoing clinical trials, and most of the literature only exists as case files. This makes it nearly impossible for pediatric oncologists to develop novel therapies tailored specifically to the treatment of esophageal cancer in children. There must be an increased collaborative effort between both pediatric and adult oncologists and oncologists on an international level to maximize the efficacy of treatment given the limited exposure to the disease. Increased physician awareness of esophageal cancer, GERD, and BE in children and the specific conditions that predispose children to those diseases are important for both prevention and early detection.

Krishna Subhas Vyas
Kelsey Snapp
University of Kentucky College of Medicine

See Also: Childhood Cancers; Esophageal Cancer; Genetics; Obesity.

Further Readings

Estrogen, Steroidal

Estrogen is a female sex hormone that plays an important role in menstrual and reproductive cycles. Natural estrogens are steroidal hormones, while some synthetic ones are nonsteroidal. This hormone is synthesized in all vertebrates as well as some insects. Their presence in both vertebrates and insects suggests that estrogenic sex hormones have an ancient evolutionary history. Estrogens are used as part of some oral contraceptives, in estrogen replacement therapy for postmenopausal women, and in hormone replacement therapy for transexual women. Estrogen also readily diffuses across the cell membrane as do all other steroidal hormones. Once inside the cell, they bind to and activate estrogen receptors (ERs), which in turn modulate the expression of many genes.

The three major naturally occurring estrogens in women are estrone, estradiol, and estriol. Estradiol is the predominant estrogen during reproductive years both in terms of serum level as well as in terms of estrogenic activity. During menopause, estrone is the predominant circulating estrogen, and during pregnancy, estriol is predominant in terms of serum level. Estradiol is the most important estrogen in nonpregnant females who are between the menarche and menopause stages of life. In females, estrogens are produced primarily by the ovaries and, during pregnancy, by the
placenta. Follicle-stimulating hormones stimulate the ovarian production of estrogens by the granulosa cells of the ovarian follicles and corpora lutea. Some estrogens are produced in smaller amounts by other tissues such as the liver, adrenal glands, and the breasts. These secondary sources of estrogens are especially important in postmenopausal women.

The actions of estrogen are mediated by the ER, a nuclear protein that binds to deoxyribonucleic acid and controls gene expression. Estrogens are present in both men and women, and they are usually present at higher levels in women of reproductive age. They promote the development of female secondary sexual characteristics, such as breasts, and are also involved in the thickening of the endometrium and other aspects of regulating the menstrual cycle. There are several other structural changes induced by estrogen, such as to accelerate metabolism, increase fat stores, stimulate endometrial growth, increase uterine growth, increase vaginal lubrication, thicken the vaginal wall, reduce bone resorption, and increase bone formation.

Scientific studies have found that estrogen is a potent growth stimulus in its target organs such as the uterus, vagina, and some ER-positive breast cancers. However, estrogen is also able to control menopausal symptoms and maintain bone density in postmenopausal women. Until recently, there was also believed to be a link between estrogen and the prevention of cardiovascular disease. For these reasons, hormone therapy (HT) with orally active estrogen and progesterone has been used routinely for more than 50 years to maintain physiologic homeostasis after menopause. Many research studies have found that HT increases the risk of developing breast cancer. Combination estrogen plus progestin significantly increases breast cancer incidence and death—based on data from the Women’s Health Initiative, a randomized, controlled trial. This evidence together with other studies led the International Agency for Research on Cancer (IARC) to classify combination estrogen plus progestin as a breast carcinogen. Evidence strongly indicates that higher circulating levels of endogenous sex hormones are associated with increased breast cancer risk among postmenopausal women.

A meta-analysis of nine prospective studies observed a twofold increase in breast cancer risk in women with estradiol levels in the highest, relative to the lowest, quintile, with similar associations noted for estrone, estrone sulfate, and testosterone. The risk of breast cancer associated with estrogen and progesterone therapy is greatest for postmenopausal women who have the lowest circulating estradiol and estrone levels. Thus, pretreatment determination of estradiol and estrone levels may be helpful in identifying women at particularly elevated risk for breast cancer with combined hormone therapy. P. P. Bao and colleagues proposed after a study of breast cancer in Shanghai that epidemiologic and biologic evidence suggests a pivotal role for estrogen and progesterone in the development of breast cancer. The effects of these hormones are mediated by their respective receptors, ER and
progesterone receptor (PR). ER and PR status are biologic markers considered to be a crucial factor in treatment recommendations. Furthermore, it has been hypothesized that hormone-related risk factors that reflect exposure to estrogen and progesterone may be predominantly associated with breast tumors that express ER and PR but not with tumors that are hormone-receptor negative.

Estrogen is considered to play a significant role in women's mental health. Sudden estrogen withdrawal, fluctuation in estrogen levels, and periods of sustained estrogen at low levels correlate with significant mood lowering. Clinical recovery from postpartum, perimenopause, and postmenopausal depression has been shown to be effective after levels of estrogen were stabilized or restored. According to some recent studies, women suffer less from heart disease due to the vasculo-protective action of estrogen, which helps in preventing atherosclerosis. It also helps in maintaining the delicate balance between fighting infections and protecting arteries from damage, thus lowering the risk of cardiovascular disease and stroke.

There has been increasing concern about the impact of environmental compounds with hormonelike action on human development and reproductive health over the past decades. An alternative but neglected source of hormone action that may be considered in this connection is hormone residues in meat from husbandry animals treated with sex steroid hormones for growth promotion. However, the major source of circulating estrogens among postmenopausal women is from the body's fat cells. Accordingly, being overweight and obesity after menopause are directly related to increased risk for breast cancer and increased risk of dying from breast cancer.

Estrogen has anti-inflammatory properties and helps in mobilization of polymorphonuclear white blood cells or neutrophils. Estrogen is also used in the therapy of vaginal atrophy, hypoestrogenism, amenorrhea, and oligomenorrhea. Estrogen can also be used to suppress lactation after child birth. Researchers have proposed from epidemiological studies that breast cancer characteristics vary among different ethnic groups. Numerous studies have shown that some ethnic groups present with more aggressive disease (higher grade and advanced stage with more ER-negative disease) and worse outcomes when compared with white women. Others have proposed that estrogen contributes to tumors by promoting the proliferation of cells with existing mutations or perhaps by increasing the opportunity for mutations that regulate the growth and differentiation of mammary cells, which may play an important role in the development of breast cancer. Many factors are involved in causing breast cancer. Women with a family history of breast cancer need to be more cautious regarding risks of breast cancer. Estrogen also drives increased risk of endometrial cancer.

In conclusion, estrogen is a sex hormone produced in both men and women but in more significant levels in women. Estrogen plays an important role in menstrual and menopausal cycles. Estrogen promotes the development of female secondary sexual characteristics, such as breasts, and is also involved in the thickening of the endometrial and other aspects of regulating the menstrual cycle. There are several other functions induced by estrogen such as protein synthesis, coagulation, increases in high-density lipoprotein, decreases in low-density lipoprotein, changes in fluid balance, reduction in bowel motility, and support for hormone-sensitive breast cancers.

Estrogen and other hormones are given to postmenopausal women in order to prevent osteoporosis as well as treat the symptoms of menopause, such as hot flashes, vaginal dryness, urinary stress incontinence, chilly sensations, dizziness, fatigue, irritability, and sweating. Long-term use of unopposed estrogen increases risk of endometrial cancer and likely breast cancer. Combination estrogen plus progestin therapy (for women who still have a uterus) increases the risk of breast cancer and death from breast cancer. IARC classifies combination estrogen plus progestin as a breast carcinogen.

Hueiwang Anna Jeng
Vinit K. Jha
Old Dominion University

See Also: Breast Cancer; Diet and Nutrition; Education; Screening.

Further Readings
Bao, P. P., et al. "Association of Hormone-Related Characteristics and Breast Cancer Risk by Estrogen Receptor/Progesterone Receptor Status in the
Ethiopia

Ethiopia is one of Africa’s oldest independent nations and home to more than 84 million people. It is the second-most populous African country (Nigeria is larger) and is expected to become the ninth-most populous country in the world by 2050. There are more than 85 separately categorized ethnic communities, with the Oromo, Amhara, and Tigre being the largest. Ethiopia’s population has traditionally been located in the highlands, with no endemic malaria or other severe vector borne diseases. Internal disruptions, including a civil war lasting three decades and recurrent famine every year during the period of 1958 to 1992 have resulted in epidemics and put a strain on health care. Communicable diseases, which have traditionally been the focus of health care, are on the decline; however, cancer incidence and mortality are expected to double in Africa by 2030.

Ethiopia’s use of modern medicine has a long history, dating back to Emperor Libne Dingel (1508–40). Emperor Menelik II (1889–1913) invited missionaries and diplomats to introduce medicines and provide medical services mainly in the capital Addis Ababa. Emperor Haile Sellassie (1930–74) introduced the country’s first national health services with the creation of the Ministry of Public Health in 1947. Throughout the 1950s, various nongovernmental organizations (NGOs) and the international community helped in developing hospitals and provided essential technical assistance to the Ethiopian government. Because of various interests by the World Health Organization (WHO), UN International Children’s Emergency Fund (UNICEF), and U.S. Agency for International Development (USAID), coordinating programs along Ministry of Health objectives proved difficult.

Community-based health programs were successful, and more were planned, but by 1967, one-third of Ethiopia’s 8,740 hospital beds and all but six of the 65 Ethiopian physicians were in Addis Ababa.

Following the revolution in 1974, the Mengistu Haile Mariam (Derg) period (1974–91) the nation’s first health plan was developed exclusively by Ethiopians. These programs were initially held in high regard but later contributed to the inequitable distribution of health resources to large cities.

Following several decades of war, the Transitional Government of Ethiopia (TGE) gained power in 1991, inheriting damage to 1,221 stations, 108 health centers, 33 hospitals, and several diseases at epidemic rates. The TGE decentralized the Ministry of Health, putting it over issuing policies, setting targets, and monitoring programs. Regional health departments in newly formed states became responsible for planning, implementation, and monitoring their respective health programs. These policies pushed for the extension of health services to pastoralists and other rural populations but not without cultural, political, and systemic challenges.

The Ethiopian government is the country’s main health care provider, with 138 hospitals and 635 health centers. Resources in these facilities are oftentimes lacking, and appropriate care is hard to obtain. The doctor- and nurse-to-population ratio is 1:42,700 and 1:4200, respectively, and their distribution throughout the country is unequal. Access to radiotherapy or chemotherapy is also limited as
Ethiopia only has only two cobalt units. A comprehensive cancer registration is yet to be completed in Ethiopia, so statistics on the country's cancer burden vary depending on the source. Clinical records from Tikur Anbessa (the Black Lion Hospital) Radiotherapy Center estimate that there are 120,500 new cancer cases per year, although Globocan estimates are much lower, at 51,000 per year and a 41,600 mortality rate per year. The prevalence from 2003 to 2008 was 224.2 per 100,000, and less than 1 percent of patients receive specialist treatment.

In 1987, biopsies of 1,154 southern Ethiopia patients were outlined. Among men, hepatic carcinoma, lymphomas, and superficial malignancies were the most common. Among women, cervical, breast, and ovarian cancers predominated. Hodgkin's disease and Burkitt's lymphoma were most common among childhood lymphomas, whereas non-Hodgkin's lymphomas of other types were found in adults. Cancer of the stomach was the second-most common internal malignancy among both men and women. Recently, the government reported that the most common types of cancer seen in hospitals for children are leukemia, lymphoma, retinoblastoma, Wilms's tumor, and bone and soft tissue sarcomas.

The most common cancers occurring in adults include breast cancer, cervical cancer, head and neck cancer, esophageal cancer, sarcoma, colorectal cancer, liver cancer, non-Hodgkin's lymphoma, and skin cancer. Both studies note that inaccessible cancer such as liver, gastric, and pancreatic are less likely to be diagnosed because of nonspecific presentation and hospitals' lack of necessary imaging technologies. Late presentations, limited resources, low awareness of symptoms, lengthy referral processes, and traditional beliefs contribute to Ethiopia's having a high mortality rate of cancer.

Tikur Anbessa hospital in Addis Ababa has 600 beds, of which 18 are for cancer treatment. There are 201 physicians at the hospital, with only four medical oncologists, two surgical, and one pediatric. There also are two hematologists, four radiotherapists, and three palliative pain specialists. Tikur Anbessa allocates only 26 of their 627 nurses to oncology and has the nation's only computed tomography (CT) scanner and magnetic resonance imaging (MRI). In 2010, the hospital saw more than 2,000 adults and more than 200 children with cancer, providing treatment with anticancer drugs, surgery, and radiotherapy. Clinical guidelines for cancer treatment have been developed at Tikur Anbessa and distributed to other university hospitals.

Hospice Ethiopia in Addis Ababa is the first professional palliative care unit in Ethiopia, founded in 2003 by Sister Tsigerada Yiswafossen in a room in her home with the help of 20 volunteers. Volunteers were trained by the local Community Health Bureau. African partners, such as Uganda's Hospice Africa, have been supportive and aided in the organization's growth. The most common sources for referrals are from Black Lion University Hospital and St. Paul's Millennium Hospital; however, referrals also come from private clinics, health centers, volunteer organizations, and charities, along with self-referrals by patients and their families.

In 2005, Ethiopia partnered with AstraZeneca and successfully developed a program to improve the support infrastructure for the management of patients with breast cancer in Tikur Anbessa. With limited investment, this program showed considerable improvement in low-resource environments. The program has provided tamoxifen freely to staff and patients to promote adherence to a well-defined protocol of care, continuous audit of patients, and cross-departmental patient management groups, as well as other methods.

Information and communications technologies and applications, including the development of specialized content, have a low cost and can be an important source of international support. Health research directly relevant to Ethiopia and cancer may be unrepresented as research conducted locally may be published in developing country journals and absent in literature searches. Language is another barrier as most of the literature and materials are in English.

An example of a successful tool and program is HealthNet, which is a knowledge network created to assist Ethiopia and several other African nations with the potential to provide health data collection and information resources through the use of personal digital assistants.

Malik Muhammad
Ashland Thompson
Synthesis Behavioral Medicine PLLC
Christopher Edwards
Duke University Medical Center
Europa Donna, the European Breast Cancer Coalition

The European Breast Cancer Coalition is an independent, nonprofit organization whose members are affiliated with groups from countries throughout Europe. The coalition works to raise awareness of breast cancer and to mobilize the support of European women in pressing for improved breast cancer education, appropriate screening, optimal treatment and care, and increased funding for research. Europa Donna represents the interests of European women regarding breast cancer to local and national authorities as well as to institutions of the European Union (EU). Europa Donna was founded in 1994 and now has 46 fora (national country organizations) across Europe.

Europa Donna Goals

- To promote the dissemination and exchange of factual, up-to-date information on breast cancer throughout Europe
- To promote breast awareness
- To emphasise the need for appropriate screening and early detection
- To campaign for the provision of optimum treatment
- To ensure provision of quality supportive care throughout and after treatment
- To advocate appropriate training for health professionals
- To acknowledge good practice and promote its development
- To demand regular quality assessment of medical equipment
- To ensure that all women understand fully any proposed treatment options, including entry into clinical trials and their right to a second opinion
- To promote the advancement of breast cancer research

As Europe’s breast cancer advocacy organization, Europa Donna has identified seven main priorities for its European breast cancer advocacy work. These are: establishing population-based mammography screening programs in all countries set up according to the EU guidelines for quality assurance in breast cancer screening and diagnosis, establishing specialist breast units in all countries set up according to these EU guidelines, ensuring an appropriate EU-wide accreditation program is developed to ensure quality standards across all countries for breast services, developing national breast cancer registries, and furthering breast cancer research, breast cancer prevention, and survivorship.

The coalition consists of a 9-person board elected from among Europa Donna’s 46-member countries. The head office of the coalition is located in Milan, Italy, and is responsible for carrying out coalition projects in the areas of information, education, and public affairs.

Europa Donna provides information that is evidenced-based in various publications, newsletters, Web sites, and social networking sites. In 2006, the European guidelines for quality assurance in breast cancer screening and diagnosis were published. This document forms the basis for much of our advocacy work as it outlines the breast cancer services that all women should have a right to receive. Europa Donna has published a short guide to these guidelines to enable women
and the lay public to understand the main points contained in this scientific document. These can be downloaded from www.europadonna.org and have been translated into 17 languages.

Breast Health Day is Europa Donna’s prevention program held annually on October 15; it provides information to women and girls about lifestyle changes that can help prevent a diagnosis of breast cancer in the future. Breast Health Day publications and campaign materials can be viewed at www.breasthealthday.org.

The Europa Donna Pan-European Conference is the only conference in Europe that is conducted for breast cancer advocates and survivors. The 11th Europa Donna Pan European Conference was held in Prague, Czech Republic, in October 2013, and the next conference will be held in Paris in October 2015. Topics of current interest are covered such as: the EU accreditation scheme for breast services, new study results on lifestyle factors, updates on progress in research, advocacy for women with metastatic breast cancer, and the challenges of survivorship. There are still vast differences in the breast services available in different countries, and the organization seeks to help national groups overcome obstacles to gain access to appropriate services.

Europa Donna is co-organizer with the European Society of Breast Specialists (EUSOMA) and the European Organisation for Research and Treatment of Cancer (EORTC) of this unique conference that brings together more than 3,500 researchers, clinicians scientists, and advocates in one arena; it is held every two years.

The European Breast Cancer Advocacy Training Course is a two-and-a-half-day training course for breast cancer advocates that is conducted annually in Milan; here, members from 46 countries learn how to initiate and carry out advocacy programs in their own countries. The course covers the biology of breast cancer, early detection, best practices in treatment of breast cancer, the EU guidelines that have been developed, and communications skills training.

The Europa Donna Advocacy Leader Conference is a new program provided for the national representatives and key leaders of member countries to discuss issues and topics of common concern and provide sessions for them to improve management and development of their local organizations.

Europa Donna is an active participant in several scientific research programs in Europe. The organization has representation on the scientific committee of Breast International Group (BIG) and serve on committees of the MINDACT trial and the new AURORA study. Europa Donna has conducted training programs for advocates concerning trials and has published two booklets “Breast Cancer and Clinical Trials” and “The Advocates Guide to Understanding Breast Cancer Research” to increase understanding of clinical trials among nonscientists.

**Public Affairs**

Europa Donna is constantly engaged in bringing about positive policy change at the European level. It has held numerous European Parliament Information meetings and exhibits resulting in two European Parliament Resolutions on breast cancer in 2003 and 2006 and the Written Declaration against
breast cancer in the EU in 2010. These form the basis of much of our work to promote change nationally. Information on these activities as well as various publications, the annual newsletter, and e-news can be found on the Web site at www.europadonna.org.

**Conclusion**

Europa Donna advocates for all women in Europe to have access to accurate, up-to-date information concerning breast cancer and to have equal access to state-of-the-art services for early detection, diagnosis, treatment, and follow-up for this disease. The strength of the organization lies in uniting women of many countries and cultures to achieve common goals based on scientific evidence.

Susan Knox

*Europa Donna, the European Breast Cancer Coalition*

**See Also:** Breast Cancer; European CanCer Organisation; European Cancer Prevention; European Society for Therapeutic Radiology and Oncology.

**Further Readings**


---

**European Association for Cancer Research**

The European Association for Cancer Research (EACR) was founded in 1968 with the aim of advancing cancer research and undertakes a variety of responsibilities in research funding and training. The EACR registered office is located in England and Wales. EACR has the largest membership of cancer researchers in Europe, with more than 9,000 current members. EACR has strong associations with other cancer societies in Europe and is one of the founding members of the European CanCer Organisation (ECCO), which works toward creating awareness of cancer patients’ needs and wishes and encourages progressive thought in cancer policy, training, and education. As a founding member of ECCO, EACR makes a valuable contribution to the biennial ECCO–European Society for Medical Oncology multidisciplinary congress and is intimately involved in the development of the charter for the scientific program of the meeting.

EACR provides educational training, opportunities for scientific meetings and conferences, and facilitates cooperation and collaboration among member cancer researchers by providing a platform for scientific interactions and exchanges between basic research scientists, translational researchers, and clinical scientists and physician researchers, covering all aspects of oncology. It also nurtures and encourages the professional development of young researchers by awarding fellowships and promotes knowledge sharing through technical exchange and training for specific techniques. EACR also advocates for persistent economic and political support for cancer research in Europe.

EACR is an inclusive organization with members from multidisciplinary fields. It encourages researchers in the field of cancer research to join the association. The costs to become an EACR member are deliberately kept low so that the cost factor does not deter membership applications. EACR also provides reduced membership rates for postgraduate students and postdoctoral fellows with less than four years of postdoctoral experience. Researchers affiliated with the national cancer societies in Britain, Belgium, Croatia, Denmark, France, Germany, Hungary, Ireland, Israel, Italy, Portugal, Serbia, Spain, and Turkey are automatically assigned membership to EACR.

EACR has the *European Journal of Cancer* (EJC) as its official international journal on oncology, covering multidisciplinary research areas. The EJC publishes 18 issues yearly on topics related to oncology, covering basic research, preclinical trials, translational research, clinical oncology, and epidemiology and cancer prevention. The articles published in the EJC undergo a rigorous peer-review process before publication and include original research and reviews, editorial comments on basic and preclinical cancer...
research, translational oncology, clinical oncology, cancer epidemiology, and prevention. EJC can be accessed as a digital or print version.

EACR also grants recognition for pioneering work on cancer research through awards. The Mike Price Gold Medal and the Pezcoller Foundation—EACR Cancer Researcher Award are among the most prestigious awards. The Mike Price Gold Medal is awarded to exceptional senior researchers contributing to cancer research in Europe. It was initiated the first time in 2012 at the EACR biennial congress in Barcelona. The Pezcoller Foundation—EACR Cancer Researcher Award recognizes academic achievements in the field of cancer research from European cancer researchers with less than 15 years of postdoctoral experience.

Additionally, EACR provides researchers with the opportunity to work across Europe at a center of excellence of their choice or to participate in practical workshops and courses by covering the travel costs through numerous travel fellowships. These travel fellowships are jointly supported by the EACR and the Association for International Cancer Research (AICR). Apart from these awards, EACR also has a Meeting Bursary scheme designed to provide economic support toward cost of travel and accommodation to the members of EACR so as to attend the Association’s Biennial Congress.

The Education Committee of EACR encourages special conferences on highly focused topics by responding to the calls from members of EACR. EACR also supports and organizes meetings such as the annual meeting of Progress in Vaccination Against Cancer, besides participating in the organization of a number of courses in partnership with other organizations, a recent example being the training course on the molecular pathology approach to cancer, jointly organized by EACR and the Organization of the European Cancer Institutes. EACR also plans to have a joint special conference with the American Association for Cancer Research (AACR) and Società Italiana di Cancerologia (SIC) on Anticancer Drug Action and Drug Resistance to be held in June 2015 in Florence, Italy, and is expected to attract global audience.

EACR partnered in the Eurocancercoms project, a two-year project funded by the European Commission with the aim of providing a proof of concept to establish an efficient network for cancer communication in Europe. The primary aim of the project was to use the World Wide Web as a one-stop information exchange platform to integrate, provide access, and share information among patients, policy makers, research scientists, and physicians. The vast scope of this project covered everything from information on the patients to educational tools for clinical scientists.

The project also included access to the latest bioinformatics tools for cancer biologists working in the laboratories. The role of EACR in this project involved collating the collective knowledge of the member researchers and identifying their information needs, attitudes, and ideas. Three Europe-wide member surveys were conducted on communication and use of the Web, usage of National Cancer Institute’s caBIG bioinformatics tools, as well as views on open access publishing. The findings of these projects have been made accessible to the public on the EACR Web site.

Poonam Balani
Independent Scholar

See Also: European Cancer Prevention.

Further Readings
European CanCer Organisation

The European CanCer Organisation (ECCO) is a not-for-profit international association, which was previously known as the Federation of European Cancer Societies (FECS). FECS was founded in the early 1980s by visionary researchers working on various aspects of oncology when multidisciplinary cancer care was a novel concept. FECS was founded with the aim of devising a coordinated, multidisciplinary approach toward cancer treatment. The members of FECS looked at oncology with a broader perspective and worked toward bringing together the major players in cancer research, cancer prevention, diagnosis, treatment, and care. The society also spearheaded the program to create awareness of patients’ wishes and needs and to encourage progressive thought in cancer policy. FECS, as an organization, also encouraged exchange of scientific ideas via multidisciplinary conference meetings.

In September 2007, after a consultation with experts in the field of oncology, FECS was renamed as ECCO at the European Cancer Conference in Barcelona Spain. Since its formation, ECCO continues to expand its outreach in research, education, as well as training to professionals covering multidisciplinary aspects of oncology through a biennial series of conferences. Educational programs such as the ECCO e-Learning and an online patient information section are some of the programs initiated by ECCO under the dedicated leadership of specialists and experts in the form of official committees. Currently, ECCO is headed by the president, Martine Piccart (2014–2015) and serves the interests of more than 60,000 professionals associated with oncology through its 24 member organizations.

ECCO strives to uphold the rights of all European cancer patients such that they have access to the best possible treatment and care. ECCO promotes interaction between associated cancer societies in Europe and creates awareness of patients’ needs and wishes, encouraging progressive thinking in cancer policy, training, and education and promoting European cancer research, prevention, diagnosis, treatment, and care through the organization of international multidisciplinary meetings.

ECCO has members of the founding member societies, the full member societies, and the advisory member societies. The founding member societies include the European Association of Cancer Research (EACR), European Society for Medical Oncology (ESMO), European Society for Radiotherapy and Oncology (ESTRO), European Oncology Nursing Society (EONS), European Society for Surgical Oncology (ESSO), and the European Society for Pediatric Oncology (SIOP Europe). The full member societies include the European Association of Neuro-Oncology (EANO), European Organization for Research and Treatment of Cancer (EORTC), European School of Oncology (ESO), European Society of Breast Cancer Specialists (EUSOMA), European Association of Urology (EAU), European Society of Gynecological Oncology (ESGO), and European Society of Oncology Pharmacy (ESOP).

ECCO is advised by members of a council that includes representatives from all voting member societies. In addition, there are also the advisory members who are representatives from other European and international organizations, with objectives consistent with the mission of ECCO. The ECCO Council of Members formally meets once a year.

ECCO is uniquely positioned to represent the consensus of oncology professionals in Europe and to engage with the European policy makers, ensuring adequate attention to cancer research, training, and patient care as a priority in the European Union (EU).

The public affairs arm of ECCO engages in Oncopolicy, which involves a coordinated and sustained effort of interaction with the policy makers in the EU as well as third-party stakeholders in shaping an effective cancer health and research policy for the EU member countries. The public affairs policy of ECCO has specific objectives that include: raising a collective voice on wider policy issues; engaging stakeholders in cancer research, innovation, treatment, care, and education; coordinating the EU oncology community under a single umbrella; and fostering a proactive approach to cancer in Europe.

ECCO is committed to engage advocates of cancer patients to uphold the rights of cancer patients in getting the best patient care in Europe. In 2009, the European Cancer Congresses started a special theme called the Patient Advocacy Track.
dedicated entirely to cancer patients. The Patient Advocacy Track has been developed by the experts from the ECCO Patient Advisory Committee (ECCO PAC). It focuses on the better understanding of cancer patients’ desires rather than their perceived needs.

Since 1999, ECCO, in collaboration with other cancer societies, organizes an annual workshop on Methods in Clinical Cancer Research, which is an introductory educational program for junior clinical oncologists and concentrates on the principles of good clinical trial design. This workshop is held yearly in the last week of June in the town of Flims in Switzerland with the goal of developing young researchers into well-trained, experienced researchers capable of designing better clinical trial and incorporating the methods for cancer therapy and prevention into everyday practice and health care.

ECCO acts as the coordinating organization for the EU-funded project Oncovideos. The project has an online video collection of 24 videos on standard procedures in different oncology disciplines filmed at 18 teaching partner institutions. The primary purpose of the Oncovideos project is to assist in the medical education of health professionals who want to further develop and acquire practical vocational skills in oncology.

ECCO is also a partner organization of the European Journal of Cancer (EJC), the monthly scientific journal with news, reviews, editorial comments, and research on experimental oncology, clinical oncology, and translational oncology. ECCO is one of the four founding members of the Web-based, open-access cancer journal ecanercmedicalsience, initiated by the European Institute of Oncology. ECCO is also a part of the online project eurocancercoms, funded by the European Commission, with the aim of integrating information resources on cancer using modern technology to provide a unique platform providing information on cancer to public, patients, as well as the medical community.

Poonam Balani
Independent Scholar

See Also: European Association for Cancer Research; European Cancer Prevention; Organisation of European Cancer Institutes.

Further Readings

European Cancer Prevention

The European Cancer Prevention organization (ECP) was established in 1981 by the founders Professor Michael Hill (United Kingdom), Professor Paul Mainguet (Belgium), Professor Attilio Giacosa (Italy), and many other clinical physicians. The aim of ECP is to promote collaborations and intellectual exchange among scientists from Europe and to study the primary causatives of cancer in European populations. ECP acts as an authority on information on the causes of cancer and prevention for European governments, health care professionals, and the media.

The majority of initial work by ECP concentrated on the comparative analysis of incidences of cancer in southern Europe, with primarily Mediterranean diet and nutrition with that of the Scandinavian countries. Attempts were also made to integrate epidemiological findings as a tool for cancer prevention in Europe. Cancer prevention by alteration of dietary intake and exercise emerged as one of the priorities that could decide the fate of cancer prevalence.

ECP is governed by a general assembly, which is selected by the board from the members of the society. The general assembly conducts meetings once a year, while the board members are elected by the members every three years. ECP has a president (Professor Jaak Ph Janssens from Belgium) and a treasurer (Dr. Belinda Johnston from the UK). The overall scientific program of ECP is managed by the scientific committee, which constitutes the
heads of all working groups of ECP as well as distinguished scientists who are experts in their chosen fields. The administrative arm of ECP carries out work at different country headquarters and is responsible for extensive communication among the members of ECP. The administrative headquarters are also responsible for organization of scientific projects, financial support, and international conferences.

One important goal of ECP includes prevention of cancer cases in developing eastern European countries, which appear to be taking the same path in the number of cancer cases as the developed world in the 20th century. A second aim of ECP is to intensify cancer prevention programs and, at the same time, promote healthy lifestyles. ECP also plans to concentrate on the screening methodologies for different forms of cancer for early detection of the disease as current evidence suggests a drop in mortality with better screening for disease.

The organization also provides funding in the form of research grants for the development of better endoscopic screening and imaging tools as well as research on genetic factors such as polymorphisms along with developments of methods for patient friendly tissue harvesting.

The *European Journal of Cancer Prevention*, the official journal of ECP, was started in 1992 to provide a dedicated platform furthering the publication of research conducted by numerous scientific research groups at ECP. The journal was started with the aim to raise awareness regarding all aspects of cancer prevention and to facilitate exchange of intellectual ideas.

The *European Journal of Cancer Prevention* covers a broad range of topics related to cancer prevention. These include topics covering descriptive and metabolic epidemiology, biochemical and molecular biological pathways important in cancer prevention and progression of the disease, histopathology as a tool for detecting cancers, clinical sciences, interventional trials and public education programs, and basic laboratory studies and special group studies concentrating on focused topics in cancer prevention.

Although the journal is based in Europe, it addresses all important aspects associated with cancer prevention internationally. Professor Jaak Ph. Janssens, from Hasselt, Belgium, and Professor Carlo La Vecchia from Milan, Italy, have served as the editors of the *European Journal of Cancer Prevention*. The *European Journal of Cancer Prevention* works in collaboration with the International Agency of Cancer Registration to combine the national and regional registries of cancer patients in European countries. This publication serves as a reliable and robust source of epidemiological data and is further used to classify the national and regional differences in the incidences of cancer in Europe.

The *European Journal of Cancer Prevention* serves as a major platform to integrate, evaluate, and publish scientific findings on cancer prevention tools and strategies. ECP informs the population of the role of lifestyle and diet and the risk of cancer through a variety of channels and media. It also fosters exchange of knowledge and research ideas by organizing international meetings and bringing together people with different disciplines, including basic research scientists, clinical researchers, pharmaceutical companies, and policy makers.

ECP encourages young researchers with no more than five years of postdoctoral experience to apply for travel grants. The selection process chooses a candidate for the award based on his or her outstanding work in cancer prevention who wishes to establish a career in the field. The award funds travel costs and visits to established scientists in the field of cancer prevention.

Another specific area where ECP is actively involved is the identification of new threats toward the development of cancer, especially in eastern Europe. The incidence of cancer is rising in the eastern European countries, in contrast to western Europe, as improved lifestyles and an adoption of Western-style diets increase the risk of obesity, which can further manifest into other diseases like type 2 diabetes and cancer. In the future, ECP plans to prioritize the efforts of cancer prevention in developing eastern European countries to minimize the new cases of cancer.

ECP also works to ensure the availability of vaccines against certain types of cancer. This is especially relevant for cervical cancer. Cervical Cancer Update was the theme of the 2013 annual ECP meeting held in Antwerp, Belgium, and ECP undertakes collaborative efforts with the pharmaceutical industry to identify regions and target
women who are at the highest risk of developing cervical cancer.

Poonam Balani
Independent Scholar

See Also: European Association for Cancer Research; European CanCer Organisation; Organisation of European Cancer Institutes.

Further Readings

European School of Oncology

The European School of Oncology (ESO) is an independent not-for-profit organization established in 1983 to improve the standards of treatment and care for cancer patients across Europe. Founded by the renowned Italian cancer surgeon Umberto Veronesi, together with international leaders in cancer surgery, radiotherapy and medical oncology, its mission is “to contribute through education to reducing the number of cancer deaths and to ensuring early diagnosis, optimal treatment, and holistic patient care.” ESO remains one of the only providers of oncology courses not tied to commercial interests. It has been able to steer its own course in pursuit of its mission thanks to generous backing from independent donors.

Educational Courses
In its early days, the concept of continuing medical education (CME) was virtually unknown in Europe, so ESO sought and gained accreditation for its courses from the American Medical Association. The school was a key player in introducing a CME system in Europe, drawing up a report to the European Commission in 1994, and then working with the Union of European Medical Specialists to lay down a framework.

Today ESO runs 20 to 25 courses a year on different cancers and aspects of treatment and care, in addition to its flagship, weeklong Masterclass in Clinical Oncology. Courses are taught by leading oncologists who are committed to student-focused teaching and patient-centered care and provide their services for free. Students come primarily from European countries and are selected on a competitive basis. The school also runs an e-ESO program of fortnightly e-grand rounds. Presented by international experts and broadcast live, these webcasts can be accessed by anyone in the world, and the audience can pose questions by e-mail before or during the session.

To help fill gaps in provision of more in-depth learning for oncologists around the world, ESO is collaborating with the University of Ulm, in Germany, to provide courses that run over 14 months, using a distance learning format.

The school also runs conferences, meetings, and symposia that provide expert overviews of key developments or hot topics. Its signature conferences focus on advanced breast cancer (the only professional conference to address the treatment and care needs of people with advanced cancer), active surveillance for low-risk prostate cancer, and breast cancer in young women.

A Multidisciplinary Organization
ESO was founded as a multidisciplinary organization at a time when medical oncology was still emerging as a specialty in its own right. As scientific director of the Istituto Nazionale dei Tumori in Milan, ESO’s founder, Veronesi, hosted the first trials of adjuvant chemotherapy in 1972, which were being boycotted by surgical departments in the United States. In 1982, he published a landmark paper showing that quadrantectomy—a technique he pioneered for breast-conserving surgery—was safe if used in combination with radiotherapy. The school remains one of the few providers of oncology education to use multidisciplinary faculties.
ESO played a key role in setting up the multidisciplinary European Society of Breast Cancer Specialists (EUSOMA) in 1986. Together with the patient advocacy group Europa Donna, EUSOMA developed, defined, and advocated for the concept of specialist multidisciplinary breast units as the best way to organize breast cancer services. The concept was adopted as policy by the European Parliament in 2003 and has influenced the way services have developed in many European countries. ESO is now backing calls from many prostate cancer specialists and patient advocates for a similar organizational model to be adopted for prostate cancer.

**A Focus on Patient Care**

ESO decided from the outset to teach all courses from the perspective of caring for the patient rather than treating the disease. While rejecting traditional paternalistic attitudes, the school sought to promote a distinctive, compassionate, European approach to patients in contrast to what it saw as a rather bleak interpretation of the truth telling then practiced in the United States.

ESO established a psycho-oncology task force in the late 1980s, at a time when the specialism was emerging in the United States. By 1989, ESO was integrating psycho-oncology into its courses. The school was also quick to recognize the importance of specialist cancer nursing and to integrate nursing into their courses. ESO has been funding training courses for nurses, designed and delivered jointly with the European Oncology Nursing Society, since 1996.

ESO sponsored the establishment of European patient advocacy groups, including the European Breast Cancer Coalition, Europa Donna, in 1994; the European Prostate Cancer Coalition, Europa Uomo, in 2002; and the European Cancer Patient Coalition (ECPC), in 2003.

**A Policy Agenda**

ESO looks for opportunities to engage with governments, policy makers, and administrators regarding policies and practices that impact on patient outcomes.

In 1985, ESO drew up the blueprint for Europe Against Cancer—Europe’s biggest ever coordinated health program—which ran between 1987 and 2000. The school also played an important role in carrying out many aspects of the program, including formulating the European Code Against Cancer, developing training courses for primary care health professionals, defining minimum standards for oncology training in universities, and convincing heads of government to back tough legislation on tobacco.

In 2012, ESO brought together leading clinicians, researchers, epidemiologists, advocates, policy makers, and industry representatives at the first World Oncology Forum, organized in collaboration with the *Lancet* “to evaluate progress in the war against cancer.” The conference issued a statement, Stop Cancer Now!, which called on world governments to implement a 10-point strategy to speed up progress in the prevention, delivery of treatment and care, and development of effective affordable therapies.

**Cancer World and the Media Service**

ESO publishes *Cancer World*, a bimonthly magazine for cancer professionals, policy makers, administrators, and advocates, which addresses social, cultural, political, economic, and organizational factors that impact patient experiences and outcomes.

The ESO Media Service promotes critical reporting of cancer issues in the European mass media through awards and grants for journalists. It also runs training courses for journalists to better equip them to report on all aspects of cancer and provides media training for clinicians and other cancer professionals to help them interact more effectively with the media.

Alberto Costa  
*European School of Oncology*  
Anna Wagstaff  
*Cancer World*

**See Also:** European Society of Surgical Oncology.

**Further Readings**


European Society for Therapeutic Radiology and Oncology

The European Society for Therapeutic Radiology and Oncology (ESTRO) was founded in 1980 by the founding fathers Maurice Tubiana, Jerzy Einhorn, Klaas Breur, Michael Peckham, and notably Emmanuel van der Schueren. The aim of the society was to establish radiation oncology as an independent specialty within a broader field of multidisciplinary oncology.

ESTRO is a nonprofit organization fostering improved patient care using multimodality treatments for cancer. ESTRO primarily focuses on the betterment of methods used in radiation oncology. ESTRO has more than 5,000 members from around the world. ESTRO provides economic as well as educational support to all professionals in the field of radiation oncology. This includes professionals in their daily practice, including radiation oncologists, medical physicists, radiobiologists, and radiation therapists. ESTRO's mission includes developing and promoting the standards of practice and education in radiotherapy and clinical oncology and encouraging cooperation between societies representing radiotherapy, clinical oncology, and related subjects within Europe and globally. ESTRO also spearheads research and development activities in clinical oncology, radiotherapy, and other allied fields.

ESTRO held its first annual congress in 1982 in London and was a success with the participation of around 500 delegates. The theme of the first congress was to integrate basic fundamentals of radiation oncology with clinical applications. At present, apart from the ESTRO conference, the association also partners in joint conferences with other societies and associations to promote networking and research initiatives striving for excellence in patient care.

ESTRO pioneered and prioritized dedicated education and training in the field of radiation oncology in Europe. The Education and Training Committee was established in 1985 and was chaired by Jens Overgaard during the Stockholm congress. ESTRO subsequently held its first training course in physics in Leuven, the Netherlands, in 1985. The teaching course was inspired by outcomes of research by physicists Andrée Dutreix (Paris, France), Ben Mijnheer (Amsterdam, the Netherlands), and Hans Svensson (Umea, Sweden), who demonstrated the large variations in standards at different radiation oncology centers. Since the first course, ESTRO regularly offers training courses and modules in Europe on a variety of topics related to radiation oncology.

ESTRO launched its official journal, the Green Journal, in August 1983, with Emmanuel van der Schueren as the editor. The European journal became one of the two leading journals in the field of radiation oncology. ESTRO also releases a bimonthly, open-access, digital newsletter highlighting current topics of interest to the community of radiation oncologists. The newsletter publishes the latest advancements, conference summaries, and other research relevant to the field.

During the past 20 years, ESTRO supported more than 40 European research projects and is recognized as an international leader in education and research-based training of professionals in the field of radiation oncology. Some of the current projects of ESTRO include development of innovative radiation treatments to improve patient outcomes, using stem cells to evaluate the risk of cancer from neutrons in comparison to photons and the induction of secondary malignant neoplasms following radiation therapy in pediatric patients.

The primary vision strategy for ESTRO, as stated during the 30th anniversary of ESTRO, held in Brussels, Belgium, is to link the development of optimal patient care to patient access to state-of-the-art radiation therapy. ESTRO aims to provide optimal, individualized patient care to every cancer patient in Europe through collaborative efforts with current and future organizations collectively involved in the development of multidisciplinary treatment modalities for cancer care. ESTRO also works in tandem with the appropriate scientific and professional societies, international agencies, national representative groups, collaborative clinical trials groups, and patient advocacy groups.
One of the future aims of ESTRO is to develop new areas of engagement with regulatory authorities within Europe, which include the European Union (EU), European Economic Area (EEA), and national regulatory agencies as well as the nongovernmental organizations.

ESTRO’s mission is to promote innovation, research, and dissemination of science through its congresses, special meetings, educational courses, and publications. The ESTRO also provides financial and material support facilitating the PhD student exchange programs and research fellowship. It also assists junior fellows to apply for EU grants to support participation in research studies and scientific meetings.

In 2010, ESTRO launched the project Health Economics in Radiation Oncology (HERO), with the aims of consolidating a knowledge base and creating a model for the evaluation of health economics of radiation therapy in Europe. The HERO project addresses questions on the accessibility versus the need for radiotherapy in Europe. The project aims to establish a cost-versus-effectiveness and cost-versus-utility program for radiotherapy treatments in Europe. ESTRO launched the ESTRO Cancer Foundation (ECF) in 2012 as a Belgian public interest foundation with the vision of improving the roles and perceptions of radiation oncology as an economical contributor toward cancer treatment modalities. The project promotes radiation oncology to patients and decision makers. The foundation can be regarded as the ESTRO arm that tangibly enforces its vision statement on the ground.

From its central position, ESTRO has developed a broad network of contacts with international, regional, and national societies as well as professional bodies and industry partners in the field of radiation oncology.

Poonam Balani
Independent Scholar

See Also: European School of Oncology; Radiation; Radiation Therapy.
European Society of Mastology

The European Society of Mastology (EUSOMA), otherwise known as European Society of Breast Cancer Specialists, was established in 1986 by a group of physicians who specialized in breast cancer to collaborate on solutions for the issues and needs that existed in the area of breast cancer. For the period between 1986 and 1990, EUSOMA’s members conducted discussions about different aspects of breast disease; the meetings were informal during this time, and the discussions did not result in any publications.

The society’s formal activities began in 1991. Starting at this time and for the next few years, the society organized conferences and scientific discussions that led to the publication of articles. Since 1998, the society has organized multidisciplinary workshops where experts collaborate to discuss their experiences and opinions as well as drawing up reference documents on different facets of breast disease. These documents resulted in the publishing of guidelines in the *European Journal of Cancer*. EUSOMA is one of three entities that organize the European breast cancer conferences that convene every other year.

Further Readings

The *European Journal of Cancer* is the official journal of EUSOMA. The journal is an oncology journal that takes a multidisciplinary approach, publishing research, reviews, and comments by the editor on basic as well as preclinical research, clinical oncology, translational oncology, and medical, radiation, pediatric, and surgical oncology, along with cancer epidemiology and methods of prevention.

After the European breast cancer conference in 1998, a working team was established to consider a Europe-wide standard, high-quality, specialist breast service. EUSOMA gave an official opinion on the standards that made up high-quality breast cancer units Europe-wide. Many facets of care and quality were considered when the statement was made regarding the guidelines, including the facility’s size, the provisions of the unit, the services offered, and much more. The hope was that the resulting standards for high-quality breast cancer care will inspire improvement in diagnostics, treatment, and care for patients suffering from breast cancer Europe-wide. EUSOMA also created a quality treatment system for auditing breast cancer facilities. The metrics used include screening, surgery, pathology, assessment, hormone therapy, chemotherapy, follow-up, and other categories.

The society has established that diagnosis and treatment of breast diseases, especially breast cancer, have wide and varying approaches across the European region. In addition, the society identified an urgent need for provision of a channel for a wider diffusion of basic research programs either by way of screening the population or through education and information. Based on these essential insights, the society established four core objectives, which have for the period of time the society has been in existence, informed and guided their operations.

Since the inception of EUSOMA, its objectives have been to promote scientific research and increase contacts between scientists and health care professionals interested in breast diseases and in particular in breast cancer and to improve and standardize the ways how patients are treated with appropriate screening and support solutions. This is for making it available for all women in Europe though a state-of-the-art treatment solution; supporting standards for managing different issues and different certification needs for offering the best solutions possible; bringing these to the attention of the appropriate authorities; and fostering training...
and postgraduate programs in breast disease at national and international levels.

The society organizes the European breast cancer conference every two years. The conferences provide platforms for the various European-based professionals in the area of breast cancer, among them doctors, nurses, health practitioners, care givers, and researchers, to meet and discuss the various key issues in the research, treatment, prevention, and advocacy of breast cancer. The objective of this activity is to reach a final consensus on the topic.

In addition to the conference held once every two years, the society organizes workshops on a regular basis. These workshops are on the different aspects of breast diseases, and the specialists from the field of oncology who attend discuss and come up with documents that are meant to provide quality assurance in the diagnosis and treatment of breast cancer.

The scope covered by the society is wide. Even though it is in the areas of breast diseases and in particular breast cancer, the society covers aspects of biology and immunology of cancer, diagnosis and screening, epidemiology and prevention, loco-regional and systemic treatment, genetics and pathology, reconstruction, patient support, and rehabilitation.

Toward these objectives, the society has made considerable achievements through the European breast cancer conferences that the society organizes together with organizations devoted to the research of cancer and how it develops. The solutions are designed to promote help for the body at large.

Other achievements by EUSOMA include the documents that are drawn up during the regular workshops organized by the society. These documents, which are developed by specialists in oncology, have helped to increase the standards in breast health care throughout Europe because they are adopted as guidelines. In addition to the documents, other scientific articles have been published by scientists after attending the workshops as well as consensus conferences and scientific meetings that have been organized by the society.

The work by the society has helped to improve the methods used in the management of not only breast cancer but also breast diseases.

Michael Fox
Independent Scholar

See Also: Breast Cancer; Europa Donna, the European Breast Cancer Coalition; European Association for Cancer Research.

Further Readings
European Society of Breast Cancer Specialists.

European Society of Surgical Oncology

Established in 1981, the goal of the European Society of Surgical Oncology (ESSO) is to advance the art, science, and practice of oncological surgery, which is surgery specifically used in the treatment of cancer. ESSO’s mission is aimed at supporting the overall health and well-being of cancer patients through multidisciplinary educational and research efforts. The guiding philosophy for ESSO is to create a system of surgical oncology within Europe’s medical establishment that focuses on a patient-centered approach rather than a disease-focused approach. This, ESSO says, helps patients become clear partners in their treatment, ultimately improving the patient’s quality of life and providing for a higher rate of survivorship.

ESSO operates under a set of core principles and goals that supports patient advocacy and multidisciplinary expertise for the field of oncology. These include education, cooperation, science and investigation, oncopolicy, and communication.

Touting a membership of 20,000 worldwide—to include individuals, groups, and corporations—ESSO members span multiple disciplines that are either directly involved or related to in the practical application, research, and care and treatment associated with surgical oncology in Europe. ESSO believes that creating a collaborative, multidisciplinary educational and research environment for
those involved in this field will help propel cancer treatment forward and help surgeons serve a crucial role in the care and treatment of cancer patients. ESSO provides standardized training and education on topics ranging from innovative surgical techniques to advising and counseling patients, to cutting-edge therapies.

As a result, ESSO does not focus solely on the technical aspects of surgical oncology; instead, ESSO supports collaboration with other specialties involved in cancer treatments, like radiologists and geneticists. This collaboration provides ESSO members with a well-rounded perspective, possible cancer treatments and research areas and connects medical professionals from a variety of disciplines and subdisciplines through shared knowledge and expertise that might otherwise have operated as disparate communities. Some examples of these multidisciplinary areas include robotic surgery, minimally invasive laparoscopic surgery for cancer patients, intraoperative chemotherapy and radiation therapy, reconstructive surgeries, and recovery programs.

ESSO is also a founding member of the European CanCer Organisation (ECCO), which is a nonprofit federation focused on the patient rights and advocacy. As of 2014, ECCO is made up of 24 other multidisciplined oncology societies and organizations in Europe. Through ECCO, the member organizations work to create awareness of patient’s rights, needs, and wishes during cancer treatment programs and advocates for progressive cancer policies, especially in the areas of training, education, cancer research, care, and treatment.

ESSO is governed by an overall general assembly, which meets once a year and gathers the ESSO members to discuss issues of strategic importance, elect members to serve on the organization’s executive committee, and approve the daily operations functions, such as budgets and changes to the organizations guiding charter. In addition to the general assembly, ESSO’s governance includes an executive committee. This committee is charged with carrying out the overall operations of the organization and is tasked with implementing any activities that support the overall goals of the organization and its members. Other governing bodies include a steering committee, which is comprised of the organization’s officers, who take care of the organization’s day-to-day operations, an education and training committee, which focuses on the development of a strategic training plan for ESSO, to include projects and activities for members, and the editorial committee, which focuses on ESSO’s communications objectives and publication of its scholarly journal.

In order to accomplish its overall goals, ESSO partners with various other organizations and cancer societies. These partner organizations include the European CanCer Organisation, the European Society for Radiotherapy and Oncology, the European Society for Medical Oncology, the Society of Surgical Oncology, the European School of Oncology, the European Society of Breast Cancer Specialists, the International Society of Geriatric Oncology, and the European Association of Urology. These partnerships enable ESSO to leverage resources, expertise, knowledge, and funding.

ESSO’s official publication is the European Journal of Surgical Oncology, a joint scholarly journal produced with the British Association of Surgical Oncologists (BASO), an association of cancer surgery. Through this publication, ESSO provides education and information on a monthly basis in the form of, but not limited to, original scientific articles, news articles, peer reviews, and clinical trials on a variety of cancer surgery subdisciplines and specialties, such as epidemiology, preventative oncology techniques, new applications and surgical treatments, and results assessments. The journal is published and distributed internationally through both print and electronic formats. Additionally, ESSO is supported, in part, through educational grants from the Genomic Health and Nutricia.

L. L. Lundin
Independent Scholar

See Also: Breast Cancer; European Cancer Prevention; European School of Oncology; Pancreatic Cancer; Prostate Cancer; Surgery; Survivors of Cancer; Survivors of Cancer, Families of.

Further Readings
Ewing’s Family of Tumors

Ewing’s family of tumors (EFT) is a group of cancers that arise in bone or soft tissues of mainly children and adolescents. This group comprises of four main tumor types:

(1) Ewing’s sarcoma of bone (ES) was first described by James Ewing in 1921 as a diffuse endothelioma of the bone. It is the second-most common bone cancer that affects children after osteosarcoma. ES occurs mainly in the pelvis, lower extremity, upper extremity, chest wall, and spine.

(2) Extraosseous Ewing’s sarcoma (EOE) acts and looks very much like ES but occurs in soft tissues around bones. The tumors can occur anywhere including the trunk, extremities, head and neck region, and retroperitoneum.

(3) Peripheral primitive neuroectodermal tumor (pPNET) is a rare tumor that occurs in bones and soft tissues and shares features with ES and EOE.

(4) Askin’s tumor is a pPNET of the chest.

The cells that make up the tumors in this group have the same unique genetic abnormalities that are not found in other cancer types. Due to this unique characteristic, there is a strong likelihood that these cancers originate from the same cell. Hence, they are all grouped as EFT and receive the same treatment. About 25 percent of patients have metastatic disease at diagnosis. While the five-year survival for patients with localized tumors is 75 percent, it is only 20 percent for patients with metastatic disease.

Epidemiology

The overall incidence of ES sarcoma is approximately three cases per 1 million per year and has remained unchanged for 30 years per data from the U.S. National Cancer Institute’s Surveillance, Epidemiology, and End Results registries. The cancer occurs most frequently in teenagers and young adults, although it can occur at any time during childhood. It is very rarely seen in adults over the age of 30. About 225 new cases of EFT are diagnosed each year in North America. The probability of Caucasians being affected is almost nine times greater than African Americans.

Diagnosis

Definitive diagnosis is based on histologic findings and immunopathology coupled with molecular pathology. On histology, ES and EOE appear as small, round cell tumors with clear cytoplasm with abundant glycogen. Neuroendocrine differentiation may be prominent in pPNET. Tumors are positive for MIC2 gene product CD99, which is a cell membrane protein. However, MIC2 positivity is not unique to ES as it is found in several other tumors, including synovial sarcoma, non-Hodgkin's lymphoma, and gastrointestinal stromal tumors. Hence, histopathological findings need to be confirmed molecularly by fluorescent in-situ hybridization-based detection or by polymerase chain reaction (PCR)-based amplification of a chimeric gene, EWS-FLI1 that results from a chromosomal translocation t(11;22)(q24;q12). This genetic feature is a molecular hallmark for this disease as it is present in approximately 90 percent of EFT cases. The remaining few cases could have lesser common translocations between the EWSR1 gene and a member of the ETS family such as ERG, ETV1, or E1AF. Rarely, other TET family members can substitute for EWS. In addition to aiding in diagnosis, PCR enables the detection of submicroscopic metastatic disease in the blood (circulating tumor cells) or bone marrow.

Tumor Staging

Pretreatment staging is important for understanding tumor extent and spread. For EFT, a localized tumor is defined as one where there is no spread beyond the primary site and no regional lymph node...
involvement by clinical and imaging techniques. Continuous extension into adjacent soft tissues may occur. Imaging guidelines from the Children’s Oncology Group bone tumor committee states that magnetic resonance imaging is the current standard of care for primary tumor assessment. Spiral computed tomography (CT) is more sensitive than traditional thin-cut CT for detection of metastasis. Additional studies should include bone scans, chest CT, and bone marrow aspiration and biopsy. Molecular analysis of bone marrow for the presence of chromosomal translocation will help detect advanced disease spread, but this staging modality is not commonly used. Results from the EURO-E.W.I.N.G. 99 clinical trial suggests that positron emission tomography (PET) using fluorodeoxyglucose and conventional imaging are both equally efficient in detecting a primary tumor, but PET alone has better detection rates for lymph node involvement and bony metastases.

**Prognosis**
The prognosis for EFT patients depends on pretreatment factors as well as therapeutic response. Pretreatment factors such as patient age, sex, and tumor features along with extent of spread influence outcomes. Younger patients (less than 15 years old) with disease and girls have a better prognosis. Cancer occurring in distal extremities performs better than tumors located proximally. Large tumors along with metastatic disease respond poorly to treatment. Primary cancer that is genetically stable with less-complex karyotype has good prognosis. Molecular biomarkers linked with aggressive tumor behavior or drug resistance are associated with inferior outcomes. Therapeutic response factors include presurgical chemotherapy response and postsurgical tumor volume. Patients with poor response to preoperative chemotherapy have an increased risk for local recurrence, while those with minimal or no residual viable tumor after presurgical chemotherapy have a significantly better chance for event-free survival. In patients with advanced disease, decreased PET scan uptake following chemotherapy correlates with good histologic response and better outcomes.

**Treatment**
The complete treatment of patients with EFT requires systemic chemotherapy together with surgery or radiation therapy for local tumor control. Most patients with metastatic disease have a good initial response to preoperative chemotherapy. However, for most, the disease is only partially controlled with a high recurrence risk. Patients with only lung metastasis have a relatively better prognosis than patients with metastases to bone or bone marrow. Treatment lengths depend on tumor location and stage of disease at diagnosis. The surgical resection may involve limb salvage or amputation. Although EFTs are radiation sensitive, radiotherapy alone for localized disease is rarely considered due to radiation-related morbidity as well as advances in orthopedic surgery. Multidrug neoadjuvant systemic chemotherapy for EFT includes vincristine, doxorubicin, cyclophosphamide with ifosfamide, and etoposide. Addition of the latter two drugs has markedly improved overall and event-free survival for patients with localized disease but does little for patients with metastasis. Increasing chemotherapy doses for metastatic disease increases acute toxicity and risk of secondary cancers. Recent clinical trials in the United States and Europe are concentrating efforts on chemotherapy regimens termed megatherapy for metastatic disease. Megatherapy involves myeloablative high-dose chemotherapy (busulphan-melphalan) with or without total-body irradiation followed by rescue with marrow or peripheral hematopoietic stem cells. Benefits of megatherapy are still uncertain for those with advanced disease. Clinical trials in the United States and Europe are underway to improve the overall survival outcomes for this aggressive disease.

**Ongoing Research**
Genomics and proteomics are being used by various researchers to identify disease-specific molecular targets that can lead to the development of novel therapeutic drugs. This may ultimately help change future treatment strategies for ES patients with improved survival without increasing drug toxicity.

Sheetal A. Mitra
Children’s Hospital Los Angeles

**See Also:** Childhood Cancers; Sarcoma, Ewing's Family of Tumors; Technology, Imaging.

**Further Readings**
Exercise

Over the past 20 years, there is a vast body of research exploring the relationship between exercise and cancer. This research explores how exercise, or physical activity, is associated with cancer risk, prevention, and survival. While evidence from epidemiological studies documents the benefits of exercise in reducing cancer mortality, there is also extensive research summarized by the International Agency for Research on Cancer (IARC) relating higher levels of exercise to reduced risk of many cancers. This entry explains the biological mechanisms that link exercise and cancers, describes the characteristics of exercise frequently studied in relation to cancer, and summarizes current epidemiological research studying the association between exercise (or the lack of it) and various cancers.

The biological mechanisms that influence the impact of exercise on cancer include a number of pathways such as the positive outcomes of exercise on reduction of body fat, improving insulin sensitivity, and improving pulmonary function. Exercise, a modifiable behavior, is known to decrease body fat, which consequently lowers levels of inflammatory markers, reduces the production of sex hormones (estrogen and testosterone), and increases levels of sex hormone binding globulin (SHBG). Moreover, reduced body fat is linked with improving insulin sensitivity and lowering plasma insulin and glucose levels. Thus, exercise may reduce the risk of certain hormone-related cancers such as postmenopausal breast, colon, endometrium, ovarian, and prostate cancers. Exercise also lowers the concentration of carcinogenic material in the lungs, which decreases lung cancer risk.

Research has studied numerous features of exercise that may be related to the development of cancer. These features or characteristics include type of exercise (leisure, household, or occupational), duration of exercise, frequency (number of days per week), intensity (low, moderate, or high), and age at which exercise started. Exercise is related to or results in other factors that are studied in relation to cancer, such as body mass index (BMI) and weight.

The link between exercise and cancer is examined and reviewed by several national and international organizations as well as individual researchers. Foremost among these is the IARC, which uses consistent systemic methods to summarize evidence and classify exposures according to their potential to cause (or prevent) cancer. The evidence shows that the strength and consistency of this association varies based on the site of cancer; that is, one cannot generalize evidence from one cancer to all cancers. Further, the findings can be classified as convincingly associated, possibly associated, and null or insufficient findings.

**Convincingly Associated With Exercise: Reduction in Colon Cancer**

More than 60 studies have been conducted across the world on the relationship between exercise and the risk of colon or colorectal cancers. These studies show that exercise results in decreasing the risk of colon cancer among men and women by 20 to 25 percent. Research found that both occupational (22 percent) and recreational (23 percent) exercise resulted in nearly the same levels of risk reduction. The evidence from studies of recreational or leisure activities suggests that 30 to 60 minutes of moderate to vigorous exercise per day can significantly decrease colon cancer risk.

**Probably Associated With Exercise Reduction in Breast Cancer.** More than 73 studies have been conducted worldwide on the link between exercise and breast cancer risk. Three-quarters of these studies have reported a positive relationship, showing a risk reduction of 25 percent. While all types of exercise were found to be beneficial in decreasing breast cancer risk, studies show that household and leisure activities reduced the risk by 21 percent, walking or cycling by 18 percent, and occupational activity by 13 percent. Research also found that, although exercise performed at any age contributed to reducing the risk of breast cancer, exercise...
done after the age of 50 had a stronger impact than exercise done when younger. The benefits of exercise were greater for postmenopausal women and women with normal BMI.

Reduction in Endometrial Cancer. A systematic review of 20 studies reported that exercise was related to a 20 to 30 percent decreased risk of endometrial cancer. While studies show that any type of physical activity reduced endometrial cancer risk, recent research evidences that a sedentary lifestyle that includes more than five hours of sitting is associated with increased risk of endometrial cancer. Indeed, emerging research suggests that moderate-intensity exercise for approximately one hour per day reduces endometrial cancer risk.

Possibly Associated With Exercise
Reduction in Lung Cancer. Most of the 20 studies conducted to investigate the relationship between lung cancer risk and exercise reported a decreased risk ranging from 20 to 40 percent. Owing to the causal link between smoking behaviors in the development of lung cancer, controlling for the effects of smoking or investigating the risk for nonsmokers is important when considering this site of cancer. Interestingly, the effects of exercise on nonsmokers is reported to be null or weakened among studies that take into account individual smoking status. Similarly, research that did not control for smoking found that exercise was a strong predictor of reduced lung cancer risk, highlighting the protective nature of exercise for this particular cancer. This effect is stronger for leisure (versus occupational) activity, is stronger in men (versus women), but is consistent across various histological (i.e., type of tissue where the cancer originates) subtypes.

Reduction in Prostate Cancer. The relationship between exercise and reduced prostate cancer risk ranges from 10 to 20 percent. However, these findings are inconsistent, lacking clarity on type of exercise, time periods in life that make exercise most beneficial for risk reduction, and duration of exercise. A methodological issue that one needs to consider is that this cancer is dormant, resulting in most men dying with undiagnosed prostate cancer. Hence, it may be problematic to identify a difference in the effects of exercise between individuals with cancer and “healthy” individuals who may be having dormant, nondetectable prostate cancer because the two groups may be too similar.

Reduction in Ovarian Cancer. Of the 20 studies conducted in exercise and ovarian cancer risk, the findings were found to be inconsistent as half the studies noted positive effects of exercise, half reported no effects, and one study observed an increased risk. A meta-analysis conducted in 2007 found that recreational activity was related to ovarian cancer risk reduction by 20 percent. Two studies reported sedentary behavior to be a risk factor for ovarian cancer, with a 55 percent risk increase when a person is sitting for six or more hours per day.

Null or Insufficient Association With Exercise
Findings from studies examining the relationship between exercise and non-Hodgkin’s lymphoma (NHL), Hodgkin’s lymphoma, leukemia, and multiple myeloma were limited due to small sample sizes. Exercise can reduce body fat, and reduced body fat is linked with improving insulin sensitivity and lowering plasma insulin and glucose levels. Thus, exercise may reduce the risk of certain hormone-related cancers such as postmenopausal breast, colon, endometrium, ovarian, and prostate cancers. (National Cancer Institute/Bill Branson)
sizes, inadequate assessments of exercise, and not controlling for confounding variables.

Few studies have investigated the association between exercise and cervical cancer risk, reporting inconsistent findings, with some studies showing increased risk and some decreased risk. Further, there is insufficient evidence for the link between exercise and various cancer sites, namely pancreatic, kidney, testicular, and bladder cancers.

There are several risk factors for cancer, with research evidence suggesting exercise to be a significant risk factor especially in the case of colon, breast, and endometrial cancers. Further research is needed to confirm the exercise—cancer risk relationship for cancers such as lung, prostate, ovarian, hematological, and other genitourinary cancers. Considering the impact of physical activity on less-researched cancer sites will add to the overall scientific knowledge of exercise as a risk factor of cancer. This information will, consequently, help develop public health interventions for physical activity, such as planning exercise programs and setting up exercise awareness initiatives.

The current World Health Organization (WHO) global recommendation for physical activity for adults between 18 and 64 years is 150 minutes of moderate-intensity aerobic exercise per week. However, understanding the role of psychosocial factors that contribute to physical activity (e.g., culture, economic status, and education) can further inform such international health recommendations on exercise.

Mahati Chittem
Indian Institute of Technology Hyderabad

See Also: Breast Cancer; Colon Cancer; Diet and Nutrition; Endometrial Cancer; Lung Cancer, Non–Small Cell; Ovarian Cancer, Childhood; Prostate Cancer.

Further Readings


Experimental Cancer Drugs

Cancer is the term used for all the malignant tumors. A malignant tumor is defined as “an abnormal mass the growth of which exceeds and is uncoordinated with that of the surrounding tissues.” Cancer is described as human consumption even in this era of unprecedented medical advancement. In 2012, there were about 8.2 million cancer-related deaths worldwide, with lung cancer accounting for the greatest number of deaths (estimated at 1.6 million), followed by liver cancer (745,000 deaths), stomach cancer (723,000 deaths), colorectal cancer (694,000) and breast cancer (521,000). This made oncology—that is, the study of cancer—one of the most attractive fields for research workers. New advances were made to seek its remedy.

Chemotherapy, Hormones, and Enzymes
Chemotherapy is the use of drugs for the treatment of diseases. Cancer chemotherapy targets one or more of the steps involved in tumor development—that is, excessive proliferation, or anaplasia (lack of differentiation), local invasion, or metastasis (development of secondary cancer at anatomically distinct sites).

The current drugs mostly act through molecular targets to inhibit the excessive proliferation of neoplastic cells. The newer classes of drugs include hormone antagonists, enzyme inhibitors, growth factor inhibitors, antiangiogenic factors, pro-angiogenic factors, and drugs that promote the body’s immune system.

Various classes of hormone antagonists are used to suppress the growth of hormone-responsive tumors. A good example is carcinoma of the breast. Two of the most striking classes of drugs for this carcinoma are selective estrogen receptor modulators (SERMs) and aromatase inhibitors.
SERMs inhibit the action of estradiol on estrogen receptors in tumor tissues of the breast and endometrium. They block the activation of genes required for cellular proliferation without interfering with the desirable effects of estrogen on bones and low-density lipoproteins (LDL) levels. Aromatase complex is responsible for the final step of estrogen synthesis. Aromatase inhibitors like aminogluthethemide inhibit cyp-450 through the interaction of nitrogen atoms of the drug with haem iron of the enzyme. Similarly acting agents with aza heterocycles in their structures are under investigation.

Estrone-3-O-sulfamate (EMATE, a steroidal sulfatase inhibitor) is an irreversible active site-directed inhibitor. It is very potent but has not been able to make its mark in the treatment of breast cancer so far. Nonsteroidal sulfatase inhibitor 667 COUMATE is in phase I trial. The results of a follow-up on phase II trial will establish its efficacy. A dual aromatase and sulfatase inhibitor compound A is expected to be more efficacious.

Prostate cancer is another example of hormone-responsive tumors that can be treated along similar lines. Signals by testosterone are required for continued proliferation of prostate cells, while 5 alpha reductase is an essential enzyme for the synthesis of testosterone. Finasteride is a potent irreversible inhibitor of 5 alpha reductase type II. It reduces the dihydrotestosterone levels incompletely, which is due to noninhibition of 5 alpha reductase type I. This led research workers to try for the development of dual inhibitors of 5 alpha reductase I and II. The Glaxo Company developed a dual inhibitor Dutasteride, which is in clinical trial phase III.

Cytochrome P17 is another enzyme for the synthesis of androgens in testes and adrenals. Liarozole is a good inhibitor of rat cytochrome P17. In humans, it reduced the plasma testosterone concentration by 80 percent. It is in phase III clinical trials. YM 116 and BW 19 act similarly and are under clinical evaluation.

Several 17-pyridyl steroids have also been tested for cytochrome P17 inhibition. One of them is a highly selective inhibitor abiraterone. The profile of this drug in phase I trial has been very promising. It reduced the testosterone plasma levels without affecting the cortisol levels. Sa 40, a compound derived from abiraterone, is even more active. More recently, compounds like MH_54, L_39, which are dual inhibitors of 5 alpha reductase and cytochrome P17, are being tested.

The use of enzymes and their inhibitors is not new to physicians. Imatinib is an inhibitor of tyrosine kinase domain of Bcr_Abl oncoprotein. The inhibition of tyrosine kinase prevents the oncoprotein from causing unlimited proliferation.

Telomerase is an enzyme that prevents the cells from senescence—that is, aging. Normal cells age after a certain period of time and undergo apoptosis. Cancer cells escape this phenomenon through continued telomerase production. A number of research projects have been carried out regarding the use of telomerase inhibitors to promote the aging and death of tumor cells.

Antiangiogenic Drugs in Chemotherapy

Every solid tumor needs to generate blood vessels to survive once it reaches a certain size. Angiostatic-based treatment prevents angiogenesis. Bevacizumab is being investigated for metastatic colorectal cancer therapy. It is a humanized monoclonal antibody directed against vascular endothelial growth factors secreted by the tumor. It inhibits its interaction with its receptors VEGFR-1 and VEGFR-2. The normal function of VEGF is the formation of blood vessels and regulation of their permeability and inhibition of apoptosis of new blood vessels. The interruption of these functions by bevacizumab kills the tumor. In a research trial carried out by Duke University Medical Center, patients who received bevacizumab along with the standard chemotherapy showed a five-month life extension.

Thalidomide is an old agent that is being exploited for multiple myeloma due to its antiangiogenic and immunomodulatory effects. Although the exact antiangiogenic mechanism has not been elucidated, several preclinical studies prove its efficacy.

Some drugs inhibit angiogenesis by a different mechanism. Gefitinib is a small molecule inhibitor of tyrosine kinase domain of epidermal growth factor receptor. It inhibits the angiogenesis caused by epidermal growth factor. Loss of blood supply starves the tumor. ZD6474 acts by plugging up small pockets inside the cell where adenosine triphosphate (ATP) would normally dock and enable the growth factors to activate. In the presence of ZD6474, the activation of vascular endothelial growth factor (VEGF) is prevented. A newer
Experimental Cancer Drugs

approach is to increase the formation of blood vessels in the tumor so that the tumor is choked. This approach has not yet proved to be as effective as antiangiogenic therapy.

Immunotherapy

Immunotherapy means to enhance the body’s immune system; it utilizes the natural components of the immune system or synthetic analogs for this purpose. The immune system of the body is suppressed in cancer patients and its enhancement would help overcome neoplasia. Immunotherapy utilizes monoclonal antibodies, cytokines and interferons, and cancer vaccines. Monoclonal antibodies are specifically directed against the antigens on the surface of tumor cells. This helps the destruction of tumor cells. Many have been developed like rituximab and trastuzumab, and many like cetuximab are being evaluated for various types of cancers. They are being used in combination with cytotoxic drugs and toxins to carry them to their targets so, in this case, these monoclonal antibodies are being used as guided missiles.

Interleukins are small proteins that enhance the T-cell immune response e.g. IL-2 activates; lymphokines activate killer cells (LAK cells). LAK cells destroy the tumor cells and benefit the patients with renal carcinoma, melanoma, and non-Hodgkin’s lymphoma.

Vaccines, Bacteria, and Viruses

Attempts have been made to develop effective vaccines to prevent cancer or treat cancerous patients. Cancer vaccines consist of a source of cancer-associated material (antigens) along with other components to stimulate the immune response against that antigen.

For example, in malignant lymphoma, a vaccine using lymphoma-associated protein called idio-type can stimulate the immune system and resist the development of lymphomas. Similarly, dendritic cell vaccines are being tried for melanomas where dendritic cells switch on the immune response.

Generally, engineered bacteria are also being used to enhance the immune system, for example, mycobacterium segments. Another study is being carried out to use anaerobic bacteria, such as Clostridium novyi, to consume the interior of oxygen-poor tumors. They do not consume the oxygen-rich side, so they are combined with chemotherapy.

T-cells may be isolated from the cancer patients and modified by induction of viruses into them that carry the receptor genes. When the modified T-cells are transfused into the patient, the receptor genes obtained from the virus enable them to attack the tumor cells with specificity. This approach has been tested for malignant melanoma.

The Duke University Medical Center developed a drug that uses targeting RNA to enter the cells and silencing RNA to stop the expression of those proteins that keep the cells alive. This drug has undergone many successful clinical trials (for prostate cancer). Attempts are being made to transform silencing RNA into natural anticancer drugs.

The University of California, San Francisco discovered an experimental anticancer drug called onyx-015. It is a genetically modified version of adenovirus (cold virus). In normal, healthy cells, the P-53 gene prevents tumor formation—that is, it checks the growth rate of cells. This virus can replicate only in those cells in which the P-53 gene is suppressed, which is the case in 60 percent of tumor cells. It also acts against the cells with intact P-53 genes but with defective P14 ARF that is located upstream in the tumor suppression pathway. The loss of P14 ARF inhibits P-53, which removes the restriction on adenovirus replication.

In contrast to P-53, Bcl-2 is a proto-oncogene that inhibits apoptosis by inhibiting the pro-death signals. Drugs like ABT-737 have been developed to release the pro-death signals from the inhibition caused by Bcl-2, which enhances the self-destruction of tumor cells.

Insulin and Gene Therapy

Insulin potentiation therapy is an unproven alternative cancer treatment. The cancer cells consume more glucose than healthy cells, so they are more susceptible to hypoglycemia caused by insulin. The chemotherapy after the injection of insulin will result in increased efficacy and decreased incidence of adverse effects because lower doses of drugs are required. However, this therapy has its own demerits.

A relatively newer approach to combat cancer is gene therapy. Genes are isolated from human cells, cloned, and altered. These genes could be put into cancer cells and then activated to produce a poison or toxin that kills the cells to make the cells more susceptible to the body’s immune system,
replace the damaged genes, or improve the effect of chemotherapy.

Sana Ghafoor
Amber Afzal
Independent Scholars

See Also: Anticancer Drugs; Chemotherapy; Drugs; Gene Therapy.

Further Readings

Explosives

Explosives, or explosive materials, are reactive substances (solids, liquids, or a mixture of substances) that, when measured in given quantities, or charges, release potential energy through a chemical reaction under certain conditions of light, heat, sound, or pressure.

Historically, explosives have been used by the military in warfare but have also been used for industrial mining, quarrying, construction, and demolition. In 1867, Alfred Nobel, a Swedish chemist and engineer, patented dynamite in both England and Sweden. Dynamite consists of sodium carbonate, diatomaceous earth, and nitroglycerin (ND). Although Nobel attempted tight control over these patents, Americans engineered a slightly different formula, trinitrotoluene (TNT).

Later, military-grade dynamite was engineered without using the highly unstable and sensitive nitroglycerin and instead using the chemical composition of cyclotrimethylene-trinitramine or cyclonite or hexahydro-1,3,5-trinitro-1,3,5-triazine, also known as the Royal Demolition eXplosive (RDX), which was used extensively in Germany during World War II.

In the process of demilitarizing off-specification, obsolete, or otherwise unserviceable munitions bases from 1940 through the 1970s, the U.S. Department of Defense began to recover TNT and TNT-containing fillers from explosives left over from the enormous quantities of RDX manufactured in World War II. According to the Environmental Protection Agency (EPA), this process allowed significant quantities of chemicals to contaminate soil and groundwater, the first report of which was in the 1980s.

Although RDX is not commercially produced in the United States, it is still widely used in commercial applications and U.S. military munitions, accounting for a large part of contamination around U.S. military installations. According to the Agency for Toxic Substances and Disease Registry (ATSDR), RDX has been identified by the EPA in at least 31 of the proposed hazardous waste sites for inclusion on the National Priorities List, 1,699, of which are targeted for long-term federal cleanup activities.

Within the new millennium, Dense Inert Metal Explosive (DIME) is a new breed of experimental military weaponry developed by the U.S. Air Force, combining RDX and a heavy metal tungsten alloy (HMTA) mixture. Tungsten is an inert metal, meaning it is not active in the chemical reaction causing the explosion but, upon detonation, acts like micro-shrapnel, embedding itself in the body's tissue and is extremely lethal within a four- to 15-meter range. DIME mixtures were used in military actions after 2000, primarily in Gaza throughout the various Israeli sieges in Palestine. While DIME technology has been lauded for its precision, accuracy, and ability to decrease the potential for collateral damage, physicians treating patients in Gaza in 2006 criticized DIME technology for causing “abnormally serious” physical injuries. Norwegian physicians Dr. Mags Gilbert and Dr. Erik Fosse have been at the forefront in bringing attention to the serious injuries incurred by Palestinians at al Shifa Hospital in Gaza City.

Many chemicals and substances used in the manufacturing or detonation of explosives are considered carcinogenic, meaning they have cancer-causing potential. Such carcinogens may directly affect DNA, leading to cancer, or could increase the likelihood that DNA changes will occur with varying levels of cancer-causing potential dependent on the degree,
limited or prolonged exposure, the intensity of those exposures, and a person’s unique genetic makeup.

Many of the substances, either on their own or in combination with other chemicals, are either grouped as carcinogenic to humans (Group 1), probably carcinogenic to humans (Group 2A), or possibly carcinogenic to humans (Group 2B), according to the classification developed by the International Agency for Research on Cancer (IARC). The U.S. National Toxicology Program (NTP) identifies these agents as known to be carcinogenic or reasonably anticipated to cause cancer.

The Occupational Safety and Health Administration (OSHA) recognizes both the evaluation of the IARC Group 1 and Group 2A carcinogens as well as the list of known and potential carcinogens published in the Annual Report on Carcinogens by the NTP as criteria for regulated carcinogens under the Hazard Communication Standard. OSHA requires all manufacturers of chemicals and mixtures to disclose the potential hazards when handling chemicals and compounds on a Material Safety Data Sheet (MSDS), which include any information regarding the carcinogenic nature of the material listed as well as allowable limits of exposure and potential health risks posed by exposure.

The most common explosives listed as carcinogens with governmental regulations are discussed in the remainder of this entry.

NT or o-NT, chemically known as nitrotoluene or ortho-nitrotoluene, may be used in the manufacturing of explosives, agricultural chemicals and pesticides, as well as the petrochemical, pharmaceutical, and rubber industries. The Report on Carcinogens (RoC) cited that o-NT be “reasonably anticipated to be a human carcinogen” based on animal studies and the IARC notes that o-NT is “probably carcinogenic in humans” in similar studies where laboratory rats were exposed to high doses for extended periods of time. Human exposure is most likely through contaminated groundwater near munitions-manufacturing facilities and military grounds and can result from ingesting orally, absorbing through the skin, or inhaling airborne particulates.

OSHA has set a permissible exposure limit (PEL) of five parts per million (ppm) and 30 milligrams per cubic meter (mg/m³) of workplace air within an eight-hour workday for a 40-hour workweek. NIOSH holds a recommended exposure limit (REL) of 0.5 mg/m³, while ACGIH recommended a more stringent TLV of 0.1 mg/m³ of workplace air within an eight hour workday for a 40-hour workweek.

RDX (chemical name: hexahydro-1,3,5-trinitro-1,3,5-triazine) has been classified as a Group C, possible human carcinogen, by the EPA based on a study wherein mice ingested RDX between one and two years, leading to the presentation of liver tumors. The ACGIH has classified RDX as not classifiable as a human carcinogen, or Group A4.

Potential routes of human exposure are through the skin or inhalation as well as ingestion of contaminated drinking water around hazardous waste sites. RDX targets the nervous system, causing seizures, nausea, and vomiting.

According to the Integrated Risk Information System (IRIS), the EPA’s database of chemical risk values, which includes health risk assessment and toxicity benchmarks, RDX was assigned a chronic oral reference dose (RfD) of $3 \times 10^{-3}$ milligrams per kilogram per day (mg/kg/day). The EPA assigned an oral slope factor for carcinogenic risk of 0.11 mg/kg/day, and the drinking water unit risk is $3.1 \times 10^{-6}$ micrograms per liter (μg/L). The EPA has issued a drinking water health advisory for RDX at varying concentrations of RDX contamination with a lifetime health advisory guidance level of 0.0002 mg/L.

The ATSDR established a minimal risk level (MRL) for varying durations of oral exposure to RDX: 0.2 mg/kg/day for acute-duration (14 days or
Extracranial germ cell tumors occur outside the brain. Germ cell tumors are abnormal growths...
Extracranial Germ Cell Tumor, Childhood

that are derived from germ cells, the cells that differentiate into the sex cells, eggs, and sperm (in contrast, the cells forming the rest of the body are called somatic cells). Tumors typically are classified in reference to the cell type from which they develop, with germ cell tumors originating in germ cells, sarcomas in nonhematopoietic mesenchymal tissue, leukemias and lymphomas in hematopoietic cells, and carcinomas in epithelial cells. Extracranial germ cell tumors may be either benign or malignant (cancerous), though even benign tumors can cause medical problems. Often, they originate as birth defects caused during embryonic development.

Extracranial germ cell tumors are classified as two types—extragonadal and gonadal, according to whether or not they are located in the gonads. This classification is in part because extragonadal germ cell tumors were originally believed to be metastasized carcinomas originating in the gonads before it was understood how common benign extragonadal germ cell tumors (many of which are called teratomas) are.

Another way to express the division between the two types of extracranial germ cell tumors is as that between germinomatous and nongerminomatous. The germinomatous germ cell tumors include germinoma of the brain, developing from the pineal gland (not discussed here, as it is not extracranial), dysgerminoma, developing in the ovary, and seminoma, developing in the testis. Nongerminomatous germ cell tumors are extragonadal.

Gonadal germ cell tumors are either testicular or ovarian. Testicular germ cell tumors usually occur during one of two windows: before age four or during adolescence. Though adolescents with gonadal germ cell tumors are often treated in pediatric cancer centers, their cancer is actually virtually the same as adult testicular cancer and develops differently than childhood gonadal germ cell tumors.

Seminoma produces hormones called beta-human chorionic gonadotropin. Testicular tumors may present as a painless lump in the testicles. Despite being difficult to diagnose until they develop more-painful symptoms, the survival rate is very high. One testicle may need to be removed surgically, but the patient will remain fertile. Childhood seminoma is unusual; germ cell testicular tumors are usually found in teenagers and young men. In about 10 percent of cases, rather than a lump presenting, testicular atrophy occurs. Lower back pain may present and is usually a sign of metastasis. The tumor may sometimes be detected by a blood test for placental alkaline phosphatase, especially if the patient has never smoked, which also increases placental alkaline phosphatase (PLAP). Often, the nature of the tumor is not certain until surgery has been performed and a biopsy can be done.

Testicular germ cell tumors can present an additional complication in the form of intratesticular masses, which need to be removed by inguinal orchiectomy.

Spermatocytic seminoma is a type of testicular germ cell tumor, constituting only about 1 percent of all testicular germ cell tumors. It is extremely rare but not unheard of as a childhood cancer, more commonly occurring in men over 50. It presents as slow and painless testicular enlargement in one or both testicles, and the tumors may sometimes show sarcomatoid differentiation. This cancer rarely metastasizes and so is fairly easily dealt with surgically. Chemotherapy and radiotherapy are rarely required.

Dysgerminoma forms in the egg-making cells of the ovary and are more common in adolescent girls. Ovarian tumors may present a lump in the abdomen, accompanied by pain, fever, or constipation as well as unusual bleeding from the vagina or, in adolescent girls, cessation of menstruation. Only about 5 percent of dysgerminoma cases occur during childhood. In 10 percent of patients, tumors occur in both ovaries. Having abnormal gonads due to androgen insensitivity syndrome or gonadal dysgenesis increases the risk of developing dysgerminoma. Tumors are usually smooth and knobby on the outside and soft and gray, pink, tan, or cream-colored on the inside. If they metastasize, they usually do so in the lymph nodes.

Certain hereditary disorders, notably Swyer syndrome, increases the odds of developing gonadal germ cell tumors, as does having an undescended testicle. The tumors are identified by physical examination, imaging including X-rays, ultrasounds, and computed tomography (CT) scans, or blood tests.

Prognosis depends on the malignancy of the tumor, the patient's age and health, and whether it has metastasized. A nonmetastatic tumor can usually be successfully removed, malignant or not. The prognosis is generally good for childhood gonadal germ cell tumors and slightly better in girls.
Chemotherapy and radiotherapy are both exceptionally effective with both ovarian and testicular childhood germ cell tumors.

Bill Kte’pi
Independent Scholar

See Also: Extragonadal Germ Cell Tumor; Ovarian Cancer, Childhood; Ovarian Germ Cell Tumor; Testicular Cancer.

Further Readings

Extragonadal Germ Cell Tumor

Extragonadal germ cell tumors originate outside the gonads. Germ cell tumors are neoplasms (abnormal growths) derived from germ cells, the cells that differentiate into eggs and sperm (all other cells in the body are called somatic cells). Tumors are neoplasms that have formed a lump, but not all neoplasms are tumors in that sense, even if they are malignant. Tumors often are classified according to the type of tissue from which they developed—sarcomas develop from nonhematopoietic mesenchymal tissue, carcinomas from epithelial tissue, leukemias and lymphomas from hematopoietic cells, and germ cell tumors from germ cells. Not all are cancerous, and they may originate as birth defects caused during the development of the embryo.

It was once believed that extragonadal germ cell tumors were carcinomas that had metastasized beyond the gonads, but it is now understood that many extragonadal germ cell tumors are in fact benign. About half of them are sacrococcygeal teratomas, located at the base of the coccyx. Teratomas are tumors with components that resemble the normal derivatives of two or more germ layers. They are most familiar to the layperson from their rarest example, fetiform teratoma, which consists of a mature teratoma that includes tissues resembling a poorly formed fetus, including not only hair, bone, or epidermis but partially or fully formed hands, feet, and eyes. There is a theory that fetiform teratoma is the result of a fetus that began development within its twin before being arrested, but this is not at all a certainty, and the mechanism is in any case unknown.

It is just as likely that these fetal features developed as a birth defect, not as a separate fetus, in the same way that a fetus may develop with a six-fingered hand or cleft palate. Other mature teratomas may be either solid or cystic, often including skin or hair, and sometimes bone. Sometimes tissues associated with organs like the liver, brain, or kidney will be present but not fully formed. Mature teratomas are almost always benign and are usually found in women. Immature teratomas, without these developed tissues, are more often found in men and are more often malignant.

Teratomas are graded 0 (mature and benign), 1 (immature and probably benign), 2 (immature and possibly malignant), or 3 (malignant) and classified according to whether they are solid (containing only tissues and the complex structures of mature teratomas), cystic (containing only pockets of fluid, like sebum, fat, or cerebrospinal fluid), or mixed, containing both. Any teratoma has the potential to become malignant, and any malignant teratoma has the potential to metastasize. Seemingly benign teratomas may become malignant in unexpected ways, such as cystic teratomas containing squamous cell carcinoma that is not discovered until surgery.
Though present before birth, teratomas are usually not diagnosed until much later—sometimes during childhood, if the tumor is large, but more often in adulthood. Even fetiform teratomas may go undetected for decades. In some cases, the teratoma is detected in a prenatal magnetic resonance imaging (MRI), and some larger teratomas are responsible for the death of a fetus or require emergency intervention, usually fetal surgery. This is particularly true if the teratoma is large enough that the fetus’s blood flow is redirected to it.

Some benign teratomas can cause difficulty simply through their physical presence, either because of obstructing some important process in the body or by stimulating antibodies or secretions. Ovarian teratomas can result in a serious illness called anti-N-methyl-D-aspartate (NMDA) receptor encephalitis, in which patients develop psychosis and memory troubles, followed by seizures, language difficulty, and finally a near-catatonic state characterized by unsteady breathing and abnormal movements. Other teratomas in both men and women can cause chest pain or breathing difficulty because they are pressing down on the lungs.

Sacrococcygeal teratomas, located at the base of the tailbone, occur in roughly one in every 35,000 people and are more likely than other teratomas to be identified in babies and children. Prenatal ultrasounds nearly always will reveal their presence. In rare cases, they may grow larger than the fetus, jeopardizing its life as previously discussed. They are found more often in girls than boys by a ratio of about four to one. Those that are not found on ultrasound or in the newborn often are discovered shortly after the child learns to talk, especially during toilet training, as the teratoma may be detectable as a periodic physical sensation that the child articulates as fecal urgency.

Teratomas are usually treated with surgery and are relatively easy to resect from surrounding tissues. This is often recommended because of the possibility of becoming malignant or of concealing malignant tissue within it. Malignant teratomas (which become adenocarcinomas) are subjected to follow-up chemotherapy. With sacrococcygeal teratomas, although it is relatively simple to remove the malignant tumor in its entirety, some functional disability is often a side effect.

Bill Kte’pi
Independent Scholar

See Also: Extracranial Germ Cell Tumor, Childhood; Ovarian Germ Cell Tumor; Testicular Cancer.

Further Readings
Family Size

Family size is the number of members that make up a family unit. There are many different definitions of family, somewhat complicating research, but in the United States, it typically means those who are tied through blood or marriage, or who live together in the same household.

Research has identified some relationships between family size and risk for cancer. However, much of the research is preliminary, and this topic warrants much further in-depth research to find concrete patterns between the two. Research on the relationship between family size and cancer is complicated by the fact that family size may correlate with other risk factors such as socioeconomic status and also that the number of children a women bears directly influences her risk for reproductive cancers (breast, ovary, and endometrium).

As the definition of a family is variable, so is the definition of what constitutes a “large” versus a “small” family. The lack of consistency across studies in defining a small and a large family is a further complication in studying this relationship, although many studies count four or more children as a large family and three or less as a small family. To advance insights from research, a more consistent application of definitions will help.

Large Family Size

One study found that individuals from larger families were less likely to develop melanoma of the skin. The study, conducted in a northern region, offered the possible explanation that larger families typically could not afford vacations to sunny climates, from their homes in the north to the south, and therefore were less likely to experience prolonged sun exposure, which has been linked to melanoma (skin cancer). Obesity, which increases risk for various cancers such as liver, breast, esophageal, colorectal, kidney, and endometrial cancer, has been linked to large family size, but this relationship is complicated by the fact that in current U.S. population surveys, poverty is related to both obesity and large family size.

Large families can also contribute to an increased risk for stomach cancer because of greater exposure to the bacterium Helicobacter pylori. Younger siblings are at the greatest risk for stomach cancer from H. pylori because they may be exposed to the bacterium at a very young age from their older siblings. Being exposed to the bacterium while one’s immune system is still developing can cause long-term effects. The bacterium will have already had a “head start” in a younger person, compared with a genetically similar older person (e.g., a younger sibling compared with an older sibling), and can attack
the younger sibling in a stronger, more disastrous way. The bacterium also has the potential to have adapted to the family's genes and can easily compromise a younger sibling's immune system, causing stomach cancer later in life.

Other cancers with infectious and viral origins also have a higher prevalence in larger families. This may be due to the fact that infections may spread more readily through a large family than through unrelated individuals because family members live in close proximity to one another. This ease of disease spread can lead to compromised immune systems and a higher likelihood of certain cancers including certain lymphomas.

In contrast, some cancers are less common in members of large families. For instance, glioma brain cancer is less prevalent in larger families, and having siblings is associated with a reduced risk of developing glioma as an adult. Unlike the case of stomach cancer, being exposed to infection at a young age from siblings actually lowers the risk for glioma, as it can stimulate the immune system and prepare the body better to fight off infection that could have led to glioma as an adult.

Small Family Size
Small families are associated with more educated women and higher socioeconomic status, and they are also associated with higher parental age at conception. Due to risks associated with having children at an older age, the last-born child may be at a higher risk of developing both childhood cancers as well as cancers later in life. These cancers can vary as there are myriad health concerns for children born to older mothers. Later age at childbirth and fewer children increase the risk for breast cancer in mothers, and fewer children is directly related to increased risk for ovarian cancer. Since the onset of industrialization, family size is becoming smaller, and an unintended consequence is higher risk for some cancers among women.

Family size has also been linked to breast cancer. A genetic breast cancer study found that women with fewer than two first- or second-degree family members living past 45 years were more likely to develop genetic breast cancer. Having a smaller gene pool from which to have potentially inherited hereditary cancer may raise the risk for cancer, but it also makes tracking the family history simpler. However, this research is complicated by the fact that though small family size makes it easier to track family history and records from small families may be more accurate, some observed results may be due to the differential quality of data from families of different sizes.

Family size has been linked to cancer risk in another way, because the number of children borne by a woman has been related to differing risks for some types of cancer. Women who have more than two children have a higher risk for cervical cancer. Yet having no children puts women at a higher risk for endometrial and ovarian cancers. Pregnancy serves as a protection for women against breast and ovarian cancer. During pregnancy and subsequent breastfeeding, women have a much lower risk of developing breast or ovarian cancer.

Prevention and Support
Family size also plays a role in norms around prevention behaviors for cancer, such as smoking, exercise, choice of diet, and getting health screenings. These behaviors may be learned from and influenced by the behavior of other family members, and the family environment may be more or less welcoming to behaviors identified as increasing cancer risk or reducing cancer risk. Of course, many of these behaviors are also related to other factors that are related to family size, such as socioeconomic status. Differing family dynamics may also play a role in the practice of health behaviors: For instance, some health risk behaviors (e.g., smoking) may be more likely to pass unnoticed in a large family than in a small one.

In some cases, the term family can include the extended family, such as grandparents living under the same roof as their children and grandchildren. Creating a multigenerational family, which may tend to be larger than a nuclear family, has been shown to increase the likelihood of following preventative measures to avoid cancer. Living with one's grandparents makes it easier to gather information about family history, and older generations are more likely to promote cancer screenings for the family in hereditary cancer cases. Older family members who have experienced cancer may understand both the medical and the social aspects of the disease better than younger family members.

They are also able to offer guidance and support to younger generations in the family if everyone lives under the same roof.
Family size can also play an important role in support systems. A diagnosis of cancer creates a very vulnerable and fearful time in one’s life, one that is best handled in a supportive environment. Two aspects of social support are network size (how many family members and friends one has) and perceived adequacy of the support to the patient. The larger the support network size, the less likely patients are to show depressed symptoms. High perceived adequacy of that support aids in lowering depression too. Coming from a larger family can automatically grant someone a higher network size, thus leading to lower levels of depression. However, even when coming from a large family, as people age, their social network diminishes in size, leading to higher incidences of depression in elderly cancer patients. This is especially true for people who do not have any or many children.

Preliminary research shows that family size can be a medical predictor of cancer incidence, as well as aid in the understanding of social support after a cancer diagnosis. Continued research into the many different types of cancers as well as the many different types of families will yield information vital for cancer research.

Courtney Vail Fletcher
Chelsea Halstead
University of Portland

See Also: Brain Tumor, Adult; Gallbladder Cancer; Gastrointestinal Carcinoid Tumor; Melanoma; Psychosocial Care/Support

Further Readings

Finland

The Republic of Finland is a Nordic nation bordered by Sweden to the north, Russia to the west, Estonia to the south, and the Gulf of Finland to the west. With a population of 5.5 million, Finland is one of the more sparsely populated members of the European Union as well as one of the most prosperous. Most of Finland’s health care system is funded by the government and is the responsibility of Finland’s Ministry of Social Affairs and Health. Research regarding various diseases and health conditions, including cancer, is provided by Finland’s National Institute for Health and Welfare.

Beginning in the 12th century, Sweden controlled most of what is present-day Finland, continuing its hegemony over the area until 1809, when Finland became a grand duchy of the Russian Empire. Achieving independence in 1918, Finland remained a mostly rural, agrarian society until after World War II. Joining the United Nations in 1955, Finland has maintained its neutrality since that time, partially in deference to concerns of the Soviet Union, now the Russian Republic. After 1950, Finland rapidly industrialized, with the majority of its citizens now living in urban areas. Economic growth was rapid, and Finland’s gross domestic product (GDP) and per-capita income were among the globe’s highest by the mid-1970s. After an economic depression during the early 1980s, Finland again enjoyed rapid economic
Finland has adopted the Nordic model of government, which combines free markets with strong social welfare programs. The first nation to grant universal suffrage to all citizens, Finland strives to provide for the educational and economic well-being of all. To do so, Finland has established a system of legal rights, including that to health care. In 1929, the Finnish government established a committee that examined the status of the nation’s health care system. At that time, it was determined that Finland was sorely lacking in access to health care. The decision was consequently made to establish a system of publicly funded hospitals, which have served as the base of the modern Finnish health system.

Government health policies are established through the Ministry of Social Affairs and Health and subsequently approved by the Finnish parliament. Each municipality is charged with offering health care services to its residents. These health care services are often provided through municipal health care centers. Local health care centers, which employ general practitioners and nurses, provide primary care, which encompasses most day-to-day medical services. Primary care health centers also specialize in health promotion activities. The primary care centers serve as gatekeepers for more-specialized services in the secondary and tertiary care sectors, and a referral from a patient’s primary care provider is needed for him or her to receive care on the secondary and tertiary levels. When secondary care is needed, it is provided through district hospitals, where more specialists are available. Tertiary care is provided by Finland’s network of five university teaching hospitals, which provide the most advanced medical equipment and facilities. Municipalities also fund both secondary and tertiary care, although the national government does assist with the cost of medical training. Tertiary care facilities are located in Helsinki, Kuopio, Oulu, Tampere, and Turku. The health care system is funded both through general tax revenues and user fees.

Finland’s Ministry of Social Affairs and Health also funds medical research, including that involving cancer, through the National Institute for Health and Welfare. The National Institute for Health and Welfare works to find solutions to certain health problems facing the Finnish public and also to affect the health services provided those citizens. With an annual budget of €100 million, the National Institute for Health and Welfare focuses upon the following:

- Promoting the health and welfare of Finns
- Preventing diseases and other social problems that threaten Finland’s health
- Developing health care and social activities and programs

As such, the National Institute for Health and Welfare works to reduce the incidence of cancer in Finland, seeking both to alter certain behaviors of the population (i.e., reducing tobacco usage) while also sponsoring research that assists in treatment of the disease. It also works with international organizations to translate research findings from abroad into improved treatment options for Finns facing cancer.

Cancer Research

The National Institute for Health and Welfare and the Cancer Society of Finland jointly sponsor the Finnish Cancer Registry, also known as the Institute for Statistical and Epidemiological Cancer Research. The Finnish Cancer Registry has since 1953 maintained a database of all incidents of cancer in Finland. This has permitted researchers and scientists to examine how rates of cancer have changed over time. Examination of this data permits policy makers and health care providers to explore why the incidence of certain types of cancer may have increased or declined over time and to take appropriate steps to deal with these changes. Alcohol consumption among Finns increased by approximately 33 percent between 1985 and 2010, with a concurrent increase in liver cancer and other alcohol-related diseases. As a result, policy efforts have begun to decrease the rate of alcohol successfully, including tax increases and a public awareness campaign.

The Finnish Cancer Registry also undertakes basic research, resulting in the publication of approximately 100 scholarly articles per year. The research funded by the Finnish Cancer Registry is broad and varied. Examples of recent research includes Marianne Hinkula’s examination of the relationship between childbearing and reproductive organ cancer incidence; Hinkula’s study found
that women who bore five or more children had a statistically significant lower chance of cancer of the breast, ovaries, or endometrium, while the incidence of cervical cancer increased for the same population.

These findings have led to further studies examining how hormonal therapy might reduce the incidence of these cancers. Another study conducted by Timo Timonen, Simo Näyhä, and Eero Pukkala examined the interaction between sunlight deprivation, influenza, and leukemia. Sunlight deprivation is of particular interest in Finland, where exposure to sunlight is severely restricted during winter months. The study found that the incidence of acute leukemia increased during the winter months, as did the incidence of influenza. The researchers posited that this occurred as a result of the dark season, which itself caused a substantial proportion of Finns to suffer from a deficiency of vitamin D. Further studies are being conducted to examine how vitamin D supplements will affect this deficiency. As a result of this and other research, the survival rate of Finns diagnosed with cancer has increased dramatically over the past 50 years.

Stephen T. Schroth
Towson University

See Also: Denmark; Drugs; Education; Future of Cancer; Hospitals; Norway; Sweden.

Further Readings

Flame Retardant

Designed to suppress, delay, inhibit, or otherwise prevent the spread of flames, flame retardants are minerals added to base materials (additive) or chemically bonded compounds applied as surface finish and coatings (reactive) in manufactured goods that might be combustible.

The two classes of flame retardants, additive and reactive, are further subdivided into families of minerals (aluminum hydroxide, hydrates, borates, etc.), organohalogen compounds (polymeric brominated compounds, brominated polystyrenes, organochlorines, organobromines, etc.), and organophosphorus compounds (organophosphates, brominated tris, chlorinated tris, and halogenated phosphates).

Coupling with a rise in global safety standards, the worldwide use of flammable materials in consumer products, including electronic, aviation and automotive components as well as insulation, roofing, clothing, upholstery, and textiles, has encouraged the use of flame retardants. There are risks of exposure through direct contact with such products, dust and airborne particles, as well as post-combustion inhalation.

Studies indicate that flame-retardant chemicals pose a health risk during combustion, emitting large amounts of carcinogenic dioxins and furans released in the smoke and dust. Inhaling, ingesting, or absorbing these toxic by-products puts firefighters at a higher risk. In a California study, incidences of breast cancer among female firefighters age 40 to 50 had six times the national average, which may be linked to the state’s early adoption of California Technical Bulletin 117 (TB 117) standards. Subsequent studies show firefighters of both genders developing cancer, including rare forms of transitional cell carcinoma typical of chemical industry workers, at higher rates than the general public.

TB 117 was enacted in 1975, requiring polyurethane foam to meet the basic flammability standard of withstanding a small open flame for at least 12 seconds. Because California represents such a large percentage of the market, the majority of furniture manufacturers met these standards in products distributed throughout the United States, using halogenated organic flame retardants. By the turn of the millennium, 80 percent of the furniture treated in the United States met TB-117 standards.

Despite their pervasive use, worldwide numerous studies have shown that flame retardants are not necessarily effective in delaying combustion or preventing the spread of flames. Testing has shown that bioaccumulation, the buildup of these
toxic chemicals in the human body as well as animals over a lifetime, never reduces, causing serious health impacts including cancer. Regulations allow for the discontinuation or ban of one chemical only to be replaced by its equivalent.

A recent *Chicago Tribune* investigative report linked the introduction of halogenated flame retardants in the United States to a 1920s strategy employed by the tobacco industry aimed at redirecting public pressure on self-extinguishing cigarettes to flame-retardant requirements in response to a rise in deaths, identifying indoor cigarette smoking where the smoker fell asleep smoking in an upholstered chair or bed.

The data collected by the *Chicago Tribune* suggested that the tobacco industry allied with various fire safety groups, inventing the National Association of State Fire Marshals, to push for fire-retardant furniture and upholstery requirements, contributing to the passage of TB 117. The campaign was effective in delaying the introduction of the self-extinguishing cigarette almost a century after the first self-extinguishing cigarette was developed.

A 1977 study explored the use of fire retardants (polybrominated biphenyls [PBBs], polychlorinated biphenyls [PCBs], and tris-[2,3-dibromopropyl] phosphate [tris-BP]) in children’s pajamas, which were added due to the Flammable Fabrics Act of 1943 to protect the public from “unreasonable risk” of fire. It suggested a more prudent alternative to using toxic chemical fire retardants in clothing would be self-extinguishing cigarettes as the cause of 30 to 50 percent of U.S. 12,000 fire deaths per year could be attributed to the use of tobacco products.

This study, among others in the 1970s, contributed to the ban of tris-BP in children’s pajamas, citing a 1973 study by the National Cancer Institute (NCI) where 50 percent of female laboratory rates developed adenocarcinomas. Effective January 2014, the flammability standard was replaced by the smolder test, such that upholstery and furniture need to withstand a smoldering cigarette rather than an open flame, expecting to reduce the use of flame retardants.

Among the earliest of flame retardants, PCBs were used as heat transfer fluids in transformers and capacitors and banned in the United States in 1977. In 1979, the U.S. Congress banned the manufacture of PCBs and later, the Environmental Protection Agency (EPA) classified PCBs as known animal carcinogens and probably human carcinogens based on animal testing.

Use of PCBs was replaced by brominated flame retardants (BFR), including trambromobisphenol A (TBBPA), hexabromocyclododecane (HBCD), and the most frequently cited polybrominated-diphenyl ethers (PBDEs). In studies where rats and mice ingested decabromodiphenyl ether (decaPBE)-laced food for the duration of their lives, they developed liver tumors, and as a result, the EPA has classified decaBPE as a possible human carcinogen.

Widely used in furniture manufacturing as an additive in furniture foam until 2000, penta-bromodiphenyl ether (pentaBDE) has been the source of growing concern for both environmental and public health risks. The EPA has partnered with the Furniture Flame Retardancy Partnership (FFRP) since 2003 to access viable alternatives to pentaBDE. PBDEs with fewer bromine atoms, such as pentaBDE and octabromodiphenyl ether (octaBDE), are not classifiable as carcinogens according to the Agency for Toxic Substances and
Disease Registry (ATSDR). This does not necessarily mean these compounds are safe or not carcinogenic but demonstrate a void of research necessitating further study. In 2001, the Stockholm Convention, an international environmental treaty, listed 22 organohalogenics and three BFRs as persistent organic pollutants (POPs).

In 2004, the only U.S. manufacturer of pentaBDE and octaBDE voluntarily ceased manufacturing the chemicals, and by 2009, the primary manufacturer of decaBDE committed to end the production, import, and sale of decaBDE by the end of 2013, although it is possible that pentaBDE continues to be used in other countries and enters the United States through imported goods.

A group of 145 prominent scientists, representing 22 countries, signed the landmark San Antonio Statement on Brominated and Chlorinated Flame Retardants 2010, the goal of which is to advocate for widespread policy changes in the use of flame retardants. The first consensus statement against flame retardants citing documented health hazards linked to high levels of flame retardant chemicals in consumer products and furniture, it questioned the usefulness of using flame retardants given the limited safety benefits and serious impacts on human health.

According to a 2014 market study performed by Ceresana Research, 2 million tons of flame retardants were used, generating projected revenue in the United States of $7.15 billion by 2021. This same study recognizes a downward trend in BFRs as well as chlorinated and halogenated flame retardants.

Because of heavy exposure of the BFRs and PBDEs over several decades, it is assumed that most people have bioaccumulated toxins as a result of exposure in furniture, infant products, electronics, computers, and foam insulation. Studies show that people living in the United States are exposed at a rate 10 to 40 times higher than their European or Asian counterparts.

The EPA has issued a proposed rule in 2012 to stop the import of products containing PBDEs, including pentaBDE, octaBDE, and decaBDE, and has formed the Design for the Environment (DfE), an EPA partnership with industries aimed at identifying safer alternatives to PBDEs, HBCDs, and other chemical flame retardants in response to human health and environmental concerns and evidence of increasing body burden in the general population.

PBDEs largely have been replaced in consumer products by tris(1,3-dichloro-2-propyl) phosphate (TDCPP) and are used in polyurethane foam padding applied to furniture and automobiles. In a 2013 survey of 101 products for infants and toddlers, TDCPP was found to be the most frequently used flame retardant.

Because TDCPP is not chemically bonded to the foam, it poses a risk of exposure through dust. Recent studies also documented the presence of the flame retardant in accumulated dust in homes, offices, and automobiles, where levels of exposure were seen to be higher than in people's homes. Two complementary studies demonstrated alarmingly high exposure to TDCPP. Unlike PBDEs, which can linger in the body for years, TDCPP is believed to have a half-life of hours or days.

The National Research Council reported TDCPP to be linked to cancer in rats. Further studies indicate that TDCPP is neurotoxic, an endocrine disruptor, and a reproductive toxicant. Although TDCPP is on California's Proposition 65 list of substances known to cause cancer, its potential carcinogenicity has not yet been classified by the EPA, International Agency for Research on Cancer (IARC) or National Toxicology Program (NTP). As of June 2014, the EPA will be assessing more than 20 flame retardants to determine the level of risk.

Another organophosphate flame retardant chemical similar to TDCPP and used to replace PBDEs, Firemaster 550, has been used in foam furniture and children's products. Firemaster 550 contains TBB, or 2-ethylhexyl-2,3,4,5-tetrabromobenzoate, and TBPH, or 2-ethylhexyl-2,3,4,5-tetrabromophthalate. The carcinogenicity and toxicity of Firemaster 550 has not yet been determined, although a recent study showed a detected presence in 96 percent of the dust samples. Detectable levels of Firemaster 550 have been found in the tissues of baby harbor seals, indicating contamination of the ocean environment and wildlife.

Tara Michele Zrinski
Northampton Community College

See Also: Carcinoma of Unknown Primary; Chlorine; Environmental Tobacco Smoke; Lung Cancer, Non–Small Cell; Plastics Industry.
Flavoring Agents

The connection between health, taste, and flavoring agents is a complex one, colored by many factors. By description, flavorings are often complex mixtures of natural and man-made substances. Some flavorings are simple and composed of only one chemical, while many others are complex mixtures of several substances. When properly combined, such mixtures can provide the aroma and taste of a specific flavor, such as butter or strawberry. This entry discusses what flavorings are in greater detail, where they come from and how they are made, potential health issues and risks surrounding them, and why they will likely continue to pose some risk to those especially who manufacture them.

The Manufacturing and Labeling of Flavoring Agents

To begin, flavoring agents are ubiquitous in the modern food supply. In fact, there are more than 2,000 substances used in flavoring manufacturing for food products today. Typically, in the United States, the Food and Drug Administration (FDA) regulates flavorings to ensure they are safe when they are eaten (but not necessarily inhaled). Any liquid extracts, essences, and flavors that are added to foods to enhance their taste and aroma are evaluated for safety and toxicity typically, regardless if naturally or synthetically derived. There are a wide number of original sources of flavorings such as: essential oils, in the cases of almond, lemon, and vanilla; fresh fruits obtained by expression methods; ginger obtained by extraction methods; mixtures of essential oils and synthetic organic chemicals or entirely from synthetic chemicals, with the aid of various solvents such as alcohol, glycerol, and propylene glycol used alone or in combination. In the manufacturing process of making the agents, water is often added as well as certified food coloring. To be precise, extracts, essences, and flavors employing only natural flavoring agents are called pure flavorings. Contrarily, those employing
synthetics (in part or entirely) are called imitation, or artificial, flavorings.

It is important to note that nearly all of these organic chemicals have been artificially synthesized as well, and it is these synthetics that are used in the manufacture of imitation flavorings. In sum, flavorings are focused on altering the flavors of natural, whole foods such as meats and vegetables, or creating flavor for food products that do not have the desired flavors as determined by manufacturers, such as candies and other snacks. Most types of flavorings are focused on enhancing the scent and taste of the product.

Depending on which country and its respective laws you examine, each country may slightly alter their definition and categorization of flavorings. For instance, in the United States, the U.S. Code of Federal Regulations describes a natural flavorant as “the essential oil, oleoresin, essence or extractive, protein hydrolysate, distillate, or any product of roasting, heating or enzymolysis, which contains the flavoring constituents derived from a spice, fruit or fruit juice, vegetable or vegetable juice, edible yeast, herb, bark, bud, root, leaf or any other edible portions of a plant, meat, seafood, poultry, eggs, dairy products, or fermentation products thereof, whose primary function in food is flavoring rather than nutritional.” The European Union’s (EU’s) guidelines for natural flavorants differ slightly. In this instance, certain artificial flavorants are given an E number, which may be included on food labels, whereas United Kingdom food law defines a natural flavor as “a flavoring substance (or flavoring substances) which is (or are) obtained, by physical, enzymatic or microbiological processes, from material of vegetable or animal origin which material is either raw or has been subjected to a process normally used in preparing food for human consumption and to no process other than one normally so used.”

**Unique Characteristics of Artificial Flavorings**

Most artificial flavors are highly specific and often complex mixtures of singular, naturally occurring flavor compounds combined together to either imitate or enhance a natural flavor. These mixtures are formulated by flavorists (i.e., flavor chemists) to accomplish a number of things including (1) to give a food product a unique flavor; (2) to maintain flavor consistency between different product batches; and (3) to maintain flavor consistency after recipe changes. The list of known flavoring agents in food manufacturing includes thousands of molecular compounds, and the flavorist often can mix these together to produce many of the common flavors found in many natural, whole foods. For instance, many flavorants consist of esters, which are often described as being sweet or fruity, which are typically highly desired flavors in many foods. However, what is considered a flavorant or not can be somewhat discretionary. Such is the case with organic acids that may enhance sour taste, such as acetic acid and citric acid, which are not regulated as flavorants by law.

Compounds used to produce artificial flavors are almost identical to those that occur naturally. Ironically, it has been suggested by some testing authorities that artificial flavors may be safer to consume than natural flavors due to the standards of purity and mixture consistency that are enforced either by the manufacturing company or by law.

Examples of artificial flavors include the chemical compound diacetyl (used to make artificial butter flavor), isoamyl acetate (used to make banana flavor), cinnamic aldehydes (used to mimic cinnamon), and benzaldehyde (which can mimic the flavor of bitter almonds).

**Safety and Health Issues Surrounding Flavoring Agents**

To begin, many flavorings have been in use for many years and are classified by the FDA as generally recognized as safe (GRAS) for oral consumption. However, the FDA does not require testing for other routes of exposure, such as inhalation, and this is where other data in a number of studies has suggested otherwise when it comes to their safety.

For example, the National Institute for Occupational Safety and Health (NIOSH) investigated the occurrence of severe lung disease in workers at a microwave popcorn packaging plant. Eight former workers at this plant developed an illness characterized by fixed airway obstruction on lung function tests linked to diacetyl exposure (i.e., artificial butter flavor) through respiration. Similar fixed, obstructive lung disease has also occurred in workers at other plants that use or manufacture flavorings, and furthermore, in animal tests, inhaling vapors from a heated butter flavoring used in microwave popcorn production caused severe injury to airways.
In general, flavoring chemicals are very volatile, making them readily able to evaporate into the air from their liquid or solid form, thus leading to likely inhalation. They also can be inhaled in the form of a powder if airborne dust is created in the production process (such as in food manufacturing plants). Many of these chemicals in studies have been shown to be highly irritating to the eyes, respiratory tract, and skin.

At flavoring and microwave popcorn production plants, where workers developed the severe lung disease, workers routinely handled or were exposed to open vessels containing flavorings or their chemical ingredients. In addition to microwave popcorn and flavorings plants, other food industries of note with potential exposure to butter flavoring chemicals include (1) snack foods (e.g., chips and pretzels); (2) commercial and retail bakeries (e.g., cakes, cookies, and bread); (3) retail baking mix production; (4) margarine and other vegetable oil–based cooking products; (5) butter and other dairy products; (6) and candy manufacturers. Furthermore, the use of butter-flavored cooking oil products to prepare meals in restaurants also may lead to worker exposure in such venues. While exposures in the flavoring industry and in microwave popcorn production have caused severe lung disease in some workers, the degree of risk to workers from exposures in other settings is currently unknown and will likely remain a risk factor for the foreseeable future due to a lack of regulatory guidelines and enforcement on such exposures.

Given the complexity of flavoring mixtures and the lack of health data for many of the component materials, identifying the relative contributions and risks of individual substances to causing flavoring-induced lung disease is very difficult. The flavorings industry has estimated that more than 1,000 flavoring ingredients have the potential to be respiratory hazards due to possible volatility and irritant properties (e.g., alpha, beta-unsaturated aldehydes and ketones, aliphatic aldehydes, aliphatic carboxylic acids, aliphatic amines, and aliphatic aromatic thiols and sulfides). Some of the most closely examined flavoring agents and their connections to potential health issues include the following: diacetyl (related to artificial butter typically); 2,3-pentanedione; 2,3 hexanedione; 2,3 heptanedione; acetoacetin (acyl methyl carbinol); and acetaldehyde.

By far, the overwhelming concern with flavoring agents primarily relates to respiratory damage and lung disease sequelae (such as bronchiolitis obliterans). This is also primarily via respiratory inhalation, not oral consumption of such agents, research suggests. The initial signs and symptoms of flavoring-related fixed airways obstruction may be subtle. These signs and symptoms seen in affected workers include cough, fatigue, and shortness of breath with exertion. Such signs and symptoms generally do not improve on weekends, brief respites, or vacations, and these same signs and symptoms may have a gradual onset. In some cases, however, severe signs and symptoms have occurred suddenly with rapid progression of lung disease. Accordingly, because of a lack of general knowledge and awareness of the risks associated with flavoring agent exposure by the medical profession, workers may be misdiagnosed with other lung diseases such as asthma or chronic obstructive pulmonary disease (which in some cases may increase the risk for certain types of lung cancer).

It may take months or years before, potentially, the real causes and issues are later revealed. Once diagnosed, unfortunately, studies have not suggested a good prognosis. Workers with flavoring-related fixed airways obstruction, including bronchiolitis obliterans, largely have not demonstrated any improved lung function with medical treatment in clinical studies. Studies also indicate that, while a small percentage of individuals have noted gradual improvement in their cough, several years after flavoring agent exposure, their pulmonary function generally has not improved. In extreme cases, individuals have developed severe, disabling lung disease requiring that they receive a lung transplant.

In addition to the plethora of lung disease problems linked to flavoring agent exposure, exposed individuals have also experienced irritation of the eyes, nose, and throat. For example, in the NIOSH study examining the popcorn manufacturing site, researchers found that nearly half of the current production and office workers and all current laboratory and warehouse workers reported having experienced nasal irritation. Furthermore, approximately half of the then-current office workers and
warehouse workers and approximately 80 percent of production and laboratory workers reported experiencing eye irritation. Lastly, skin problems were most common in current production workers (36 percent), especially in workers who made mostly liquid flavorings (60 percent).

**Conclusion**
As has been detailed, flavoring chemicals are very volatile, so they easily evaporate and can be readily inhaled. They can also be inhaled in the form of a powder if airborne dust is created in the production process. Many of these chemicals are highly irritating to the eyes, respiratory tract, and skin and can be linked to chronic and progressive lung diseases. Thus, for as long as we continue to use them in the food manufacturing process and also not require proper ventilation and protection for workers and office staff in food manufacturing and preparation sites, health risks and lung disease in particular will continue to be issues for those chronically exposed.

Eric Wood
Hawthorn University

**See Also:** Food and Drug Administration; Lung Cancer, Non–Small Cell; Lung Cancer, Small Cell.

**Further Readings**

**Food Additives**

Any substance added to food to preserve the color, flavor, texture, or appearance or to extend the shelf life of a food product for storage can be considered a food additive regardless of whether it is natural (caffeine, vanilla, etc.) or artificial (yellow dye #5, aspartame, etc.).

Within the second half of the 20th century, factory-processed foods have introduced more than 3,000 food additives, both natural and artificial, to the global food supply and have significantly changed the standard American diet, raising concerns about the adverse impact that these food additives may have on human health.

The Food and Drug Administration (FDA) regulates the safety of food and responds to petitions by companies requesting approval for new chemical ingredients and food additives. After the review process, the FDA will either deny the petition or approve the request, granting the label generally recognized as safe (GRAS), with recommendations on the terms of use within food.

The GRAS designation was established in the Food Additives Amendment of 1958, an amendment to the Food, Drugs and Cosmetic Act of 1938. Under the Delaney Clause of the 1958 amendment, new food additives (pesticides, chemical ingredients, and organic compounds) must be tested, and if found to be carcinogenic in humans or animals, the law requires the FDA to ban the usage of such additives.

Several ingredients that have been banned in other countries have been granted approval by the FDA, including various food dyes, azodicarbonamide, potassium bromate (brominated flour), artificial sweeteners, nitrates and nitrites, acrylamides, butylated hydroxanisole (BHA), and butylated hydroxytoluene (BHT).

Azodicarbonamide is the latest food additive to come under speculation. Used in bread as a food additive, and industrially for yoga mats and shoe soles, azodicarbonamide breaks down and forms high levels of urethane, a known carcinogen. Even though it has been approved for use in food not to exceed 0.0045 percent by weight of the flour used in bread, the FDA recommends manufacturers voluntarily remove the ingredient. In 2014, the food chain Subway voluntarily discontinued use of azodicarbonamide under public pressure.
Potassium bromate, also used in bread making, is classified as a Group 2B possible carcinogen by the International Agency for Research on Cancer (IARC) based on studies of exposed rats that developed renal cancer. Although the European Union, Canada, and several other countries have banned potassium bromate, the FDA sanctioned its use prior to the Delaney Clause and has asked bakers to voluntarily discontinue its use.

Artificial sweeteners have received a great deal of attention as possible carcinogens, historically. The prevalence of their usage throughout the world, marketed as sugar-free products to diabetics and as a lower-calorie substitutes for weight watchers, has raised questions about the allowable limits of daily and lifetime consumption and the links to cancer.

In 1969, the FDA banned the use of cyclamate as a result of studies on laboratory rats that demonstrated an increased risk of bladder cancer in humans. Even though this study was reevaluated by the Office of Food Additive Safety (OFAS), determining that cyclamate was not carcinogenic, the petition for reapproval with the FDA is being held in abeyance, a category which includes petitions found to be deficient, and as of March 2014, the status of the petition shows no new evidence to satisfy the deficiency.

Drawing much concern and attention to artificial sweeteners, studies performed in 1977 on laboratory rats linked saccharin (Sweet ‘N Low) to the development of bladder cancer. Subsequent studies showed that these results only apply to rats and not humans. Epidemiological studies show that there are no consistent patterns of evidence that would support incidences of cancer in human beings, and in 2000, saccharin was taken off the list as reasonably anticipated to be a human carcinogen, published in the “11th Report on Carcinogens” (RoC) by the U.S. National Toxicological Program (NTP).

Aspartame is another artificial sweetener composed primarily of two common amino acids, aspartic acid and phenylalanine. Although aspartame (NutraSweet and Equal) was approved by the FDA in 1981, a 1996 report linking an increase of brain tumors between 1975 and 1992 with the introduction of aspartame renewed concerns in the link between artificial sweeteners and cancer. After further analysis, the report failed to show conclusive evidence that the overall rise in brain tumors could be attributed to the introduction of aspartame.

In 2005, the European Food Safety Authority (EFSA) released a statement declaring aspartame carcinogenic based on long-term studies performed by the European Ramazzini Foundation (ERF) where laboratory rats fed high doses of aspartame developed lymphoma and leukemia. The FDA evaluated the findings and, upon completion of its review in 2007, reported the ERF’s findings unsupported and insufficient in evidence for the FDA to change its conclusion that aspartame is safe for human consumption, a conclusion based on more than 100 toxicological and clinical studies.

In addition to saccharin and aspartame, four other artificial sweeteners are currently approved by the FDA for use in food:

- Acesulfame potassium (Sweet One) was approved in 1988 for use in specific food and beverage categories and was later approved as a general-purpose sweetener (except in meat and poultry) in 2002.
- Sucralose (Splenda) was approved as a tabletop sweetener in 1998, followed by approval as a general-purpose sweetener in 1999.
- Neotame was approved as a general-purpose sweetener (except in meat and poultry) in 2002.
- Advantame was approved as a general-purpose sweetener (except in meat and poultry) in 2014 based on findings from more than 37 animal and human studies failing to demonstrate any clear evidence of a cancer risk.

Sodium nitrate and sodium nitrite are added as preservatives to delay the growth of botulinal toxins, which cause botulism, and to enhance the color as well as flavor of processed meats. Nitrites and nitrates are also found in some vegetables and even baby food.

A 1971 study raised concern that nitrites have the potential to form N-nitrosamines when the nitrites are heated and combined with amines, the natural by-product of the breakdown of protein, to form N-nitrosamine, a known carcinogen in animals. In 1972, the FDA approved nitrites and nitrates as GRAS, stating that meats containing high levels of nitrates and nitrites are not carcinogenic but that N-nitrosamines still poses a human health hazard.
In 1982, the National Academy of Sciences requested additional evaluation, and the FDA nominated nitrites for NTP study, which was completed and reviewed, and the findings were reported in 2001. The proposed conclusion was such that no evidence of carcinogenic activity was found in male mice, and equivocal evidence of carcinogenic activity was found in female mice.

In 2006, the IARC conducted a working group of epidemiologists and toxicologists to perform another review of the carcinogenicity of nitrite and nitrates, resulting in their classification as probably carcinogenic to humans based on an extensive review that links consumption to bowel cancer and places high on the priority of sodium nitrates and sodium nitrites for consideration as possibly carcinogenic for human beings.

Citing the conflicting evidence in the link between nitrates and nitrites and cancer, the EPA regulates the amount sodium nitrate to no more than 500 parts per million (ppm) in finished meat products and the amount of sodium nitrite to not more than 200 ppm in finished meat products. The World Health Organization recommends eating no more than 3.7 milligrams of nitrates for each 2.2 pounds of body weight.

Acrylamide is a chemical used for industrial purposes in manufacturing paper, dyes, and plastics and in treating both drinking water and sewage. Acrylamides have been found in certain foods (potato chips, French fries, and other fried foods) and tobacco smoke. The NTP and the IARC consider acrylamide to be a probable human carcinogen based on studies in laboratory rodents ingesting acrylamide in drinking water, even though toxicological studies show differing rates of absorption between humans and rodents.

Current case-controlled studies investigating the link between consumption of acrylamides and developing cancers of the oral cavity, pharynx, esophagus, larynx, large bowel, kidney, breast, and ovary have found no excess of tumors associated with acrylamide intake. Because much of the data collected was based on personal interviews, the accuracy is subject to individual recall of exposures. Concerned about the major hazard to human health, the World Health Organization and the Food and Agriculture Organization of the United Nations have called for more research to determine the dietary risk of acrylamide.

Sodium benzoate and benzoic acid are food additives used as preservatives in a wide variety of processed foods and beverages. Listed as a GRAS, the FDA has found no evidence to list these ingredients as hazardous for food consumption after addressing concerns that sodium benzoate in soft drinks reacts with added vitamin C to form benzene, a known carcinogen. In a 2007 study published in *Lancet*, 200 beverages with sodium benzoate and vitamin C were sampled and tested, with four beverages exceeding federal safety standards for benzene levels.

BHA, an antioxidant and preservative in foods, is listed as reasonably anticipated to be a human carcinogen in the 12th Report on Cancer published by the NTP. Another preservative, BHT, has been on the GRAS list since 1959, and NTP studies have been inconclusive in rats or mice, although the FDA has noted concerns that BHT may transform

Potassium bromate, used in bread making, is classified as a Group 2B possible carcinogen by the International Agency for Research on Cancer (IARC). (Photos.com)
Food and Drug Administration

The U.S. Food and Drug Administration (FDA) is a government regulatory agency concerned with protecting the health of Americans. The agency is housed under the Department of Health and Human Services and is responsible for assuring foods, medicines, medical devices, cosmetics, and dietary supplements are safe. It also regulates electronic equipment that produces radiation and tobacco products. This broad responsibility translates into regulatory actions such as reviewing the results of clinical trials and approving new drugs, ensuring consumers are adequately informed of the risks and benefits of new drugs, monitoring approved drugs already on the market to ensure their continued safety and efficacy, assuring food and drug products are adequately and accurately labeled, inspecting manufacturing plants, and ensuring overall compliance with the various acts that pertain to food and drug products.

While the agency’s regulatory function is very broad and extends to the 50 United States, the District of Columbia, the Virgin Islands, Puerto Rico, Guam, American Samoa, and other U.S. territories, it does not regulate all consumer products, and some of its responsibilities are shared by other government departments and agencies. For example, the FDA regulates game meats, such as moose, deer, rabbit, wild ducks, and wild turkeys, but it has no control over other meats and poultry frequently found on the American table. Additionally, it has no jurisdiction over vaccination for infectious animal diseases and shares the responsibility for regulating pesticides with the U.S. Department of Agriculture and the Environmental Protection Agency.

Some critics of the FDA believe its regulatory role is too broad and intrusive, while others believe the role should be expanded and the agency given greater autonomy. The debate about the reach of the FDA is probably most intense in the drug industry, where government control meets science and research.

FDA and Cancer Research

In recent years, the FDA has taken decisive steps to reconcile between maintaining consumer safety and facilitating the speedy development of drugs to treat cancer and other chronic diseases. Researchers in

substances into cancer-causing additives, a concern that warrants further investigation. BHT has been banned in the United Kingdom.

Tara Michelle Zrinski
Northampton Community College

See Also: Dyes and Pigments; Flavoring Agents; Meat Processing; Water Treatment.

Further Readings


oncology had repeatedly complained that the FDA bureaucracy was stymieing progress in the field; critics charged the FDA was slow and inefficient in reviewing new drugs. In an attempt to improve efficiency, the FDA established in 2005 an Office of Oncology Drug Products (ODP). The move was intended to centralize the review of cancer drugs application and expedite the review process without compromising safety. Prior to 2005, the review of cancer drug applications was shared across different offices in the FDA.

This resulted in reviewers without expertise in oncology making final decisions about cancer drugs and reviews taking an inordinate amount of time. The establishment of ODP has significantly improved this situation. In the first two and a half years of its existence, the office reported approving 50 of the 58 new drugs that were submitted for review. The FDA has also developed expedited drug review programs with the aim to make available as quickly as possible new drugs that demonstrate the potential to address unmet medical needs in the treatment of cancer and other life-threatening diseases. Since the introduction of these programs, almost half of all cancer drugs submitted to the FDA for review have an expedited status categorization, and on average, oncology drugs are reviewed faster than other drugs.

Critics of the expedited review program argue the process is making available to patients drugs that have not been adequately tested and for which the risk and benefits have not been clearly established. New drugs that receive an expedited status are approved based on preliminary clinical evidence and are made available to patients even while clinical tests are still being conducted. Critics argue the FDA is compromising safety in order to facilitate innovation and access. They cite the later withdrawal of some drugs approved under the expedited review process as evidence of the FDA's betrayal of its mandate to ensure drugs sold on the U.S. market are efficacious and safe.

**History of the FDA**

In spite of the criticisms and limitation in some of its oversight capacities, the FDA has helped to significantly improve the quality of America's food and drug supply. Prior to the establishment of the FDA in 1906, the food and drug industries were largely unregulated, and consumers had no protection from corporate greed. Foods were being manufactured under very unsanitary conditions, manufacturers adulterated foods by mixing together anything that would cut their manufacturing cost (e.g., chalk was added to flour and insects were ground up and added to sugar), chemicals were used to disguise rotting foods offered for sale to consumers, labels were nonexistent or misleading, and "medicines" ranged from simple water mixed with alcohol or sulfuric acid to lethal and addictive concoctions made from narcotics and other substances not fit for human consumption.

Drugs were released to unsuspecting consumers without any form of clinical trial or safety mechanism and were often marketed as panaceas for a range of diseases on which they had no positive effect. With no way to verify the claims of the powerful businesses, consumers were left extremely vulnerable. While there is no certainty about the precise number of people who were affected by contaminated foods and deadly drug concoctions, it is believed thousands of adults and children were either killed or permanently maimed.

The free-for-all and corruption in the pharmaceutical and food industry received its first major challenge from Harvey Wiley, a medical doctor and chemist. Wiley was pro-commerce but believed businesses had a responsibility to deal honestly. He was also concerned about adulterated foods and the health effects of chemicals that were being used as preservatives. Through his lobbying, the Pure Food and Drug Act was passed in 1906 under the presidency of Theodore Roosevelt. The food and drug regulatory agency, which was then named the Bureau of Chemistry, was born. The agency was renamed the U.S. Food and Drug Administration in 1930.

Even many years after the FDA was established, it was troubled by corruption, weak regulatory powers, inaction in the face of pressure from powerful business interests, and political manipulation. The Kefauver–Harris bill of 1962 that came in the wake of a near thalidomide drug disaster increased the power of the FDA and demanded the agency adopt a more scientific approach to carrying out its function. Among other mandates, the law demanded drug companies use carefully designed and controlled scientific studies to prove the efficacy and safety of drugs being introduced to consumers. Before 1962, drugs were considered safe and effective based on the "expert testimonies" of doctors.
The FDA Today
The FDA still faces many challenges, some of which existed since its inception. The agency continues to struggle to reconcile maintaining consumer safety and facilitating science and innovation, it lacks adequate funding to fully carry out its regulatory role, and its power is limited by restriction on its legal authority. The globalized context in which the FDA now operates also creates added challenges. A large portion of the U.S. food and drug supply is imported from other countries. This makes monitoring an even more complex and expensive undertaking.

The passing of the Food Safety and Modernization Act (FSMA) of 2011 represents the most recent legislation aimed at aligning the agency’s function and authority with its vastly expanded 21st-century role. The FSMA has been described as a comprehensive reform of food safety laws that takes a risk-based prevention approach to food safety. The aim of FSMA is to prevent food-borne diseases and promote public health.

The act expands both the responsibility and authority of the FDA. Under the new legislation, the FDA is mandated to develop model standards for food safety and disseminate them to international and domestic food suppliers. The agency is also required to increase surveillance of domestic and international food facilities, improve its record keeping and food tracking capacities, and apply a scientific food monitoring and protection system. In addition, the act gives the agency greater access to records pertaining to all stages of food preparation and distribution and gives the FDA the power to order a product recall without prior approval from the court or prohibit the distribution of food from a facility that is deemed unsafe.

Today, the FDA continues to face criticisms about its authority and the way it carries out its role. The question of whether the FDA is overregulating or under-regulating is yet to be decided. In spite of criticisms and challenges, however, most agree the FDA's regulatory function is crucial to the safety of the U.S. food and drug supply.

Andrea McDonald
Lenna Dawkins-Moultin
Texas A&M University

Further Readings

Forest Labs
(United States)

Forest Laboratories, Inc., headquartered in New York, City, is a specialty pharmaceutical company that researches, develops, manufactures, and sells pharmaceutical products used in the treatment of various diseases and medical conditions in the United States. The company’s pharmaceutical portfolio includes both brand-name and generic drugs developed to treat a variety of illnesses and medical conditions to include, but not limited to, diseases and medical conditions affecting the central nervous and cardiovascular systems; conditions associated with gastroenterology, urology, and women’s health; and the treatment of Alzheimer’s disease. From a cancer treatment perspective, the company primarily develops medications used to treat cancers affecting the thyroid and pituitary glands as well as medications used to prevent infections in patients recovering from other medical treatments such as chemotherapy and radiation. These medications include products such as Armour Thryoid, Thyrolar, and Levothroid, to name a few.

In July 2014, the pharmaceutical company Actavis completed its $25 billion acquisition of Forest Laboratories, Inc., which was first announced in February of the same year. This merger created one of the largest specialty pharmaceutical companies in the United States, with an expected annual revenue amount of more than $15 billion in 2015. The combined company’s business model places emphasis on lower-risk drug development by implementing a flexible manufacturing model that

See Also: American Society of Clinical Oncology; Anticancer Drugs; Meat Processing; Radiation.
can be easily adapted to better meet any changing needs the medical community and pharmaceutical industry may encounter as a whole. By leveraging Forest Laboratories, Inc. strong product development options, including nine clinical-stage drugs, the merger will build on both companies’ strong foundations of research and development, poised to serve not only the United States but also to take part in pharmaceutical growth in other areas of the world such as Canada and Latin America. Additionally, the merger will allow Actavis to begin performing some functions in-house that they currently outsource by leveraging existing functions already being performed in Forest Laboratories, resulting in further savings.

In order to support its U.S.-based operations and sales, Forest Laboratories, Inc. has three major subsidiaries located in the United States in addition to the company’s two subsidiaries in Canada and Europe. These U.S. subsidiaries include Forest Pharmaceuticals, Inc., a St. Louis, Missouri-based company; Forest Research Institute, Inc., with operations in both Jersey City, New Jersey, and Long Island, New York; and Cerexa, Inc., located in Oakland, California.

The company’s first U.S. subsidiary—Forest Pharmaceuticals, Inc.—is responsible for the manufacture, sale, and distribution of Forest Laboratories’ name-brand prescription medications and products in the United States. Forest Pharmaceuticals operates by marketing and selling its products directly to U.S. health care networks and the medical industry, to include health care professionals, hospitals, and pharmacies.

The company’s second subsidiary—Forest Research Institute—is a wholly owned subsidiary and is tasked with the research and development mission of Forest Laboratories, Inc., which includes product development, preclinical and clinical trials, and the overall evaluation success of the company’s medications. This research and development arm of Forest Laboratories, Inc. provides the company with an opportunity to invest in scientific research and pharmaceutical development that incorporates the many facets of a drug’s life cycle and helps the company gain appropriate approvals from the U.S. Food and Drug Administration at the appropriate times in a product’s development.

As is the case with the Forest Research Institute, the company’s third subsidiary—Cerexa—is also a wholly owned subsidiary of Forest Laboratories, Inc. Cerexa is a biopharmaceutical company solely focused on the development of an anti-infective therapy portfolio. Founded in 2005, Forest Laboratories, Inc. acquired Cerexa in early 2007.

As with other pharmaceutical companies in the United States, Forest Laboratories, Inc. is required to implement post-marketing requirements (PMRs) as part of its overall drug development initiatives. These PMRs include the company gaining a sponsor for a particular drug after gaining FDA approval and conducting appropriate studies and clinical trials designed to garner information on the product’s safety, efficacy, and use. On the other hand, Forest Laboratories, Inc. also conducts post-marketing commitments (PMCs), which are not required by any statute or FDA regulation but indicate a drug sponsor’s agreement with the FDA to conduct studies or trials to gain information on a drug’s overall safety and use.

In recent years, mainly 2009 through 2010, Forest Laboratories, Inc. suffered from a series of legal complications after being accused by the U.S. Department of Justice of criminal negligence and defrauding the federal government by illegally marketing some of the company’s drugs but namely surrounding the evaluation, promotion, and distribution of the company’s thyroid and antidepressant drugs. The U.S. government alleged that Forest Laboratories, Inc. and Forest Pharmaceuticals, Inc. illegally marketed their products, deliberately slowed manufacturing and availability of other drugs, and essentially provided payments to doctors for prescribing specific drugs to patients—such as promoting Cerexa and Lexapro, which are antidepressants, in unapproved pediatric patients.

These charges led the company and its subsidiary, Forest Pharmaceuticals, Inc., to plead guilty to a number of criminal charges, both felonies and misdemeanors. Other charges alleged the illegal distribution of drugs and therefore a violation of the Food, Drug, and Cosmetic Act. This issue also led to a class-action lawsuit, resulting in the company paying more than $300 million as part of an agreement, both in a civil and federal component of the settlement, in order to rectify the civil and criminal liability charges the government and patients had brought against them. In the end, the federal prosecutors working the case said they gathered the evidence against Forest Laboratories with the help of whistle-blowers.
Despite the legal setbacks and issues Forest Laboratories, Inc. experienced, the company remains a top pharmaceutical company in the United States, and its merger with Actavis poises the company to play a dominant role in the American pharmaceutical industry.

L. L. Lundin  
Independent Scholar

See Also: Drugs; Food and Drug Administration; Marketing, Drug; Marketing, Hospitals and Clinics; Pharmaceutical Industry; Thyroid Cancer.

Further Readings

Fox Chase Cancer Center

The Fox Chase Cancer Center is devoted to cancer treatment, prevention, and research. In 1974, the National Cancer Institute designated the center as one of the first comprehensive cancer centers in the United States. Located in Philadelphia, Pennsylvania, Fox Chase is the fourth-largest hospital in the United States dedicated to cancer care. It regularly appears on the America’s Best Hospitals list published by U.S. News & World Report.

The center can trace its history back to 1904 and the founding of the first cancer hospital in the United States, the American Oncologic Hospital. The hospital’s first facility was a west Philadelphia Victorian home. At the time, cancer was widely considered incurable. The hospital would go on to become a leader in radium treatments of cancer. The Fox Chase Cancer Center was established in 1974 via the merger of the American Oncologic Hospital and the Institute for Cancer Research, founded in 1927. Fox Chase remained an independent, nonprofit institution until joining the Temple University Health System in 2012.

The Fox Chase Cancer Center and its precursors have contributed to improved treatments in cancer care. These contributions date back to 1917, when research studies were started to investigate the fundamental biological processes in cancer. Prior to that time, cancer research focused primarily on studies of tumor tissue. Researchers at the American Oncological Hospital, however, were convinced that it was necessary to understand normal cell growth and functioning in order to understand cancer. In 1931, the Marine Experimental Station was established at the hospital to focus on the biological basis of cancer.

By the 1940s, some researchers began focusing on genetics and its relationship to cancer, leading them to establish some of the basic concepts of what would become the discipline of molecular genetics. Hugh P. Creech, Ph.D., joined the staff in 1945 and conducted groundbreaking research on chemotherapy agents over the next three decades. In 1959, two researchers at the institute, David A. Hungerford, then a graduate student at Fox Chase, and a University of Pennsylvania pathologist, Peter C. Nowell, M.D., identified a chromosomal abnormality that led to the first conclusive evidence that cancer is a genetic disorder of the somatic cells.

Other important contributions would also come from Fox Chase, including identifying in 1967 the hepatitis B virus, which is the primary cause of liver cancer. In 1969, Fox Chase researchers developed a vaccine for hepatitis B, thus developing the first vaccine to prevent a human cancer. In 1995, Fox Chase further advanced cancer research as a founding member of the Comprehensive Cancer Network, which includes 21 leading academic cancer centers in the United States.

Fox Chase continues to conduct a wide range of basic and clinical research focusing on the diagnosis, treatment, and prevention of cancer. Overall, the center’s research programs include efforts in cancer biology, prevention and control, immune
cell development and host defense, developmental therapeutics, and women's cancer. Approximately 200 clinical trials are normally underway at the center. These include testing new agents and compounds to prevent cancer in high-risk individuals.

Throughout the years, Fox Chase has also provided clinical care to cancer patients. The center accepts patients with all types of cancers and is known for its treatment of rare and difficult-to-manage tumors. Fox Chase also features special programs in cancer prevention, detection, and survivorship, as well as community outreach programs.

Fox Chase’s 100-bed hospital sees more than 8,400 new patients each year on an inpatient or outpatient basis. It admits approximately 4,800 patients to the hospital each year. Overall, Fox Chase physicians record approximately 88,000 outpatient office visits yearly. Fox Chase is recognized for its programs in medical, radiation, and surgical oncology and for its diagnostic imaging programs. Other areas of special expertise include diagnostic pathology and pain management.

Fox Chase has made several innovations in cancer care, such as its contributions to the development of three-dimensional conformal radiation therapy (3D-CRT). This approach involves shaping beams of radiation to match the tumor’s shape and size. Fox Chase was also the first center in the world to use magnetic resonance imaging (MRI) to help plan for treatments. The center features surgeons who specialize in da Vinci robot-assisted surgery for a broad range of cancers. It is also one of the few centers in the United States to offer advanced minimally invasive surgical techniques for patients with cancers of the lung, gallbladder, liver, pancreas, and bile ducts.

Fox Chase also specializes in the treatment of lung cancer and mesothelioma, including the surgical management of mesothelioma. Fox Chase’s research programs on mesothelioma include studies of new methods for early detection and treatment. Fox Chase researchers are also searching for the genetic roots of the disease.

In 2013, Fox Chase opened its Cancer Genome Institute to provide an innovative clinical service that guides cancer patients’ treatment or their potential to participate in specific new drug trials. The institute features advanced DNA technologies to compare patients’ tumors with a panel of 50 cancer-related genes. The tumors are examined for genetic alterations to determine whether or not they match one or more of the cancer-related genes. The goal is to match patients suffering from advanced cancers to specific gene-altering therapies, either established or experimental.

Fox Chase also heads an outreach program called the American–Russian Cancer Alliance. The alliance is a consortium of cancer research institutes from both countries established to promote increased collaboration among cancer scientists and physicians from the two nations. Fox Chase employs more than 2,000 people, including a staff of 358 physicians and scientists.

David Petechuk
Independent Scholar

See Also: Bile Duct Cancer, Extrahepatic; Lung Cancer, Non–Small Cell; Lung Cancer, Small Cell; Mesothelioma, Adult Malignant; Mesothelioma, Childhood.

Further Readings

France

The western European nation officially termed the French Republic has undergone many political variations in its long and storied history, from
France

In opposition to the monarchy of King Louis XVI, the citizens of France declared the first French Republic in September 1792, and since this date, the nation has experienced several renditions of republican governance, which have led up to the establishment in 1958 of the modern French government, the Fifth Republic.

In 16th-century Europe, the ancient Roman theory that cancer was caused by excessive amounts of bile, or humors, circulating in one's system was still commonly held by practicing physicians, while in the 17th-century, European physicians such as the Italian Gaspare Aselli purported that an incidence of cancer was the result of abnormalities within an individual's lymphatic system. During this time, these theories were consequently espoused in France due to the traffic of ideas on the continent. Another common belief in France during this period was that cancer was contagious; in fact, France's first cancer hospital was forced to move from the city of Reims as late as 1779 because the local populace was anxious that the city would be contaminated.

As the nation entered the 18th century, French physicians such as Claude Deshais Gendron (1653–1750) began to reject these theories in favor of a more modern understanding of the disease. Gendron discerned in his research that cancer arose locally in tissues or organs as a thick, developing mass of cells, which he maintained could not be remedied by drugs but only through surgical removal. Furthermore, later in the 18th century, two French scholars created a new field of research in Pierre and Marie Curie in their lab. The Curies were awarded the Nobel Prize for physics in 1903 for their research regarding radioactivity and their discovery of radium and polonium. Soon after, French scientists made the historic observance that consistent doses of radiation over a series of multiple weeks strongly increased an individual's chance for beating cancer. (Wikimedia Commons)
the campaign against cancer: experimental oncology. Jean Astruc, a physician, and Bernard Peyrilhe, a chemist, began to initiate calculated experiments in a concerted attempt to officially affirm or negate particular theories regarding cancer; in their research, they sought to better understand how cancer progressed and how the disease could be more efficiently diagnosed and treated. In a similar vein of research, the French gynecologist Joseph Recamier intensively studied how cancer cells spread through a person's bloodstream in 1839.

Twentieth-century France experienced many important scientific breakthroughs that became extremely relevant in the global battle against cancer. Pierre and Marie Curie were awarded the Nobel Prize for Physics in 1903 for their research in Paris regarding radioactivity and their discovery of radium and polonium. Soon thereafter, French scientists made the historic observance that consistent doses of radiation over a series of multiple weeks strongly increased an individual's chance for beating the cancer.

In contemporary times, France has the highest survival rates for cancer on the continent. Incidences of cancer have been on the decline for the past two decades. In spite of this fact, France unfortunately has one of the highest rates of male cancer incidences in all of Europe. As stated earlier, though, cancer rates have been steadily waning in the country's male and female populations, and many commentators attribute this to the nation's strong health care system, its effective diagnostic services, its advanced treatment capabilities, and vocal public campaigns that warn against the dangers of smoking and alcohol use with regard to cancer. In recent years, a large amount of domestic institutions has been created in an effort to help combat the disease, such as the Institut National du Cancer in 2004 and the Association Laurette Fugain in 2002.

Currently, though, France does not have a national cancer registration program; information from particular domestic departments has been used to help track the most widespread forms of cancer incidence in the country. Regardless of gender, the most prevalent forms of cancer in France are bowel, breast, lung, oral, and prostate cancer. Bowel, lung, and prostate cancers make up more than one-quarter of all cancer incidences in France, while bowel, breast, and lung cancers account for more than half of all cancer incidences in females there. Moreover, within the past 30 years, certain cancers such as bowel cancer, kidney cancer, leukemias, liver cancer, and prostate cancer have seen a nationwide increase in prevalence, while incidences of cervical cancer and lung cancer have been consistently decreasing.

Sadly, and like the rest of the world, many citizens of France have had cancer. Pierre and Marie Curie, as mentioned earlier, are said to have died from the radiation poison that they acquired during their years of research handling radioactive materials. The once-emperor of France, Napoleon Bonaparte, died in exile on the island of Saint Helena from what was believed to be stomach cancer. Laurent Fignon, who was a two-time winner of the Tour de France cyclist, passed away from lung and intestinal cancer in his Parisian home in 2010.

France is world renowned for being home to as many as 20 cancer specialist centers, each staffed with advanced equipment and highly trained staff. For example, Dr. François Pein, who oversees all research undertaken at the Centre René Gauducheau in Nantes, is a leading expert in the battle against cancer in France. Professor Jean-Yves Blay, who is head of the Medical Oncology Department and the Translational Research Pole at the Centre Léon Bérard in Lyon, received the prestigious Hamilton Fairley Award in 2012 for his research regarding translation issues related to cancer.

William M. Peaster
Independent Scholar

See Also: Breast Cancer; Lung Cancer, Non–Small Cell; Oral Cavity Cancer, Lip and; Prostate Cancer.

Further Readings
Fred & Pamela Buffett Cancer Center

Located in Omaha, Nebraska, the Fred & Pamela Buffett Cancer Center serves a vital role in the mission of the University of Nebraska Medical Center. The Fred & Pamela Buffett Cancer Center, formerly the Eppley Cancer Center, conducts cancer research and provides patient care that includes obtaining information from the patient’s tumor to develop and design a specific cancer treatment for each patient based upon his or her human genome information. This personalized approach at the cancer center undergirds and informs clinical research, patient care, and education programs to facilitate the application of new knowledge regarding the etiology, diagnosis, treatment, and prevention of cancer.

The future of the Fred & Pamela Buffett Cancer Center shines brightly. By 2017, a new facility with an estimated investment of $323 million will house the Fred & Pamela Buffett Cancer Center. This is the largest project ever at the University of Nebraska. The cancer center will consist of three components under one roof: a 10-story, 252,000-square-foot research tower with 98 laboratories; a seven-story, 325,000-square-foot, 108-bed hospital tower; and a multidisciplinary ambulatory care clinic. The cancer center’s multidisciplinary, comprehensive, and translational approach to cancer care will allow researchers to accelerate breakthroughs in the laboratory and clinicians to provide personalized care plans for patients. The new facility represents a key strategy in efforts to achieve status as a National Cancer Institute (NCI) Comprehensive Cancer Center, an achievement by only 41 other centers nationwide by 2014. Director of the cancer center, Dr. Ken Cowan, observed, “The Fred & Pamela Buffett Cancer Center will enhance the already excellent research programs by bringing scientists and clinicians together in the same building to share and exchange ideas.”

Internationally recognized scientists and clinicians at the center study the mechanism of action that causes cancer and translates these findings into new approaches for the prevention and treatment of cancer. Their goal is to pursue innovations to eradicate cancer. There are four basic science, clinical, and translational research programs at the cancer center that provide education and collaborative discussion, which generate further study:

1. Cancer Genes and Molecular Regulation Program
2. Molecular Biochemical Etiology Program
3. Gastrointestinal Cancer Program
4. Cancer Prevention and Control Program

The most notable research at the cancer center includes ongoing scientific inquiry and treatment in the areas of lymphoma and bone marrow transplantation, pancreatic cancer, and breast cancer. The cancer center is also a founding member of the National Comprehensive Cancer Network (NCCN). The NCCN is an alliance that develops standards and sets guidelines for the treatment and prevention of cancer. Throughout their history, the NCI-designated cancer centers have contributed to extraordinary advances in the understanding of cancer mechanics as well as prevention, diagnosis, treatment, and care of diverse populations. A formal academic affiliation agreement has also been secured with Children's Hospital, and as a result, pediatric clinical cancer trials are increasing.

The cancer center is designed as a single-use or one-stop facility, which means that patients only have to go to one place and be seen by the entire oncology team (medical, surgical, and radiation oncology) as well a physical therapists, dieticians,
and social workers for their diagnosis, plan of care, and treatment. The inpatient cancer facility is located next to the cancer outpatient center. With 108 inpatient beds, people can go seamlessly from the clinic to the hospital and back. When a patient is tired from rigorous treatment, saving steps can make a big difference. Likewise, the patient care philosophy at the Fred & Pamela Buffett Cancer Center includes helping patients navigate their health journeys by focusing on wellness and disease prevention while maintaining family and professional support through the continuum of care. This is achieved by the following:

- Focusing on families and individuals
- Restructuring primary care services for personalized care
- Population-based health management based on the latest science
- System integration including seamless research and clinical practice
- Cost containment

The goal is to have each patient receive the right care, in the right place, at the right time, with the right quality, and at the right cost.

The cancer center provides leadership and coordinates regional, national, and international relationships and alliances as well as facilitates outreach education and cancer screening programs.

Kimberly McFarland  
David Dunning  
University of Nebraska Medical Center

See Also: Herbert Irving Comprehensive Cancer Center; Lombardi Comprehensive Cancer Center.

Further Readings
“JAMA Publication Features Study on Depression and Head and Neck Cancer.” http://esciencenews.com/articles/2008/05/21/jama.publication.features.study.depression.and.head.and.neck.cancer (Accessed September 2014)
prevention. In 1988, scientists from the center started working on the understanding of human immunodeficiency virus (HIV), and the research extended to include other infectious diseases. Presently, the Vaccine and Infectious Disease Division at the center is one of the largest HIV research units in the world. It also acts as a center for HIV Vaccine Trials Network, which is a global initiative to fast-track the development and testing of successful HIV vaccines.

Hutchinson Center has more than 200 research groups, laboratories, and project groups in five scientific divisions, occupying the 15-acre Robert W. Day Campus in Seattle, Washington. In addition to the research laboratories, the Fred Hutchinson Cancer Research Center campus houses core facilities, which are operated by the center's shared resources department. These core facilities provide products, services, and equipment, which are shared amongst researchers.

Fred Hutchinson Cancer Research Center houses biological scientists, clinical scientists, and public health scientists working in tandem to apply the fundamental research toward diagnosis and therapy as well as implementing the new knowledge toward the reduction of deaths in the community from cancer and related diseases. The Hutchinson Center has staff and faculty members in excess of 2,700, working toward the elimination of cancer, HIV, and other related diseases.

In 1982, the Cancer Prevention Program was established at the Fred Hutchinson Cancer Research Center and has made substantial contributions to the current understanding of the role of diet, exercise, and other factors that may be associated with the risk of acquiring cancer and related diseases. Scientists at Fred Hutchinson Cancer Research Center work on diverse aspect of the diseases like cancer and HIV/acquired immune deficiency syndrome (AIDS), covering both the fundamental questions related to the disease as well as clinical treatment options. The most basic aspects of the diseases are investigated at a molecular level and are studied parallel with epidemiological and population-based approaches. These multidisciplinary studies help in unravelling the risks associated with all possible factors affecting the person's likelihood of getting cancer.

Research at Fred Hutchinson Cancer Research Center can be classified broadly into five categories, which include basic sciences, prevention, early detection and diagnostics, treatment and cures, and survivorship, studying the long-term physical, psychological, and social effects of cancer and cancer treatment.

Fred Hutchinson Cancer Research Center considers science education is an essential tool to advancing biomedical research. Apart from its involvement in the training and education of researchers, postdoctoral fellows, graduate students, and high-school fellows, the center also provides opportunities for professional development, internships, and opportunities to gain research experience. Community programs and events creating awareness about the progress in the fight against cancer and related diseases are also organized to raise the awareness of the general public on issues related to cancer. These programs also serve as fund-raising events.

Fred Hutchinson Cancer Research Center works in partnership with numerous other American institutions to further the development of novel therapies and provides the highest quality of health care in the world. As an academic, teaching, and research institution, the interinstitutional relationships allow sharing of ideas, information, as well as resources.

Other scientific initiatives of the Hutchinson Center include the Hutchinson Institute for Cancer Outcomes Research (HICOR), working toward the improvement of the effectiveness of cancer prevention, treatments, and therapy and, at the same time, reducing the costs of cancer care. The Hutch Integrated Data Repository and Archive (HIDRA) is a joint effort of the Fred Hutchinson Cancer Research Center and University of Washington Cancer Consortium, with the aim of the creation of a database enabling scientists and physicians to access information and learn from each new patient. This database is expected to enable the integration of knowledge and application for patient care.

The HIV Vaccine Trials Network (HVTN) is the largest publicly funded international collaboration in the world facilitating vaccine development against HIV/AIDS. The network conducts all phases of clinical trials for safety and efficacy. Project Violet involves researchers developing a new class of anticancer compounds, which are specifically engineered to attack cancer cells. The Solid Tumor Translational Research (STTR) is a
collaborative effort of scientists and physicians at the Fred Hutchinson Cancer Research Center, UW Medicine, and Seattle Cancer Care Alliance with the aim of translating bench research to precise treatment options for solid tumor cancers.

In 1998, the Hutchinson Center joined the University of Washington and Seattle Children’s to form the Seattle Cancer Care Alliance (SCCA), which is a leading cancer treatment center in the United States.

SCCA provides clinical care to patients from the three partner organizations and also acts as the contact center for the Cancer Information Service (CIS) of the National Cancer Institute. The CIS is a cancer education program providing accurate, up-to-date, and reliable information on cancer free of cost by trained information specialists to the people in the United States, Puerto Rico, the U.S. Virgin Islands, and the U.S. Associated Pacific Territories.

In the year 2002, the Hutchinson Center and University of Washington Cancer Consortium was formed to accelerate cancer research at the Hutchinson Center, UW, and Seattle Children’s. The consortium together has more than 400 faculty members with research interests across basic, clinical, and public health sciences related to cancer. The consortium strengthens the collaborative efforts toward fighting cancer while maintaining the autonomy of each institute.

Poonam Balani
Independent Scholar

See Also: Fox Chase Cancer Center; Herbert Irving Comprehensive Cancer Center; Huntsman Cancer Institute.

Further Readings

Freon

Freon is the trade name for chemicals (chlorofluorocarbons [CFCs]) developed in the United States in the 1920s and 1930s. Freon has many uses and was labeled a miracle compound at the time of its development. Freon’s history includes remarkable stories of science and their playing out in society and nature.

Freon has several uses, and DuPont sold a majority of Freon for industrial applications, but it was more visible as a refrigerant. This is the story of how humans overcame the limiting effects of summer heat. Prior to the availability of technology to keep cool, people had to accommodate to heat by drinking fluids, staying in the shade, and restricting their physical activity. Fresh food could not be stored or shipped, so families depended on their gardens in the country and on peddlers bringing fresh food into city neighborhoods.

Refrigeration developed in stages in the United States. People have known for millennia that evaporation has a cooling effect, so that, for example, water was stored in a porous clay container to keep it cool to drink. The old fashioned name for household cold storage was ice box, even though it was also called a refrigerator. It literally was a storage place kept cool with a block of ice. There were no machines to produce that ice, so it was a product of the frigid winters of northern regions. The technology of ice storage was to cut ice blocks on frozen rivers and lakes and store them in warehouses insulated with sheets of cork. Then the ice man would bring those blocks of ice to the family home on his daily rounds between the warehouse and the neighborhood.

Late in the 19th century, this ice industry would change with the development of refrigeration technology. The machines that cooled the air and its contents made possible many new industries and contributed to the basis for our modern society. Refrigerated railway cars made it possible to ship fresh meat instead of bringing live animals to the neighborhood butcher. Chicago became the hog butcher of the world as the meat packing industry developed. The availability of a central source of animal by-products led to other industries, such as leatherworks. With home refrigerators, people were not dependent on the daily delivery of ice and could even make their own.
The technology of refrigeration was severely limited by one factor: the chemicals used as refrigerants were dangerous. When they leaked into the air and were breathed in, they caused lung injuries and deaths. Some households kept their refrigerators in the backyard for safety, but this was not convenient, safe, or even possible for large commercial installations, nor for apartment dwellers. This problem opened the way for the introduction of an odorless, colorless, nontoxic, and nonflammable chemical to replace the original refrigerants: Freon. Scientist Thomas Midgley Jr. at the Frigidaire division of General Motors, working with the DuPont chemical corporation developed the miracle compound and patented it in 1928. It replaced other refrigerants when put on the market by DuPont.

Within a few years, the Frigidaire Corporation and others had sold 8 million home refrigerators at the height of the Great Depression. A similar widespread adoption of air-conditioning came after the Carrier Engineering Corporation developed the world’s first self-contained home air-conditioning unit in 1932.

Once Freon became available for the everyday use of air-conditioning, it spread from specialized application in theaters to workplaces, then in homes, and eventually in automobiles. Our modern skyscrapers and even low-rise, modern buildings do not have windows that open for fresh air; temperature-controlled ventilation provides it. Windows in these modern buildings are now window walls. Because ventilating air is filtered and monitored, even in private homes, the air inside is healthier than outside “fresh” air. One consequence is that, if the electric power fails, then the occupants in a modern building will have to evacuate; they no longer can open a window. Thus, we see our dependence upon this modern technology; we cannot live our daily lives without it.

Freon led to human control of the enclosed environments of our buildings and autos. It also supported new applications. Among them was the development of the aerosol spray can. This became the second-most common application of Freon, used to spray all matter of substances, from paint and lubricants to cosmetics and cooking spray. Aerosol cans even were developed to spray air. These cans had the effect of releasing Freon directly into the atmosphere. As aging refrigerators and air-conditioners are discarded, their Freon will eventually make its way into the atmosphere as well.

While Freon had made its appearance as a miracle compound, some scientists became concerned that the chemical had unanticipated effects on the environment. The potential risks of adding this new chemical to the atmosphere in large quantities led to its detailed study. Scientists found that a series of reactions between CFCs and ultraviolet rays led to the release of the element chlorine into the stratosphere. Chlorine is rare as a natural component of the atmosphere and would measurably increase from CFC breakdown. Then it would catalyze the reaction that removes ozone (a form of atmospheric oxygen) from the atmosphere. Scientists calculated that one atom of chlorine would result in the loss of 100,000 molecules of ozone.

Ozone has the property of blocking the passage of high-frequency (energetic) ultraviolet sun rays. These rays are damaging to life through their harm to cells’ DNA and are carcinogenic to skin. Early studies indicated that there would be a significant loss of atmospheric ozone of several percent, a thinning of the Earth’s protective layer of ozone from the expected release of Freon. Even though this reduction would take place several decades in the future, it created alarm. So Freon, introduced as a miracle compound that was completely safe and the basis for the modern industry of refrigeration, had now become unsafe and a threat to life on the planet. Chemists and other scientists concluded that the production of Freon should be reduced and protective measures taken. For example, Freon in refrigerant units could be extracted and recycled rather than be allowed to decay until they were leaking from landfills.

Now a billion-dollar industry involving manufacturing, construction, and people’s private comfort, Freon could not simply be eliminated, unless new, safer chemicals could be substituted for the CFC compounds. What was emerging was a conflict that allied environmentalists and advocates for public health against industry and public indifference. This is the same confrontation that has been repeated as hidden risks have been found in various aspects of modern life.

In the developing confrontation, the DuPont Corporation was in a leading position as the largest manufacturer of Freon. It also had an interest in altering the technology based on Freon. There were several factors in play as found by James Maxwell and Forrest Briscoe in their study of these
developments. The DuPont patent on Freon had ended, so other manufacturers were competing with DuPont. The company was oriented toward an environmentally friendly posture and was questioning its potential contribution to an environmental disaster. DuPont chemists already had replacement chemicals for Freon, although they would be more costly. Nonetheless, if the government were to legislate against Freon, then competitors would not be able to undercut DuPont's more expensive substitutes. By selling those substitutes at a higher price and with renewed patent protection, DuPont would be the beneficiary of laws that banned its own best-selling product. Just as Freon had replaced chemicals found to be hazardous to the public, now Freon was to assume the position of the hazard to be replaced.

What would resolve the Freon problem worldwide would be an international agreement to phase out the chemical with effective enforcements against its manufacture and sale. There had been international concern since laboratory studies by Mario J. Molina and F. Sherwood Rowland found in 1974 that CFCs acted under ultraviolet light to break down ozone catalytically. International meetings and discussions continued without a clear outcome.

The potential for accomplishing this goal came with an international meeting over Freon in Montreal in 1987. The prospects for agreement at this meeting were no better than those from earlier international meetings, although progress was made. The same problem that faces public health and environmental protection in general applied to Freon. An apparently necessary product was opposed by scientists, doctors, and environmentalists. The harm that the experts were forecasting was invisible and in the future. The solution would be costly. The public had not been favorable toward the experts when this kind of situation has arisen. People asked, “Why change,” when the danger only existed “in theory.” Opposition challenging the scientific consensus arises and is included in the media as a “debate” even when the scientific results are already known in situations like this.

This opposition did arise in this case, but it was not effective or large enough to stop the Montreal Protocol of 1987 and its implementation. The reason for this came in part from an unexpected scientific finding that changed public opinion. The second reason is the refusal of DuPont to join other chemical manufacturers in opposing the regulations.

This part of the story begins with the scientific study of the weather, leading to satellite images of the ozone layer over the Antarctic. In 1985, those images disclosed the famous ozone hole. Now, the public could see for themselves the effects of Freon. Scientists also were surprised as the effects were revealed to be more extreme than expected from laboratory studies. In subsequent years, the ozone hole and thinning of the ozone layer elsewhere has been continuously monitored by satellite and ground observations.
The outcome was swayed by DuPont representatives lobbying behind the scenes for enactment of the protocol. The unexpected resolution came from several events coming together to forge the agreement: the various scientific discoveries, the dramatic appearance of the ozone hole that swayed the public, the development of viable (although more costly) alternatives to Freon, and the support of the main Freon producer for phasing out its own product. Thus, the Freon example serves as a model for how to gain international agreement on protecting the environment.

Keith R. Johnson
Oakton Community College

See Also: Australia; Natural Causes of Cancer; Skin Cancer, Melanoma; Skin Cancer, Non-Melanoma.

Further Readings

Future of Cancer

In 2010, the World Health Organization (WHO) announced that, for the first time on record, cancer deaths exceeded deaths from ischemic heart disease—making cancer the world’s leading cause of death. In 2009, an article in the *Journal of Clinical Oncology* projected that the incidence of cancer in the United States is likely to increase by 45 percent between 2010 and 2030. The study was based on U.S. Census data and specifically census data projecting a higher rate of cancer among elderly residents and people of color alongside a significant increase in both populations, necessitating new public health initiatives to increase the odds of early diagnosis. This increase in cancer cases is likely to be reflected in developing nations as well, where access to care is even less of a guarantee and more often results in death; according to WHO, wealthy nations, the only nations where a full range of treatment options are available to an average citizen, account for only 28 percent of cancer deaths.

In the coming decades, the incidence of cancer is projected to increase in both the industrialized world and the developing world. Alongside this increase will likely come innovations in experimental cancer treatments, new corporate and regulatory environmental interventions, and vaccinations for oncoviruses, leading to a scenario where cancer will become more prevalent even as the tools used to prevent and treat it will become more sophisticated. Placing these tools in the hands of health providers in developing nations, and making them accessible to low-income cancer patients in the industrialized world, is likely to pose a significant public health challenge.

Prevention

The majority of cancer cases are not preventable using any known mechanism. While this situation is unlikely to change within the near future, some forms of cancer can be traced to known, treatable causes. These include oncoviruses, tobacco use, ultraviolet light exposure, and exposure to known environmental carcinogens.

An estimated 12 percent of cancer cases are caused by eight oncoviruses (HIV, HPV, MCV, HLTV-1, Epstein-Barr, Kaposi’s sarcoma, and hepatitis B and C viruses), all of which are potentially subject to future vaccination efforts. Universal vaccination of children against human papillomavirus (HPV) would prevent cervical cancer in more than 99 percent of cases and could, alongside increased screening efforts, functionally eliminate this particular form of cancer, but universal access to the HPV vaccine is unlikely. Its effectiveness is also reduced when used on patients who already have one or more types of HPV, which is a
demographic that includes more than three-quarters of adults.

Tobacco use is gradually declining in most of the industrialized West, but it remains high in eastern Europe, Asia, and north Africa; the world’s largest market for cigarettes is now China, where an estimated 52.9 percent of adult men smoke tobacco in some form (the majority, 45.4 percent, smoke cigarettes). If ozone depletion continues (and it is projected to do so), ultraviolet light exposure will increase and, with it, the rate of skin cancer; this can be mediated by protection, such as sunscreen, which is (like most mitigating interventions) less available to residents in the developing world than it is to residents of the industrialized world.

The discovery of environmental carcinogens is an ongoing process and, presumably, still a science in its infancy. The degree to which future carcinogens will be discovered, and cancers attributable to the same, is difficult to predict.

Treatment
There have been a wide range of experimental cancer treatments that have achieved some measure of documented success. Two of the most innovative categories of experimental cancer treatments are targeted cell treatments (including photodynamic therapy, bioluminescent-activated destruction, and photoactivated peptides) and the engineering of oncolytic viruses, by which viruses are programmed to target cancer cells while leaving healthy cells intact. With respect to the latter category, scientists have achieved some success using modified forms of human immunodeficiency virus (HIV), HPV, the measles viruses, adenovirus, reovirus, the Newcastle virus, and vaccinia.

Scientists at the University of California, Los Angeles (UCLA) have also achieved some success in starving leukemia cells by pharmacologically blocking their nucleotide pathways, a treatment option that may be applicable to other forms of cancer as well.

Advancements in chemotherapy and cancer surgery may ultimately help these traditional forms of cancer treatment continue to outpace experimental cancer treatment options; new classes of chemotherapy drugs have proven more effective than their predecessors at treating specific types of cancer, and health professionals have successfully mitigated the dangerous side effects of chemotherapy in some cases. Laser microsurgery has also proven effective at treating some forms of cancer that have historically proven inoperable. In principle, nanotechnology is likely to become an effective long-term cancer treatment option. In practice, the science behind nanotechnology is still very young, and it may be decades before nanotechnology becomes an effective routine cancer treatment, even in the industrialized world. The prospects of wide-scale application of nanotechnology in the developing world assume a public health apparatus of unprecedented size and scope.

Thomas L. Head
Edith Cowan University

See Also: Environmental Justice and Cancer; Environmental Tobacco Smoke; HPV Vaccination; Tobacco Smoking; Tobacco-Related Exposures; Vaccines.

Further Readings
Radu, Caius and David A. Nathanson. “Experimental Treatment Eradicates Acute Leukemia in Mice.” UCLA Jonsson Comprehensive Cancer Center (February 24, 2014).
SAGE was founded in 1965 by Sara Miller McCune to support the dissemination of usable knowledge by publishing innovative and high-quality research and teaching content. Today, we publish more than 850 journals, including those of more than 300 learned societies, more than 800 new books per year, and a growing range of library products including archives, data, case studies, reports, and video. SAGE remains majority-owned by our founder, and after Sara’s lifetime will become owned by a charitable trust that secures our continued independence.
# Contents

## Volume 2

<table>
<thead>
<tr>
<th>List of Articles</th>
<th>vi</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reader's Guide</td>
<td>xiv</td>
</tr>
</tbody>
</table>

## Articles

<table>
<thead>
<tr>
<th>Letters</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>G</td>
<td>477</td>
</tr>
<tr>
<td>H</td>
<td>521</td>
</tr>
<tr>
<td>I</td>
<td>573</td>
</tr>
<tr>
<td>J</td>
<td>627</td>
</tr>
<tr>
<td>K</td>
<td>643</td>
</tr>
<tr>
<td>L</td>
<td>657</td>
</tr>
<tr>
<td>M</td>
<td>719</td>
</tr>
<tr>
<td>N</td>
<td>793</td>
</tr>
<tr>
<td>O</td>
<td>849</td>
</tr>
<tr>
<td>P</td>
<td>879</td>
</tr>
<tr>
<td>R</td>
<td>967</td>
</tr>
</tbody>
</table>
List of Articles

A
Abbott Laboratories (United States)
Acrylic Rubber and Fibers
Adrenocortical Carcinoma
Adrenocortical Carcinoma, Childhood
Advertising
Aerospace Industry
Afghanistan
Age
AIDS-Related Cancers
Albert Einstein Cancer Center
Alcohol
Algeria
Allergan (United States)
Alternative Therapy: Diet and Nutrition
Alternative Therapy: Herbs, Vitamins, and Minerals
Alternative Therapy: Manual Healing and Physical Touch
Alternative Therapy: Mind, Body, and Spirit
Alternative Therapy: Pharmacological and Biological Treatment
American Academy of Pediatrics, Section on Hematology/Oncology
American Association for Cancer Education
American Association for Cancer Research
American Brain Tumor Association
American Cancer Society
American College of Gastroenterology
American College of Radiation Oncology
American Joint Committee on Cancer
American Lung Association
American Psychosocial Oncology Society
American Society for Radiation Oncology
American Society of Clinical Oncology
American Society of Hematology
American Society of Pediatric Hematology/Oncology
Amgen (United States)
Anal Cancer
Angola
Antibiotics
Anticancer Drugs
Argentina
Asbestos
Asian Diet
Aspirin
Assisted Suicide
Association for the Cure of Cancer of the Prostate
Association of Cancer Online Resources
Association of Community Cancer Centers
Association of Freestanding Radiation Oncology Centers
Association of Oncology Social Work
Association of Pediatric Hematology/Oncology Nurses
Astellas Pharma (Japan)
<table>
<thead>
<tr>
<th>Country/Institution/Topic</th>
</tr>
</thead>
<tbody>
<tr>
<td>AstraZeneca (United Kingdom)</td>
</tr>
<tr>
<td>Australia</td>
</tr>
<tr>
<td>Austria</td>
</tr>
<tr>
<td>Automobiles</td>
</tr>
<tr>
<td>Azerbaijan</td>
</tr>
<tr>
<td>Battery Acid</td>
</tr>
<tr>
<td>Belarus</td>
</tr>
<tr>
<td>Belgium</td>
</tr>
<tr>
<td>Benin</td>
</tr>
<tr>
<td>Bereavement Issues</td>
</tr>
<tr>
<td>Beta-Carotene</td>
</tr>
<tr>
<td>Bicycles</td>
</tr>
<tr>
<td>Bile Duct Cancer, Extrahepatic</td>
</tr>
<tr>
<td>Biologic Therapy</td>
</tr>
<tr>
<td>Bladder Cancer</td>
</tr>
<tr>
<td>Bladder Cancer, Childhood</td>
</tr>
<tr>
<td>Bolivia</td>
</tr>
<tr>
<td>Bonadonna, Gianni</td>
</tr>
<tr>
<td>Bone Cancer, Osteosarcoma/Malignant Fibrous Histiocytoma</td>
</tr>
<tr>
<td>Bone Marrow Transplants</td>
</tr>
<tr>
<td>Brain Stem Glioma, Childhood</td>
</tr>
<tr>
<td>Brain Tumor, Adult</td>
</tr>
<tr>
<td>Brain Tumor, Cerebellar Astrocytoma, Childhood</td>
</tr>
<tr>
<td>Brain Tumor, Cerebral Astrocytoma/Malignant Glioma, Childhood</td>
</tr>
<tr>
<td>Brain Tumor, Childhood</td>
</tr>
<tr>
<td>Brain Tumor, Medulloblastoma, Childhood</td>
</tr>
<tr>
<td>Brain Tumor, Supratentorial Primitive</td>
</tr>
<tr>
<td>Neuroectodermal, Childhood</td>
</tr>
<tr>
<td>Brain Tumor, Visual Pathway and Hypothalamic Glioma, Childhood</td>
</tr>
<tr>
<td>Brazil</td>
</tr>
<tr>
<td>Breast Cancer</td>
</tr>
<tr>
<td>Breast Cancer, Male</td>
</tr>
<tr>
<td>Breast Cancer, Sociocultural Differences and</td>
</tr>
<tr>
<td>Breast Cancer and Pregnancy</td>
</tr>
<tr>
<td>Bristol-Myers Squibb (United States)</td>
</tr>
<tr>
<td>Broad-Spectrum Ultraviolet (UV) Radiation</td>
</tr>
<tr>
<td>Bronchial Adenomas/Carcinoids, Childhood</td>
</tr>
<tr>
<td>Bulgaria</td>
</tr>
<tr>
<td>Burkina Faso</td>
</tr>
<tr>
<td>Burma (Myanmar)</td>
</tr>
<tr>
<td>Burundi</td>
</tr>
<tr>
<td><strong>C</strong></td>
</tr>
<tr>
<td>Calcium</td>
</tr>
<tr>
<td>California Blood Bank Society</td>
</tr>
<tr>
<td>Cambodia</td>
</tr>
<tr>
<td>Cameroon</td>
</tr>
<tr>
<td>Canada</td>
</tr>
<tr>
<td>Canadian Association of Medical Oncologists</td>
</tr>
<tr>
<td>Canadian Association of Pharmacy in Oncology</td>
</tr>
<tr>
<td>Canadian Cancer Society</td>
</tr>
<tr>
<td>Canadian Red Cross</td>
</tr>
<tr>
<td>Canadian Society of Surgical Oncology</td>
</tr>
<tr>
<td>Canadian Urologic Oncology Group</td>
</tr>
<tr>
<td>Cancer Association of South Africa</td>
</tr>
<tr>
<td>Cancer Communication</td>
</tr>
<tr>
<td>Cancer Council Australia</td>
</tr>
<tr>
<td>Cancer Drugs, Cost and Benefits of</td>
</tr>
<tr>
<td>Cancer Therapy Evaluation Program</td>
</tr>
<tr>
<td>Candlelighters Childhood Cancer Foundation</td>
</tr>
<tr>
<td>Carcinoid Cancer Foundation</td>
</tr>
<tr>
<td>Carcinoid Tumor, Childhood</td>
</tr>
<tr>
<td>Carcinoid Tumor, Gastrointestinal</td>
</tr>
<tr>
<td>Carcinoma of Unknown Primary</td>
</tr>
<tr>
<td>Careers</td>
</tr>
<tr>
<td>Caregivers</td>
</tr>
<tr>
<td>Celebrities and Cancer</td>
</tr>
<tr>
<td>Celgene (United States)</td>
</tr>
<tr>
<td>Cell Phones</td>
</tr>
<tr>
<td>Central African Republic</td>
</tr>
<tr>
<td>Central Nervous System Lymphoma, Primary</td>
</tr>
<tr>
<td>Cervical Cancer</td>
</tr>
<tr>
<td>Chad</td>
</tr>
<tr>
<td>Chao Family Comprehensive Cancer Center</td>
</tr>
<tr>
<td>Chemical Industry</td>
</tr>
<tr>
<td>Chemoprevention</td>
</tr>
<tr>
<td>Chemotherapy</td>
</tr>
<tr>
<td>Childcare and Cancer Risk</td>
</tr>
<tr>
<td>Childhood Brain Tumor Foundation</td>
</tr>
<tr>
<td>Childhood Cancers</td>
</tr>
<tr>
<td>Chile</td>
</tr>
<tr>
<td>China</td>
</tr>
<tr>
<td>Chlorine</td>
</tr>
<tr>
<td>Chloroform</td>
</tr>
<tr>
<td>City of Hope</td>
</tr>
<tr>
<td>Clinical Trials</td>
</tr>
<tr>
<td>Clothing</td>
</tr>
</tbody>
</table>
List of Articles

Coal Industry
Cold Spring Harbor Laboratory
Colombia
Colon Cancer
Colorectal Cancer, Childhood
Comprehensive Cancer Center of Wake Forest University
Congo, Democratic Republic of Cosmetics
Cost of Therapy
Costa Rica
Côte d’Ivoire
COX-2 Inhibitors
Croatia
Cuba
Czech Republic

D
Daiichi Sankyo (Japan)
Daily Life
Dana-Farber Cancer Institute
Danish Cancer Society
DDT
Denmark
Deodorizers
Detergents
Developing Countries
Diesel Exhaust
Diet and Nutrition
Disability
Disinfectants and Antiseptics
Disparities Within Nations (Elimination of Cancer)
Dominican Republic
Drugs
Duke Cancer Institute
Dyes and Pigments

E
Ecuador
Education
Egypt
Eisai (Japan)
El Salvador
Electrical Industry
Electronics
Eli Lilly and Company (United States)
Embalmig Fluids
Endometrial Cancer
Environmental Justice and Cancer
Environmental Tobacco Smoke

Ependymoma, Childhood
Eritrea
Esophageal Cancer
Esophageal Cancer, Childhood
Estrogen, Steroidal
Ethiopia
Europa Donna, the European Breast Cancer Coalition
European Association for Cancer Research
European CanCer Organisation
European Cancer Prevention
European School of Oncology
European Society for Therapeutic Radiology and Oncology
European Society of Mastology
European Society of Surgical Oncology
Ewing’s Family of Tumors
Exercise
Experimental Cancer Drugs
Explosives
Extracranial Germ Cell Tumor, Childhood
Extragonadal Germ Cell Tumor

F
Family Size
Finland
Flame Retardant
Flavoring Agents
Food Additives
Food and Drug Administration
Forest Labs (United States)
Fox Chase Cancer Center
France
Fred & Pamela Buffett Cancer Center
Fred Hutchinson Cancer Research Center
Freon
Future of Cancer

G
Gallbladder Cancer
Gasoline
Gene Therapy
Genentech
Genetics
Genzyme (United States)
Georgia
Germany
Gestational Trophoblastic Tumor
Ghana
Glass Industry
GlaxoSmithKline (United Kingdom)
Global Health Issues and Cancer
Government
Greece
Green, Adele
Gregoire, Christine
Guatemala
Guinea

H
H. Lundbeck (Denmark)
Haemophilia Society (United Kingdom)
Hair Dye
Haiti
Head and Neck Cancer
Health Advocacy
Healthy People
Hepatitis B
Hepatitis C
Hepatocellular (Liver) Cancer, Adult (Primary)
Hepatocellular (Liver) Cancer, Childhood
(Primary)
Herbert Irving Comprehensive Cancer Center
Herbicide
History of Cancer
Holden Comprehensive Cancer Center at
the University of Iowa
Honduras
Hong Kong Anti-Cancer Society
Hospice Care
Hospitals
HPV Vaccination
Hungary
Huntsman Cancer Institute
Hypopharyngeal Cancer
Hypothalamic and Visual Pathway Glioma,
Childhood

I
Immigrant Populations
India
Indonesia
Infection
Insecticides
Insurance
International Agency for Research on Cancer
International Association for the Study of
Lung Cancer
International Association of Cancer Registries
International Cancer Alliance for Research and
Education
International Committee of the Red Cross
International Myeloma Foundation
International Psycho-Oncology Society
International Society for Cutaneous
Lymphomas
International Society for Experimental
Hematology
International Society for Preventive
Oncology
International Society of Nurses in Cancer Care
International Society of Paediatric Oncology
International Society on Thrombosis and
Haemostasis
Intraocular Melanoma
Iran
Iraq
Ireland, Republic of
Ireland (Ohio) Cancer Center
Irish Cancer Society
Islet Cell Carcinoma (Endocrine Pancreas)
Israel
Italy

J
Japan
Japan Lung Cancer Society
Japanese Cancer Association
Japanese Gastric Cancer Association
Japanese Society for Therapeutic Radiology and
Oncology
Jet and Rocket Fuels
Jimmy Fund
Johnson & Johnson (United States)
Jordan

K
Kaposi’s Sarcoma
Kazakhstan
Kenya
Kidney (Renal Cell) Cancer
Kidney Cancer, Childhood
Kidney Cancer Association
Kimmel Cancer Center
Kyrgyzstan

L
Laos
Laryngeal Cancer
Laryngeal Cancer, Childhood
Latitude
Lead
Leukemia, Acute Lymphoblastic, Adult
Leukemia, Acute Lymphoblastic, Childhood
Leukemia, Acute Myeloid, Adult
Leukemia, Acute Myeloid, Childhood
Leukemia, Chronic Lymphocytic
Leukemia, Chronic Myelogenous
Leukemia, Hairy Cell
Leukemia & Lymphoma Society
Libya
Liver Cancer, Adult (Primary)
Liver Cancer, Childhood (Primary)
Lombardi Comprehensive Cancer Center
Lung Cancer, Non–Small Cell
Lung Cancer, Small Cell
Lymphoma, AIDS-Related
Lymphoma, Burkitt's
Lymphoma, Hodgkin's, Adult
Lymphoma, Hodgkin's, Childhood
Lymphoma, Hodgkin's, During Pregnancy
Lymphoma, Non-Hodgkin's, Adult
Lymphoma, Non-Hodgkin's, Childhood
Lymphoma, Non-Hodgkin's, During Pregnancy
Lymphoma, Primary Central Nervous System
Lymphoma Research Foundation of America
Memorial Sloan Kettering Cancer Center
Menarche, Early
Merck (Germany)
Merck & Co. (United States)
Merkel Cell Carcinoma
Mesothelioma, Adult Malignant
Mesothelioma, Childhood
Mexico
MIT Center for Cancer Research
Moldova
Morocco
Mozambique
Mozambique
Multiple Endocrine Neoplasia Syndrome, Childhood
Multiple Myeloma/Plasma Cell Neoplasm
Mycosis Fungoides
Myelodysplastic Syndromes
Myelodysplastic/Myeloproliferative Diseases
Myeloma, Multiple
Myeloproliferative Disorders, Chronic

N
Nasopharyngeal Cancer
Nasopharyngeal Cancer, Childhood
National Alliance of Breast Cancer Organizations
National Cancer Institute
National Cancer Policy Board
National Cancer Registrars Association
National Childhood Cancer Foundation
National Marrow Donor Program
National Causes of Cancer
Nepal
Netherlands
Netherlands Cancer Institute
Netherlands Hemophilia Patients Society
Neuroblastoma
Neutrons
New Zealand
Nicaragua
Nickel Compounds
Niger
Nigeria
Nixon, Richard (War on Cancer)
North American Association of Central Cancer Registries
North Korea
Norway
Novartis Group (Switzerland)
Novo Nordisk (Denmark)
Nuclear Industry

O
Obesity
Occupational Therapy
Ohio State University Comprehensive Cancer Center
OHSU Knight Cancer Institute
Oncology Nursing Society
Ono Pharmaceutical (Japan)
Oral Cancer, Childhood
Oral Cavity Cancer, Lip and
Organisation of European Cancer Institutes
Oropharyngeal Cancer
Ovarian Cancer, Childhood
Ovarian Epithelial Cancer
Ovarian Germ Cell Tumor
Ovarian Low Malignant Potential Tumor

P
Pain and Pain Management
Paint
Pakistan
Pancreatic Cancer
Pancreatic Cancer, Childhood
Pancreatic Cancer, Islet Cell
Paper Industry
Papua New Guinea
Paraguay
Paranasal Sinus and Nasal Cavity Cancer
Parathyroid Cancer
Passive Smoking
Penile Cancer
Perfume
Perlmutter Cancer Center
Peru
Pesticides
Pfizer (United States)
Pharmaceutical Industry
Pheochromocytoma
Philippines
Photodynamic Therapy
Physical Therapy
Pineoblastoma and Supratentorial Primitive Neuroectodermal, Childhood
Pinkel, Donald
Pituitary Tumor
Plasma Cell Neoplasm/Multiple Myeloma
Plastics Industry

Pleuropulmonary Blastoma
Poland
Polishes
Pollution, Air
Pollution, Water
Portugal
Poverty
Prostate Cancer
Proton Therapy
Psycosocial Care/Support
Purdue University Center for Cancer Research

R
Radiation
Radiation, Gamma
Radiation, Ionizing
Radiation Therapy
Raloxifene
Rectal Cancer
Religion
Religion: Jewish Women and Cancer Risk
Religion: Meditation and Risk
Religion: Preventability Versus Preordained
Religion: Use of Interventions
Retinoblastoma
Rhabdomyosarcoma, Childhood
Roche Group (Switzerland)
Romania
Rosenberg, Barnett
Roswell Park Cancer Institute
Russia
Rwanda

S
Salivary Gland Cancer
Salivary Gland Cancer, Childhood
Salk Institute for Biological Studies
Sanford-Burnham Medical Research Institute
Sarcoma, Ewing’s Family of Tumors
Sarcoma, Soft Tissue, Adult
Sarcoma, Soft Tissue, Childhood
Sarcoma, Uterine
Sarcoma Foundation of America
Saudi Arabia
Screening
Screening, Access to
Sedentary Occupations
Selenium
Senegal
Serbia
List of Articles

University of Colorado Cancer Center
University of Hawai’i Cancer Center
University of Michigan Comprehensive Cancer Center
University of Minnesota Masonic Cancer Center
University of New Mexico Cancer Research and Treatment Center
University of North Carolina Lineberger Comprehensive Cancer Center
University of Pittsburgh Cancer Institute
University of Southern California Norris Comprehensive Cancer Center
University of Texas MD Anderson Cancer Center
University of Virginia Cancer Center
University of Wisconsin Carbone Cancer Center
Unknown Primary Site, Cancer of, Childhood
Unknown Primary Site, Carcinoma of, Adult
Unusual Cancers of Childhood
Ureter and Renal Pelvis, Transitional Cell Cancer
Urethral Cancer
Uterine Cancer, Endometrial
Uterine Sarcoma
Uzbekistan

V
Vaccine Workers, HPV and HCV
Vaccines
Vaginal Cancer
Vanderbilt-Ingram Cancer Center
Venezuela
Vermont Cancer Center
Vietnam
Vinyl

Visual Pathway and Hypothalamic Glioma, Childhood
Vitamins
Vulvar Cancer

W
Waldenström’s Macroglobulinemia
War Gases and Chemicals
Water Treatment
Western Diet
Wilms’ Tumor
Wistar Institute
Women’s Cancers
Wood Dust
Wood Preserver
Workplace Wellness Programs
World Health Organization
World Health Organization Framework Convention on Tobacco Control
Wynder, Ernst

X
X-Rays

Y
Yale Cancer Center
Yemen
Young Adult Cancer Prevention
Yul Brynner Head and Neck Cancer Foundation (Head and Neck Cancer Alliance)

Z
Zambia
Zimbabwe
Reader’s Guide

Alternative Treatments and Therapies
Alternative Therapy: Diet and Nutrition
Alternative Therapy: Herbs, Vitamins, and Minerals
Alternative Therapy: Manual Healing and Physical Touch
Alternative Therapy: Mind, Body, and Spirit
Alternative Therapy: Pharmacological and Biological Treatment

Associations by Cancer Type
American Brain Tumor Association
American College of Gastroenterology
American Lung Association
Association for the Cure of Cancer of the Prostate
Candlelighters Childhood Cancer Foundation
Carcinoid Cancer Foundation
Childhood Brain Tumor Foundation
International Myeloma Foundation
Kidney Cancer Association
Lymphoma Research Foundation of America
National Alliance of Breast Cancer Organization
National Childhood Cancer Foundation
National Marrow Donor Program
Sarcoma Foundation of America
Yul Brynner Head and Neck Cancer Foundation (Head and Neck Cancer Alliance)

Associations: Others
American Academy of Pediatrics, Section on Hematology/Oncology
American Association for Cancer Education
American Association for Cancer Research
American Brain Tumor Association
American College of Radiation Oncology
American Joint Committee on Cancer
American Psychosocial Oncology Society
American Society for Radiation Oncology
American Society of Hematology
American Society of Pediatric Hematology/Oncology
Association of Community Cancer Centers
Association of Freestanding Radiation Oncology Centers
Association of Oncology Social Work
Association of Pediatric Hematology/Oncology Nurses
California Blood Bank Society
Canadian Association of Medical Oncologists
Canadian Association of Pharmacy and Oncology
Canadian Cancer Society
Canadian Red Cross
Canadian Society of Surgical Oncology
Canadian Urologic Oncology Group
Cancer Association of South Africa
Danish Cancer Society
Europa Donna, the European Breast Cancer Coalition
European Association for Cancer Research
European Cancer Organisation
European CanCer Prevention
European Society for Therapeutic Radiology and Oncology
European Society of Mastology
European Society of Surgical Oncology
Haemophilia Society (United Kingdom)
Hong Kong Anti-Cancer Society
International Agency for Research on Cancer
International Association for the Study of Lung Cancer
International Association of Cancer Registries
International Committee of Red Cross
International Myeloma Foundation
International Psycho-Oncology Society
International Society for Cutaneous Lymphomas
International Society for Preventive Oncology
International Society of Experimental Hematology
International Society of Nurses in Cancer Care
International Society of Paediatric Oncology
International Society on Thrombosis and Haemostasis
Irish Cancer Society
Japan Lung Cancer Society
Japanese Cancer Association
Japanese Gastric Cancer Association
Japanese Society for Therapeutic Radiology and Oncology
Lymphoma Research Foundation of America
National Alliance of Breast Cancer Organizations
National Cancer Policy Board
National Cancer Registrars Association
National Marrow Donor Program
Netherlands Hemophilia Patients Society
North American Association of Central Cancer Registries
Oncology Nursing Society
Organization of European Cancer Institutes
Society of Gynecology Oncologists
Society of Surgical Oncology
Turkish Society of Haematology
Union for International Cancer Control
World Health Organization

Business of Cancer
Abbott Laboratories (United States)
Allergan (United States)
Amgen (United States)
Astellas Pharma (Japan)
AstraZeneca (United Kingdom)
Bristol-Myers Squibb (United States)
Celgene (United States)
Cost of Therapy
Daiichi Sankyo (Japan)
Eisai (Japan)
Eli Lilly & Co. (United States)
Forest Labs (United States)
Genentech
Genzyme (United States)
GlaxoSmithKline (United Kingdom)
H. Lundbeck (Denmark)
Johnson & Johnson (United States)
Marketing, Drug
Marketing, Hospitals and Clinics
MedImmune (United States)
Merck (Germany)
Merck & Co. (United States)
Novartis Group (Switzerland)
Novo Nordisk (Denmark)
Ono Pharmaceutical (Japan)
Pfizer (United States)
Roche Group (Switzerland)
Shire UK
Taisho Pharmaceutical (Japan)
Takeda Pharmaceutical (Japan)

Cancer Around the World
Afghanistan
Algeria
Angola
Argentina
Australia
Austria
Azerbaijan
Bangladesh
Belarus
Belgium
Benin
Bolivia
Brazil
Bulgaria
Burkina Faso
Burma (Myanmar)
Flame Retardant
Flavoring Agents
Freon
Gasoline
Genetics
Glass Industry
Hair Dye
Hepatitis B
Hepatitis C
Herbicide
Immigrant Populations
Infection
Insecticides
Jet and Rocket Fuels
Latitude
Lead
Meat, Cooking
Natural Causes of Cancer
Neutrons
Nickel Compounds
Nuclear Industry
Obesity
Paint
Paper Industry
Passive Smoking
Perfume
Pesticides
Pharmaceutical Industry
Plastics Industry
Polishes
Radiation, Gamma
Radiation, Ionizing
Smokeless Tobacco
Solar Radiation
Solvents
Stainless Steel
Sunlamps or Sunbeds, Exposure to
Textile Dyes
Tobacco-Related Exposures
Tobacco Smoking
Toxic Mold
Ultraviolet A Radiation
Ultraviolet B Radiation
Ultraviolet C Radiation
Ultraviolet Radiation Related Exposures
Vinyl
War Gases and Chemicals
Water Treatment
Wax and Soap
Wood Dust
Wood Preserver
X-Rays

Major Cancer Associations
American Association for Cancer Research
American Cancer Society
American Society of Clinical Oncology
Association of Cancer Online Resources
Association of Community Cancer Centers
Cancer Therapy Evaluation Program
International Cancer Alliance for Research and Education
Massachusetts Medical Society
National Cancer Institute
National Cancer Registrars Association
Union for International Cancer Control
World Health Organization

Major Hospitals and Treatment Centers
Albert Einstein Cancer Center
Barbara Ann Karmanos Cancer Institute
Chao Family Comprehensive Cancer Center
City of Hope
Cold Spring Harbor Laboratory
Comprehensive Cancer Center of Wake Forest University
Dana-Farber Cancer Institute
Duke Cancer Institute
Fox Chase Cancer Center
Fred & Pamela Buffett Cancer Center
Fred Hutchinson Cancer Research Center
Herbert Irving Comprehensive Cancer Center
Holden Comprehensive Cancer Center at the University of Iowa
Huntsman Cancer Institute
Ireland (Ohio) Cancer Center
Jimmy Fund (DFCI)
Kimmel Cancer Center
Lombardi Comprehensive Cancer Center
Massey Cancer Center
Mayo Clinic Cancer Center
Mayo Clinic Cancer Center, Jacksonville
Mayo Clinic Cancer Center, Scottsdale
Memorial Sloan-Kettering Cancer Center
MIT Center for Cancer Research
National Cancer Institute
Ohio State University Comprehensive Cancer Center
OHSU Knight Cancer Institute
Purdue University Center for Cancer Research
<table>
<thead>
<tr>
<th>Testicular Cancer</th>
<th>Urethral Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thymoma, Childhood</td>
<td>Uterine Cancer, Endometrial</td>
</tr>
<tr>
<td>Thymoma and Thymic Carcinoma</td>
<td>Uterine Sarcoma</td>
</tr>
<tr>
<td>Thyroid Cancer</td>
<td>Vaginal Cancer</td>
</tr>
<tr>
<td>Thyroid Cancer, Childhood</td>
<td>Visual Pathway and Hypothalamic Glioma, Childhood</td>
</tr>
<tr>
<td>Trophoblastic Tumor, Gestational</td>
<td>Vulvar Cancer</td>
</tr>
<tr>
<td>Unknown Primary Site, Cancer of, Childhood</td>
<td>Waldenström’s Macroglobulinemia</td>
</tr>
<tr>
<td>Unknown Primary Site, Carcinoma of, Adult</td>
<td>Wilms’ Tumor</td>
</tr>
<tr>
<td>Unusual Cancers of Childhood</td>
<td>Women’s Cancers</td>
</tr>
<tr>
<td>Ureter and Renal Pelvis, Transitional Cell Cancer</td>
<td></td>
</tr>
</tbody>
</table>
Gallbladder Cancer

The biliary tract cancers are composed of gallbladder cancer, intrahepatic cholangiocarcinoma, and extrahepatic cholangiocarcinoma. Gallbladder cancer is the fifth-most common gastrointestinal (GI) malignancy in the United States and is the most common cancer to arise out of the biliary tract, with an estimated U.S. incidence of 10,650 in 2014 and deaths in 3,630 cases (according to the American Cancer Society). Gallbladder cancers behave very aggressively, and most are unresectable or metastatic at the time of diagnosis. Compared to other biliary tract cancers, gallbladder cancer tends to have early metastatic spread, shorter time to recurrence, and shorter median survival.

Risk Factors

The pathogenesis of gallbladder cancers is felt to be related to chronic inflammation, and several risk factors have been identified. Underlying gallstone disease, gallbladder polyps, and chronic infection with *Salmonella typhi* have been implicated in the development of gallbladder cancer. Other identified risk factors include female gender, obesity, and smoking.

Diagnosis and Workup

Gallbladder cancers are most often diagnosed at an advanced stage. The disease can spread rapidly; however, the diagnosis is often delayed due to presenting symptoms similar to those seen with cholecystitis. Symptoms include biliary colic (abdominal pain especially after fatty meals), development of jaundice, and findings of a mass in the gallbladder on imaging.

The initial workup for gallbladder cancer includes imaging of the abdomen and pelvis (generally computed tomography [CT] or magnetic resonance imaging [MRI]), labs to evaluate liver function, and evaluation for metastatic disease (with additional imaging of the chest). Imaging is also used to determine if cancer appears to be resectable. If the patient has jaundice, then additional workup is needed to determine if placement of a stent is necessary to relieve obstruction.

Other relevant labs that are monitored include the tumor markers carcinoembryonic antigen (CEA) and cancer antigen 19-9 (CA 19-9). Higher levels are suggestive of cancer; however, these tumor markers are nonspecific for gallbladder cancer. They can be elevated in other cancer states and also from benign causes such as inflammation.

Staging and Prognosis

The most common histology is adenocarcinoma (65–90 percent), followed by squamous cell or adenosquamous (10–15 percent), or undifferentiated (5 percent). Staging of gallbladder cancer is done using the 2010 American Joint Committee on
Cancer (AJCC) staging system. Staging consists of examination of the depth of invasion, involvement of surrounding lymph nodes, and invasion into surrounding or distant organs. There are four stages in the AJCC staging. Stage I cancers invade into the muscular layer of the gallbladder without nodal involvement. Stage II cancers invade beyond the muscular layer into the perimuscular connective tissue, without nodal involvement. Stage III cancers invade through the serosa (outer layer of the gallbladder) or invade into surrounding adjacent organs or involve adjacent lymph nodes. Stage IV cancers invade into the vasculature, multiple adjacent organs, distant lymph nodes, or distant organs.

Staging of gallbladder cancer is the most important prognostic factor. Staging is also used to determine whether patients can undergo surgical resection. Estimates of five-year survival rates in more than 10,000 patients diagnosed between 1989 and 1996 were 50 percent, 28 percent, 7 to 8 percent, and 2 to 4 percent, respectively, for stage I, II, III, and IV disease. Another poor prognostic factor is involvement of cancer in the liver at the time of presentation.

TREATMENT: RESECTABLE DISEASE
The only curative treatment for gallbladder cancer is surgical resection. Surgical resectability is determined by degree of vascular involvement, penetration into adjacent organs, degree of nodal involvement, and presence of distant metastatic disease. Staging laparoscopy is sometimes used to evaluate for peritoneal disease as occult disease not seen on imaging is common.

Surgical resection should include complete removal of the gallbladder with limited hepatic resection and removal of the adjacent lymph nodes (including the porta hepatitis, gastrohepatic ligament, and retroduodenal lymph nodes). Negative margins are necessary for cure, and further extensive resection of the liver or bile ducts may be required in order to achieve an R0 resection (defined as surgery with negative margins).

Adjuvant chemotherapy following curative resection has not been clearly defined. There are few prospective clinical trials due to the low incidence of gallbladder cancer, and most of the data has been obtained from retrospective analyses, which are limited by small numbers of patients. The National Comprehensive Cancer Network (NCCN) guidelines provide options for adjuvant treatment, including gemcitabine or fluoropyrimidine chemotherapy or use of chemoradiation (except in stage I disease). However, despite use of adjuvant therapy, rates of recurrence can be up to 80 percent in resected patients.

Surveillance after curative resection is recommended given the high likelihood for disease recurrence, even in early-stage disease. This often will include imaging studies, labs, and exams, typically done every six months for the first two years, with further surveillance dependent upon individual patient cancer characteristics.

UNRESECTABLE OR METASTATIC DISEASE
Due to the insidious nature of the disease, most cases are either unresectable or metastatic at time of presentation. In this setting, biopsy is needed to make a pathologic diagnosis. In cases of disease presenting with jaundice, biliary drainage will be required up front before any chemotherapy and can be done with biliary stent placement via endoscopic retrograde cholangiopancreatography (ERCP) or percutaneous drain placement (PTC).

Cytotoxic chemotherapy remains the mainstay for treatment of unresectable or metastatic disease. The combination of chemotherapy with gemcitabine plus cisplatin is considered to be standard first-line treatment, based upon results of the large, randomized, controlled phase III ABC-02 trial. Alternative active chemotherapy options include combinations of gemcitabine with oxaliplatin or capecitabine, capecitabine with cisplatin or oxaliplatin, fluorouracil with cisplatin or oxaliplatin or single agent fluorouracil, capecitabine, and gemcitabine. Response rates are in the range of less than 10 percent in single-agent therapy to up to 40 percent in combination regimens; however, prognosis is poor, with median overall survival of less than one year. Several ongoing clinical trials are being performed to improve the prognosis in advanced and metastatic gallbladder cancer.

CONCLUSION
Gallbladder cancers are aggressive cancers with an overall poor prognosis. Staging workup is necessary to determine if the disease is resectable. The only curative treatment is surgical resection; however, rates of recurrence remain high. The ability to achieve an R0 resection is the most important
prognostic factor in patients undergoing surgical resection. Advanced disease is treated with cytotoxic chemotherapy; however, median overall survival remains less than one year. Ongoing clinical trials are being performed to improve the outcomes of this aggressive cancer.

Kelly Shimabukuro
Moores UCSD Cancer Center

See Also: American Joint Committee on Cancer; Chemotherapy; Surgery.

Further Readings

A link between male breast cancer and gasoline and gasoline combustion exposure was found in a 2000 study, concluding that occupational exposure to gasoline vapors may increase the risk of breast cancer. (Kenneth Gabrielsen Photography)

---

**Gasoline**

Commonly referred to as gas, petrol, or motor fluid, gasoline is a pale brown or pink liquid produced from refining petroleum that is extracted from beneath the ground.

Petroleum is extracted by drilling a long hole, or well bore, into the earth with an oil rig or apparatus similar to a mobile crane attached to a drilling auger that drives a rotating drill bit through the ground to an identified petroleum reservoir. After the well bore is created, a steel pipe casing is fitted to maintain the structural integrity of the hole, and crude oil is brought to the surface by regulating the pressure and flow with a complex system of valves.

While there are many stages of petroleum recovery, the end product is the extraction and drainage of all petroleum from the reservoir, which is then distributed through a network of pipelines for storage and processing. For automotive gasoline, processing occurs at a refinery where the crude oil is distilled of impurities and the various petrochemical products (gasoline, kerosene, natural gas, etc.) are separated.

In 1859, Edwin Drake dug the first oil well, distilling kerosene for lighting; the other products, for which he had no use, were waste products. The invention of the automobile in 1892 created a need for suitable automotive fueling alternatives to kerosene and coal tar distillates, but these products caused what is called knocking, a phenomenon whereby fuel compression causes spontaneous ignition after spark ignition, rather than spark plug ignition, resulting in the rapid increase in pressure and engine damage. Several additives, including tetraethyl lead, detergents, ethanol, methanol, and lead, were used to improve the octane rating.

From the 1950s through the 1970s, lead was added to improve engine performance and octane ratings in gasoline. As the apparent health problems of lead emerged, the Environmental Protection Agency (EPA) established standards to phase out lead in gasoline through the 1980s, and by 1995, the U.S. Clean Air Amendment of 1990 banned the use of leaded fuel for automotive vehicles.

In recent years, the EPA has attempted to regulate hazardous air pollutants resulting from the
emissions of automotive gasoline by controlling the content of benzene, 1,3-butadiene, acrolein, and formaldehyde.

According to the Monograph Program of the International Agency for Research on Cancer (IARC), an agency of the World Health Organization specializing in global cancer research, five classification categories exist, ranging from carcinogenic to humans (Group 1), probably carcinogenic to humans (Group 2A), possibly carcinogenic to humans (Group 2B), not classifiable as to its carcinogenicity to humans (Group 3), and probably not carcinogenic to humans (Group 4). The U.S. National Toxicology Program (NTP) identifies these agents as known to be carcinogenic or reasonably anticipated to cause cancer. Many chemicals in gasoline fall in Group 1 through Group 2B or have been identified by the NTP as known to be carcinogenic.

The Occupational Safety and Health Administration (OSHA) recognizes both the evaluation of the IARC Group 1 and Group 2A carcinogens and also the list of known and potential carcinogens published in the Annual Report on Carcinogens by the NTP as criteria for regulated carcinogens under the Hazard Communication Standard. OSHA requires all manufacturers of chemicals and mixtures to disclose the potential hazards when handling chemicals and compounds on a Material Safety Data Sheet (MSDS), which would include any information regarding the carcinogenic nature of the material listed as well as allowable limits of exposure and potential health risks posed by exposure.

Gasoline is a mixture of approximately 150 chemicals depending on the manufacturer. According to the MSDS, the mixture of chemicals in gasoline contains at least 15 hazardous chemicals, including (measured as a percent by volume) benzene (5 percent), toluene (35 percent), napthalene (1 percent), trimethylbenzene (7 percent) and methyl tert-butyl ether (MTBE, 18 percent), as well as 1,3-butadiene, 1,2-dibromoethane, and 1,2-dichloroethane and polycyclic aromatic hydrocarbons (PAHs), or hydrocarbons, organic compounds of carbon and hydrogen, the configuration of which consists of aromatic rings, or rings alternating double and single bonds between carbon atoms. Seven PAHs are classified by the EPA as probably human carcinogens.

The most common exposure to gasoline is through inhaling vapors at a service station when refueling or when using equipment that requires gasoline. Attendants at fueling stations, truck drivers, or those who work with gasoline are at risk for breathing excessive vapors and therefore have an increased risk for negative health impacts. According to the Agency for Toxic Substances and Disease Registry (ATSDR), inhaling vapors at 10,000 to 20,000 parts per million (ppm) or swallowing about 12 ounces can cause death. High concentrations of chronic vapor exposure can cause lung damage, stomach lining irritation, and skin irritation, and swallowing large amounts of gasoline can harm the nervous system.

After long-term exposure (two years) to high concentrations of unleaded gasoline vapors, laboratory animals developed liver and kidney tumors, although the ATSDR does not recognize this as sufficient evidence to determine human carcinogenicity resulting from gasoline exposure. The Department of Health and Human Service (DHHS) has not classified automotive gasoline for carcinogenicity, but the link between automotive gasoline and certain cancers is currently under review.

Studies from 1985 and 1993 suggest that there is no or inadequate epidemiological evidence, consistent with the findings of the IARC that no link between kidney cancer and occupational exposure to gasoline for refinery workers exists.

Benzene naturally occurs in crude oil and gasoline and is a by-product of automotive exhaust; it has industrial uses in oil refineries, chemical plants, and the manufacturing of lubricants, dyes, detergents, drugs, pesticides, and cigarettes. Studies show that lab rodents exposed to benzene developed different types of tumors, supporting the risk of leukemia in humans. The IARC determined that long-term exposure to high levels of benzene may increase the risk of leukemia.

A 2000 study suggested a link between male breast cancer with gasoline and gasoline combustion exposure, concluding that occupational exposure to gasoline vapors may play a role in the increased risk of breast cancer due to benzene, 1,3-butadiene, 1,2-dibromoethane, 1,2-dichloroethane, and PAHs.

Benzene was classified as a known carcinogen by the IARC based on evidence that shows workers exposed to high levels of benzene are found to be at a great risk of acute myeloid leukemia and some
studies suggesting links between benzene exposure and childhood leukemia, acute lymphocytic leukemia, chronic lymphocytic leukemia, non-Hodgkin’s lymphoma, and multiple myeloma (adults).

The IARC designation is supported by the NTP classification of benzene as known to be a human carcinogen, and by the 2007 EPA listing of benzene as a known human carcinogen in the Integrated Risk Information System (IRIS), an electronic database cataloging the human health impacts of environmental exposure to various hazardous substances.

OSHA maintains a recommended exposure limit (REL) to one ppm during an eight-hour workday and a maximum REL of five ppm over a 15-minute period. OSHA also requires employers to provide personal protective equipment (PPE) to workers at risk of exposure, which may include respirators and gloves. The IARC also identifies ethylbenzene, styrene, naphthalene, gasoline, and gasoline engine exhaust as possibly carcinogenic Group 2B materials based on studies in laboratory rodents.

At the 2013 International Scientific Symposium from the IARC, Kurt Straif, M.D., M.P.H., Ph.D., presented the findings of the IARC, citing the difficulty of separating diesel and gasoline exhaust, leading to inadequate evidence to determine carcinogenicity of gasoline engine exhaust. The Working Group, 24 experts from seven different countries, found sufficient evidence through animal experimentation such that they designated gasoline engine exhaust as possibly carcinogenic to humans (Group 2B), publishing their findings in 2012 in The Lancet.

Tara Michele Zrinski
Northampton Community College

See Also: Detergents; Dyes and Pigments; Kidney (Renal Cell) Cancer; Leukemia, Acute Myeloid, Adult; Leukemia, Chronic Lymphocytic.

Further Readings


Gene Therapy

Gene therapy is the use of DNA as a disease treatment, one that is administered by delivering DNA to a patient's cells. Typically, healthy, functional DNA is delivered in order to replace a mutated or damaged gene, but there are more complex therapies that use DNA to encode a protein drug that provides treatment. Gene therapy is also used to assist the immune system in recognizing a threat; in cancer patients, because the tumor is composed of the host's own mutated tissue, the immune system is little help against it when left to its own devices. In cancer treatments, the greatest successes with gene therapy have been in treating leukemias and blood cancers.

Gene therapy was conceptualized in 1972, and the first gene therapy clinical trial was approved 18 years later. At the time, gene therapy was seen principally as a potential remedy for hereditary diseases, not cancer (except insofar as several hereditary conditions predispose the patient to cancer). However, gene therapy throughout the 1990s saw few successes, and the field's current growth and confidence dates back only to the mid-2000s, when clinical successes began to flourish in the gene therapy treatment of leukemias, Parkinson's disease, and hemophilia. As of 2014, more than 2,000 clinical trials had been conducted or approved in the gene therapy field. The first gene therapy treatment approved for prescription in the West, alipogene tiparvovec, was approved by the European Medicines Agency in 2012 and was introduced commercially in 2014 under the trade name Glybera.

At $1.6 million for a course of treatment, it is the most expensive medicine in the world. While out of reach for most cancer patients for the moment, recent breakthroughs in clinical trials indicate that gene therapy in the future will join surgery, chemotherapy, immunotherapy, and radiotherapy as a standard oncology therapy. It will be especially welcome for cancer patients who, for one reason or another, are poor candidates for the other standard treatments. In 2014, for instance, Forbes reported on a young girl whose acute lymphoblastic leukemia recurred twice after chemotherapy until a gene therapy treatment using a modified human immunodeficiency virus (HIV) virus; she nearly died from the fever caused by her immune system attacking both the virus and her cancer, but within two weeks, she was cancer free and, for the first time, remained so.

Cancer did not originally seem like a candidate for gene therapy as, in most cases, it results not from the expression of a specific gene but following a complex multistep process in which a variety of somatic genes are altered. Gene therapy seemed not only ineffective in correcting this but too cumbersome because, at first blush, it might appear necessary to correct each of those alterations—not all of which are even known or understood yet—and to restore the original gene function to each cancer cell. Despite these initial and reasonable doubts, as the science of gene therapy matured, cancer turned out to be an ideal subject for it. Treatment strategies augment standard treatments by restoring normal DNA or expressing important proteins rather than rebuilding all of the cancerous cells. (In this sense, though, modern gene therapy as a cancer treatment does differ from the classical conception of gene therapy in that it is not gene-replacement therapy but rather gene therapeutics.)

The first gene therapy approved for use in humans was Gendicine, approved in China to treat head and neck cancers in 2010. Not yet approved in the West—and in order to encourage medical tourism, the Chinese manufacturer Shenzhen SiBiono GeneTech may not be motivated to seek approval overseas—Gendicine uses a recombinant adenovirus as a vector for a treatment for patients with mutated p53 genes. It is administered in conjunction with chemo- and radiotherapy, especially for patients who are resistant to one or both.

Gene therapy is a subset of biologic therapy, which uses biological substances to treat disease. Like other biologics, gene therapies can be either autologous—using the patient's own tissue, which is extracted, modified in the lab, and then returned—or allogenic, using donor tissue. While gene therapy shows promise in treating many different types of diseases, it especially makes sense as a treatment for cancer—the propagation of mutated cells—and hereditary diseases. Cancer treatment strategies using gene therapy include the augmentation of chemotherapy and immunotherapy treatments, such as through drug sensitization with genes for prodrug delivery, the delivery of drug-resistant genes to protect bone marrow during high-dosage chemotherapy, gene replacement for tumor suppressor genes, inactivation of oncogene expression,
and ex vivo and in vivo cytokine gene transfer. Though gene therapy initially focused on delivering a gene that would cause a particular protein to be expressed, a better understanding of nucleases—enzymes in the body—has led to gene therapies that deliver DNA that encodes nucleases into chromosomes. The nucleases then edit the chromosomes and disrupt disease-causing genes.

One of the uses of gene therapy is to deactivate oncogenes. Oncogenes are specific genes that contribute to cancer. Once activated, they cause the cells normally programmed for rapid cell death to survive instead, resulting in cancer’s proliferation. Oncogenes alone rarely cause cancer but are critical to its spread and survival once it has developed. Different oncogenes are associated with different types of cancer. Gene therapy can be used to deactivate these oncogenes or reduce or block their expression. Similarly, gene therapy can be used to restore tumor suppression genes—genes in the body that protect from cancer by preventing cellular mutations, which leave the body vulnerable to cancer when they are themselves mutated. Using gene therapy to replace the mutated tumor suppressor genes with functional healthy tumor suppressor genes is a common strategy.

Gene therapy can also be used to affect the efficacy of chemotherapy and other cancer drugs. Delivering drug-resistant genes to bone marrow or blood-derived stem cells, for instance, helps them survive radiation treatment, which reduces the complications and chances of infection that are attendant to radiotherapy. Drug-sensitivity genes can be delivered in order to enhance the effectiveness of anticancer drugs.

The vector is the package in which DNA is delivered to the patient. Vector development is an important area of gene therapy research, and key areas of study include methods to increase the transduction efficiency of nonviral vectors, identifying the synergy between gene therapies and other therapeutics, vector targeting, and specificity and reducing the toxicity and immunogenicity of viral vectors.

Viral vectors may come from either of the two main types of viruses, lytic and lysogenic. Lytic viruses produce more viruses quickly, spreading infection rapidly. Lysogenic viruses, on the other hand, may remain in the body for years before spreading infection in response to a chemical trigger. Viral vectors are generally safe, the virus having been modified in order to prevent it from replicating. Some viruses pose a stability problem, though, being genetically unstable and capable of rearranging their genomes.

Viral vectors using retroviruses are most subject to the problem of missing the target by inserting the genetic material into the wrong part of a chromosome, which can result in cancer if the disrupted gene happens to regulate cell division. This is the problem that caused a small number of patients in both French and British clinical trials treating X-linked, severe, combined immunodeficiency to develop leukemia, which halted a similar American trial.

Perhaps the greatest drawback to a viral vector, assuming nothing goes wrong, is that it can be used only once on a given patient. There is a limited number of viral vectors to choose from, and once the patient has been exposed to one, he or she develops an immune response that will result in the immune system attacking it if it is used again. If the gene therapy works the first time, this is fine, but many cancer therapies presuppose the possibility of being needed more than once.

Vectors need to be nontoxic in order to avoid side effects as well as destruction by the body’s immune system. Viral vectors have been used traditionally. Viruses like retrovirus, adenovirus, herpes simplex virus, pox virus, and adeno-associated virus can be modified in the lab in order to remove their toxic effects (i.e., using a modified herpes virus to deliver
a gene therapy does not infect the patient with herpes). Viruses have naturally evolved with the ability to transfer their genetic materials to host cells. Indeed, this is the source of cancer in several cases, including liver cancer, cervical cancer, and most Merkel cell carcinomas. Nonviral vectors, though, offer the promise of greater safety. Most are cationic (meaning that, at the molecular level, they possess an active ion with a positive charge), including cationic peptides, cationic liposomes, and cationic polymers like polyethylenimine and poly L-lysine. Cationic lipids, for instance, can condense negatively charged DNA in order to encapsulate it into liposomes for delivery.

The introduction of nucleic acids into cells is called transfection, as opposed to transduction, which is the use of a viral vector to introduce DNA. The simplest form of transfection is an intramuscular injection of naked DNA. In clinical trials, expression as a result of naked DNA injection has been very low, and various methods have been developed to improve on the results. Electroporation, for instance, uses short pulses of high-voltage electricity to transfect DNA across the cell membrane to its target. Electroporation has a high rate of cell death, which makes it inappropriate for some applications. Sonoporation uses ultrasonic bursts instead, which disrupt the cell membrane through acoustic cavitation. Magnetofection, as the name implies, uses magnetic particles to bring DNA into contact with the target cell. And the so-called gene gun uses DNA coated in gold particles with which the target cell is bombarded in a process that leaves the gold behind.

Some studies have used inorganic nanoparticles, such as gold, silica, or calcium phosphates, for gene delivery. Inorganic vectors have a significantly cheaper manufacturing cost (in both materials cost and time), are resistant to microbial attack, and have a low immunogenicity. Quantum dots also have been used. Some hybrid methods of delivery have tried to address the shortcomings of individual methods, such as combining liposomes with a virus to create a virosome that is more efficient at gene transfer than either a viral or liposomal vector.

Laypeople are sometimes confused by the term gene therapy. It does not necessarily involve changing anything about the individual that will be passed on to his or her subsequent offspring through heredity—nor does any treatment used on humans do so, at least not yet. Gene therapy is either somatic or germ line. Somatic gene therapy transfers the therapy to the somatic cells (nonsenes) of the body, and any modifications to the patient’s DNA are limited only to that individual—the DNA encoded in any sex cells (sperm or eggs) remains the same. All gene therapies performed on humans so far have been somatic gene therapy.

However, somatic gene therapy has limitations. No one has yet developed a therapy that replaces multiple genes, for instance, such as the genes that interact in order to cause heart disease, arthritis, diabetes, or Alzheimer’s disease. Germ-line gene therapy could do so. In germ-line gene therapy, which has been performed only on animals, it is the genes of germ cells (sperm or eggs) that are modified in order to correct a genetic disease and prevent it from being expressed by any offspring conceived by those germ cells. Despite the United States’ conservative stance on many forms of medical research, there is actually no legislation preventing this or preventing federal funding for it—federal legislation does not address the difference between somatic and germ-line gene therapy at all, unlike the legislation of several European countries, Canada, and Australia, which ban germ-line therapy for humans. That said, there is as yet no clinical work being done in this area, but a long and justified history of fear of eugenics.

Until the 2000s, most gene therapy had focused on hereditary diseases. In 2006, two significant breakthroughs helped usher in the current age of gene therapy. In May, an Italian team at the San Raffaele Telethon Institute for Gene Therapy overcame the immune rejection problem—whereby the immune system rejects the vector virus or the newly delivered gene—by using microRNA to selectively turn off the identity of the therapeutic gene. In August, a National Institute of Health team in Bethesda, Maryland, treated metastatic melanoma in two patients in one of the first successful uses of gene therapy as a cancer treatment. Five years later, two of three patients in a pilot study were cured of their chronic lymphocytic leukemia by University of Pennsylvania researchers using genetically modified T-cells. The subsequent larger study saw 26 out of 59 patients achieve complete remission. Exciting advances and successes continued to be seen in gene therapy in general.
and gene therapy as a cancer treatment specifically throughout the 2010s.

In the United States, there is no specific gene therapy protocol, but gene therapies are subject to relevant legislation and regulations pertaining to investigational new drug applications, the use of human test subjects, and so on. The National Institute of Health provides additional oversight for federally funded gene therapy research, including a mandatory registry of human genetic engineering research protocols from federally funded projects and a set of guidelines for good practices in the manipulations of genes, prepared by an advisory committee.

Gene therapy poses a number of risks. The immune system may attack a viral vector, which can result not only in failure of the attempted therapy but also in inflammation and other side effects, even including organ failure. In a patient already suffering from the effects of cancer and possibly of other cancer treatments, these side effects can be significant. Virus vectors also may infect the wrong cells, which can lead to effects ranging from mild illness to the growth of a new cancer. Viruses also can recover their original toxicity once in the body. Further, in clinical trials, genes delivered to the wrong part of the DNA have mutated the target gene and created a new tumor instead of helping to eliminate the existing tumor.

Furthermore, three patients have died in gene therapy trials, at least one as a direct result of his trial. (Jesse Gelsinger died in 1999 of organ failure and brain death caused by a massive immune response to the viral vector used in his therapy.)

Closely related to gene therapy is RNA interference as a cancer therapy. RNA interference is the process by which RNA molecules inhibit gene expression, often by destroying specific mRNA molecules. It is a process only recently understood, long thought to consist of several unrelated processes. RNA interference can silence the genes involved in a tumor’s cell division in order to stop its growth or genes implicated in the spread or origin of the cancer. Like gene therapy, RNA interference therapy has relied primarily on viral vectors but is looking further afield. The frequency or result of off-target effects is not yet fully understood, though in one major study of RNA interference to treat liver disease in mice, the death rate from off-target effects was unexpectedly high.

Initial tests suggest that, assuming off-target effects and similar problems are resolved methodologically, RNA interference has great potential as a breast cancer therapy because it has been shown to be effective in targeting the receptors associated with breast cancer proliferation. It also has shown potential in treating chronic myelogenous leukemia and colon adenocarcinoma.

Bill Kte’pi
Independent Scholar

See Also: Biologic Therapy; Future of Cancer; Genetics.

Further Readings
Herper, Matthew. “Is This How We’ll Cure Cancer?” Forbes (May 26, 2014).
Genentech is a biotechnology company that was founded in April 1976 and is headquartered in San Francisco, California. Genentech was founded by Robert A. Swanson and Dr. Herbert Boyer. The company is considered to be the first biotechnology company and, since its inception, has focused on the discovery of drugs that address significant, unmet medical needs. Genentech has multiple products on the market for serious or life-threatening medical conditions, and the organization focuses on basic and applied research in the areas of oncology, immunology, neuroscience, metabolism, and infectious disease. In March 2009, the Roche group acquired Genentech; Genentech now serves as the headquarters for Roche pharmaceutical operations in the United States. Genentech has a number of drugs that are designed to address the needs of cancer patients, including individuals suffering from breast cancer and non-Hodgkin's lymphoma (NHL).

History of Genentech

The idea for the company began in 1973, when Dr. Boyer and a colleague, Stanley Norman Cohen, found that genes from bacteria could be combined with genes from eukaryotes—recombinant DNA. Boyer and Cohen’s discovery opened the door to a new scientific field called recombinant DNA technology. Boyer went on to partner with Robert A. Swanson, a graduate of the Sloan School of Management at the Massachusetts Institute of Technology, and the two left their jobs in order to found Genentech. The duo then formed a partnership with Kleinman, Perkins, Caufield, and Byers, a high-tech venture capital firm also located in the San Francisco area. The group contracted with the City of Hope National Medical Center to conduct their early biomedical research using recombinant DNA.

Genentech pioneered the organizational model that most biotechnology firms would eventually use to grow their businesses: First, create a startup to capitalize on publically funded discoveries that were made by scientists at academic institutions; next, locate venture capital or government funding to develop and test biomedical applications of the research; last, license the rights of the research to a larger pharmaceutical company for the production, marketing, and distribution of the product. In 1977, Genentech used recombinant DNA to produce the first human protein, somatostatin, and one year later, in 1978, it was used in the first genetically engineered, synthetic “human” insulin. By 1982, Genentech partnered with Eli Lilly and Company to become the first biotechnology company to launch a commercial product, biosynthetic human insulin, marketed as Humulin. Today, most of the insulin used throughout the world is a form of biosynthetic recombinant human insulin. Since conception, Genzyme has developed and marketed many other successful biomedical pharmaceuticals, including therapies for breast cancer, colon cancer, lung cancer, non-Hodgkin’s lymphoma, age-related macular degeneration, rheumatoid arthritis, lung cancer, non-Hodgkin’s lymphoma, psoriasis, cystic fibrosis, heart attack, stroke, and growth hormone deficiency.

Genentech Today

Since 1990, the Swiss company Roche has owned a majority of Genentech, and in 2009, the company acquired full ownership of Genentech for $46.8 billion. Roche markets medicines and diagnostic tests in more than 150 countries worldwide. The United States accounts for approximately 42 percent of Roche’s pharmaceutical sales; during 2013, Roche had approximately $18.299 million (CHF 17.428 million) in net sales in the United States, which was a 9 percent increase in sales from 2012.

Genentech’s original manufacturing facility was located in South San Francisco, California; however, as demand for Genentech’s expanding product line grew, the company acquired an additional manufacturing facility at a 100-acre site in Vacaville, California. Genentech also has manufacturing and supply facilities in Hillsboro, Oregon, and Singapore. In 2014, Genentech had 35 drugs available on the market with approximately 19 products in the research and development (R&D) pipeline. In 2013, Roche spent about $9.000 million (CHF 8.700 million) in R&D. Genentech employs nearly 13,300 individuals from around the world and is consistently named by Fortune Magazine as one of the 100 best companies to work for.

Controversy

In 1999, Genentech agreed to pay $200 million to the University of California San Francisco (UCSF) to settle a nine-year dispute over a patent
underlying the drug Protropin, a growth hormone used to treat dwarfism. UCSF claimed that Genentech scientists had taken a DNA sample from a lab at the university in 1978 and then used the specimen to develop Protropin; by the end of the 1990s, the drug had generated almost $2 billion in sales. The university asked for $400 million in lost royalties from the theft and other damages. Genentech claimed they had developed the drug independently from UCSF; however, a jury ruled that the university’s patent on the drug was valid but could not determine if Protropin was definitively based on UCSF research. Genentech settled the lawsuit with UCSF, but the controversy left a legal blemish on Genentech’s record.

**Oncology**

Roche is the world’s leading provider of cancer drugs, and about 62 percent of all pharmaceutical sales for Roche derive from the oncology department. Currently, Genentech is focused on several projects related to the understanding and treatment of cancer, including better understanding of complex signaling pathways and critical aspects of the cell cycle, metabolic regulators, the immune response to cancer, and cancer stem cell research. Rituxan is the company’s top-performing oncology drug, and today it has become the standard of care for NHLs and chronic lymphocytic leukemia (CLL). The drug has been used to treat nearly 3 million cancer patients, and in 2013, Genentech received FDA approval for an additional drug, Gazyva, to work with Rituxan to improve cancer treatments. In 2013, Rituxan had $7.298 million in net sales (CHF 6.951 million) and was responsible for 19 percent of all pharmaceutical sales for Roche.

Herceptin is a drug used in metastatic breast cancer patients with tumors that overexpress the HER2 gene. The drug gained FDA approval in 1998 and has subsequently been a key treatment for many breast cancer patients. In 2013, the drug accounted for 16 percent of all Roche pharmaceutical sales and generated $6.383 million in net sales (CHF 6.079 million). Genentech also markets many other key oncology drugs, including Avastin for the treatment of metastatic colorectal cancer, Tarceva for patients with small cell lung and pancreatic cancer, and Erivedge, which is used to treat advanced basal-cell carcinoma. Genentech currently has several additional oncology drugs that are in the R&D pipeline, with several that will undergo the FDA approval process throughout 2014 and 2015.

Emily Hammad  
David P. Tracer  
*University of Colorado Denver*

**See Also:** Genetics; Pharmaceutical Industry; Roche Group (Switzerland).

**Further Readings**


**Genetics**

Genetics involves the science of trait inheritance from parents to progeny, including the hereditary and evolutionary similarities and differences of related organisms, as produced by the interaction of the genes. It pertains to the origins or development of inherited features and characteristics of an organism or group or type of organisms. Because genes are ecumenical to living organisms, genetics is, therefore, applicable to the study of all living systems, including animals, humans, bacteria, and plants. Genetics acts in conjunction with an organism’s environment and experiences to impact development and behavior. Genes principally signify their functional effect through the production of proteins, which are complex molecules responsible for most of the functions in the cell.

Abundant studies that have been devoted to the genetics of human cancer predisposition have supported indications of inheritance as a component of the etiology. Also, sufficient research efforts have been invested in the understanding of the etiology of cancer and of the interaction of genetic and environmental factors that are involved in the disease development. Genes are found in every cell of the human body and control each cell function by
making proteins that have specific functions and act as messengers for the cell.

Changes in genes, referred to as mutations, which occur during a person’s life, either inherited from father and mother or from damage, may contribute to the growth and development of cancer. Cancers commonly begin when one or more genes in a cell are mutated (changed), consequently creating an abnormal protein or no protein at all. It is estimated that there are about 30,000 different genes in each cell, controlling how each cell functions, how quickly it grows, how frequently it divides, and how long it lives. The human body consists of more than a trillion cells, organized into organs, such as the lungs, and organ systems, such as the respiratory system.

Although cancer is prevalently caused by multiple mutations to several different genes, many of the genes that contribute to the development of cancer fall into broad categories. Chromosomes are made up of genes. Humans each have between 20,000 and 25,000 different genes. Genes are composed of deoxyribonucleic acid (DNA), located on 46 chromosomes, which are arranged in pairs. The DNA is created from four chemical compounds known as adenine (A), thymine (T), guanine (G), and cytosine (C). Humans have two sets of 23 chromosomes, one set of which they inherit from their mother and the other from their father. The first 22 chromosome pairs are numbered (chromosome 1, 2, 3, etc.). These chromosomes determine people’s physical features and are called autosomes. The chromosomes of the twenty-third pair, which are referred to as the sex chromosomes, determine whether a person is female or male. These are called the X and Y chromosomes. A human female inherits two copies of the X chromosome, one from each of the parents, constituting an XX pair, while a human male inherits one copy of the X chromosome from the mother and one copy of the Y chromosome from the father, constituting an XY pair.

Cancer can occur in three primary paths: sporadic cancers, familial cancers, and hereditary cancers. Approximately 60 percent of cancers are sporadic. Sporadic cancers occur by chance or occur from environmental exposures, usually over many years, in persons who have no known genetic risk factors and no cancer-relevant family history. Although familial cancers have a tendency to cluster in families, they also tend not to follow the typical rules of inheritance. Commonly, familial cancers are caused by variants in multiple genes working together with environmental factors. A person’s risk of developing cancer is contingent on the number of cancer risk genetic variants that the individual inherits and the environmental factors that come into interaction with those genes. Hereditary cancers are caused in part by gene changes that are passed on from parents to their children. Although not everyone who is born with a gene change will eventually develop cancer, people with inherited gene changes have a 50 percent chance of passing the mutation to each of their offspring. Other blood relatives may share these same gene changes as well. Those individuals who have inherited a gene change may be at a higher risk for developing more than one type of cancer.

In cancer research, the dictation of certain types of genes that contribute to cancer has been an important development in recent times. More than 90 percent of cancers are observed to have some type of genetic alteration. While some of these alterations are inherited, others are sporadic. Two basic types of genetic mutations are acquired and
Germline. The most common types of cancers result from acquired mutations that occur from damage to genes during an individual's life and are not passed from parent to child. These kinds of mutations may result from tobacco use, exposure to ultraviolet (UV) radiation, viruses, and aging factors. On the other hand, cancer caused by germline mutations is referred to as inherited cancer, which makes up approximately 5 to 10 percent of all cancers.

Genetic cancer research has identified three main types of genes that can affect cell accretion and are altered, that is, mutated, in certain types of cancers as oncogenes, tumor suppressor genes, and mismatch-repair genes. Oncogenes are involved in the regulation of the normal growth of cells and can turn a healthy cell into a cancerous cell. Common oncogenes include a specialized protein that controls cancer growth and spread, referred to as HER2, found on some cancer cells, such as breast and ovarian cancer cells, and the RAS family of genes, which make proteins involved in cell communication pathways, cell growth, and cell demise. Genetic cancer scientists usually describe oncogenes to be like a cancer switch that exists in most people's bodies. For some unknown reason, the switch flips to cause these oncogenes to impetuously become unable to control the normal growth cells and allowing abnormal cancer cells to begin to grow.

Tumor-suppressor genes are protective genes. These genes have the capacity to acknowledge abnormal growth and reproduction of damaged cells, or cancer cells, and can interrupt their reproduction until the defect is corrected. Examples of tumor suppressor genes are BRCA1, BRCA2, and p53. Germline mutations in BRCA1 or BRCA2 elevate a woman's risk of developing hereditary breast or ovarian cancers. The most habitually mutated gene in individuals who have cancer is p53, with more than 50 percent of all cancer involving a missing or damaged p53 gene. Mismatch-repair genes are viewed as DNA repair genes that fix mistakes made when DNA is replicated (copied). These genes help in identifying errors when DNA is replicated to produce a new cell. In the event that the DNA does not consummately match, these genes repair the mismatch and correct the error. These genes must be working properly because any errors in DNA can be transmitted to new cells, causing them to become damaged. The number of cells in the human body tissues is tightly regulated so that new cells are made for normal growth and development in addition to replacing dying cells.

Cancer is often referred to as a disease of cells and as a disease of uncontrollable cell proliferation. A cluster of cancer cells in the body is referred to as a tumor. It is also known that not all tumors are cancerous. Tumors are often categorized as benign or malignant. Although benign tumors normally do not threaten the patient's life, benign tumors that develop in the brain can cause grave health effects or even death because of the brain's location within the skull. Furthermore, as the swelling involved in the benign tumor expands, the brain can be damaged because it has nowhere to go to get out of the way of the growth within the skull. Malignant tumors often metastasize to other organs of the body. Metastasis is the spread of cancer to other locations in the body, and the symptoms are dependent on the location of the tumor, which can include enlarged lymph nodes. These symptoms can also be felt or sometimes seen under the skin and are a particularly hard, enlarged liver or enlarged spleen, which can be felt in the abdomen region, pain or fracture of affected bones, and neurological symptoms. Malignant cancer or tumors are serious and will commonly lead to death if not treated promptly. The chances of surviving the disease vary significantly by the types and locations of the cancer and the extent of the disease at the beginning of treatment.

The causes of cancer are diverse, complex, and only partially understood, just as there are so many different cancers that affect humans. There are more than 200 different types of cancers. Cancer can be detected in a number of ways, including recognizing the presence of certain symptoms and signs, screening tests, or imaging. Although cancer symptoms and signs do not commonly appear when the cancer begins, they do appear as the mass continues to grow or ulcerates. Cancer commonly is treated with chemotherapy, radiation therapy, and surgery. Accumulation of genetic information provides resources for identifying those persons who have an increased risk of cancer. Genetic information generation sources include samples of biologic DNA, information gathered from a person's family disease history, diagnostic results from physical examinations, and medical records of the individual and his or her relatives. With conclusive information that indicates that a person is at
increased risk of developing cancer, intervention initiatives can be activated with life-saving management implications that may lead to specific treatment methodologies aimed at ameliorating risk. Such action plans may include tamoxifen for breast cancer, colonoscopy for colon cancer, or risk-reducing Salpingo-oophorectomy for ovarian cancer. Information regarding a person’s genetic predisposition to cancer may also provide a direct health advantage by establishing the absence of an inherited cancer susceptibility. Furthermore, the cognizance of a cancer-predisposing mutation can be informative data for other family members, not only for the individual tested. Genetic information may also provide direction that affects medical and lifestyle decisions.

Felix O. Chima
Prairie View A&M University

See Also: Brain Tumor, Adult; Breast Cancer; Sarcoma, Ewing’s Family of Tumors.

Further Readings

Genzyme (United States)

Genzyme Corporation is an American biotechnology company headquartered in Cambridge, Massachusetts. The company was founded by George M. Whitesides, Sheridan Snyder, and Henry Blair in 1981 and was originally focused on the discovery of drugs for use with lysosomal storage disorders (LSDs) but today has expanded to other disease areas including renal disease, a range of genetic disorders, cancer, and multiple sclerosis (MS). Genzyme is one of the world’s largest biotechnology companies and employs more than 12,000 people in 40 countries. In 2011, the company was acquired by Sanofi and is a fully owned subsidiary of the organization.

Initially, Genzyme was a small partnership; however, using provisions of the Orphan Drug Act, Genzyme gained exclusive rights to the National Institute of Health (NIH)–discovered replacement enzyme for glucocerebrosidase. In 1991, Ceredase became the first orphan drug developed by Genzyme and Food and Drug Administration (FDA) approved as a replacement therapy for people with Type-1 Gaucher disease. Individuals afflicted by Gaucher disease lack the glucocerebrosidase enzyme, which is responsible for the breakdown of the fat molecule glucocerebroside. Cerezyme replaced Ceredase in 1994 as a treatment for Gaucher disease, and the drug continues to contribute approximately one-third of Genzyme’s annual net sales. Since 1985, Genzyme has branched out into other areas of research, and today, the company runs two business units—MS and rare diseases (RD). The RD unit is focused on LSDs, rare forms of cancer, renal diseases, and genetic cardiovascular diseases known as familial hypercholesterolemia (FH).

In 2013, Genzyme reported $2.944 million net sales (2.142 million euros), a 25.9 percent increase in annual net sales from the previous year. Currently, Genzyme is actively marketing more than eight drugs that have been approved by the FDA and at least eight drugs currently in the Genzyme Research and Development (R&D) pipeline. During 2013, Genzyme invested approximately $580 million (415 million euros) in R&D. Genzyme operates four flagship offices located in Cambridge, Massachusetts; Framingham, Massachusetts; Geel, Belgium; and Waterford, Ireland, with other key operational facilities located at sites around the world that are located near centers of scientific innovation.

Sanofi acquired Genzyme in 2011 for approximately $20.1 billion. The acquisition was an opportunity for Sanofi to grow its specific expertise in rare diseases and also offered the company a presence in
the biotechnology sector. In 2004, Sanofi-Synthé-labo merged with Aventis to become the world’s fifth-largest pharmaceutical company with headquarters located in Paris, France. The company primarily engages in the R&D, manufacturing, and marketing of pharmaceutical drugs available in the prescription market; however, the organization also develops over-the-counter medications. Following the merger, the company officially changed its name to Sanofi in May 2011. The company focuses on seven key areas of medicine: cardiovascular disease, neurology, diabetes, internal medicine, oncology, thrombosis, and vaccines. Today, Genzyme is led by CEO and Chairman of Sanofi Christopher A. Viebacher and David Meeker, M.D., the president and CEO of Genzyme.

**Orphan Drug Act**

In 1983, the U.S. Congress passed the Orphan Drug Act, which designated orphan drugs, vaccines, and other diagnostic agents as those intended to treat rare diseases. Rare diseases are defined as diseases affecting fewer than 200,000 American citizens. The Orphan Drug Act incentivized companies to develop drugs for orphan diseases by providing seven years’ market exclusivity to developers of drugs for rare diseases and tax credits equal to half of the cost of development. At the time when the Orphan Drug Act was passed, Genzyme had already developed a strategy of thinking small, making the company primed to take advantage of the incentives included in the Orphan Drug Act. The opportunity to hold the sole marketing rights of its drugs for seven years made Genzyme an attractive company for many investors. In 1986, Genzyme went public and raised $27 million from investors who saw a valuable opportunity to invest in the company’s orphan drugs for rare diseases.

Since going public, Genzyme’s enzyme replacement therapies for LSDs, including Gaucher disease, remain the company’s biggest source of profit. Correspondingly, the company remains focused on orphan drugs; however, Genzyme has expanded the types of diseases it treats. Other biotechnology companies are trying to re-create the business model that Genzyme perfected, exclusively focusing on rare diseases, even at the expense of a more diversified portfolio. By focusing on small patient populations, the company receives steep reimbursement rates; this demonstrates that leveraging enzyme replacement therapies across multiple rare diseases can be profitable. Genzyme continues to grow through purchases of other companies and has developed and is selling medications for many other areas of medicine. In January 2014, Genzyme announced that it would invest $700 million in Alnylam Pharmaceuticals, a U.S. biotechnology company that develops RNAi therapies.

**Oncology Drugs**

Over the past three decades, health care providers have observed a steady increase in the incidence of thyroid cancer. In order to manage thyroid cancer, oncologists often rely on thyroidectomies or surgeries that partially or completely remove the thyroid gland from the affected individual. Thyroidectomies are often followed by radiiodine ablation and thyroxine therapy. Genzyme’s most successful oncology drug is Thyrogen (thyrotropin alfa for injection), a synthetic product that is similar to the naturally occurring human thyroid-stimulating hormone (TSH) and was developed as an alternative treatment for thyroxin therapy in thyroid cancer patients.

Individuals diagnosed with thyroid cancer and planning to undergo surgery to remove all or part of the thyroid gland may be prescribed Thyrogen prior to surgery in order to continue stimulation of the remaining thyroid tissue. Thyrogen has been used as a thyroid hormone replacement after surgery in order to ameliorate the patient’s quality of life by avoiding thyroid hormone withdrawal. Thyroid hormone withdrawal may include symptoms such as extreme fatigue, depression, and feeling consistently cold and may result in a reduced quality of life. Additionally, Thyrogen has been used successfully as a tool in the identification and diagnosis of thyroid cancer.

Emily Hammad  
David P. Tracer  
*University of Colorado Denver*

**See Also:** Food and Drug Administration; Genetics; Pharmaceutical Industry; Thyroid Cancer.

**Further Readings**

In its early history, Georgia was a powerful kingdom, experiencing its peaks in the 10th and 13th centuries. Georgia owes much of its modernization to Russia, including adopting free health care. The country has moved from tax-funded health care to providing health care for the most at-risk citizens (children under 6, elders over 60) and the poor, while those above their poverty line deal with private-sector health insurance companies. The government has also taken steps to provide free cancer screenings for its citizens.

The country of Georgia is geographically located east of the Black Sea and is bordered to the north and northeast by Russia. In the year 1801, Georgia was annexed by the Russian empire, and remained that way until a brief independence in the 1900s. It functioned as an independent state from 1918 to 1921, when it became part of the Soviet Union. From 1921 to 1991, Georgia's health care system was intertwined with the Soviet system. While health care was supposed to be free, some health professionals took illegal, out-of-pocket fees. While it was part of the Soviet Union, Georgia became more advanced and enjoyed greater diversity. Georgians living below the poverty line were provided services including surgery, radiation, chemotherapy, palliative care, and outpatient care. In regard to palliative care, the center ensures that all palliative care employees are instructed at national and international levels. They organize and oversee training in academia at national and international levels for medical practitioners under Tbilisi State University and Tbilisi State Medical University. The staff works with both adult and pediatric individuals.

In the 1990s, Georgia had a health care system that was funded entirely by taxes. Changes in 1995 resulted in a system with social insurance that operated through the State Medical Insurance Company. This covered basic health care. In 2009, primary care costs were paid for mostly by public sources—namely the Ministry of Labor, Health, and Social Affairs for the rural families and the urban population under age six and over age 60.

In 2000, the Cancer Prevention Center (CPC) was founded. The center has legal union status as a nongovernment, nonprofit organization. It provides both medical and teaching programs to patients, doctors, families of the patients, and medical students. CPC's focus is on preventative care as well as early detection techniques and treatment of cancers with known cures. The CPC offers inpatient palliative care, home care, support for those in the early stages, counseling and social support of both the patient and the patient's relatives, and education for both the patients and their families about the illness.

In Georgia, as in many places throughout the world, breast cancer is the main cause of death among women in their reproductive years. This was in part because women tended to get diagnoses in the later stages of cancer when it is harder to treat. In 2005, John Snow, Inc. (JSI) supported Georgia's first-ever walk to raise awareness of the issue, and in 2009, the event became part of the Susan G. Komen Foundation Race for the Cure. The Georgian government set up a national screening center in 2008 and offered free breast cancer screening for the women living in their capital city, Tbilisi. Just two years later in 2010, the government offered this screening nationwide.

In 2009, the rural population had their health care funded through public avenues. The population in urban areas under the age of 6 and over the age of 60 also had their health care funded. Georgians living below the poverty line were provided...
vouchers to purchase private health insurance. Anyone above the poverty line had to pay out of pocket for health insurance or services. In 2010, the Black Sea Countries Coalition on Breast and Cervical Cancer Prevention was held in Tbilisi. The goal of this coalition is to make an agreement to boost early detection and prevention of breast and cervical cancer in the area. The formation of this coalition began with Georgian first lady Sandra Elisabeth Roelofs in 2009, and it is made up of individuals from the health ministries, health policy managers, and clinicians from the area.

In 2013, the Women’s Empowerment Cancer Advocacy Network (WE CAN) and the Georgia National Screening Center held a summit in Tbilisi to raise awareness and promote education on the subject. Dr. Julie Gralow, WE CAN’s founder and director of the breast medical oncology program, Seattle (Washington) Cancer Care Alliance, oversaw the summit.

Georgia has taken great strides in being proactive. Many cancer-related deaths were due to the fact that the cancer had not been screened for, meaning the individuals were being diagnosed when they were in more severe and life-threatening stages.

According to the National Screening Program Web site, the program was started by the Georgian National Council of Reproductive Health. The government now offers free screenings for cervical cancer, bowel cancer, and prostate cancer in addition to breast cancer. For breast cancer, the screenings are free every two years, cervical cancer screenings every three years, and bowel cancer screenings every year for both men and women between the ages of 50 and 70. Prostate screenings are available every year for men ages 50 to 70.

One pitfall of Georgia’s health care system is that it is inaccessible. There are many doctors per capita in Georgia, and in that nation’s capital city of Tbilisi, the number of doctors per capita is three times that of rural locations. Even with the large number of medical professionals, Georgia still sees a low rate of utilization for both in- and outpatient services, including pharmaceutical medications, which suggests that people experience barriers to accessing health care, primarily cost. The poorest are covered by the government, but for anyone above the poverty line, family health emergencies contribute to many families becoming impoverished.

Even with its shortcomings in terms of accessibility, the Georgian government has taken strides to give its people access to cancer screening and the treatment they need. By sponsoring summits in Tbilisi, offering free screenings to its citizens, and giving health care access to the poor, Georgia is improving the quality of life and care of its people. Every step in technology and education for the masses is one step toward a lower rate of cancer mortality.

Michael Fox
Independent Scholar

See Also: Breast Cancer; Cervical Cancer; Prostate Cancer; Radiation Therapy.

Further Readings

Germany

The western European nation officially termed the Federal Republic of Germany has ancestral roots stemming all the way back to 962, when King Otto the Great united the various Germanic tribes of Germania to form the Holy Roman Empire. In the centuries that followed, Germany’s humanities and sciences flowered, though war also abounded. In the 20th century and four years after the conclusion of World War II, the modern Federal Republic of Germany was officially founded. In 1990, the previously Soviet-controlled East Germany was reunified with the Federal Republic of Germany, and this has remained as the nation’s modern rendition.

In 19th-century Europe, many European physicians following the lead of the Italian Gaspare Aselli purported that incidences of cancer were the result of anomalies occurring within an individual’s lymphatic system. The German pathologist...
Johannes Muller directly rejected such a theory in 1838. In his studies, he deduced that cancer is constituted by cells and that it is not inherently derived from the lymphatic system; however, he mistakenly also maintained that cancer cells were not derived from regular cells but from the connections between tissues called blastema. In this regard, Muller would later be corrected by one of his students, Rudolph Virchow, who in 1858 ascertained that cancer cells were in fact derived from regular cells. Virchow is now often referred to as the father of cellular pathology, and his work led to breakthroughs regarding how surgery was performed on tumors.

However, even Virchow had mistaken theories. In the second half of the 19th century, he mistakenly proposed that cancer cells were distributed throughout the body as if they were liquid-like in nature. In an attempt to better understand the disease, German surgeon Karl Thiersch negated this notion of Virchow’s throughout the 1860s by demonstrating that cancer cells were distributed by the growth of malignant cells and were not spread through the body by the action of a liquid. Another German surgeon active in the second half of the 19th century was Theodor Billroth, who gained worldwide acclaim for his mastery and innovation of radical surgical techniques on cancerous tumors. Billroth is held in high regard in contemporary medical circles for his pioneering of techniques to effectively remove stomach tumors.

As the German nation entered the 20th century, a German physics professor named Wilhelm Conrad Roentgen was the recipient of the inaugural Nobel Prize in physics for his work in the field of X-ray technologies. Soon after, the first X-ray machines were developed in an attempt to offer more efficient diagnoses. For the rest of the century, treatment capabilities and diagnosis options for the German public advanced. The treatment options in the country were advanced enough that the then-acting United States president Ronald Reagan visited the nation in 1985 to receive treatment for colon cancer from the esteemed German doctor Hans Nieper.

Contemporaneously, Germany is internationally recognized as having some of the best cancer specialists and best cancer treatment centers in the world. In the past several decades, German doctors have pioneered a new form of treating the disease that has been termed hyperthermia therapy, otherwise known as fever therapy, by practitioners in the field; the process is less expensive than other treatment options and involves using a very specialized machine to overheat the specific site of an individual’s tumor, which then consequently stems its growth. Moreover, unlike some other European nations, Germany has a well-established national cancer registry, which was initiated by the Federal Cancer Registry Data Act in August 2009.

In the past decade, the most prevalent incidences of cancer in Germany have been bowel, breast, lung, prostate, and stomach cancer. Intestinal, lung, and prostate cancers are the most prominent cancer incidences in males in Germany, while bowel, breast, and lung cancers are the most prevalent cancer incidences in females there. In the past several years, certain cancers such as gall bladder, liver, and bowel cancer have seen an increase in incidence in Germany, while cases of larynx cancer and cervix cancer are slowly declining.

As around the rest of the globe, many Germans have been affected by cancer. The critically acclaimed and Oscar-winning German actor Ulrich Mühe passed away at his house in Walbeck in 2007 as a result of stomach cancer. The popular comedian and entertainer Dieter Hildebrandt died in 2013 after only recently being diagnosed with prostate cancer. More historically, the German emperor Frederick III died of complications arising from larynx cancer in 1888.

As mentioned earlier, Germany is renowned for its extremely skilled cancer specialists. For example, Dr. Richard P. Baum is the chairman and clinical director of the Department of Nuclear Medicine at the Bad Berka Center of Neuroendocrine Tumors in Bad Berka, Germany, where he oversees interdisciplinary treatment approaches to battling cancer. Another prominent German cancer specialist is Dr. Bertram Wiedenmann, who is currently the chair of hepatology and gastroenterology at Humboldt University in Berlin, Germany, where he specializes in all aspects of gastrointestinal oncology.

See Also: Breast Cancer; Lung Cancer, Non–Small Cell; Prostate Cancer; Stomach (Gastric) Cancer.
Further Readings
Scholberg, A. “German Cancer Breakthrough.” Online Publishing and Marketing (February 2008).

Gestational Trophoblastic Tumor

Gestational trophoblastic tumor (GTT), also known as gestational trophoblastic neoplasia, may refer to any of three related types of malignant tumors (i.e., invasive mole, choriocarcinoma, and placental-site trophoblastic tumor), which originate in the placenta. Unlike in a normal pregnancy, wherein placental and trophoblastic cells facilitate the implantation of the fertilized egg into the uterine wall, in a pregnancy affected by GTT, the regulatory mechanisms that typically control the growth of these cells fail, and they develop into invasive, metastatic, and vascular tumors.

The benign premalignant tumor, which along with the aforementioned types of tumors may collectively be referred to as gestational trophoblastic disease, is a hydatidiform mole, in which the chorionic villi cells surrounding the fetus develop improperly and form a benign growth that may be either a complete or partial hydatidiform mole. In the event that a mole develops, the woman is said to be experiencing a molar pregnancy. Complete hydatidiform moles are usually composed completely from the paternal genome and account for around 70 percent of molar pregnancies. Partial moles, however, are comprised of both paternal and maternal genomes.

An invasive mole, or chorioadenoma destructum, begins as a hydatidiform mole, which is by definition restricted to the endometrial cavity but then develops to the point of invading the uterine wall. This type of tumor is seen in 10 to 20 percent of all molar pregnancies.

While invasive moles are composed of placental cells, choriocarcinoma is a cancer composed of only trophoblastic cells, the trophoblast being the membrane that forms the wall of the blastocyst in the early stages of fetal development. Choriocarcinoma can develop subsequent to any type of pregnancy, whereas an invasive mole may only generate from a hydatidiform mole. Around 50 percent of choriocarcinoma cases occur after a hydatidiform mole, 25 percent follow a spontaneous abortion or tubal pregnancy, and the remaining 25 percent occur subsequent to a normal pregnancy.

Placental-site trophoblastic tumors (PSTT) are the rarest of these malignancies, accounting for less than 1 percent of all cases of GTT. PSTTs, which develop at the site where the placenta and uterus join, may develop following a normal pregnancy, abortion, ectopic pregnancy, or molar pregnancy. As opposed to the other types of GTT, in cases of PSTT, the woman’s human chorionic gonadotropin (hCG) levels remain low despite the tumors’ metastasizing. This coupled with the fact that prognostic staging scores are of limited reliability makes detection and diagnosis difficult. In most cases, the tumors affect the uterus only, however, pelvic involvement and metastasis to the lungs and other organs have been documented.

In rare cases, a fetus may coexist with an evident mole, a case referred to as a twin molar pregnancy. There are no clear guidelines for medical
management of these cases. An increased risk of GTT development has been identified for women who continue the pregnancy into the second trimester but who experience complications leading to termination of the pregnancy prior to the stage of fetal viability. Previous recommendations were for the fetus in all twin molar pregnancies to be aborted; however, recent studies have found that around 40 percent of infants born in this scenario experience no significant congenital abnormalities, and so this recommendation is now considered outdated.

**Incidence and Risk Factors**

Worldwide occurrence of GTT is believed to be around 1 in 1,000 pregnancies, with rates perhaps twice as high in some Asian countries, especially in Japan.

Known risk factors associated with GTT include limited consumption of dietary carotene, vitamin A, and animal fat, and either extremely young or very advanced maternal age, specifically in women either younger than 15 or older than 40. Some evidence suggests that advanced paternal age may contribute to risk of complete, but not partial, hydatidiform mole development. Having experienced a prior molar pregnancy additionally has implications for recurrent GTT, with one study reporting that the risk for a second molar pregnancy was one in 76 and that, after two molar pregnancies, the risk for a third was one in 6.5.

**Symptoms and Diagnosis**

The most prominent symptom of complete hydatidiform mole is vaginal bleeding in early pregnancy, which can range from spotting to hemorrhage requiring transfusion. Pain, elevated hCG levels, and rarely, the passage of visible villi tissues may also indicate the presence of GTT. Other medical comorbidities associated with molar pregnancy, including anemia, tachycardia, preeclampsia, hyperemesis, hyperthyroidism, and respiratory distress are now rarely seen, likely due to the now-routine use of ultrasonography to aid in diagnosis of complete hydatidiform mole in the first trimester. Partial hydatidiform moles develop more slowly and are thus not often diagnosed until the second trimester, though vaginal bleeding is still the hallmark symptom of this type of tumor.

Ideally, all products of conception from nonviable pregnancies should be subject to histological examination irrespective of ultrasonographic findings, given that ultrasonography, especially in the first trimester, cannot completely reliably confirm the presence of GTT.

This histological exam, however, is not always performed on evacuation of conception, which can problematically delay the detection of GTT, thus increasing risk for requiring chemotherapy and surgery. Therefore, it is recommended that serum hCG levels be obtained within one week of evacuation, every one to two weeks while levels remain elevated, and then at one- to two-month intervals for up to one year. Most instances of GTT are evident within six months following evacuation, though rare cases of late-developing GTT have been documented.

**Treatment**

For most women experiencing hydatidiform mole or GTT who wish to retain fertility, the preferred evacuation method is suction dilation and evacuation. Some women may elect to undergo a hysterectomy in the event that future pregnancy is desired or that hemorrhagic bleeding is severe. However, it is crucial that women choosing hysterectomy be informed that this procedure prevents only local invasion of tumors but that, given the potential development of metastasizing tumors, it does not negate the need to routinely monitor hCG post-evacuation nor to receive chemotherapy in some cases.

If chemotherapy is recommended following molar evacuation or in response to choriocarcinoma or PSTT development, a typical regimen may include methotrexate, sometimes in conjunction with leucovorin. Dactinomycin may also be used. Effectiveness of treatment is determined through the measurement of hCG levels, and treatment typically concludes following the reduction of hCG levels to expected ranges, though one to two additional chemotherapy cycles may be recommended.

PSTT tumors specifically tend to be less responsive than other subtypes of GTT to chemotherapy, and the highest success rates to date have been found following multi-agent chemotherapy treatments, specifically etoposide, methotrexate, and dactinomycin alternating with cyclophosphamide.
and vincristine (EMA/CO) or etoposide, methotrexate, actinomycin, and cisplatinum (EMA/EP) treatments. The best prognosis is associated with growths localized to the uterus and with an elapsed time of less than two years between diagnosis of PSTT and the antecedent pregnancy.

Some oncologists have assessed whether a prophylactic course of chemotherapy following molar evacuation may reduce the subsequent incidence of GTT. The resulting research indicated that, while incidence was reduced for patients with high-risk moles, those with low-risk moles did not experience a diminishment in GTT development. Furthermore, in cases where GTT developed in spite of preventative chemotherapy treatment, more chemotherapy was required to achieve curative effects, and researchers thus concluded that the development of chemoresistance negated the minimal benefit of prophylactic chemotherapy administration.

Overall, GTT is regarded as the most curable gynecologic malignancy due to recognition of hCG as a tumor marker, the responsiveness of GTT to various chemotherapeutic agents, and the cataloging of risk factors that enable individualization of treatment. Overall cure rates are more than 98 percent with fertility retention, which represents a dramatic improvement over the overwhelming fatality associated with these tumors as little as 60 years ago.

Christopher L. Edwards
Rosellen Reif
LaBarron K. Hill
Duke University Medical Center

See Also: Breast Cancer and Pregnancy; Lymphoma, Hodgkin’s, During Pregnancy; Trophoblastic Tumor, Gestational.

Further Readings

Ghana

The West African country of Ghana is located along the Gulf of Guinea and Atlantic Ocean in the south, bordered by Côte d’Ivoire to the west, Burkina Faso to the north, and Togo to the east. The word Ghana means “warrior king.” The Republic of Ghana is named after the medieval west African Ghana empire. Historically, complex societies have existed in the Ghana (Wagadu) empire, including the region that is now southeastern Mauritania and western Mali, since about 1500 B.C.E. and around Ghana’s core regions since around 300 C.E. Various salient civilizations thrived in the general core region of Ghana until the 13th century. Beginning in the 13th century, the Akan peoples established the next dominant civilization which then was followed by the Ashanti empire, which flourished in the 18th and 19th centuries.

Health care practices in Ghana include the prevention, care, and treatment of diseases, such as cancer and other maladies. Until the introduction of Western medicine by Christian missionaries to the Gold Coast in the 19th century, traditional village healers and clerics were the primary caregivers, providing herbal remedies. In 16th century Ghana, traditional herbalists offered treatment of illnesses that stressed the combination of spiritual and physical healing. A recent 2012 World Health Organization (WHO) statistic has revealed that cancer accounted for 8.2 million deaths globally, more than deaths from human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS), malaria, and tuberculosis (TB) combined. It is projected that, without immediate action, the number of deaths from cancer will increase globally by nearly 80 percent by 2030, with most of the deaths occurring in the world’s developing nations and other low- and middle-income countries. More than 14 million people develop cancer globally each year. While many different types of cancer diseases exist, the two most common and deadly types in the sub-Sahara region of Ghana are breast and prostate cancers.

In Ghana, many cancer patients currently are unable to access curative therapies, state-of-the-art surgery, or expensive cancer drugs that are the mainstay of cancer care in developed nations. The government of Ghana provides most of the health care, which is administered largely by the Ministry
of Health and Ghana Health Services. There are five levels of providers within the health care system: health posts, which are first-level primary care for rural regions, health centers and clinics, district hospitals, regional hospitals, and tertiary hospitals. Funding for these health care programs is provided by the government of Ghana, financial credits, the Internally Generated Fund (IGF), and Donors-Pooled Health Fund. Additional health care services are also provided by the Christian Health Association of Ghana through hospitals and clinics.

Ghanaians living in the urban centers, which contain most of the hospitals, clinics, and pharmacies, are relatively well served by the country’s health care system. Rural areas, however, often lack modern health care technologies, causing patients in these areas either to depend on traditional medicine or to travel long and expensive distances for health care. Ghana currently has a universal health system, the National Health Insurance Scheme (NHIS), which was passed into law in 2003 by former president John Kufour. Until the establishment of the Ghana National Health Insurance, many Ghanaians lost their lives when they became ill because of their inability to pay for their health care needs.

The system of health care that operated before the establishment of the NHIS was commonly known as the cash-and-carry system. Under this system, a patient must make an estimated initial payment before any health care attention will be rendered. The cash-and-carry system was the practice even in emergency situations. It was a requirement that patients needing emergency treatment in hospitals or clinics must pay money before treatment and at every point of service delivery. While overall health care accessibility has improved since the enactment of NHIS, cancer control and care remained a low priority.

The government is ill prepared to combat the dramatically growing cancer burden. Breast cancer is the leading cause of death in Ghana. Despite the efforts devoted to preventing and treating breast cancer, about one-third of individuals diagnosed as having breast cancer die annually. Health professionals in the 2014 World Cancer Day contend that the high rate of death resulting from cancer has been attributed, primarily, to ignorance and delay in reporting the health condition to health agencies for evaluation and treatment. Explanations for the delay in seeking treatment among Ghanaian women also have been documented to include feelings of hopelessness and helplessness and cost of and access to routine screening mammography.

Furthermore, close to 70 percent of the women with breast cancer in Ghana present at hospitals and clinics in the advanced stages of the disease, when a cure is commonly impracticable. Breast cancer accounted for 15.4 percent of all malignancies in 2007 and continues to increase annually. A recent study has indicated that women in Ghana are more likely to be diagnosed with high-grade tumors that are negative for expression of the estrogen receptor, progesterone receptor, and HER2/neu marker. Triple-negative breast tumors are known to be more aggressive and result in higher breast cancer death rates.

Prostate cancer in Ghana and most African societies is the most fearsome and common disease in males after hepatocellular carcinoma. Globally, incidence of prostate cancer is higher among black men than any other male group. Each year, almost 1,000 Ghanaian men are diagnosed with prostate cancer, and about 750 men die of prostate cancer annually. Because prostate cancer is a genetic disease, it is difficult to prevent a man from developing it. A man is commonly at greater risk of developing prostate cancer if his father, grandfather, brother, or uncle had lived with the disease. Although prostate cancer tends to develop in men over the age of 50, recent reports show that it is also becoming more prevalent in Ghanaian men in middle age. In many cases, in men who lack the means and access to receive early diagnosis and adequate or any medical therapy, prostate cancer metastasizes and becomes fatal.

Prostate cancer in its early stage does not present any particular symptoms. Some observable signs may include swelling, needing to urinate often, inability to freely urinate, experiencing weak or interrupted urine flow, difficulty in having an erection, noticing blood in the semen or in the urine, a burning sensation when urinating, pain, abnormal test results, and nausea.

Felix O. Chima
Prairie View A&M University

See Also: Breast Cancer; Liver Cancer, Adult (Primary); Lung Cancer, Non–Small Cell; Prostate Cancer; Stomach (Gastric) Cancer.
Further Readings

Glass Industry

Glass objects date back to 3500 B.C.E. in Mesopotamia and Syria, with the first stable flat glass industry recorded in 1550 B.C.E. in Egypt. In 650 B.C.E., the practice of glass-making furnaces and glass blowing arose in Syria; then during the Roman Empire in 20 B.C.E., glass objects were documented in Italy, France, Germany, and Switzerland. From 1173 to 1271, Venice started to regulate the glass trade and published guild rules. In the Middle Ages, glass mosaics and stained-glass windows came into vogue.

By 1910, glass was rolled into a sheet between mechanical rollers, and this initiated some automation into the process. Glass windows became common in homes in the early 1900s. Glass windshields also appeared in cars. By 1959, the Float or Pilkington process was initiated for flat glass. The current processes involve automation of much of the process of making flat glass.

Cancer occurs from changes in the cell's DNA in the human body. Environmental factors can cause these changes to the cell's DNA. The production of glass in the workplace, in the home, or in art can produce some of these changes to produce cancer. Cancer also can be generated by prolonged, high-level contact. Individuals possess varying risks of cancer due to exposure to carcinogens, the extent of exposure, and the genetic makeup of the person.

The main organizations classifying carcinogens comprise the World Health Organization's (WHO's) International Agency for Research on Cancer (IARC), the National Toxicology Program in multiple countries, and the Environmental Protection Agency, whereas other agencies (e.g., National Institute for Occupational Safety and Health [NIOSH], the Food and Drug Administration, and the National Cancer Institute) give expert testimony or comments on the substances being classified as carcinogenic.

The glass industry consists of five main manufacturing sectors. The sectors comprise flat glass, container and pressed ware, art glass, special glass (optics or electronics), and fiberglass. The basic phases in producing glass products consist of melting, fining, homogenization, annealing, and forming.

Over the last century, the assembly of flat glass and container glass emerged from traditional batch processes to extremely automated procedures. The current production of flat glass involves substantially automated methods with continuous feeding of ingredients and floating for the forming technique, whereas container and pressed ware use primarily mechanized blowing or pressing of the heated glass. In addition, modern plants for glass production use physical engineering controls (ventilation systems, government-approved respirator masks, and monitoring the size of fibers) to alter exposure to harmful elements. Thus, flat glass and container glass fail to come in contact with humans during the manufacturing process and do not pose a risk to humans.

Art and special glass continue to be made by pot processes that entail manual batch methods. Consequently, art glass manufacturing has changed little over time and even now necessitates blowing the glass by oral breaths. If cutting or grinding of the glass occurs without wearing a particulate mask, lead or borosilicate also can cause cancer. The particulate mask filters the offensive fibers. Arsenic, a metal, may be used in glass production as well. Arsenic possesses an association with skin, lung, bladder, kidney, and liver cancers.

Human exposures transpire in the glass industry to noxious substances (e.g., lead, arsenic, and antimony oxides) when individuals employ traditional, nonautomatic methods with art or crystal glasses. Other possible contact with harmful materials in the glass industry consists of silica, asbestos, other metal oxides, and polycyclic aromatic hydrocarbons.

Glass Production and Cancers
The IARC lists arsenic as known to be a human carcinogen, whereas inorganic lead compounds used
in glass production are listed as probably carcinogenic to humans (Group 2A), and ceramic fibers and glass wool fibers are reasonably anticipated to be human carcinogens.

In the 1980s and 1990s, a cohort study in Finland and a case-control study in Sweden both showed a high incidence of stomach cancer in glass blower workers. Research in the same time frame revealed an increased risk for lung cancer in ceramic and glass workers in Austria, Finland, and Sweden. An Italian cohort study demonstrated an increased risk of laryngeal cancer in glass workers. The Finnish cohort research observed an elevated risk of basal cell carcinoma of the skin in male glass workers.

R. Sankila and colleagues studied workers in Finnish glass factories. The research analyzed all types of cancer but found only significantly elevated risks for lung cancer in men and skin cancer among glass blowers. Previous studies indicated an increased risk of stomach and colon cancer, but this study failed to show any increased risk for these two cancers.

**Glass Fibers**

L. Lipworth and colleagues conducted a meta-analysis of individuals employed in the production of rock wool and glass wool. A small elevation in the relative risk of glass workers involved in man-made vitreous fibers occurred, but the results argue against a carcinogenic effect of man-made vitreous fibers, rock wool, or glass wool in the production workers.

According to T. W. Hesterberg and colleagues, the WHO held a symposium on synthetic vitreous fibers in Copenhagen in 1986. Studies by researchers that covered the period from 1946 to 1982 demonstrated significant increases in deaths in all malignant cancers and lung cancer in employees with more than 20 years working in the fiberglass industry. The highest rates existed for mineral wool workers.

Others have studied the effect of man-made vitreous fibers (MMVF) on the health of glass workers in the United States. No adverse lung effects appeared with exposure to MMVF in this population.
Researchers carried out studies in rats and hamsters to ascertain the effect of glass fibers (e.g., glass wool, continuous glass filaments, rock or stone wool, slag wool, refractory ceramics, and special purpose glass) on carcinogen formation. This study showed only refractory ceramics and special purpose glass with possible human carcinogenic effects. By comparison, all forms of asbestos fibers (actinolite, amosite, anthophyllite, chrysotile, crocidolite, and tremolite) exhibited carcinogenic effects in humans.

In the process of animal research, the scientists found that fiber length and diameter must match human situations. The glass fibers inhaled by humans consisting of a diameter less than three micrometers and a length longer than five micrometers may cause cancers. Studies conducted on animals after the 1990s utilized these measurements. Fiberglass fell into the dimensions that cause lung cancers.

The controlled studies in rats demonstrated carcinogenic capability in the asbestos groups (amosite and rocidolite) and two of the synthetic fiber groups (special purpose E glass and refractory ceramic fiber). The key factor in the rats that produced tumors turned out to be biopersistence. Biopersistence describes the capability of fibers to persist in the lung over prolonged periods of time. Longer fibers produce more toxicity in the body than shorter fibers no matter what the glass substance is.

The European National Toxicology Program conducted a review of all the evidence about the carcinogenesis of glass wool fibers. Their recommendation stated that “glass wool fibers . . . not be classified either as known to be a human carcinogen or reasonably anticipated to be a human carcinogen.”

A 2002 IARC report indicated that a European cohort study of glass fiber workers demonstrated an increased risk of lymphatic and hematopoietic neoplasms in workers with more than 20 years of exposure to styrene. The glass fiber industry employs styrene in the process of making glass fiber-reinforced plastic products.

H. Shannon and colleagues conducted a historical prospective study of 2,557 male subjects working in the glass wool industry in Ontario. The results of the study demonstrated a significant increase in lung cancer mortality in glass wool workers. This study laid the groundwork for later research on the glass industry and lung cancer.

**Glass Protection From Skin Cancer**
Most glass fails to block ultraviolet radiation. Consequently, glass fails to prevent damage from ultraviolet radiation that causes sunburn. Melanoma, basal cell carcinoma, and squamous cell carcinoma can occur from long-term exposure under plain glass.

**Glass Microspheres**
Cancer articles published descriptions of Dr. Delbert Day, Curators’ professor emeritus of materials science and engineering at the Missouri University of Science and Technology, receiving the 2012 Phoenix Award Glass Person of the Year. This award honors a living person for superior contributions to the glass industry. Day performed a critical role in creating radioactive glass microspheres to treat individuals with inoperable liver cancer. He also formed the MO-SCI Corporation for the production of glass microspheres and a variety of glass merchandise for the health care industry. This innovator developed a product to treat cancer using glass.

**Protective Measures in the Glass Industry**
The NIOSH recommends certain protective practices for individuals working in the glass industry. For high exposure areas, practices to reduce worker exposures are implemented. These personal protective equipment recommendations include gloves, long sleeves, long-legged pants, and respirator masks for individuals working in the cutting, cleanup, or releasing containers processes. Glass companies further measure the fibers in the air to determine areas of high exposure to fiber or dust.

The glass industry realized that long-time drivers develop damage to the skin on the side facing the driver-side windows. Transparent ultraviolet filtering film became available for vehicles to reduce the chance of contracting skin cancers. Recently, residential and commercial window films came onto the market. These films block out about 99.9 percent of the ultraviolet rays and prevent skin aging and risks from skin cancer.

**Conclusion**
Research carried out in the glass industry shows only certain areas of production cause individuals to be exposed to high levels of cancer-producing
GlaxoSmithKline (United Kingdom)

The sixth-largest pharmaceutical company in the world, according to 2013 revenue, GlaxoSmithKline (GSK) is a British multinational based in Brentford, London. The company was formed in 2000 with the merger of SmithKline Beecham, which was itself formed through a series of mergers of the Beecham Group with the SmithKline Beckman Corporation formed from the Smith, Beckman, and Kline & French corporations, and Glaxo Wellcome, which had been formed when Glaxo (originally a New Zealand company that relocated to London) acquired Wellcome (founded in London by American pharmacists).

The fourth-largest company listed on the London Stock Exchange, GSK has roughly 100,000 employees and develops treatments and vaccines in major disease areas including mental health, infectious disease, gastrointestinal disease, asthma, diabetes, and cancer. Among its best sellers are the asthma/chronic obstructive pulmonary disease (COPD) treatment Advair, the generic of which has been delayed for five years and counting due to the Food and Drug Administration’s (FDA’s) lack of a set standard for the bioequivalence of inhaled steroids in multidose inhalers; the erectile dysfunction pill Avodart; the corticosteroid Flixotide, used primarily for asthma and allergic rhinitis but also prescribed for nasal polyps, skin disorders, and Crohn’s disease; Augmentin, a trade name of the antibiotic amoxicillin; the prescription dietary supplement Lovaza; and the anticonvulsant Lamictal, used to treat epilepsy, bipolar, and clinical depression. Its consumer health care division’s portfolio is also deep, including products like Aquafresh and Sensodyne toothpaste, Breathe Right nasal strips, Nicorette nicotine gum, and Boost health drinks.

GSK has had a checkered legal history. In 2012, it pled guilty to criminal charges for promoting Paxil and Wellbutrin for off-label uses, reporting false prices to Medicaid, and failing to report important safety information about Avandia, resulting in a $3 billion settlement, the largest paid by a drug company up to that point. It faced similar class action suits and criminal fines for marketing off-label uses of paroxetine for child patients; has faced charges of bribery in multiple countries, including being found guilty of systematic bribery by a Chinese court in 2014, resulting in a suspended prison sentence for the former head of GSK’s Chinese operations; and recent bribery investigations in the United Kingdom, United Arab Emirates, Lebanon, Jordan, Syria, and Iraq. Among other allegations in these investigations, GSK representatives are alleged to have made direct payments to health care professionals and institutions in order to assure their business.
At the end of 2013, amid several years of increasing complaints about pharmaceutical industry practices by consumer advocates and public health officials, GSK adopted new ethical standards in its practices, including no longer paying medical or health care professionals for speaking at medical conferences, no longer compensating doctors who prescribe their products, and no longer requiring prescription-related sales targets of its representatives. Doctors would continue to be compensated for GSK-sponsored clinical trials, market research, and advisory services, which the company defends as necessary to disease research. It has further shored up its reputation with a joint project with the Bill and Melinda Gates Foundation, developing a malaria vaccine that it submitted for approval in 2014, with the intention of selling it in developing countries at 5 percent over cost. In late 2014, amid fears of Ebola, GSK announced it had begun the first-ever human trials for an Ebola vaccine.

GSK had a long history of successes in oncological treatments, including recent approvals of Tafinlar and Mekinist to treat melanoma. In early 2014, it sold off most of its cancer portfolio to pharmaceutical company Novartis, with a deal to co-market future oncology products in return for a $16 billion cash payout. Though a leading pharmaceutical company, GSK’s ranking in cancer drugs was disproportionately low relative to its size, and selling off most of its cancer division allowed it to refocus on its strengths while also taking a needed cash injection. At the same time, it retained key elements of its cancer research and development programs with serious long-term potential, including epigenetics research and immunotherapy—programs that could not be sold today for a fraction of what they may someday be worth when that research has borne fruit.

Less than two months after the sale to Novartis, GSK entered into a $350 million, seven-year collaboration with Adaptimmune, a biotech company developing immunotherapy treatments for blood, skin, and ovary cancers. Adaptimmune is based in Oxford, England, part of the UK’s cancer research Golden Triangle (along with Cambridge and London).

Bill Kte’pi
Independent Scholar

See Also: AstraZeneca (United Kingdom); Pharmaceutical Industry; Shire UK.

Further Readings

Global Health Issues and Cancer

The concept of global health (GH) is relatively recent, and it encompasses diverse aspects of population and health in a world context. It covers areas such as epidemiology in a wide sense, public health, and demography. In fact, we cannot understand this concept without framing it in other conceptual elements related to measurement (statistical data, quality of life, life expectancy, mortality, or morbidity); health conditions (geographical, human, economic, sociocultural and political circumstances, and situations where access to wealth and basic services or resources, equality, or equity are involved); intervention (planning, prevention, impact, efficacy, and efficiency); and environment (sustainability). It is a concept whose reach goes beyond any border and that intends to fight disparities and to give global protection to all human groups regardless of their origin, status, or location. The concept of GH began to be used instead of international public health because there is a general concern about the state of health of every citizen of the world and a literal conviction that the commitment with health in a specific region of the world implies an involvement with the health of any person everywhere.

Because this topic is visibly interdisciplinary, it is essential to determine the limits and frames of some terms involved in it. One first step is to define what global means and if GH relates somehow to...
globalization and to what extent. A further step would be to specify what kind of disciplines deal directly with this matter.

The interest in global health coincides with the new millennium. In a few years, GH became a discipline in most departments and universities in the United States. It emerged from several perspectives and ways of understanding and interpreting health and its improvement and the different strategies to reduce, eradicate, or prevent some specific (infectious) diseases. Although it became a hegemonic term, many critical voices affirm that GH is a concept not totally new—in the 1950s, the World Health Organization (WHO) used it in its campaign for the eradication of malaria—and sometimes, it has been manipulated by that same institution for political reasons in order to concentrate power in its main role of coordinator and leader.

Currently, the concept of GH goes beyond the idea of health in itself in the sense that it also covers aspects like welfare and well-being. In addition, from the point of view of global health—where risk factors, measurements, analysis of determinants, and comparison of trends are main tools—cancer, both as a disease and as a social reality, has gained a central place, and it plays a relevant role.

Cancer Onto Global Health Agendas: Organization of Data

However, that relevance must be clarified because, while cancer has been raised onto GH agendas of high-income countries, it receives less attention in low-income countries, where according to statistics, cancer also has a big impact. In order to monitor cancer incidence and to have a proper identification of new cases, many countries have established a national registry, even though most registries are transnational, which is also an aspect related to the general idea of GH. For example, the International Association of Cancer Registries (IACR) has existed since 1966, and its fundamental mission is to collect data of quality and, eventually, to compare them. The European Network of Cancer Registries (ENCR) was created in 1990 with the purpose of facilitating exchange of data among the different national cancer agencies, monitoring cancer incidence, and making these incidence data available. On the other hand, umbrella institutions like WHO bring together global health topics, data, and analysis, highlighting the need of avoiding exposure to risk factors and the significant amount of cancers that can be cured. A database is an elemental tool to evaluate and understand the morbidity and mortality in several regions around the world. They are also common and reliable sources of information on cancer survival.

All the institutions linked somehow to cancer from the perspective of globalization keep in mind that their actual challenges are advanced research, good expertise, implementation and consolidation of clinical trials, and the creation of resources that allow reducing the incidence of cancer worldwide.

Cancer Control in the Framework of Global Health

From 11 million cases occurring annually worldwide, just 6 million are in low-income countries. More than 50 percent of those cases result in a patient’s death. It is clear that cancer is a global disease. But this affirmation deserves some consideration in terms of epidemiology and causality. Whereas in high-income countries, most cancer cases are related to lifestyle (like cancer of the colon, lung, or even breast), in low-income countries, infectious agents are usually involved in the incidence rate, impact, and development of that disease. Coordinated approaches and efforts in several fields had as an immediate result an effective control of some risk factors, following the successful example of what happened with noncommunicable diseases, especially infectious diseases, and the mitigation of their impact. Certainly although GH guidelines may not be applicable at a universal level, there are some care programs that include basic outlines, like prevention, early detection, and best treatment (adapted to each case). Prevention is a form of control, and it proved to be useful in the case of tobacco consumption (that factor is generally recognized as the most preventable cause of death), diet, alcohol use, and infections. Some organizations like the IARC, belonging to the WHO, insist on effective prevention measures more than on treatment to win the global battle against cancer. But the application of the three basic program clauses previously mentioned has to overcome substantial obstacles in terms of knowledge and awareness, culturally and socially different backgrounds, lack or deficiency of resources, and the limitations of access to them.
In spite of the differences in the ways of fighting cancer, there is also a growing awareness among the world population. On the other hand, public health systems provide possibilities of screening for the cases of breast, stomach, or colon cancer. One of the problems here is, however, that not every country has the proper equipment to provide specialized services for diagnosis or care resources for surgery, the treatment before and after that, and pain control. For that reason, many cancers that could be cured remain as causes of death among people worldwide.

Cancer Burden Worldwide
There is no doubt that cancer is one of the leading causes of death in the world. Population aging, particularly in Western societies, explains the fact that, every year, the number of cancer patients increases. Reliable statistical data let us know that about 11 million cases of cancer are diagnosed every year worldwide. Those data don’t include, however, cases of skin cancer. Of all these cases, 53.4 percent are male and 46.6 percent are female. Around 45 percent are cases diagnosed in Asia, 26 percent in Europe, 15 percent in North America, 7 percent in Latin America, and approximately 6 percent in Africa. For males and females, the most common cancer is lung; the second-most common is colon (with a stronger incidence in males than in females). Among females, the most common cancer is breast, followed by cervix and colon. Among men, the most common are lung, prostate, and stomach.

According to official data, in 2008, and in the context of Asia, more than 6 million new cases were detected. Most of them were males, although there is practically the same number of cases in males and females. About 60 percent of the cases supposed the death of the patient in both males and females. In the same period of time, the registered cases in Africa were approximately 750,000. From them, around 320,000 were male and the rest female. The cases resulting in the patient’s death were about 260,000 for men and 283,000 for women. The number of detected cases in North America in 2008 was 1,603,900, with the proportion of males a little higher than females. Among them, the number of deaths was 332,500 for males and 305,900 for women. Instead, in the rest of America (Central and South America and the Caribbean), the number of cases was 825,000, most of them registered in South America. The incidence of cancer is higher among the female population in the case of Central and South America and a little bit lower in the Caribbean. Instead, the number of deaths is higher among the male population (a total of 280,000 in the whole region) than among females (except in the case of Central America, where the number of women’s deaths overtakes the number of men’s deaths).

For the same period, the number of registered cases in Europe was 2,300,000. The highest incidence concentrates in western Europe (1,034,300) and the lowest in northern Europe. In the whole region, men are more affected by the disease than women, although in eastern and central Europe the number of cases for men and women are quite similar (around 490,000 cases in both groups). However in terms of deaths, in northern Europe, there is a balance in the cases of males and females, but the dominant factor in the whole region is that there are more men’s deaths than women’s. The total number of deaths reaches 1,800,000 people. In the austral region, the total amount of cases is 140,000, most of them in Australia. Although the dominant factor is a higher incidence in the case of males, in Melanesia and Micronesia, the number of women affected by cancer is notably higher (3,700 in Melanesia, as opposed to 3,300 men; and 400 in Micronesia, as opposed to 300 men). The total of deaths in the whole region is 56,000, of which 24,000 are women and the rest men.

With respect to main causes and risk factors, in the case of developed countries, diet and nutrition are implied in 30 percent of the cases, followed by tobacco, which represents about 16 percent; infections, which represent 8 percent; occupational exposures, which represent 5 percent, and environmental elements, which represent 2 percent. The rest of the cases have different causal backgrounds. In the context of developing countries, infections are in the first place, involved in 26 percent of the cases, followed by diet and nutritional factors, which represent 20 percent of the cases, and tobacco, which represents about 10 percent. The rest of the cases also have different causal backgrounds.

In respect to the kinds of cancer, lung is at the top, with a total of 1,800,000 new cases in 2012, which represents 13 percent of the total diagnosed cases. In second place is a cancer that affects basically the female population, breast cancer, with an incidence of 1,600,000 new cases, representing 11.6 percent of the total diagnosed cases. In third place is colorectal
cancer, with 1,361,000 annual new cases, representing 9.7 percent. In last place, with only 44,000 new cases (0.3 percent of the total) is Kaposi’s sarcoma. Actually, the most common cancers for men are lung, prostate, and colorectal, nearly 42 percent of all cancers, and liver or stomach, at about 5 percent. In the case of women, breast cancer leads to 25 percent of the total diagnosed cases every year. For women, breast, colorectal, and lung cancers represent more than 43 percent of all cancers. Cervical cancer represents about 8 percent of all cancers in women.

Cancer survival is measured taking into consideration the percentage of patients who are alive five years after the diagnosis. But that measurement is not absolute; it includes many other factors, like the type of cancer, the initial stage at the moment of the diagnosis, or even the availability of treatment for each case. For those cancers whose survival rates are high—like breast or colorectal cancer—the differences between developing and developed countries are enormous. For example, whereas in the United States, the survival rate for breast cancer after five years is 85 percent, in countries of northern Africa, it gets down to 39 percent.

**Toward Global Intervention: Prevention Policies and Analysis of Risk Factors**

As most studies suggest a direct link between cancer risk and lifestyle, prevention policies play a fundamental role in the eradication of cancer worldwide. Those policies could be indirect—campaigns in order to make the population everywhere aware of messages about eating healthy and getting active—or direct monitoring and (opportunistic or organized) screening of potential or actual patients or high-risk groups. Indirect strategies appeal to individual responsibility. Instead, direct intervention supposes organizational support and a public health system providing specialized services. In countries where a health infrastructure cannot be afforded, programs for raising awareness should be implemented so that populations can become more sensitive to signs and symptoms, a first step to early diagnosis of the disease, and report any change or abnormality.

According to recent data, about one-third of cases are preventable, and for that reason, prevention used to be considered the best long-term strategy of controlling such a disease. The global policy frameworks are described as follows.

**Tobacco.** Tobacco is the most common preventable risk for cancer mortality at the global level. It causes an estimated 22 percent of cancer deaths annually. Tobacco is not only behind cases of lung cancer but also esophagus, mouth, tongue, larynx, cervix, bladder, throat, kidney, pancreas, and stomach. It affects smokers and nonsmokers, and some cases are already detected in children. Chewing tobacco leaves, a custom of the native populations of both South and North America, increases the risk of mouth cancer. On the other hand, smokeless products like electronic cigarettes need further research in order to know their effects on a person’s health. In the United States, tobacco use is responsible for approximately one in five deaths. Tobacco consumption in Latin America is higher—perhaps even epidemic—and it will be the main killer in the continent in a few years. Smoking causes directly 270,000 cancers every year in Europe. Africa, where the incidence of lung cancer was relatively low, is experiencing an important increase of cases as the number of smokers has become four times higher in the last years due to the influence of Western habits. In Asia, lung cancer deaths attributable to smoking ranged from 0 to 40 percent in females and from 21 to 49 percent in males.

**Physical Inactivity.** Regular activity or sport practice mean some direct benefits for health because they allow keeping a healthy weight and prevent becoming obese or simply overweight (it is proven that there is a link between being overweight and the incidence of some cancers, like breast, esophagus, colorectal, endometrium, and kidney). The combination of activity with a balanced diet rich in vegetables and fruits supposes a powerful protective against cancer. On the other hand, it seems plausible that a high consumption of red meat increases the risk of colorectal cancer.

**Infections.** Infections are active agents in the incidence of cancer in developing countries (it is believed that they are the main cause in 22 percent of the cases as opposed to 6 percent in developed countries). Hepatitis B and C are behind liver cancer; infection by human papillomavirus behind cervical cancer, and *Helicobacter pylori* can produce cancer of the stomach, or at least it increases its risk. Nearly 18 percent of cancers worldwide are attributable to infections, but again, there are big differences between the regions. In Africa, it
reaches 25 percent of the cases, and in developed countries scarcely 10 percent.

**Occupational Cancer.** The exposure to some agents in the context of workplaces and what is worked with seems to be the main cause of some types of cancer, like lung, bladder, skin, and larynx or leukemia in documented cases. Actually, more than 40 carcinogenic occupational agents have been identified. For example, mesothelioma is a lung cancer produced by exposure to asbestos. Despite all evidence, it is estimated that, every 52 seconds, occupational cancer produces another victim (about 600,000 deaths annually worldwide)—it used to be a hidden cause of the disease. According to a report from the WHO, between 7 and 19 percent of all cases of cancer are directly attributable to toxic exposure to carcinogen elements. The highest incidence of occupational cancers occurs among workers of uranium mining, with 54 percent.

**Environmental Pollution.** According to WHO, the environment could be defined as all the physical, chemical, and biological factors external to the human host and all related behaviors but excluding those natural environments that cannot reasonably be modified. Human beings are exposed to many carcinogenic agents through inhalation, eating, drinking, and skin contact. Pollution affects water, air, and soil through chemical elements in a way that may cause about 1 to 5 percent of cancers. Arsenic or coal use is widespread in Asia. Arsenic is a direct agent related to a notable number of deaths in poor countries like Bangladesh, and coal use causes lung cancer in nonsmoking people. Among them, women have more possibilities of contracting that disease. Benzidine is linked to bladder cancer. Other toxic substances behind a vast majority of cancers attributed to environmental factors are asbestos, radon, and silica. Actually, humans do not live in contaminant-free surroundings, and it provokes a permanent interaction.
with their internal genetic makeups that may lead to a fatal mutation able to destabilize the organism. Even so, it is estimated that almost one-third of the cancers caused by environmental elements could be prevented by a simple modification of lifestyle.

**Alcohol Use.** Alcohol use is an important risk factor in several types of cancer, like liver, breast, stomach, larynx, pharynx, ovaries, oral cavity, or esophagus. Despite its high incidence in cancer, it affects men and women in different ways. In men, heavy consumption of alcohol becomes a risk factor for oral cavity, liver, and pharynx cancer in almost 22 percent of cases. Instead, in women, the incidence is smaller—only 6 percent—and 3.5 percent of cancers and deaths caused by cancer are attributable to alcohol use. The incidence is much higher in women than in men.

**Radiation.** Radiation as a risk is well known after strong evidence in epidemiological studies with Japanese survivors of atomic bombs. Ionizing radiation causes leukemia in young people and thyroid cancer (affecting the female more than the male population); radon gas is the second cause of lung cancer, after tobacco; and ultraviolet radiation is behind most skin cancers in the world. In this latest case, the solution seems to be quite simple, just by avoiding excessive exposure and by using proper sunscreen and clothes.

On the other hand, these specific fields of intervention need to be combined with other intervention policies that cover research, application of preventive treatments like vaccines (particularly useful in those countries affected by epidemic or generalized infections), clinical trials, and regular screening of potential patients and people belonging to groups at risk in order to guarantee an early detection and diagnosis of the disease. Early detection makes sense, in the last instance, only when it leads to a follow-up and effective treatment.

**Risk Factors and Genetics**

Lifestyle factors, geographical distribution, and incidence of infections are just elements that interact with genetic susceptibility. Inherited circumstances and conditions may raise a person’s risk of cancer of any kind. Some mutations can be predicted—approximately between 5 and 10 percent of cancers can be traced directly from genetic defects—but unfortunately sometimes anything can be changed.

Variant identification in cancer genomes has to be placed in a context of global challenges because the link between cancer and genetic mutations is a global concern. But there are many questions that remain, so far, with no answer, for example, if generalized mutational profiles could be identified in a determined type of cancer. Even in the case that mutational variables could be identified, there are specific personal variations that interfere with such identification of patterns, making it, and any further therapeutic strategy, extremely complex. One first step is to create a large database with information of a homogeneous population. Some sophisticated registries were already created about 20 years ago in Poland. On the other hand, the Cancer Genome Atlas project applied epigenetic assessment together with sequencing and classifying genomic definition of molecular subtypes, an indispensable tool with global range this is statistically valuable worldwide.

**Toward Global Care**

A diagnosed cancer means a coordinated response that involves experts, personalized treatment, and proper tools and information. An integral treatment should also include psychological help for the patient and his or her family. At the same time, in cases with no possibility of cure or total remission (no cancer signs), an adequate service of palliative care and control of pain (pain relief) must be offered. The principles of GH assume not only the application of those policies at home but also the possibility of exporting the know-how to less-privileged countries.

Although the steps to be taken are clear, it is an incontrovertible reality that the access to essential therapies is far from being global and that barriers to information and to treatment exist. A priority is, then, to create opportunities for improving global access to cancer therapies. One eventual solution that committed oncologists offer is the training of sanitary personal to deliver medical care, surgery, and radiation oncology in a resource-limited context as the best way to maximize their implementation and access to diagnostic facilities.

The greatest challenge is the differences between high-income countries and low- or middle-income countries. Whereas in high-income countries, services include the opportunity of an early diagnosis, proper treatment and surgery, and even
some extra services to reinforce the welfare and well-being of the patient and his or her family—for example, emotional support, practical information, community cancer programs, volunteers’ work, personal coaching, organized supportive care or follow-up care—in low- or middle-income countries, sometimes they need to import others’ experiences.

In Western countries, it is common that each patient receives an individualized survivorship plan, including guidelines to control his or her disease and maintain his or her health. In the last 25 years, the priority is patient’s quality of life.

In a vast majority of regions in the world, a great number of cancer cases are diagnosed in advanced stages. For these patients, there is no realistic treatment for cure, and the only possibility is to follow a pain relief treatment and palliative and supportive care. Most of those treatments are oral pills against pain, which usually are inexpensive, and they range from simple painkillers to powerful opiates, depending on patients’ needs. Opioid drugs are not easily available in developing countries, sometimes due to their price, the lack of knowledge about them, or—more often—because of regulatory policies that limit their access and use. Although WHO establishes a clear normative in regard to drug policies for scientific purposes, the reality is that, in many countries, there are barriers and false beliefs that cannot be overcome. Sometimes, chemotherapy or radiotherapy is prescribed as a part of the palliative treatment.

Natalia Fernández Díaz-Cabal  
Free University of Barcelona

See Also: Chemical Industry; Coal Industry; Developing Countries; Disparities Within Nations (Elimination of Cancer); Exercise; Future of Cancer; Infection; National Cancer Registrars Association; Natural Causes of Cancer; Obesity; Pollution, Air; Pollution, Water; Screening, Access to; Statistics; Tobacco Smoking; Vaccines; World Health Organization.

Further Readings

Government

The international cancer community drew attention for the responsibility of governments in developing effective programs, public policies, convenient legislation, and regulation setting with the focus on cancer management at different levels through policies implemented by the national health systems. But cancer is also affected by governmental decisions and practices that are far beyond the reach of medicine and the health systems, for example, when regulating the transportation, household and industrial energy, water and waste, housing, education, agriculture, and industry’s production.

Political initiatives such as the World Cancer Declaration outline a common strategy to reduce the global cancer burden by increasing cancer’s visibility on the international political agenda and setting a common strategy. Still, in many low- and middle-income countries, cancer is absent on the political agenda when compared to the visibility and resources given to other diseases such as human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS), even though enough evidence has demonstrated that low- and middle-income countries endure a double burden of communicable and noncommunicable chronic diseases.

Cancer is today one of the most common health problems in the world, with a burden that represents a crisis for public health for which governments
attempt to find responses, basically to cancer control. This strategic approach defines primary prevention, early diagnosis, treatment, palliative care, and surveillance as the arenas for current governments' interventions.

Prevention and Early Stages
Cancer primary prevention means identifying the risk determinants or causes of cancer among those factors that epidemiological studies have associated with the development of the disease. Many modifiable risk factors for cancer have been identified: tobacco smoking, alcohol consumption, excessive exposure to sunlight, lack of physical activity, overweight and obesity, dietary factors, occupational exposures, and chronic infections. For reducing tobacco smoking—the most important human carcinogen—governments include restrictions on advertising cigarette products and forbidding smoking in workplaces and public settings. Such restrictions on indoor smoking are effective strategies for reducing the prevalence of smoking.

Prevention programs can reduce the level of exposure of populations to the common modifiable risk factors for cancer as well as other noncommunicable diseases. However, the cancer-causing infections human papillomavirus (HPV) and hepatitis B (HBV) are still not covered by universal vaccination programs worldwide.

As Peter Boyle argues, the major issue in the low- and middle-income countries is the delivery of the prevention action in a way that is affordable for the countries' health systems. One of the main barriers of preventive programs pointed out by anthropologist George Foster is not including a combined basis of the programs offered: health programs based on externally defined health priorities. Another barrier is stigma associated with cancer and the lack of inclusion of people's conceptions in order to understand different perceptions of cancer within different populations. Juliet McMullin has said that only by taking local perspectives into account can changes proposed in social policies be incorporated.

The other arena of governmental intervention is secondary prevention, which includes early detection by cancer screening. Detecting cancers at an early, asymptomatic stage could lead to a decreased mortality rate in certain cancers, such as breast, cervical, prostate, and bowel. As Ichiro Kawachi argues, governments play a major role in financing and delivering cancer screening and treatment services. Nonetheless, population-based screening and early detection programs are still not universally implemented for some types of cancers (screening anyone within specific age-groups) nor selected screening for people who are known to be at a higher risk of developing cancer. Public education and awareness about important cancer warning signs and symptoms also need to be improved as another target for government action.

Cure, Care, or Alleviating Suffering
Known as tertiary prevention, national health systems offer cancer treatments that lead to cures for some. Governments are encouraged in the World Cancer Report to strengthen their health systems to ensure sustained delivery of comprehensive patient-centered cancer control programs across the life course, improving the accessibility of affordable, effective, and quality medicines and technologies.

In low- and middle-income countries, access to treatment is scarce and inequitable because most of the services are provided in health centers located in big cities, leaving a rural population with no access. The high cost of medicine and technologies almost makes these services inaccessible for the poor population. Other barriers to quality access to cancer treatments identified by Paul Farmer and colleagues is a shortage of oncologist specialists, treatment guidelines, and regulatory mechanisms; restrictions on importation of drugs, resulting in limited access to cancer medication; lack of affordable disease-control programs; advanced stages of diagnosis; and lack of availability and quality of cancer treatment centers.

With regard to palliative care, there are wide disparities in the capacity, resources, and infrastructure dedicated to the care of people with life-limiting illnesses. Most countries have neither formal palliative care policies nor integrated palliative care services; they do not meet basic international guidelines in the provision of palliative care and have legislation or policies whose effect restricts the availability of opioids for medical purposes.

Pain control is typically low cost and easily delivered, but there are still barriers that prevent the full implementation of palliative care within many sanitary systems, meaning many patients die with preventable suffering. These barriers are distribution
of resources, availability of opioids, insufficient professional training, morphine's myths among patients and professionals, substance controls that lead to blocking health care providers from supporting needs, and absence of specialists, facilities, and treatments.

**Research and Surveillance**

Governments also have a main role in defining debates about funding research for cancer and setting priorities within the cancer program, for example, the proportion allotted to basic biological research, clinical trials, and cancer prevention programs.

Strategies to control cancer need local data for adapting international guidelines to specific contexts. However, neither the number of new cases of cancer nor the number of deaths is available in many parts of the world. The World Cancer Report states that, in 2000, less than 20 percent of the world’s population was covered by cancer registration and 35 percent by vital statistics schemes based on medically certified cause of death, which gives greater priority to surveillance. According to the Cancer Declaration, population-based cancer registries and surveillance systems are needed to measure the global cancer burden and the impact of national cancer control programs. Governments are called to improve surveillance of cancer morbidity, mortality, and prevalence by establishing population-based cancer registries and for identifying priorities in public health. It can also contribute to programs aimed at reducing inequalities in health outcomes.

**Conclusion**

It was addressed that the primary role of governments in generating multi-sectoral public policies and action plans to control cancer are at different levels, but there are still important differences across and within nations in how they deal with this disease. As a result, a wide and unequal range of responses are being implemented.

These disparities among regions must be remarked upon, noting the inequalities in cancer incidence, mortality, quality of life, and survivorship. The lack of recognition of cancer as a major public health issue has been recognized as one of the main barriers. In that sense, governments' implementation of educational interventions to increase community understanding of cancer is promoting early detection and adherence to treatments. Many interventions to culturally diverse target audiences are being adapted to become more appropriate; considering the complexity of cancer, this requires a comprehensive approach. Further difficulties in cancer control in some low- and middle-income countries are compounded by inadequate government budgetary allocation to cancer management.

Finally, for successful strategies in cancer control, not only is the government necessary but also the engagement of the rest of society: nonprofit organizations, health voluntaries, and private-sector businesses, among others.

Natalia Luxardo

*University of Buenos Aires/CONICET*

**See Also:** National Cancer Institute; Smokeless Tobacco; World Health Organization.

**Further Readings**


Greece

Ancient Greece played a very significant role in the development and evolution of medical history. Hippocrates is a renowned figure in medicine and had so much influence that medical providers today take the Hippocratic oath before they are allowed to serve their patients. One of the Greeks' strong points was that, while they explained away natural phenomena as the work of the Gods, they practiced secular medicine and attempted to find natural explanations for the ailments people faced. Not all of the ancient Greeks were so accepting, though, and preferred relying on the gods—Apollo in particular—to alleviate their conditions.

Hippocrates is so famous that even Plato and Aristotle wrote about him. He believed that the work of priests and doctors should be segregated and that doctors should observe their patients. This was the framework for what would be later known as clinical observation, and this insight is part of the reason that Hippocrates is considered the father of modern medicine. He suggested examining a patient and inquiring about his or her appetite and sleep, and he also kept a detailed book of symptoms and ailments so that doctors could forecast the turn a disease would take. This method spread throughout Greece and the eastern Mediterranean, and writings that survived have provided historians with excellent study resources.

In Hippocrates's day, hospitals did not exist in the way that they do now. The sick made their way to temples dedicated to the healing god Aesculapius, or Asclepieia, which functioned as places of worship as well as a place of healing. Hippocrates set forth the belief that all illnesses had a natural explanation and cure as opposed to a divine origin or curse.

The origin of the word cancer was Hippocrates using commonplace words like carcinos and carcinoma to describe tumors that respectively do not and do have tumors that can form ulcers. In Greek, these terms meant crab, which was likely named as such because of the fingerlike projections from cancer. Galen, another Greek physician, utilized the common word oncos, a Greek term to describe swelling. Hippocrates was a proponent of the humoral theory, which was that everybody had four humors. These were bodily fluids, namely blood, phlegm, yellow bile, and black bile. All of these were balanced in a healthy person, but too much or too little occurred in a person who was sick. Too much black bile was believed to cause cancer, a belief that was carried on by the Romans and continued on through the Middle Ages for more than 13 centuries.

In the days of Hippocrates, physicians knew that cancer could return even when it had been taken out surgically. A second-century Greek physician by the name of Galen, whose writings were kept for centuries, viewed cancer in the same way Hippocrates did: The afflicted were incurable. Cancer treatment barely progressed even as breakthroughs were made in other areas.

Because cancer was considered incurable, treatment went through a very slow evolution. Galen described surgically removing tumors in breast cancer and stated that it could be cured through removal if it could be caught in an early stage. Surgery was much more dangerous at this time because there was the potential for many more complications, including blood loss. This was a time when anesthesia was not available, so surgery was extremely painful for the patients. It was only in the 19th and early 20th centuries that surgical cancer treatment became more effective.

Before the discovery of anesthesia, doctors who could operate swiftly and precisely were in high demand. Once anesthesia was introduced in the mid-1800s, surgical knowledge and techniques advanced so quickly that the time came to be called the century of the surgeon.

The Greek beliefs about cancer carried on throughout the centuries and were expanded upon or debunked over the centuries. The evolution of cancer understanding and treatment ranged from the belief that cancer was contagious to the belief that it spread through the blood and only seeded in parts that could host it.

In 1830 until the close of the 19th century, less than 10 percent of the population of Greece had health care coverage. In 1922, the Ministry of Hygiene and Social Welfare was founded. The quality of health care service was primitive by comparison with other European countries. The first serious attempt by the government to provide better health care for the masses involved establishing the Social Security Organization in 1934. This gave health care and pension coverage to blue-collar and white-collar workers in urban areas as well as in industries with more than 70 employees. It resulted in
health care access for more than one-third of the population.

In 1941, temporary hospitals were set up for the war effort and remained afterward. The next plateau was 1953, when the government passed legislation to found a National Health Service. The aim was decentralizing health care competencies to the health regions and, through them, to the district health councils. Regional councils gave their insight on the health care needs by population, morbidity, and other factors and would get the required equipment and buildings. This marked the first time a needs-based approach to health care was used; however, the law was not implemented, and the chance was lost.

In the 1960s, a period of fast economic growth saw a number of institutions establishing their own insurance funds. These funds were mainly financed by employer contributions, and the funds provided high-quality insurance for their employees.

Farmers made up more than half of the Greek population at this time, and in 1961, legislation was passed to provide health care for them as well—the founding of the Agricultural Insurance Organization. This marked the first time that farmers ever had had access to health insurance.

Between 1967 and 1974, the dictatorship consolidated these health care services. It was during this period that the idea of a comprehensive health care system came about. In 1968, plans were made for an overhaul of the health care system. The Ministry of Health had many goals in this, not the least of which was improving health care for the rural population, instituting a family doctor system, improvements in psychiatric care, and more.

By the end of 1973, only a fraction of the health care policies had come into fruition. Public funding of health care had actually decreased, and the rest of the proposals on the establishment of a national health service died out. Once democracy was restored in 1974, public pressure and problems with the existing health care system were amplified, making this a heavy issue for the new government. Problems with health care continued on into the late 1990s and early 2000s.

Michael Fox
Independent Scholar

Further Readings

Green, Adele

Applying sunscreen for extended time spent in the sun seems now to be common sense—parents at pools or beaches with their children, those over 55, and those simply wishing to prevent the effects of aging apply sunscreen almost automatically. But the extensive oncological research that went into first defining the effects of the sun's ultraviolet (UV) rays on the development of a variety of skin cancers and, in turn, first provided the scientific data that backed up the use of sunscreen is barely two decades old and initially faced doubts and skepticism even within the scientific community. Cancers, it was long held, are largely genetic, and environmental factors and even personal decisions were marginalized as risk factors. Australian cancer researcher Adele Green was among the most diligent and dedicated of that first generation of oncology researchers whose groundbreaking research led, in her case, to a lifetime of tireless promotion of sunscreen, a practice, Green and others argued, that made skin cancers not merely treatable but actually preventable. Born in the late 1950s, Green grew up in a generation in which cancer was a bugaboo, a hobgoblin to be feared for its apparent and evident randomness. To that point, save avoiding tobacco products, the scientific community was largely committed to cancer treatment studies. Green challenged that mind-set. Her work and her public advocacy of sunscreen as well as her message that personal decisions played a large role in cancer prevention led to much recognition and prestigious accolades in her native country, among them being named to the Companion of the Order of Australia and being short-listed in 2013 for Australian of the Year.

Australia was, oddly, a nearly perfect research laboratory environment for the study of melanomas.

See Also: Breast Cancer; History of Cancer; Insurance.
It is the world’s largest island with more than 16,000 continuous miles of coastline (the sixth-longest coastline in the world). Add to that an average six-month summer season where daily high temperatures can range between 75 and 95 degrees and a majority population of people with European ancestry and fine white skin. Adele Green, in 1979, then a graduate from the prestigious medical program at the University of Queensland and a practicing physician, treated case after case of melanomas that were far too established to provide much hope to her patients (later she would describe skin cancer as an epidemic in Australia). She began to believe that research would be far more valuable and help far more people than her work as a doctor treating, one by one, skin cancers after they had already been established. What caused the spike in skin cancers in Australia? She returned to complete her doctoral research in epidemiology, completing her degree from the University of Queensland in 1984. She studied tropical medicine and treatment abroad, first in England and then at Harvard before returning to her native country in 1996, certain now that the particular environmental conditions of Australia were key to melanoma prevention. She was appointed director of the University of Queensland’s Epidemiology and Population Health Unit, a forward-thinking facility that saw as its mission nothing less than the promotion of the general health of the state’s residents. Although her research would come to include work in ovarian cancer and in esophageal cancer in men, she pioneered research into the impact of the sun’s UV rays on melanomas.

Her groundbreaking work centered on a four-year study of a group of selected residents, all under the age of 55, in the southeast Queensland coastal town of Nambour, a thriving beach community at the heart of Australia’s so-called Sunshine Coast, a tourist paradise. Green eliminated narrowing the pool by race or general skin color, cancer history, weight, or gender—she even used smokers. It was a radical notion—Green wanted to test a random sampling of Australians. The results were stunning—residents who used sunscreen daily and broadly (i.e., all over the exposed body) not only preserved the natural smoothness of the skin lost in the process of aging but, far more important, actually avoided the onset of skin cancers. It was the first conclusive data linking exposure to the sun to melanomas; previous work had been limited to studying the effects of UV rays on hairless mice in controlled laboratory conditions. As the study’s lead author, Green began what would become a decades-long public campaign to get her fellow Australians to use sunscreen of sun protection factor (SPF) 15 daily and to reapply it throughout the day. Although cosmetic companies would attempt to take advantage of the public’s use of sunscreen by providing increasingly expensive sunscreen with higher SPF numbers, Green’s research definitively showed that the increase in protection beyond 15 was minimal.

Green’s message to her island country became clear—skin cancers and melanomas could be avoided. She took to any public forums to spread the message. Indeed, although her unconventional research methodologies are certainly part of her legacy, she has had far more impact as a public spokesperson and as a mentor of an entire generation of Australian oncology students, inspired by her message that skin cancer was impacted, of course, by genetics but that personal decisions and choices contributed to it. Green was a charismatic and engaging speaker—she never came across as scolding or judgmental. A regular on television programming and radio talk shows as well as appearances in public forums across her country, she became a kind of celebrity, the family doctor to her nation-continent (she is frequently compared to Dr. Mehmet Oz, or “Dr. Oz,” on American television). In addition to advocating sunscreen, Green also pioneered the relationship between leafy green vegetables and cancer prevention as well as regular exercise (she was particularly fond of dancing). Although other oncology researchers believed time would be better spent in researching the mechanisms of melanomas, Green argued that preventing skin cancer through a simple protocol of common-sense decisions made far more sense.

Joseph Dewey
Broward College

See Also: Education; Sun Exposure (Australia); Sunscreen.

Further Readings
Gregoire, Christine

At the turn of the 20th century, cancer was among the most mysterious and terrifying diseases. Unlike tuberculosis or yellow fever, which had heroic narratives of medical research and survival stories among patients, because of the limited treatments developed, a cancer diagnosis was considered a death sentence, and those who had to deal with the agonizing dying process itself were viewed as victims, not patients. Families often kept the diagnosis a private matter or gave cancer elaborate euphemisms. With the exponential growth of cancer research and treatment options in the post–World War II boom in the biomedical field, with President Richard Nixon’s call for a war on cancer in 1973, and with a growing public awareness that cancer, if caught early enough, could actually be treated successfully, there has grown a subgenre of medical narratives and cancer survivor stories.

These people, whichever gender, whatever age, became inspiration models; their tales of courage and endurance, featured in magazines and talk shows and most recently in Internet videos, have lifted the spirits of those others who face similar diagnoses. Among the most prominent cancer survivors of this era is Christine Gregoire, a two-term governor of Washington, whose doctor, during a routine checkup in anticipation of Gregoire’s run for the governorship, detected early-stage breast cancer. Because the cancer was detected early enough, treatment was a viable option. Gregoire decided on a mastectomy and returned to full vigor and the public spotlight within a week. Over the next decade, as she dominated the state’s Democratic Party, she never forgot the importance of early detection and tirelessly championed the cause among women age 40 and above.

Born in 1947 in Michigan, Christine O’Grady grew up the only child of a single mom who worked as a line cook in a restaurant and never completed high school. Her mother relocated them to Washington before O’Grady was three. O’Grady was taught early on by her mother the importance of education, and she devoted herself to her studies. Graduating in speech and sociology from the University of Washington in Seattle, she initially wanted to teach public school. But finding no opportunities, she returned to school to study law and earned her Juris Doctorate from Seattle’s Gonzaga University in 1977. Inspired as so many of her generation by John Kennedy’s call for community involvement, Gregoire, now married, knew public service was her ambition.

After a brief stint as a typist-clerk in the parole and probation offices and then in the state’s Department of Ecology (she had grown up in love with the state’s wilderness), she moved to the state’s attorney general’s office, where she worked initially with social services in investigating and ultimately protecting children from abusive parents. She became known quickly as one of the Democratic Party’s rising stars. Energetic and charismatic, she spoke in a straightforward manner that gained wide voter trust. She decided in 1991 to run for attorney general. She was elected (the first woman to hold that position) and once again distinguished herself as a fighter and champion of populist causes, most notably successfully spearheading the state’s massive lawsuit against several tobacco companies for misinforming the public over the dangers of smoking. Reelected twice, she decided she would make a run for the governorship. In an effort to present the voters a clean bill of health, she underwent a standard set of physical examinations. In her early 50s and quite active and hands-on as attorney general, she felt fine and considered the tests as a mere formality.

It was her routine mammogram, however, that detected a ductal carcinoma in one of her breasts, undetectable by standard manual examinations. That the cancerous cells had gotten no further than the duct, that is, noninvasive, located just under the skin, gave doctors two treatment options: She could undergo intense radiation therapy that would take six grueling weeks and would leave Gregoire physically exhausted and, more problematically, it could not discount a return of the cancer, or she
Two-term Washington state governor Christine Gregoire became a famous anti-cancer advocate after her bout with breast cancer. (Washington State Office of the Governor)

could elect a mastectomy, a more radical option but one that had had far more promising long-term results. Gregoire did not dwell in self-pity or depression—rather she made a quick decision.

Doctors removed the breast and did standard reconstructive work in a single day, all under the relentless scrutiny of the state’s media. To doubters who thought a cancer survivor so soon after treatment would not be up for the campaign, much less the daily 16-hour grind of a governor, Gregoire demonstrated in her campaign a resilience and grace that convinced voters to vote on the basis of her politics, not her disease. When asked, she stressed that her recovery was thanks to early detection and the advances in cancer treatment, among the first public figures to make such public pronouncements about breast cancer.

She was elected after a difficult challenge (by a margin of just under 160 votes and that was resolved by a recount) and quickly established a national presence for her campaigns to address a variety of populist causes from education reform to welfare reorganization, from tax initiatives geared to help the poor and middle class to gay rights. But she also vigorously pushed for state support of stem cell research, citing such controversial biomedical research as the best promise not only in cancer treatment but in a variety of diseases, most prominently in treating dementia and catastrophic nervous system conditions. Her own cancer never returned, never interfered with her managing the responsibilities of the office—and she was reelected in 2008, becoming something of national figure when she endorsed Barack Obama rather than Hillary Clinton. Gregoire was reelected handily.

In May 2012, as her second term was ending (she had announced she would not seek a third term), she and her husband made a difficult public announcement that her husband, Mike, had been diagnosed with colon cancer during a routine checkup. He had been in no pain and had evidenced none of the symptoms. Surgery immediately removed the cancerous segment, and doctors predicted a full recovery. Once again, Gregoire emphasized the importance of early screening. Once out of office, although she was courted by the Obama administration for a cabinet-level job, Gregoire retired from public life to spend time with her family—however, she did accept a trusteeship on the board of the Fred Hutchinson Cancer Research Center, one of the state’s top-rated cancer research and treatment facilities.

Joseph Dewey
Broward College

See Also: Breast Cancer; Colon Cancer; Fred Hutchinson Cancer Research Center.

Further Readings
Guatemala

The Central American Republic of Guatemala, independent since 1821, is home to 15 million people who have witnessed major changes in their disease profile. Whereas preventable upper respiratory tract and gastrointestinal infections were once the biggest health threats, Guatemalans now experience increasing rates of noncommunicable diseases, including many cancers. Much of Guatemala’s Maya population also suffers high rates of malnutrition and poverty, compounding their already difficult health picture. Mayas and others who live in marginal areas should an especially heavy cancer burden that centers on five types.

Major Cancers
Since at least 2005, more Guatemalans have died from stomach cancer than from any other cancer. Mortality from this disease has been especially marked among Guatemalan men, for whom it is the most frequently diagnosed cancer. Guatemalans as a whole, though, suffer heavily from this malignancy and were ranked fourth globally in its occurrence in 2012. But while stomach cancer remains the leading cancer cause of death among Guatemalan men and women, women are also very vulnerable to liver cancer. In fact, Guatemalan women had the third-highest rate of liver cancer in the world in 2012. Liver cancer is the second-most prevalent cancer in Guatemala, and though it affects men and women, its diagnosis has been uneven across these groups. Given the high rates of drinking and alcoholism among men, the underreporting of this cancer among men is cause for concern.

The cancer most frequently diagnosed among women, meanwhile, is cervical cancer. In Guatemala’s rural areas, where many women marry early and have short intervals between births, women face an increased overall risk of developing this cancer. To address this, in the 1980s, health workers began making the Pap test more widely available. Persisting problems with cytology lab work and patient follow-up visits, though, limited the test’s effectiveness. In 2002, then, the Pan American Health Organization (PAHO) and some nongovernmental organizations (NGOs) began promoting the VIA/Cryo diagnostic protocol, in which trained health personnel apply a 3 to 5 percent acetic acid solution to the cervix, which causes abnormal cells to temporarily turn white under bright light. Abnormal lesions can then be treated immediately by cryotherapy. The entire process is as reliable as cytology but much faster and more cost-effective. This process has limitations, though, because it relies on subjective visual reading and is not suitable for women over age 50. The Ministry of Public Health and Social Services (MSPAS) and other stakeholders are currently studying how to administer human papillomavirus (HPV) vaccines to the country’s most vulnerable women.

Research is also under way to limit the mortality tied to prostate cancer, considered the fourth-leading cause of all cancer deaths in 2011. Worth noting, though, is that, whereas most health agencies point to stomach cancer as the leading cancer cause of death, in Guatemala City’s public oncology hospital (INCAN), prostate cancer was detected more often in men than stomach cancer in 2012. This suggests that where screening and diagnostic resources are concentrated, more detection of prostate cancer occurs, despite national trends. The fewer screening opportunities in rural areas may be associated with how Guatemalan men had the fourth-highest rate of prostate cancer in the world in 2012.

Limited diagnostic resources in the countryside, together with other factors like smoking and wood smoke inhalation, have imperiled lung health and contributed to lung cancer prevalence. This cancer is now the fifth-leading cancer cause of death in Guatemala. With smoking on the increase, the high rates of upper respiratory tract infections are on track to worsen, along with overall vulnerability to cancers. Among Mayas, moreover, as tobacco use stems from ancestral practices, it is deeply entrenched in some quarters of community ritual life. And with the widespread visibility of cigarette smoking, including in TV advertising, smoking is attracting younger Guatemalans. Poor indoor environmental quality, especially in smoke-filled kitchens in rural homes, also threatens respiratory health and may contribute to rising rates of lung cancer.

System Challenges
Guatemalans face many challenges with cancer, but diagnostic screening remains a top issue. Many cancers in rural areas go undiagnosed, partly because many women are reluctant to reveal intimate parts of their bodies to screeners, and partly because many men resist getting medical attention at all, much less
screening. But in view of how Mayas make up half
the population, the MSPAS has long tried to reach
indigenous people, and especially women, through
Maya midwives, something it will likely continue
doing to broaden screening services. At the urging
of NGOs, more health personnel are also trying to
improve their outreach and service efforts. Part
of this requires addressing how health personnel
in rural areas seldom speak one of the country’s
22 Maya languages. This language divide dissuades
many Mayas, particularly women, from going to
clinics or from returning for follow-up care.

Some Western groups have been involved in can-
cer capacity building in conjunction with INCAN,
the only publicly operated oncology hospital. Their
work has included (1) helping update INCAN’s
record keeping system and cancer registry, which
until recently were paper based, (2) identifying trans-
mittance vectors of infectious agents linked to stom-
ach and cervical cancers, and (3) helping improve
the screening infrastructure. Mammography, for
example, is still not widely available in the public sec-
tor, and even at INCAN, it is expensive. A mammo-
gram there costs around $18, which is about twice the
average daily wage of $9.70, itself far more than most
rural people make in a day. Health centers and posts
throughout Guatemala remain poorly staffed and
underequipped, and with the state devoting less than
0.05 percent of gross domestic product (GDP) to can-
cer research, cancer mortality is expected to increase.

Affluent Guatemalans, meanwhile, have a wider
range of health choices, including private hospitals
and physicians trained in the United States or Europe.
Many seek treatment at U.S. centers like MD Ander-
son Cancer Center in Houston. Their situation, of
course, contrasts starkly with that of most Guatema-
lans, who wrestle with marginalization and whose
lives are more likely to be irreparably disrupted by a
cancer diagnosis. With cancer impeding the social
mobility of many poorer Guatemalans, the country as
a whole will continue feeling the effects of this disease.

Servando Z. Hinojosa
University of Texas–Rio Grande Valley

See Also: Cervical Cancer; Liver Cancer, Adult (Primary);
Stomach (Gastric) Cancer; Tobacco Smoking; Vaccines.

Further Readings
Worldwide.” Lyon, France: International Agency for

Instituto de Cancerología. “Cancer Registry of INCAN
Guatemala.” http://regcangua.zzl.org (Accessed April
2014).

Pan American Health Organization. “Situation
Analysis: Strategies for Cervical Cancer Screening
With Visual Inspection With Acetic Acid and
Treatment With Cryotherapy in Latin America and
the Caribbean.” Washington, DC: Pan American
hq/index.php?option=com_docman&task=doc_
download&gid=17337&Itemid= (Accessed March
2014).

Guinea

Guinea has been in the process of reorganizing
its health care system since the Bamako Initiative
in 1987. It formally endorsed community-based
activities to increase access to drugs and health care
services to the population, in part by implement-
ing fees. This strategy saw a spike in accessibility
through community-based health care. The services
provided experienced a boost in quality as well.

The Bamako Initiative aimed to resolve dif-

Guinea has joined a growing number of countries

In June 2011, the Guinean government instituted
a levy on all air traffic taking off from the country.
These funds were given to UNITAID to increase
the reach of programs to treat human immuno-
deficiency virus (HIV), acquired immune deficiency
syndrome (AIDS), tuberculosis, and malaria.
who are using transactional taxes and other such methods as vehicles for increasing health care to its people. In 2014, the life expectancy in Guinea reached 59.6 years.

Although Guinea has seen some improvement when it comes to health care access, Guinea also suffers from severe problems on the same front. Like many countries in Africa, many of Guinea’s people fall prey to HIV and AIDS. In 2001 and 2002, studies concluded that HIV was higher in urban areas, with prevalence in some cities as high as 7 percent of the population. Forty-two percent of commercial sex workers were afflicted as well as 6.6 percent of active military, 7.3 percent of truck and taxi drivers, 7.3 percent of miners, and 8.6 percent of adults who also suffered from tuberculosis. In 2004, it was estimated that more than 170,000 children and adults were afflicted with these diseases. HIV is spread primarily by way of heterosexual intercourse with multiple partners. Both genders are basically at the same risk, with young people between the ages of 15 and 24 most likely to become afflicted.

The epidemic of HIV is fueled by several different factors including unprotected sex, multiple sexual partners, poverty, illiteracy, unstable borders, lack of civic responsibility, refugee migration, and scarce access to medical care as well as public services.

Another serious problem plaguing Guinea’s population is malnutrition. In 2012, a study reported chronic malnutrition rates as high, with levels ranging from 34 to 40 percent according to region. Acute malnutrition rates in mining zones were reported as above 10 percent. About 139,200 children were suffering from acute malnutrition and 609,696 from chronic malnutrition, and another 1,592,892 were afflicted with anemia. The factors behind these high levels of malnutrition include limited medical access, degradation of care practices, poor hygiene practices, and low levels of food diversity.

In 2014, the Ebola virus broke out in the highly populated capital city of Guinea: Conakry. The health ministry prohibited sale and consumption of bats, which were thought to carry the pathogen, but the virus spread out from the rural areas in spite of this measure. With limited access to health care and a capital city with 2 million people, the emergence of Ebola is a thing of nightmares. Ebola is passed from person to person by close contact and has a mortality rate of between 25 and 90 percent.

The people most affected thus far have been living in rural areas. The victims are commonly impoverished people who have little to no access to any health care system. There is also very little in the way of incentives for major companies to make any sort of investment in medical solutions for these people when there would likely be no return on the investment.

Cancer has become a health problem in Africa. As screening has become more widespread, it has been reported that 715,000 new diagnoses were made, and 542,000 deaths as a result of cancer occurred in 2008. These numbers have been hypothesized as nearly doubling by 2030 simply due to population aging and growth. Despite these worrying figures, cancer is not as highly prioritized due to other public health concerns. The magnitude of this cancer burden is lost on many policy makers as well as the general public.

Most of the cancers in Africa are related to infectious agents. These include but are not limited to Kaposi’s sarcoma, urinary bladder cancer, and cervical cancer. Some areas are experiencing an increase in the cancers most common in North America as lifestyles change, such as taking up smoking, an increase in inactivity, and weight gain. The cancers cropping up include breast, colorectal, and prostate cancers.

Unfortunately, most cancers in Africa are diagnosed at a late stage. This is from many different factors such as lack of access to medical care, lack of knowledge or limited knowledge about the signs and symptoms of cancer, and a stigma associated with the cancer diagnosis in Africa. In addition to this lack of knowledge, most cancers are only found at an advanced stage because of nearly nonexistent screening or early detection services. As a result, the mortality rate of cancer is much higher than the rate for the same type of cancer would be in developed countries. The five-year survival rate for women suffering from breast cancer is less than half in Gambia, Algeria, and Uganda, as opposed to nearly 90 percent in the United States. This is, in part, because a late cancer diagnosis means that the cancer is in or nearing its final stages, and treatment options become severely limited.

While Guinea is making strides to create a health care system for its people, it is also afflicted with diseases and hunger, both of which are ravaging its citizens. Guinea has quarantined people known to have been exposed to the Ebola virus,
but the fruits of this effort will only be seen in the coming years. Still, Guinea has been working against obstacles to its citizens’ overall health for many years now, with marked improvements in the metrics of accessibility and quality. Hopefully in the years to come, Guinea will resolve its health care problems. With the public health crises in full effect, however, public exposure to cancer information may take a while.

Michael Fox
Independent Scholar

See Also: Breast Cancer; Cervical Cancer; Colorectal Cancer, Childhood.

Further Readings
H. Lundbeck (Denmark)

In the last generation of television medical dramas and in the small, but significant genre of antibusiness films, writers and directors, needing a clear and easy villain to generate drama, have often demonized without much subtlety pharmaceutical companies, faceless drug companies that cynically rush poorly tested drugs into the market, that care only about the bottom line, that dump potentially dangerous drugs into unsuspecting Third World markets, or that employ elaborate armies of legal counsel, conversant in legalese, to deflect any responsibility, legal or moral, away from pharmaceutical companies’ obvious agenda of making profits off the victims of sickness.

Given the paranoia and suspicion such mainstream productions inevitably generate, it is easy to forget that, in addition to university researchers and laboratory teams in high-profile cancer facilities, pharmaceutical companies are in fact often at the forefront of cutting-edge research. Certainly compelled by profit margins and shareholder interests, these companies nevertheless fund massive research efforts to bring to market revolutionary medicines that have in fact radically altered the approach to cancer treatment. H. Lundbeck, a global pharmaceutical conglomerate headquartered in Valby, just outside Copenhagen, is an example of just such a company, working with government agencies, university facilities, and even patients themselves to alter the public’s perception of drug companies. Over the last decade, Lundbeck has patented two revolutionary drugs that specifically target cancer treatment: Treanda and Trisenox. But more importantly, Lundbeck has used its global social media reach to begin a landmark effort on the part of a drug company to become involved with the psychological effects of disease: It has begun a major push to work with families, especially children, traumatically impacted when a member of the family has been diagnosed with cancer.

The story of H. Lundbeck is one of both savvy business evolution and the rich potential of globalization. Founded by Hans Lundbeck at the height of World War I, Lundbeck was initially conceived as a kind of old-school trading company to assist war-ravaged Denmark, trading in everything from aluminum foil to biscuit mix. With the end of the war, the company quickly expanded initially into beauty products. Research teams eventually began testing the lucrative market for newer and more effective painkillers, and by World War II, Lundbeck had established a national reputation as a pharmaceutical company. In the 1950s, the company pioneered research into drugs that would help in treating Alzheimer’s disease, although at the time it was known as dementia or senility, and by the late 1970s, with the introduction of the drug Truxal to diminish the effects of schizophrenia, Lundbeck
was an international pharmaceutical player, phasing out its other agencies to focus on drug research. Initially, the company became known for its major advances in drug protocols for a wide range of brain disorders, including incipient Alzheimer’s, depression, insomnia, bipolar disorder, schizophrenia, and even epilepsy. All the while, the business divisions oversaw the careful expansion of the company into new markets, establishing bridgeheads into most of Europe, the United States, and most revolutionary of all, the Peoples’ Republic of China. By 2013, H. Lundbeck was a $2 billion conglomerate that employed more than 6,000 researchers and technicians in 57 countries.

Beginning in the early 1990s, Lundbeck branched into funding major research into cancer treatment. Its initial success came with the drug Trisenox. The drug, which used a variant of the poison metal element arsenic (arsenic trioxide), was targeted to treat specifically acute promyelocytic leukemia (APL), a relatively rare type that affects adults after age 40, and then largely for APL patients who had experienced a radical relapse after a period of apparent remission. Anterior cruciate ligament (ACL) devastates the white blood cells in bone marrow and in the blood itself. Patients struggle with fatigue and frequently develop anemia and in extreme cases internal hemorrhaging. Although many variants of leukemia have become treatable, ACL has for the most part resisted treatment protocols. Licensing of Trisenox faced some resistance as the drug, with its extremely toxic arsenic base, despite its remarkable success in clinical tests, caused significant side effects—most centrally to the heart’s ability to maintain rhythmic beating and keep blood circulating. The reality was that the side effects of the treatment drug could themselves be fatal. But countries approved the drug for use but only under doctor’s direction because, as an injected drug, it eased the patient’s need to endure often difficult chemotherapy sessions, bringing not only hope, given the drug’s success, but also relief to thousands of cancer patients worldwide.

But in 2010, the remarkable success of bendamustine hydrochloride, its brand name Treanda, became Lundbeck's signature contribution to cancer treatment. Targeted to treat relapsed indolent B-cell non-Hodgkin's lymphoma and chronic lymphocytic leukemia (which together account for about 6 percent of all cancer deaths), Treanda, an injection, had proven effective in clinical trials involving both patients with an extended history of cancer treatments and those just diagnosed—in short, it held promise for virtually the entire range of patients with non-Hodgkin’s lymphoma and leukemia. What perhaps best indicates Lundbeck’s concern for intensive testing, the drug was introduced into a study involving 319 patients with leukemia, patients selected without regard to ethnicity, age, or gender. It was a random test—many drug companies routinely adjust their demographics for drug testing in an effort to earn drug licensing and approval to market. A remarkable 76 percent of patients treated with Treanda responded to the treatment, and even more promising, in follow-up studies, patients showed no signs of the disease in the bloodstream up to 21 months (previous drug protocols averaged nine). Patients could return to relatively normal life, although the drug had notable side effects, including prolonged nausea, headaches, and vomiting.

What made Treanda such a revolutionary cancer drug was how it killed infected cells—although researchers admitted they were not entirely sure how the drug did what it did. Cells can die two ways: (1) a process known as necrosis, a relatively unpleasant process in which some external trauma (infection, blunt force, as in a car accident, or the introduction of a poison) kills the cells or (2) a process known as apoptosis, in which the cell is actually told to die, to commit a kind of tidy cellular suicide in a controlled and directed fashion. Although it is the basis of radiation treatments and chemotherapy sessions, apoptosis in cancer treatments can often leave the patient physically exhausted. Like radiation or chemotherapy, an injection of Treanda, by short-circuiting the wiring of the DNA, sent a signal for diseased cells to die, leaving the patient with much milder side effects. Approved first in Europe and then in the United States and Canada, Treanda is now available virtually worldwide and has become a new and promising option for cancer patients.

Joseph Dewey
Broward College

See Also: Chemotherapy; Leukemia, Acute Lymphoblastic, Adult; Leukemia, Acute Myeloid, Adult; Radiation Therapy.
Further Readings

Haemophilia Society (United Kingdom)

The UK Haemophilia Society was founded in 1950 to serve the needs of people with hemophilia and related bleeding disorders, including hemophilia A, hemophilia B, von Willebrand disease, and risk factors associated with the development of inhibitors against the treatment (depending on ethnicity and severity of the bleeding disorder). It is the only independent society with a presence across the United Kingdom. It is a charitable organization working toward providing the best medical care for patients with hemophilia. The Haemophilia Society is currently headed by President Baroness Molly Meacher, who has been active in the field of mental health and drug reform at the House of Lords. She has served as president of the society since March 2013. She has extensive expertise in issues related to health and social care, and involvement with UK National Health Service (NHS) supports.

It is estimated that hemophilia and related disorders affect around 15,000 people in the United Kingdom, who are drawn from all racial groups. Furthermore, von Willebrand’s is believed to affect up to 1 percent of the population, many of whom currently remain undiagnosed. The Haemophilia Society’s mission is to provide patients with necessary information and treatment options for hemophilia and other bleeding disorders, the freedom to choose medical interventions, and the ability to seize opportunities available to them. The society is led by people affected by hemophilia and works in close partnership with the NHS. The society has over 4,000 members, 60 percent of whom have bleeding disorders. The other 40 percent are primarily family members or friends of people with bleeding disorders.

The Haemophilia Society has worked hard to disseminate information through Web sites, magazines, pamphlets, and research. The society also has individual advocacy and support for patients in the form of consultation and advice through telephone helplines, enabling patient access to physiotherapy clinics, and the organization of community fundraising efforts. The society encourages patients to meet other people with bleeding disorders, and it helps in the organization of events for children and families of affected people, and people with human immunodeficiency virus (HIV) or hepatitis C, with support via a Facebook page. The society has been supporting a campaign to raise awareness about contaminated blood. One important agenda for the Haemophilia Society is to campaign for better societal treatment and care for people affected by blood disorders. Members of the Haemophilia Society regularly participate in meetings with the UK Department of Health.

Important activities of the Haemophilia Society include providing members with up-to-date information on hemophilia treatment and care; providing assistance with application procedures for Disability Living Allowance and other applicable social benefits; providing information on special travel arrangements, treatment centers, and documentation procedures for patients traveling abroad for treatment; and raising awareness among women regarding bleeding disorders. The Haemophilia Society also advises and supports patients with hepatitis C and HIV through its wide network of volunteers. Parents with newly diagnosed children are also counseled and informed regarding treatment options and management of the disorder. The Aventis Alert pager service of the Haemophilia Society enables parents to be contacted if their children suffer from bleeding disorders.

The Haemophilia Society started the innovative Get Involved, Get the Best (GIGTB) project in 2009, to support active involvement of people affected by bleeding disorders in improving options for care and treatment. The project aims to bring a patient perspective to three main arenas involving local commissioning, auditing of hemophilia centers every three years, and the establishment of a Pan-Thames Haemophilia Consortium and services reconfiguration. Long-term volunteers are actively involved in this program, and youth leaders
are encouraged. The society has a presence through local groups across the United Kingdom, with 17 local groups in England, 2 in Wales, 4 in Scotland, and 1 in Northern Ireland.

In May 2011, as an attempt to increase awareness in the society regarding the challenges faced by people with bleeding disorders, the Haemophilia Society launched its Buddy Award scheme, sponsored by Novo Nordisk. The event was inaugurated at a launch event held at the House of Commons in London. The annual awards recognize the pivotal support provided from family members, caregivers, friends, and teachers of children who suffer from bleeding disorders. Because there is a severe lack of public awareness for bleeding disorders, families and friends have immense responsibility for their sibling/friend, and the Buddy Award recognizes and appreciates the valuable contribution made by friends and family. In 2014, 70 nominations were received for the buddy awards from all across the United Kingdom, and the award function was held at the London Zoo, with more than 200 guests attending. The award ceremony was held on April 17, which is the World Haemophilia Day, and winners included friends and family of patients with bleeding disorders, teachers, and social workers, as well as nurses and caregivers for patients.

The Haemophilia Society initiated a program called Talking Red, in order to tackle the problem of poor understanding of bleeding disorders and to raise awareness about bleeding disorders among women who suffer from bleeding disorders without realizing it. The first Talking Red awareness week was held on June 21, 2014, and encouraged women to be aware of bleeding disorders manifesting as frequent and heavy periods, easy bruises, frequent or heavy nosebleeds, heavy bleeding after surgery or dental procedures, and abnormal bleeding after childbirth. Talking Red encourages people not to be embarrassed to talk about bleeding and to raise awareness.

Poonam Balani
Independent Scholar

See Also: AIDS-Related Cancers; Hepatitis C; United Kingdom.

Further Readings

Resources/CharitiesEvaluationServices/Documents/haemophiliassocie
have considerable public health implications. It is for this reason that hair dye represents one of the most researched cosmetic products, having been the subject of both longitudinal and experimental scientific investigation.

Following development of the *Salmonella typhimurium* mutagenicity assay in the mid-1970s, it was reported that just over 50 percent of the amine ingredients of oxidative hair dyes had mutagenic properties. This test, which uses several strains of the bacterium *Salmonella typhimurium* to assess the carcinogenic potential of various chemicals, is beneficial in that it is significantly less time and resource intensive than rodent studies, though there are instances in which false positives and false negatives result. Ultimately, it was determined that this assay was of limited predictive value for the rodent carcinogenicity of the ingredients of oxidative hair dyes as species-specific metabolic differences have been found to be major determinants of the carcinogenic properties of aromatic amines.

**Regulation**

Beginning in the mid-1970s, due to the recognition that oral administration of certain aromatic amines was linked to cancer in rodents, many industrialized countries introduced regulations to prevent the use of those ingredients found to be toxic in rodent studies from use in commercially available hair dyes. This historical shift is of key importance in understanding the links that may exist between use of hair dyes and the development of cancer, given that certain cancers such as urothelial cancers may have latency periods of two or more decades. Thus, studies examining cases of cancer diagnosis occurring in the 1990s and 2000s may, in fact, be detecting carcinogenicity associated with dye products that have become unavailable due to heightened regulatory restrictions.

Today, government regulation of hair dyes varies throughout the world. In the European Union (EU), the safety of hair dyes and their ingredients is reviewed by the Scientific Committee on Cosmetic Products and Non-Food Products Intended for Consumers (SCCNFP), an independent agency whose role is to advise EU member states on any safety concerns regarding cosmetic ingredients. Those ingredients found to pose confirmed or presumed carcinogenic or reproductive risk are prohibited from use in products marketed to EU consumers.

Under federal regulations in the United States, the Food and Drug Administration is responsible for evaluating the safety of cosmetics and hair dyes, though the safety of specific ingredients is largely self-regulated. In 1976, the independent Cosmetic Ingredient Review was established to evaluate the risks of cosmetic ingredients. Since its founding, this group has written safety assessments of more than 650 ingredients, nearly all of which have been identified as safe or acceptable for use within certain parameters.

In Japan, hair dyes and their ingredients are considered by the Ministry of Health, Labor, and Welfare to be quasi-drugs and are subject to approval, which may include evidence of their safety. Similar agencies and regulations also exist in other Asian countries.

**Research**

Research on the development of cancer in both professional and personal consumers of hair dye has not resulted in clear conclusions. While some large-scale epidemiological studies have found that cancer risk increased in association with hair dye use, other prospective investigations have not demonstrated this link.

**Personal Hair Dye Use**

A pooled analysis of four smaller studies examining hair dye use and the development of non-Hodgkin’s lymphoma in women found that women who used hair dye prior to 1980 demonstrated a 30 percent higher risk of developing non-Hodgkin’s lymphoma than did women who had never used hair dye. Women who used oxidative dyes beginning in 1980 or later were not found to exhibit this increased cancer risk, with one exception: Women who used darker-colored dyes after 1980 were found to have an increased risk of follicular lymphoma. When contrasted with nonhair dye users who developed cancer, women who used hair dye prior to 1980 were significantly more likely to develop follicular lymphoma and chronic lymphocytic leukemia or small lymphocytic lymphoma.

Studies examining the personal use of hair dye and the risk of leukemia development have also had unclear results. In one case-controlled study, a slight leukemia risk was associated with use of
Hair Dye

pre-regulated dyes, though the increase was not statistically significant. Of note, researchers found that this minimal increase in risk was associated with oxidative as well as semipermanent and temporary hair colorants. In contrast, a similar investigation conducted in Italy found that only users of black dyes exhibited an increased cancer risk. This study’s results must be considered cautiously, as the frequency and timing of use of hair dye products were not evaluated as a component of the study, despite other researchers having acknowledged the importance of considering these factors when assessing carcinogenicity in oxidative hair dye products.

Individual studies and meta-analyses examining personal hair dye use and the risk of bladder cancer have produced especially conflicting results. While some researchers have found evidence of an increase in rates of bladder cancer associated with personal hair dye use, other research has not.

The relationship between breast cancer development and use of hair dye in women has been examined frequently since the late 1970s, with no studies to date finding any association of increased breast cancer risk for women who use hair dyes relative to those who do not.

There is limited research examining whether hair dye use is related to other types of cancers, and it may be some time before samples and results from available studies can be pooled due to significant variations in study designs.

Professional Hair Dye Use

One recent meta-analysis concluded that professional hairdressers do experience an increased cancer risk for several anatomic sites. Specifically, researchers reported a 62 percent increase in the development of multiple myeloma, a 52 percent increase in rates of larynx cancers, a 30 percent increase in rates of bladder cancers, and a 27 percent increase in lung cancer. These postulated that this increase in rates across these various sites reflected the multiple pathways, including respiratory, dermatologic, and systemic exposure, whereby industrial hair colorists may be exposed to carcinogenic agents. This analysis additionally indicated that professional hairdressers’ risk is not significantly increased for Hodgkin’s disease, non-Hodgkin’s lymphoma, leukemia, or ovary, breast, kidney, or colon cancers.

In 1993, the International Agency for Research on Cancer (IARC) conducted a meta-analysis that indicated that, relative to nonhairdressers, the risk of bladder cancer development for professional hairdressers was 1.6 times greater for male hairdressers and 1.1 times greater in females. The agency cautioned against assuming a direct corollary relationship between professional oxidative hair dye application and the increased risk for bladder cancer development, noting that hairdressers experience professional exposure to thousands of chemicals, including volatile solvents, propellants, formaldehyde, and methacrylates in the routine tasks of their chosen profession.

Conclusion

Ultimately, several factors may explain the relative inconsistency of findings regarding hair dye and cancer risk. Some research has examined age cohorts that may have been too young to assess the risk for certain types of cancers. Other studies have not properly controlled for other potential
confounding factors, such as ventilation, smoking history, glove use, and dye strength, in the case of professional hairdressers, or frequency or length of hair dying in the case of consumers. The largest study examining this relationship to date found a decreased mortality due to bladder cancer in women who had used dyes compared to those who had not, a finding that other researchers have labeled implausible. It is clear that to question the relationship between ever using hair dye and death due to cancer may represent too broad a question, which is likely to be influenced by any number of confounds. In response to the admittedly limited available research on the topic, the IARC recently stated its position that professional exposure to hair dyes was likely carcinogenic to humans, while personal use of oxidative hair dyes could not be classified as carcinogenic.

Christopher Edwards
LaBarron K. Hill
Rosellen Reif
Duke University Medical Center

Haiti

A Caribbean nation of close to 10 million people, Haiti shares the island of Hispaniola with the Dominican Republic. Unlike its neighbor, however, Haiti lacks the robust tourism and consistent gross domestic product (GDP) often associated with Caribbean countries and is the poorest country in the Western Hemisphere. The World Health Organization (WHO) reported in 2014 the life expectancy of Haitian men to be 61 and Haitian women 64.

National data on cancer incidence and mortality are difficult to ascertain. Haiti does not maintain a national cancer registry. E. J. Mitacek, D. St. Vaillieres, and A. P. Polednak reported in the International Journal of Cancer that the major types of cancer recorded from 1979 to 1984 were stomach, intestine, primary hepatic, cervix, penis, and Kaposi’s sarcoma. Although the American Cancer Society reported in 2007 that Haiti has the highest liver and cervical cancer incidence and mortality rates of any Caribbean country, it had the lowest incidence and mortality rate from breast cancer. Another recent study indicated that Haiti had a higher incidence rate of cervical cancer than any other country in the world; in fact, the World Health Organization (WHO) reported that the incidence of cervical cancer in Haiti is 12 times that of the United States.

The 2010 earthquake in Haiti destroyed a large portion of the health infrastructure, including the Ministry of Health building. An estimated 150 nurses were killed when a nursing school collapsed, further exacerbating an already poor public health environment. Multiple other hospitals, clinics, and public health facilities were destroyed. Following the event, government and aid agencies immediately focused resources on epidemic diseases such as cholera and other waterborne diseases. Cancer control and care initiatives received very little post-earthquake support. Following the earthquake, international funds flowed into Haiti for reconstruction along with experienced medical professionals and administrators. It remains to be understood or measured if this influx will provide, over time, new and improved health facilities and programs across the medical continuum, including cancer prevention and care.

According to the Global Task Force on Expanded Access to Cancer Care and Control in Developing
Countries Innovation (GTF.CCC), in 2011, Haiti had one national oncologist who was trained in Mexico. Like many physicians in Haiti, this clinician works in the private sector, and only the wealthiest can afford services. Haiti does have in-country resources for Pap smears with two pathology labs, one private and one public. Currently, cancer detection occurs late. Treatment regimens typical to First World countries are not available. Radiation and chemotherapy are financially out of reach for most. Surgical cancer treatment is most common but often inappropriate due to the advanced state of most diagnosed cancers. Due to the absence of detection and treatment options, outcomes are generally poor to mixed.

Prior to the 2010 earthquake, Haiti possessed the world’s second-highest concentration per capita of nongovernmental organizations (NGOs). Many of these NGOs have access to medical professionals and services from wealthier nations. Zanmi Lasante (ZL, Partners in Health in Haitian Kreyol) employs close to 5,000 doctors, nurses, and community health workers. They serve an estimated 3.4 million, primarily in the central plateau and lower Artibonite, and are the only consistent source of free oncological care in Haiti.

As the largest health care provider in Haiti, the primary ZL Sociomedical Complex is located in Cange and supports not only the complex but more than 15 public health facilities throughout the area. The Cange complex houses a 104-bed, full-service hospital with two operating rooms, adult and pediatric inpatient wards, an infectious disease center, an outpatient clinic, a women’s health clinic, ophthalmology and general medicine clinics, a laboratory, a pharmaceutical warehouse, a blood bank, and radiographic services. In 2013, Hospital Universitaire de Mirebalais (University Hospital) opened. This 205,000-square-foot facility with 300 beds not only serves the people of the central plateau and lower Artibonite but provides education and training for Haitian community health workers, physicians, and nurses. Oncology care at University Hospital includes cancer screening, education, oral and intravenous chemotherapy, and palliative care.

Palliation outside of hospital facilities is not an integrated or even accepted feature of care within the country. A cultural reticence to administering narcotics and government controls make access to pharmaceutical pain management difficult. Because of the lack of formal and diffuse oncology care, informal family caregivers are common and are often the only medical line of care experienced by a household. Many Haitians also rely heavily on spirituality and religion in medical care.

Critical to many cultures, the concept of God, as well as other forms of spirituality and the supernatural, plays an important role in cancer and other health narratives. Studies have shown that culture and religion can significantly influence a patient’s perception of illness and treatment, making Western-based cancer care treatment problematic due to stigmas, fears, and previous negative experiences with “modern” healers. These factors may prompt the patient to seek indigenous and traditional medical practices instead. Although Haitians primarily identify themselves as Roman Catholic, many continue to follow varying forms of voodoo or a combination of the two.

The Haitian health literacy rate is extremely low due to lack of contact with formal and trained medical practitioners, both in person and in the media. Haitians also have little access to technology, which significantly limits the available channels of intervention communication. While a majority of Haitian households possess a radio, which provides daily broadcasts, few own or watch television. Although well over half of the population is literate, Haitians have a low rate of newspaper readership. Few Haitians use a computer, and even fewer use the Internet. Therefore, any type of media communication intervention, community awareness or detection campaign, or public education regarding cancer is difficult, if not circumstantially impossible. This absence of media outreach has a deleterious effect on early intervention for oncology care, oncology outcomes, and survivorship.

Christine M. Platt
Joy V. Goldsmith
University of Memphis

See Also: Cuba; Dominican Republic.

Further Readings
Head and Neck Cancer

Head and neck cancer (HNC) usually refers to cancers arising within the upper aerodigestive tract, the paranasal sinuses, and the salivary glands. While the incidence of some subtypes of HNC is declining in the United States, rates within Europe and Asia have either remained stable or increased. Risk factors include substance use, social deprivation, and exposure to the human papillomavirus (HPV). Symptoms, treatment, and outcomes vary according to tumor type, stage, and a variety of demographic and biological factors.

Risk Factors

Differences in the use of substances such as tobacco and alcohol may account for the geographical variations described above. Tobacco use and alcohol consumption are the leading risk factors for HNC, and they have a synergistic effect when used together, accounting for around 75 percent of HNC globally. Head and neck cancer is linked to social deprivation with increased incidence and worse survival associated with more adverse social circumstances. The mechanisms for this are unclear but are thought to relate to tobacco and alcohol use, diets deficient in fresh fruit and vegetables, increased presence of comorbidities, and a tendency for later presentation with advanced disease. HPV is a known risk factor for oropharyngeal cancer, and it may be implicated at other associated sites. HPV-associated tumors are most likely found in males, those age 50 or under and from black and minority ethnic groups; these tumors are also strongly associated with risky sexual behavior. They are also associated with better individual outcomes after treatment: a reduced mortality risk compared to non-HPV cancers and an increased three-year survival rate.

Many approaches aimed at reducing the incidence of HNC are intended to reduce tobacco and alcohol consumption and improve detection of early-stage lesions and tumors. There is also interest in prophylactic vaccines used to treat cervical cancer.

The Physical and Psychosocial Impact of Head and Neck Cancer

Presentation of HNC may include facial swelling, nonhealing ulcers, change in voice, problems with swallowing, or persistent sore throat and earache. After diagnosis is confirmed, a treatment plan will be developed by a team of clinicians including surgeons, oncologists, radiologists, specialist nurses, dentists, and psychologists. The treatment plan is influenced by site, histology, stage, and extent of disease. It is likely to include surgery to the primary tumor site and lymph nodes in the neck as well as radiotherapy and chemotherapy. Some patients will require nutritional support provided via a percutaneous endoscopic gastrostomy (PEG), and others may require a potentially permanent tracheostomy.

The effects of treatment for HNC vary according to tumor characteristics and treatment modality and are ongoing after treatment has finished. They can include significant systemic upset, scarring and hair loss in visible areas, loss of teeth and taste, xerostomia, impaired swallowing, speech alteration or loss of voice, shoulder weakness, and osteoradionecrosis of the jaws. Consequently, there may be a considerable impact on quality of life (QoL).

QoL generally worsens after diagnosis of HNC, reaching a nadir around the end of treatment. Around 12 months after diagnosis, it returns to pretreatment levels, although symptoms such as dry mouth, sticky saliva, and altered taste may remain with continued negative impact on mouth opening, intimate relationships, and perceptions of role and function. There is evidence that those with pharyngeal cancer show greatest deterioration compared to other sites, and speech scores are worse in those with laryngeal tumors.

Single therapy treatment (surgery or radiotherapy) may reduce symptom burden compared to combination therapy: Treatment with surgery alone seems
to avoid symptoms of dry mouth and sticky saliva. The use of PEG tubes to support nutrition is widely established but reported to be the strongest independent predictor of poor QoL. This may be related to physical weakness associated with compromised nutrition, discomfort and systemic upset, or perceptions of the PEG as a reminder of the cancer and a barrier to intimate relationships.

The impact of demographic factors including age, gender, marital status, and employment on QoL is less clear, and studies report conflicting findings. Women with HNC are reported to have worse QoL outcomes than men, supporting findings elsewhere in the oncology literature. However, despite no impact of marital status on QoL, cohabiting is associated with earlier diagnosis, reduced risk of gastrostomy dependence, and improved survival. Conversely, continued substance use is associated with adverse outcomes: tobacco use is associated with reduced QoL, and continued alcohol consumption is associated with worse survival.

Anxiety and depression are associated with HNC and predicted by living alone, being male, lower educational attainment, younger age, and unemployment at diagnosis. They are associated with longer hospital stays, increased treatment complications, malnutrition, and increased mortality, with suicide rates four times higher in those with HNC than the general population. There is a relatively high risk of recurrence or new tumor development, and many people report anxiety due to fear of recurrence. Body image concerns are also frequently reported, especially by those with oral and oropharyngeal tumors.

Rates of HNC vary according to various social and physical factors as do individual outcomes, including persistence of symptoms and survival. While the personal costs of a diagnosis of HNC can be great, societal costs for treatment and aftercare are considerable. Although estimates of those returning to work after treatment vary, there is evidence that people with HNC are less likely to return to work than breast, colon, or prostate cancer patients. Further rigorous and good-quality research is required to improve the quality of our knowledge regarding this condition.

**See Also:** Alcohol; Laryngeal Cancer; Oral Cavity Cancer; Lip and; Oropharyngeal Cancer; Tobacco-Related Exposures.

**Further Readings**

---

**Health Advocacy**

Health advocacy is the mobilization of people or organizations to address a specific health concern. Health advocacy often is political because it seeks to amend existing health-related policies or implement new ones. Therefore, health advocacy can be an important tool for indirectly helping people with cancer better manage their disease. For instance, a health advocacy effort may convince policy makers to implement a law that would grant cancer patients more affordable medical treatments through improved health insurance coverage. In this entry, an overview of health advocacy is presented and a recommendation for how health advocacy may be systematically performed is offered.

**Overview of Health Advocacy**

Historically, advocacy has been used in the legal profession to describe a lawyer representing a client and speaking on behalf of the client. Rhetoricians who study advocacy examine the art of negotiations, persuasions, and argumentations that occur in court-oriented dialogue. In this context, the term advocacy implies reasoned argument toward change rather than pleading for change. There are various forms of advocacy, such as citizen advocacy, environmental advocacy, and health advocacy, among others. In citizen advocacy, professionals represent
people within an institution to speak up for their rights. In environmental advocacy, professionals represent the environment to preserve and safeguard it. In health advocacy, professionals, caregivers, or community members represent clients or patients to advance better solutions to address the health-related problems they face. For example, one may advocate for cancer patients by persuading the government that more resources should be allocated for the construction of cancer-support facilities. Those who advocate are not limited to lawyers but include people with other occupational and community roles, such as social workers, academics, health care professionals, caregivers, and patients.

Because health advocacy may require much effort, it is often carried out by a group of people or an organization rather than an individual. Therefore, health advocacy often involves coordinated action to bring about change in health policies. For instance, organizations such as clinics and grassroots cancer organizations may unite to form a cancer coalition to advocate for greater affordability in cancer treatment. Group-level health advocacy started in the early 20th century in volunteer organizations and social movements. Early health advocates were activists in civic organizations, women’s associations (e.g., Young Women’s Christian Association), labor organizations (e.g., American Association for Labor Legislation), and nonprofit organizations (e.g., American Cancer Society).

Health Communication Advocacy Model
There are a variety of ways to approach health advocacy. This entry presents a revised version of Marifran Mattson’s Health Communication Advocacy Model as one framework that people or organizations may utilize to guide them through the health advocacy process. The model emphasizes the crafting of persuasive messages that communicate advocacy goals to audiences and incorporate a social marketing perspective in developing and implementing an effective health advocacy campaign. Crafting messages refers to the effective creation and dissemination of advocacy messages using communication theories. Social marketing refers to the use of marketing concepts to relay messages and generate responses in target audiences to calls for social action. When theories and concepts of communication and social marketing are fused together in this way, advocacy efforts are more effective in compelling audiences to support advocacy goals. There are three phases in the Health Communication Advocacy Model: the assemble team phase, the formative research and message development phase, and the implementation and evaluation phase. Advocacy practitioners who utilize the model should proceed systematically through each phase.

Practitioners utilizing this model begin their advocacy campaigns with the assemble team phase. In this phase, a team of people with relevant expertise is put together to work toward a shared advocacy goal. In the context of cancer-related advocacy, the team should be comprised of individuals with expertise regarding cancer. These experts have knowledge of or experience with cancer and may include physicians, cancer patients, and caregivers. The team also should include representatives from community partners, which may be clinics, grassroots organizations like cancer associations, or large, networked organizations such as cancer coalitions.

Community partners are important as they enable advocacy efforts to have more resources and further reach. The team also would benefit from recruiting public health and communication specialists as they are proficient in communicating health-related concerns efficaciously to small and large audiences. Last, a lobbyist is recommended to be part of the advocacy team. A lobbyist is a professional who provides advice on political strategies and has considerable political knowledge and network connections. A lobbyist may help an advocacy team weave through political complexities and be connected with policy makers to persuade them to support the advocacy goals. When the team is assembled, its members construct a position statement regarding the health issue that they wish to address. For instance, if lack of affordable care for cancer patients is the health issue, an advocacy team’s position statement may be “to persuade legislators to pass a law that requires health insurance companies to provide better coverage for cancer treatment.” After the position statement is constructed, the team proceeds to phase two of the model.

Phase two is the formative research and message development phase. In this phase, the advocacy team identifies the legislators, activists, media, and other audiences who may influence policy-making decisions and develops messages to persuade these audiences to be in favor of the advocacy goal. Grounded in communication theories, the messaging process
Health Advocacy

involves crafting messages that are stimulating and motivational. This may be achieved through emotional appeals, immersive audio and vivid imagery, and portraying the threat of the disease or illness. For example, a message may depict, through a patient’s testimonial, the difficulties of managing cancer and the deleterious consequences of not being able to afford managing cancer in order to persuade legislators to support policies that provide insurance coverage for cancer treatment. Messages also should address barriers that may hinder audiences from supporting the advocacy goal. For instance, if some audiences are not familiar enough with using the Internet to access and sign online petitions, then messages should include instructions on how to support the advocacy campaign in other ways, such as rallying at the statehouse. Messages also should be culturally consistent and relevant. In other words, messages should adopt the language and norms recognized by an audience of a specific culture. An advocacy team also should consider their resource capabilities in developing and disseminating messages, including time, money, and staffing.

The message design process also should take into account social marketing strategies. Philip Kotler and Gerald Zaltman posited four elements vital for successful social marketing: product, promotion, place, and price.

Product in the context of an advocacy campaign refers to the advocacy goal; the advocacy team needs to present their advocacy goal clearly to audiences.

Promotion refers to the method by which the goal is brought to the attention of audiences. An advocacy team may achieve promotion in several ways, including raising awareness of the goal online, through the radio, or through publicity events.

Place refers to the channels through which audiences translate motivation into action. An advocacy team needs to provide specific directions for audiences to know how to support the goal. For example, an advocacy team may need to provide a URL for signing online petitions supporting the goal.

Price refers to the costs that audience members may incur in supporting the advocacy goal. An advocacy team must take into consideration the psychological, monetary, energy, and opportunity costs that audiences may face in supporting the advocacy goal and address these concerns in the campaign messages. Draft messages should be pre-tested to determine what needs to be improved or added before disseminating the messages to target audiences.

The next phase in the model involves implementing and evaluating the advocacy messaging strategies. The advocacy team may assess the progress toward the advocacy goal through methods such as monitoring media coverage; recording the frequency of traffic on its Web site, blogs, or social media sites; and tracking the number of legislative votes in favor of the advocacy goal. If the result of the advocacy effort is considered successful by the team or if the advocacy goal is achieved, the advocacy team should disseminate information to patients and relevant others who may benefit from the campaign’s progress or policy change. For example, if resulting legislation mandates health care coverage for the majority of cancer treatment expenses, the advocacy team should attempt to inform cancer patients and their caregivers that the legislation has passed and how they can acquire the benefits. If the result of the advocacy effort is unsatisfactory for the advocacy team or if the advocacy goal is not achieved, the advocacy team may choose to return to the formative research and message development phase of the model to reattempt achieving the advocacy goal by improving their messages to persuade their target audiences. Alternatively, the advocacy team may withdraw from the campaign. However, even if the team abandons the advocacy campaign, they should inform patients and relevant others about the progress of the campaign.

Health advocacy is important as it may help people with cancer better manage their disease. Advocacy efforts may lead to policy changes that provide support for cancer patients or remove obstacles that cancer patients may face. Marifran Mattson’s Health Communication Advocacy Model is one framework that practitioners may use to guide them through the health advocacy process.

Marifran Mattson
Chervin Lam
Purdue University

See Also: Cancer Communication; Government; National Cancer Policy Board.

Further Readings
The Healthy People Initiative is a comprehensive, nationwide health promotion and disease prevention agenda set by the U.S. Department of Health and Human Services. The Healthy People Initiative began in 1979 with Healthy People: The Surgeon General’s Report on Health Promotion and Disease Prevention. This was followed by the Healthy People 1990, Healthy People 2000, Healthy People 2010, and most recently, Healthy People 2020. Each initiative is released at the dawn of the previous decade (i.e., the current 2020 initiative was released in the early 2010s) and provides a list of health promotion and disease prevention objectives the United States hopes to achieve before the next decade arrives.

The overarching vision of the initiative is “a society in which all people live long, healthy lives.” This vision is guided by two main goals. The first goal is to increase quality and years of healthy life without preventable disease, disability, and injury. Quality of life refers to how happy or fulfilled an individual is with his or her life and is often measured using self-report data, number of healthy days over a certain period of time, or the number of healthy years without chronic or acute health problems. Years of health life, or life expectancy, refers to the average number of years of life remaining at a given age. For example, the current life expectancy for a child born in the United States is nearly 79 years. However, females tend to live longer than males, and whites tend to live longer than minorities, which brings us to the second main goal of the Healthy People Initiative: to eliminate health disparities among all segments of the population (e.g., gender, race, ethnicity, socioeconomic status, etc.). One example of a health disparity concerns the fact that African American men have higher rates of cancer than men or women of any other race/ethnicity.

Healthy People 2020 includes more than 1,200 measurable objectives and evidence-based resources for 42 different topics ranging from access to health services to human immunodeficiency virus (HIV) to vision care. This has increased considerably since its inception in 1979, when there were just 226 objectives in 15 topic areas. Further, Healthy People 2000 contained 312 objectives in 22 areas, and Healthy People 2010 had 467 objectives in 28 areas. A few of the 12 new areas included in Healthy People 2020 include adolescent health; genomics; lesbian, gay, bisexual, and transgender health; preparedness; and social determinants of health. And while new topic areas and objectives are added every decade, it is worth noting that cancer has been an important focus of all Healthy People initiatives to date. This is not surprising given that cancer has been the second-leading cause of death—following heart disease—for more than 50 years.

The overarching goal of the cancer section is to “reduce the number of new cancer cases as well as the illness, disability, and death caused by cancer.” This section contains 27 objectives and sub-objectives. For example, the first objective (C-1) is to “reduce the overall cancer death rates.” Also for example, objectives C-2 through C-8 focus on
Hepatitis B

reducing death rates from specific types of cancer (i.e., lung, breast, cervical, colorectal, throat, prostate, and melanoma, respectively). To provide an example of an objective with multiple subobjectives, objective C-20 reads, “Increase the proportion of persons who participate in behaviors that reduce their exposure to harmful ultraviolet (UV) irradiation and avoid sunburn”; and one of its subobjectives (C-20.5) reads, “Increase the proportion of adolescents in grades nine through 12 who follow protective measures that may reduce the risk of skin cancer.”

In addition to the section on cancer, many of the other sections and objectives target modifiable health risk behaviors that have been linked to one or more types of cancer such as tobacco use, obesity, exposure to UV light, poor nutrition, and physical inactivity. For example, one of the 15 physical activity objectives (PA-2) aims to “increase the proportion of adults who meet current federal physical activity guidelines for aerobic physical activity and for muscle-strengthening activity.” Other objectives focus on vaccinations against diseases that cause cancer such as the human papillomavirus (which causes cervical and other types of cancer) and hepatitis B virus (which causes liver cancer). For example, one of the 33 immunization and infectious disease objectives (IID-15) aims to “increase hepatitis B vaccine coverage among high-risk populations.” On a related note, as screening and early diagnosis can reduce death rates for certain cancers, some objectives deal with increasing early detection via screenings for certain types of cancer, including breast cancer (i.e., mammography), cervical cancer (i.e., Pap test), and colorectal cancer (i.e., occult blood test, colonoscopy, etc.). For example, another of the 20 cancer objectives (C-16) aims to “increase the proportion of adults who receive a colorectal cancer screening based on the most recent guidelines.”

An early report released by the Centers for Disease Control and Prevention in 2013 indicates, since the 27 cancer objectives and subobjectives were released, two have been met (i.e., those dealing with adolescent and adult use of artificial light for tanning), 11 are moving in the desired direction, four have seen little to no change, and two have gotten worse (i.e., those dealing with melanoma deaths and cervical cancer screening). Four of the remaining eight were considered developmental (meaning no baseline data is available, so there is no point of reference to assess), and only baseline data exists for the other four (meaning it is not yet possible to assess if they are getting better or worse). In sum, the Healthy People Initiative sets an ambitious agenda for the nation’s health in a wide variety of areas including cancer prevention and detection. It also provides measurable benchmarks and ways to check changes in the nation’s health over time.

Anthony J. Roberto
Arizona State University

See Also: Breast Cancer; Cervical Cancer; Colon Cancer; Hepatitis B; Lung Cancer, Non–Small Cell; Lung Cancer, Small Cell; Melanoma; Oropharyngeal Cancer; Prostate Cancer; Skin Cancer (Melanoma); Screening; United States; Vaccines.

Further Readings


Hepatitis B

The liver is one of the largest and most important organs in the body. Among other things, the liver filters harmful chemicals from the blood, stores
vitamins and minerals, helps fight infection, and aids in the digestion of food. *Hepatitis* is a general term used to refer to an inflammation of the liver. Hepatitis can be caused by excessive alcohol consumption, an autoimmune disease where the body starts to attack the liver, or one of at least five different viruses (i.e., hepatitis A, B, C, D, and E) that can be contracted in a variety of different ways. For example, hepatitis A and E are contracted primarily through ingesting contaminated food or water, and hepatitis B, C, and D are contracted primarily through contact with infected blood and body fluids. This entry focuses on hepatitis B and the hepatitis B vaccine, which has the distinction of being the first vaccine that prevents both a sexually transmitted disease and a type of cancer. More recently, a vaccine was developed for the human papillomavirus (HPV), which is another sexually transmitted disease that causes cervical and several other types of cancers.

The hepatitis B virus (HBV, Hep B) can damage the liver and cause liver cancer. HBV is transmitted from person to person through contact with infected blood or body fluids (i.e., semen, vaginal fluid, etc.). Thus, HBV is most commonly transmitted through sexual contact, contact with contaminated injection drugs, tattooing, and body piercing needles, or from mother to child. HBV is not spread by animals or insects, through food, water, or air, or via casual contact like holding hands, kissing, or hugging (though it can be transmitted by sharing toothbrushes and razors contaminated with infected blood). Because HBV is a communicable disease that can be spread from person to person, it is one of more than 80 diseases that must be reported to government authorities so public health officials can monitor the occurrence and spread of diseases (i.e., it is a nationally notifiable disease).

HBV is a fairly resilient virus. It can survive on an untreated surface for more than seven days and is 50 to 100 times more contagious than human immunodeficiency virus (HIV, the virus that can lead to acquired immunodeficiency syndrome [AIDS]). According to the Centers for Disease Control and Prevention's (CDC's) most recent fact sheet, more than 1 million individuals in the United States have chronic HBV, and approximately 40,000 new people become infected with HBV every year. Further, each year HBV-related liver disease results in approximately 3,000 deaths in the United States (and more than 600,000 deaths worldwide).

HBV may be either acute or chronic. Acute HBV (lasting less than six months) includes new infections with more mild symptoms such as jaundice (yellow skin and eyes), fever, fatigue, loss of appetite, nausea, and so on, that your immune system is able to cure after a few weeks or months. Chronic HBV (lasting more than six months) occurs when your immune system cannot fight off the virus, so it never goes away completely and can be accompanied by more severe symptoms such as cirrhosis (scaring) of the liver, liver failure, and liver cancer. Acute HBV is not usually treated unless it becomes chronic. Chronic HBV is treated with medicines that help manage or treat the disease by slowing or stopping the virus from damaging the liver. When the liver has deteriorated to the point that it is no longer adequate to sustain life, a liver transplant will become necessary.

People with acute or chronic HBV are often asymptomatic and may not be aware that they are infected. In fact, it is not uncommon for those with chronic HBV to be symptom free for many years or even decades. For this reason, HBV is sometimes referred to as a silent killer because it can progress to a very severe state over time with little to no warning. However, it is important to note that, while many people with HBV may appear healthy, they are still capable of spreading the disease to others.

There is also a simple blood test that a health care provider can order if a patient thinks he or she is at risk or may have been exposed to HBV. The HBV blood panel uses a single blood sample but actually includes three different tests, all of which are needed for proper diagnosis. HBV typically takes a month or more before it can be detected in the blood, so it may be necessary to conduct a second blood test to confirm the status if possible infection may have occurred recently. It is also important to note that the sooner a person gets tested, the sooner he or she can start treatment (which gives the best chance of treating the disease and preventing damage to the liver).

**The HBV Vaccine**

HBV is a preventable disease. Risk of contracting HBV can be reduced by avoiding the main sources
of infection such as unprotected sex and contaminated needles. However, the best way to prevent HBV is to get vaccinated (making it one of 27 vaccine-preventable diseases according to the CDC). The three-dose HBV vaccine is typically administered over a six-month period. The first injection can be administered any time, the second injection should be administered at least one month after the first dose, and the third injection should be administered six months after the first dose. All three doses of the vaccine are necessary to provide the best protection. The vaccine has proven to be both safe and efficacious. The most common side effect is soreness and redness at the injection site. Approximately 95 percent of individuals who receive the vaccine develop effective protection against HBV. To illustrate, the steep declines in HBV rates in the United States over the last two decades are attributed largely to the increase in HBV vaccine rates over this same time period.

The CDC recommends the HBV vaccine for all infants at birth, older children who did not receive the vaccine at birth, and adults in high-risk situations. This latter group includes, but is not limited to, health care and public safety workers, people living with someone who has HBV, men who have sex with men, individuals with multiple sexual partners, injection drug users, and those traveling to countries with higher HBV rates. While the HBV vaccine typically costs up to $150 per dose, it is often available for free or at a significantly reduced price via most insurance plans or at public health clinics.

The Global Vaccine Action Plan (GVAP), a framework approved by the World Health Organization (WHO) in May 2012, aims to improve global health by providing universal access to vaccination. The HBV vaccine is included among the recommended vaccinations, and the WHO works in partnership with Gavi: The Vaccine Alliance, an international organization founded in 2000, to increase access to new and underused vaccines for children in low-income countries. Gavi support of the HBV vaccine began in 2001, when the vaccine was administered to over one million children in Mozambique, and by 2004, half of the world’s low-income countries included the HBV vaccine in their routine immunization programs. As of 2013, the HBV vaccine was included on the national immunization schedule of 179 countries. However, the vaccine is not always delivered, and the WHO estimates that 5.3 to 6.0 million deaths (8.3 deaths per 1,000 persons vaccinated) could be prevented in the years 2011–2020 if the HBV vaccine were routinely provided (against a counterfactual of no HBV vaccination). One goal of the GVAP is to increase coverage with the pentavalent vaccine (providing protections against diphtheria, tetanus, pertussis, hepatitis B, and Hib) in 94 primarily low- and middle-income countries; coverage is projected to increase from 50 percent in 2011 to over 90 percent by 2020.

Anthony J. Roberto
Arizona State University

See Also: Cervical Cancer; Liver Cancer, Adult (Primary); Liver Cancer, Childhood (Primary); Vaccines.

Further Readings


Hepatitis C

Hepatitis C is an infectious disease caused by the hepatitis C virus (HCV). HCV predominantly affects the liver but can also affect the brain,
Hepatitis C

This blood-borne virus causes inflammation and damage to the liver, preventing it from performing its essential functions within the body. An HCV infection is insidious and can eventually result in cirrhosis (scarring of the liver), liver failure, or hepatocellular (liver) carcinoma. Most people are asymptomatic.

In 2011, worldwide cases of the chronically HCV infected were estimated to be between 130 and 170 million. Annually, there are about 3 to 4 million new infections and 350,000 HCV-related deaths. Globally, HCV prevalence rates are estimated at around 2 to 3 percent, with rates being over 3.5 percent in north Africa, the Middle East, and central and east Asia. Some populations in the Middle East have very high rates, such as Pakistan (4.8 percent) and Egypt (22 percent). Egypt's elevated rate is attributed to parenteral therapy for schistosomiasis (also called Bilharzia). Countries with rates around 2.5 percent include most populations in Africa, Europe, southwest Asia, and the Americas. July 28 of every year is World Hepatitis Day.

Having a chronic HCV infection for decades can develop into cirrhosis. HCV patients with cirrhosis have an increased chance (about one in five) of developing hepatocellular cancer, liver failure (acute and chronic), or esophageal or gastric varices, which are life-threatening conditions. Overall, up to about 4 percent of the HCV infected will develop hepatocellular cancer, and 2.5 percent will experience liver failure, although developing cirrhosis is more common in patients with hepatitis B, blood flukes (schistosoma), and human immunodeficiency virus (HIV), as well as in chronic alcoholics. Excessive alcohol intake increases the risk of developing cirrhosis as does having a coinfection with hepatitis B. Globally, HCV causes about one-third of cirrhosis cases and one-quarter of the cases of hepatocellular cancer. In multiple countries worldwide, HCV is the primary reason for liver transplants. Other HCV-caused or associated conditions not related to the liver include: cryoglobulinemia, diabetes, lichen planus, necrolytic acral erythema, pancreatic cancer, thrombopenia, and Sjögren's syndrome.

Classification

The Centers for Disease Control and Prevention classifies HCV as a biosafety level two, considered a medium potential hazard to the environment and persons. HCV is listed under the World Health Organization International Classification of Diseases (ICD) as 10 B17.1. HCV is a small (55–65 nanometers), enveloped RNA virus that belongs to the genus *Hepacivirus* in the *Flaviviridae* family. There are at least two members of the genus *Hepacivirus*, which are HCV and canine *hepacivirus*, and other viruses that infect horses, bats, and rodents. There are seven major genotypes of HCV, with several subtypes.

Since the 1970s, HCV was suspected to be a different type of hepatitis than either A or B. When found, it was identified as a non-A non-B hepatitis (NANBH). It was confirmed in 1989, and a screening test was developed, resulting in blood transfusion-derived HCV infections being reduced to almost zero by 2000. Hepatitis C infects only humans but has been experimentally transmitted to chimpanzees. Humans’ immune response to an HCV infection does not prevent chronicity in the majority of cases, nor does the immune system response prevent reinfection. An HCV-infected person can acquire the other hepatitis types, such as A and B.

There are two phases of HCV: acute and chronic. HCV starts as an acute infection that can last up to six months, and if not resolved, the virus stays in the body, becoming a long-term condition (chronic), and can cause lasting liver complications. Chronic HCV is associated with persistently elevated or fluctuating liver enzymes in many patients. Approximately 60 to 85 percent of the acute HCV-infected adults advance to the chronic phase. Some patients, typically younger or female, are more likely to clear the virus spontaneously.

Symptoms

The majority (about 80 percent) of HCV patients are asymptomatic. When symptoms do present, they are nonspecific and may include anorexia, polyarthritis, vague abdominal discomfort, malaise, emesis (vomiting), fever (greater than or equal to 100 degrees F [38 degrees C]), rash, and fatigue. These symptoms can last about a week (range of 3–10 days). Symptoms in the chronic stage may include depression, mild cognitive problems (troubles with concentrating and short-term memory), behavior (mood swings), pain (headaches and joint [arthralgia] and muscle aches and pains [myalgia]), pain in the abdominal and liver region, digestive
problems, itching, and fatigue. In the chronic stage, the onset of jaundice (yellowing of the skin and eyes) is possible. Chronic HCV infection is a major risk factor for serious liver complications (e.g., cirrhosis or hepatocellular cancer).

**Transmission**

HCV is transmitted primarily parenterally (e.g., intranevous, intra-arterial, intraosseous, intramuscular, or intrathecal). The foremost sources of HCV infection include intravenous drug use (IDU); anyone who received blood from an unscreened donor, such as a blood transfusion (pre-1992 in particular) or clotting factor concentrates (pre-1987 in particular); anyone who received or is receiving hemodialysis; anyone who works at a job that exposes them to blood from medical-associated needles (needle-stick injuries), blood transfusions, organ transplants, or infected or improperly sterilized instruments; and persons exposed to unsterilized items used in rituals (e.g., scarification or circumcisions [male and female]), traditional medicine (e.g., bloodletting), or other means of piercing the skin barrier, such as tattooing or ear and body piercings.

Prison inmates are a group with elevated HCV infection rates compared to the general population due to the high-risk behaviors of prison life, such as IDU and nonsterilized instruments used for tattooing. Another group with higher-than-normal prevalence rates are those with HIV, people with abnormally low levels of immunoglobulins (e.g., hypogammaglobulinemia), and persons who have had an organ transplant. This risk group is associated with a rapid progression to cirrhosis.

Household exposures that involve sharing personal care items, such as a toothbrush or razor, or casual contact, such as hugging, kissing, or sharing eating utensils, are not considered risk factors for acquiring HCV. Sexual contact with an HCV-infected person and vertical transmission (mother-to-child) transmissions have been documented but are either not conclusive or are rare. Breast-feeding is not considered a transmission route; however, caution is advised with any exposure to blood from an HCV-infected person, such as from cuts, sores, or if breast-feeding, cracked or bleeding nipples.

The transmission route changes from the developed to developing world. In the developed world, the primary route of transmission is IDU, while in the developing world, it is from unhygienic medical practices and blood transfusions. Risk groups for HCV infection include IV drug users (past and present). IDU is considered a major risk factor throughout the world for acquiring HCV. It is estimated that 60 to 80 percent of intravenous drug users are infected with HCV, accounting for approximately 10 million cases in the developed countries, such as China, the United States, and Russia.

**Diagnosis, Treatment, and Prevention**

Diagnosis is initially based on blood tests that detect antibodies against HCV (anti-HCV) but do not make a distinction between acute, chronic, or resolved infection. There are a number of diagnostic and monitoring tests for HCV, such as enzyme-linked immunoassay (ELISA or EIA), protein immunoblot, and RNA polymerase chain reaction (PCR). Tests that detect and measure antibodies in blood are ELISA or EIA and immunoblot assays. If antibodies are detected, a confirmatory test (e.g., HCV RNA or PCR) is performed to establish the infected person's viral load.

If there is no RNA and the immunoblot is positive, it is assumed that the person has a resolved infection; however, if the immunoblot is negative, it is assumed that the ELISA or EIA was a false positive. Some patients appear to have a resolved infection but continue to be infected. These patients have elevated liver enzymes, but conventional testing is unable to detect the presence of HCV antibodies. This is called a cryptogenic occult infection. If the person has HCV, there are several blood tests to determine the degree of hepatic fibrosis. If these tests are inconclusive, a liver biopsy can be used to determine the amount of liver damage.

Treatment for HCV is not always necessary and depends on the extent of liver disease as well as HCV genotype and whether the genotype will be responsive to treatment. Genotypes 2 and 3 are generally considered treatable. The diagnostic tests will aid in determining the best treatment options. When warranted, a common treatment will be a combination of the antiviral drug ribavirin (pill) and interferon (injection). HCV genotype 1 is treated with either protease inhibitors (Simeprevir, Victrrelis, or VX-950) or a nucleoside
inhibitor (ribavirin) in pill form with an antiviral drug (peginterferon alfa-2b and 2a).

Recently approved medication called sofosbuvir (pill) inhibits HCV from replicating its RNA. The treatment with sofosbuvir is 12 weeks for HCV genotypes 1, 2, and 4 and treats genotype 3 in 24 weeks, with a cure rate up to 90 percent. Other HCV combination treatments last between 24 and 48 weeks, depending on the infecting genotype. These treatments have cure rates for HCV genotype 2 and 3 at 70 to 80 percent, while other genotypes range from under half up to 70 percent. A combination treatment of ribavirin and pegylated interferon for genotype 6 has a cure rate ranging from 60 to 90 percent. The newer medications are less reliant on interferons, making it so most patients will only need to take ribavirin and an oral protease inhibitor.

The goal of treatment is to have a sustained virological response (SVR), which is defined as HCV being absent from the blood for six months after treatment. Treatment for patients with cirrhosis or hepatocellular cancer is limited, with many requiring a liver transplant. Alternative medicine of milk thistle, licorice root, ginseng, schisandra, St. John's wort, colloidal silver, and thymus extract are inconclusive or there is no evidence these therapies are effective against HCV.

Prevention

Presently, there is no vaccine for HCV like there is for Hepatitis A and B. In health care settings, universal precautions for preventing transmission of blood-borne infections are the best strategy for reducing HCV infections. These precautions include avoiding contact with bodily fluids or patients (in particular, blood) with medical gloves, face shields, and eye protection. Other HCV-prevention strategies include screening blood and donors, implementing safe injection practices, such as needle-exchange programs for intravenous drug users as well as substance abuse treatment, and medications administered in pill form if syringes are limited or will be reused (if possible).

Andrew Jon Hund
United Arab Emirates University

See Also: Hepatitis B; Hepatocellular (Liver) Cancer, Adult (Primary); Liver Cancer, Adult (Primary).

Further Readings


Hepatocellular (Liver) Cancer, Adult (Primary)

Hepatocellular carcinoma (HCC), commonly referred to as liver cancer, is the most common primary cancer that occurs in the liver (primary meaning it originates from the affected organ). HCC is one of the leading causes of cancer-related death worldwide. While HCC is common throughout the world and has a poor prognosis overall, the risk of HCC can be lowered through prevention (through both education and the use of vaccination). New antiviral medications show significant promise in reducing the number of patients with chronic hepatitis B or hepatitis C, which are the most common causes of cirrhosis leading to HCC worldwide.

Prevalence and Outcomes

Worldwide, HCC is one of the most common and deadly cancers diagnosed due to the poor prognosis and late diagnoses common in HCC. The rate of HCC is increasing worldwide, with the fastest increases in developing countries with high rates of hepatitis B or C infection. Approximately 600,000 deaths worldwide per year are attributed to HCC. In the United States, HCC was responsible for more than 20,000 deaths in 2013, and approximately 30,000 new cases are diagnosed annually. HCC is more common in men than in women, though this varies by geographical region.
Causes
HCC develops as a result of cirrhosis, or scarring, of the liver. Cirrhosis is often caused by the hepatitis B virus, hepatitis C virus, alcohol abuse, and autoimmune disease. The rate of cancer worldwide correlates directly with the rates of hepatitis B and C.

In spite of the fact that cirrhosis is known to be the biggest factor in developing HCC, only a small number of those with cirrhosis, including cirrhosis from alcohol use and from hepatitis B and C virus, go on to develop HCC. Chronic (long-term) infection with hepatitis B and C viruses are known to cause cirrhosis (scarring), which can lead to HCC. About 15 to 25 percent of individuals with chronic hepatitis B or C develop HCC, and an individual is often infected for between 20 and 30 years prior to the onset of cancer. Worldwide, hepatitis B virus is the most common cause of cirrhosis leading to HCC and is responsible for between 50 and 80 percent of HCC cases. Hepatitis C infection is responsible for 10 to 25 percent of all HCC cases worldwide. Developing countries, especially those in Asia and Africa, have the highest rates of HCC as well as the highest rates of hepatitis B virus. In the United States, chronic hepatitis C virus infection is the most common cause of cirrhosis leading to HCC.

Excessive or prolonged use of alcohol is also a cause of cirrhosis of the liver. Because of this, individuals with excessive or prolonged alcohol use leading to cirrhosis of the liver are at a higher risk for HCC. Alcohol-related cirrhosis is the third-most common cause of HCC in the United States. Other causes of HCC have been identified. These include autoimmune disease and nonalcoholic fatty liver disease (NAFLD).

Symptoms and Detection
Symptoms of HCC may be nonspecific and can result in late diagnosis. Symptoms include unintentional weight loss, loss of appetite, upper abdominal swelling and pain, nausea and vomiting, general weakness and fatigue, white chalky stools, and jaundice.

HCC is diagnosed through imaging, such as X-rays, ultrasounds, computerized tomography (CT) scans, or magnetic resonance imaging (MRI) followed by biopsy to determine the nature of the mass. Blood tests, such as liver function tests, are also used during investigation of potential liver cancer.

Outcomes and Treatment
Left untreated, patients with HCC rarely live past one year, with many patients succumbing to HCC within six months. HCC has a low survival rate overall, with the best outcomes (five-year survival rates) for those who are able to have the portion of the liver that is affected by HCC removed.

There are a number of available treatments for HCC, and treatment varies depending on the liver’s condition, location and size of the tumors, and the individual’s health and age.

Surgery is the traditional method of dealing with cancer. Surgery is possible either when the cancer is limited in size with significant amounts of healthy liver available or when the cancer is limited only to the liver and the individual is a candidate for liver transplant. Liver transplant is not common due to scarcity of livers for transplant and, in the cases of hepatitis, the risk of infection of the donor liver.

Other treatments have been used with various rates of success. These include chemotherapy (the use of chemicals introduced to the bloodstream to destroy cancer cells), radiation therapy (the use of targeted, high-intensity energy from outside the
body through the skin to the location of the tumor to kill cancer cells), cryosurgery (the use of extreme cold to freeze and destroy tumor cells), radiofrequency ablation (the use of heat to destroy tumor cells), and ethanol injection (injection of alcohol into the tumor to destroy tumor cells).

Prevention of Hepatocellular Carcinoma
Prevention and treatment can lower the rate of HCC. Vaccination is possible for hepatitis B virus, though no vaccines are available for hepatitis C. Proper hygiene to prevent transmission through bodily fluids is important in preventing hepatitis, though new antivirals hold the most promise of reducing the number of chronic hepatitis cases. Education on proper hygiene, proper screening of blood products, and early intervention with those with heavy alcohol use, autoimmune disease, and other risk factors are also important in terms of reducing the number of HCC cases.

Antiviral medications show promise in treating hepatitis. Effective antiviral medications have the ability to prevent cirrhosis, leading to fewer cases of HCC, and will be helpful in preventing re-infection in transplant scenarios.

Conclusion
HCC is a primary cancer that usually results from cirrhosis of the liver, most often from chronic hepatitis B or C virus infection. There are a number of treatments available for HCC, and prevention is a key in lowering the number of HCC cases. Vaccination and new antiviral medications hold promise in lowering the number of HCC cases and deaths.

Bridget Lepore
Kean University

See Also: Hepatitis B; Hepatitis C; Hepatocellular (Liver) Cancer, Childhood (Primary).

Further Readings


Hepatocellular (Liver) Cancer, Childhood (Primary)

Hepatocellular carcinoma (HCC), commonly referred to as liver cancer, is a very rare form of liver cancer in children. HCC is a primary cancer that occurs in the liver, primary meaning it originates from the affected organ and is able to metastasize (or spread) to other organs. HCC is one of the leading causes of cancer-related death in adults worldwide; however, HCC is very rarely diagnosed in children, and when found in children, the causes are often different than those in adult cases.

Prevalence and Outcomes
HCC is a very rare cancer in children, with most cases diagnosed in older children and adolescents. Current estimates regarding the prevalence of hepatocellular carcinoma in children and adolescents is approximately 0.5 cases per million.

The prognosis for children with hepatocellular carcinoma is poor due to both tendency toward late diagnosis and the complications due to underlying medical conditions or disease. Surgery is the most effective of treatments, with full remission most likely to be possible in those who have small tumors and successful removal of either the tumor or entire liver followed by a liver transplant.

Causes and Risk Factors
In adults, HCC commonly develops as a result of cirrhosis, or scarring, of the liver. In children and teens, however, HCC is often due to other conditions. Childhood risk factors for developing hepatocellular liver cancer include genetic conditions, liver abnormalities, and disease, as well as infection with the hepatitis B or C virus.

Genetics, specifically inborn errors of metabolism, increase the risk of HCC. Inborn errors of metabolism are conditions, present from birth, where an individual is not able to break down components
of food (usually due to an enzyme deficiency), leading to a buildup of that component, which affects the liver. Some inborn errors of metabolism that increase the risk of HCC include alpha-1 antitrypsin deficiency, hereditary tyrosimia, Gaucher’s disease, and urea cycle defects. Liver abnormalities and diseases, including biliary atresia (a malformation of the bile ducts, which leads to liver damage), also increase the risk of hepatocellular carcinoma.

Conditions that cause severe iron overload or require frequent blood transfusion may also contribute to the development of HCC. Exposure to the hepatitis B virus or hepatitis C virus at a very early age is related to the development of HCC. Hepatitis B is more likely to be related to development of HCC in children than hepatitis C, which typically takes a longer time frame for HCC to develop. Although the hepatitis virus usually progresses slowly in individuals with chronic infection, the earlier that a person is infected, the higher the risk is of developing HCC. Children who contract hepatitis B or C virus at extremely young ages are more likely to develop chronic hepatitis B or C and HCC in childhood or adulthood.

Symptoms and Detection
Symptoms of HCC may be nonspecific and can result in late diagnosis. Symptoms include unintentional weight loss, loss of appetite, upper abdominal swelling and pain, nausea and vomiting, general weakness and fatigue, white chalky stools, and jaundice. HCC is diagnosed through imaging, such as X-rays, ultrasounds, computerized tomography (CT) scans, or magnetic resonance imaging (MRI) followed by biopsy to determine the nature of the mass. Blood tests, such as liver function tests, are also used during investigation of potential liver cancer.

Treatment
Left untreated, patients with HCC rarely live past one year, with many patients succumbing to HCC within six months. HCC has a low survival rate overall, with the best outcomes (five-year survival rates) for those who are able to have the portion of the liver that is affected by HCC removed. Many cases of HCC require treatment before surgery in order to limit the size of the tumors in order to have the best chance at removal.

There are a number of available treatments for HCC, though surgery is standard for children with HCC, typically in combination with other methods. Surgery is possible either when the cancer is limited in size with significant amounts of healthy liver available or when the cancer is limited only to the liver and the individual is a candidate for liver transplant.

Other treatments have been used with various rates of success. These include chemotherapy (the use of chemicals, introduced to the bloodstream to destroy cancer cells), radiation therapy (the use of targeted, high-intensity energy from outside the body through the skin to the location of the tumor to kill cancer cells), cryosurgery (the use of extreme cold to freeze and destroy tumor cells), radiofrequency ablation (the use of heat to destroy tumor cells), and ethanol injection (injection of alcohol into the tumor to destroy tumor cells).

Early Detection of Hepatocellular Carcinoma
Frequent screening of high-risk children is key for early detection and treatment of HCC in children. Children who are at high risk of developing hepatocellular carcinoma due to chronic disease that affects the liver, liver abnormalities, or genetic issues such as inborn errors of metabolism require frequently monitoring and screening to ensure early diagnosis and proper treatment.

Vaccination against the hepatitis B virus is suggested for children in order to lower the chances of contracting it. There is no vaccine currently available for the hepatitis C virus; however, new antiviral medication shows promise in lowering the number of children who contract chronic hepatitis C virus.

Conclusion
Childhood HCC is a very rare primary cancer that can result from genetic issues (most commonly inborn errors of metabolism), liver abnormalities and diseases, or infections that affect the liver such as the hepatitis B or C virus. Surgery is the typical treatment for children with HCC. HCC in children differs from adults in that most cases arise from conditions other than cirrhosis (scarring) of the liver. Vaccination and antiviral therapy have shown promise in reducing the number of children with HCC due to the hepatitis B or C virus.
See Also: Hepatitis B; Hepatitis C; Hepatocellular (Liver) Cancer, Adult (Primary).

Further Readings

Herbert Irving Comprehensive Cancer Center

The Herbert Irving Comprehensive Cancer Center (HICCC) was created in 1911. It was initially named the Institute for Cancer Research. The center at Columbia University was designated as a National Cancer Institute (NCI) cancer center in 1972, and it was upgraded to the status of comprehensive in 1979. HICCC conducts basic research, clinical research, and research based on population demographics as well as providing patient care.

The center’s main objective is to better comprehend the biology of cancer, how it spreads, and what preventative measures might be used to lessen the occurrence of the disease. This research is then put into practice by designing procedures, therapies, and prevention education. Their aim is to reduce the incidence of cancer progression as well as making the quality of life better for cancer sufferers. The HICCC helps to alleviate some of the problems related to cancer and cancer treatment through scientifically improving methods and collaborating with multiple disciplines.

HICCC’s research is split between three main divisions: the Basic Science Division, the Disease-Specific Division, and the Population Science Division. These different divisions focus on different facets of cancer, from its cellular construction to its prevalence among different demographics. In addition to this, the HICCC has taken measures to include underrepresented ethnicities and races in its research.

The Basic Science Division houses research into topics such as cancer genetics and cancer regulatory networks. Essentially, this division seeks to understand the molecular and cellular reactions that cause cancer to develop and spread. Research in this division delves into genetics and epigenetics of cell division and the biological reactions that occur in it, the stability of genes, and what part genetics plays in cancer.

The Disease-Specific Division includes programs researching breast cancer, malignancy and development of lymphoid cancer, neuro-oncology, and prostate cancer. Cancers in each system of the body have different characteristics that require different treatment and different challenges in diagnosis. This division takes a look at the individual cancers and researches them in depth.

The Population Science Division looks into cancer epidemiology alongside prevention, disparities, and control. This division explores cancer as it relates to populations and finding patterns that indicate cause-and-effect relationships. They apply statistics to find these correlations. When the relationships are found, more knowledge about prevention can be gleaned from the data.

Currently, HICCC works with the Clinical Protocol & Data Management (CPDM) Office. The CPDM serves a managerial function. It coordinates and reports on the clinical trials of the center, wherever the study is taking place. They have the infrastructure and the ability to oversee HICCC’s clinical research program. The services this office performs include prioritization of clinical trials, screening and following up with patients, identifying individuals for the study, and regulating other clinical research items.

HICCC is in the Washington Heights area of New York City. This area has more people of differing racial and ethnic genealogy than most places in the city. This positioning allowed the center to add three additional programs to their offerings. The Research Recruitment and Minority Outreach program brought people into the trial who have been underrepresented in research. The Columbia University Screening and the Women at Risk programs were both founded and used to educate and provide services related to breast cancer to populations who were statistically more at high risk of developing the disease.
The center also provides training programs in a partnership with the university. The curriculum includes basic lab research, epidemiology, clinical science, and public health. The focuses of these programs are cancer biology, pediatric and adult oncology and hematology, and environmental health and epidemiology. As the HICCC provides support for cancer research, the infrastructure already exists for the university students to utilize.

Membership with HICCC is reviewed and renewed each year based on the required characteristics of membership. Members are expected to benefit the center through the following: collaborating with the center's other investigators; offering support in achieving the center's main mission, goals, and priorities; and providing the center with an annual report of research activity. In exchange for this, members are able to utilize the center's shared resources; apply for research funding and developmental aid; and participate in member seminars, special events, and retreats. To date, the HICCC has more than 200 members across six different schools.

The HICCC provides access to shared resources for use by its members to facilitate cancer research. These shared resources include everything from biostatistics and genomics technology to small animal imaging and transgenic mice. Biostatistics is paramount in cancer investigating, and the HICCC provides the infrastructure to do so with the help of a biostatistician. They provide statistical consulting and collaboration in the design, procedures, and interpretation of experiments. Genomics technology provides the infrastructure and knowledge to compare genetic sequences, and transgenic mice are genetically modified for testing.

Some doctors in Columbia Urology are also faculty with the HICCC. Here, they are able to design and complete research related to prostate cancer treatment. This includes clinical trials on new and potentially life-saving treatments for both aggressive and less-aggressive types of cancer. These doctors generally collaborate with other departments and other cancer centers nationwide. The ultimate goal is the improvement of diagnostic accuracy and effectiveness of treatment.

There are more than 200 researchers working with the HICCC. The NCI's funding for members is more than $33 million, but researchers at the cancer center have been awarded more than $95 million in cancer research funding from their peers. Their activity focuses on various facets of cancer research, from cellular mechanisms and interaction with tissue to the statistics of cancer occurrence across different population demographics. The researchers may work with vastly different aspects of cancer, but they all have the common goals of reducing the occurrence of cancer, reducing the progression of tumors, and creating a better quality of treatment and life for cancer patients.

The Herbert Irving Comprehensive Cancer Center facilitates research into cancer on the genetic as well as the social front. Every different facet of the disease that the center researches or provides the means for other organizations to research brings more innovation, new techniques and therapies, and overall improvement in the quality of treatment and quality of life of the patients. From genetically modified lab mice to exploring the structure of genes, the HICCC supports cancer research as well as cancer researchers.

Michael Fox
Independent Scholar

See Also: National Cancer Institute; Ohio State University Comprehensive Cancer Center; Prostate Cancer; Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins.

Further Readings

Herbicide

An herbicide is a type of pesticide used for preventing, reducing, or destroying unwanted weeds and plants. Approximately 10 percent of all plant species are weeds; of these, nearly 10 percent plague cultivated crops worldwide. Herbicides are some of the most commonly used pesticides in the world and account for billions of dollars in pesticide sales.
Glyphosate, atrazine, and 2,4-dichlorophenoxyacetic acid (2,4-D) are the top three most frequently applied herbicides on agricultural land in the United States. This entry provides an overview of the history of herbicide development and ways that these substances have been used in agriculture; sources and routes of human exposure; environmental and human health effects; and regulatory strategies to prevent exposure.

**History of Herbicide Development and Uses**

Weed control was initially conducted by mechanical or manual means such as cultivation, hoeing, and hand pulling. These labor-intensive methods were gradually replaced by simple chemicals used as general herbicides, including inorganic compounds such as brine and a mixture of salt and ashes. In the late 1800s, copper sulfate was used specifically to kill weeds in grain fields. Sodium arsenite solutions were also developed and used as the standard herbicide until 1960. Although some inorganic herbicides continue to be used, most were eventually restricted by the U.S. Environmental Protection Agency because of their persistence in soil. This contributed to the development of organic, synthetic herbicides that are now heavily used where intensive and highly mechanized agriculture is practiced (e.g., North America, western Europe, Latin America, Japan, and Australia).

Herbicides can be classified several ways. In general, selective herbicides kill weeds without harming the crop or plant of interest. Truly selective herbicides are active only against a certain species of plants but not against others. On the other hand, nonselective herbicides kill all vegetation. The placement, dosage, and timing of herbicide application are important determinants of selectivity. Herbicides can also be characterized on the basis of contact (surfaces) versus translocation (distant plant tissues), timing (preplanting, preemergence, and postemergence), area covered (band, broadcast, spot treatments, or directed spraying), and chemical groups.

There are more than a dozen major chemical classes of herbicides including phenoxyxs, organophosphates, triazines, carbamates, and arsenicals. The first of the phenoxy herbicides was 2,4-D, which was introduced in 1944 as a selective agent that could be translocated throughout the plant. In agriculture, 2,4-D is applied on cereal, grain crops, and sugarcane. Other phenoxy herbicides include 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) and 2-methyl-4-chlorophenoxyacetic acid (MCPA). Some nonagricultural uses of phenoxy herbicides are for clearing weeds on rights-of-way, on turf and lawns, and in forest conservation programs. 2,4-D and 2,4,5-T were also used in the Vietnam War as defoliants. Glyphosate, a phosphorous-based herbicide, is the most widely used pesticide in the United States and in the world. Atrazine, a common triazine herbicide, is mainly applied on corn, sorghum, and sugarcane to control broadleaf and grassy weeds in the United States. Carbaryl is a type of carbamate herbicide that is popular in Canada for lawn use. Organic arsenical agents, such as monosodium methanearsonate (MSMA) and disodium methanearsonate (DSMA), were used for many purposes but are gradually being phased out, eliminated, or prohibited as they transform over time to a more toxic, inorganic form of arsenic in soil that can migrate to drinking water sources.

In the mid-1990s, genetically modified or biologically engineered seeds were designed to be tolerant to certain herbicides. The purpose of this development was to allow for broad, over-the-top application of herbicides while minimizing damage to crops of interest. For example, crops tolerant to glyphosate are able to be sprayed with this chemical. Soy was the first type of crop to be grown in this manner, followed by alfalfa, corn, cotton, spring canola, sugar beets, rice, wheat, and winter canola.

**Sources and Routes of Human Exposure**

Herbicides are used extensively in agriculture and outside of farms. Occupational exposure to herbicides in agricultural environments may occur from loading, mixing, spraying, applying, and harvesting treated crops. Herbicides may be sprayed on foliage or applied directly into soil, among other application methods. Other important occupationally exposed populations are golf course workers who spray large areas of grassy turf as well as pesticide applicators who clear rights-of-way, roadsides, or train track brush. Herbicide manufacturing workers may also be exposed to chemicals individually and in combination, their by-products, contaminants, and inert agents that are part of herbicide formulations.

Environmental herbicide exposure can occur in public, home and garden settings, and daily
activities. Children may be exposed from playing in schools, parks, and home lawns and gardens. Children and youth who are part of farm families may also be exposed to herbicides. This type of exposure, called para-occupational exposure, is defined as exposure that occurs to people living in households where occupationally exposed workers reside but who are not themselves occupationally exposed. Exposure can also arise through drift of pesticide mists among those who live in close proximity to agricultural areas, golf courses, or other large areas where herbicides are sprayed.

As with all pesticide exposures, human contact with herbicides may occur through skin, inhalation, or oral ingestion. Workers can encounter dermal exposure and inhale fine mist particles from spraying. Children's high level of hand-to-mouth activity increases the likelihood of oral ingestion of residues, and both children and adults can consume herbicides through dietary sources. Herbicides can also leech or run off from soil into ground and drinking water.

**Environmental and Human Health Effects**

The health impacts of herbicides have been studied for several decades and remain an area of active research. Environmental effects vary and depend on factors such as degree of toxicity in different species, persistence or half-life, volatility and the potential for runoff or leaching, and the dose and number of applications usually required for the pesticide to be effective against target species. Herbicides may damage more than just weeds, especially for nonselective agents that are applied in close proximity to nontarget vegetation. Generally, insecticides are more toxic to wildlife than herbicides. However, some forms of herbicides (like certain 2,4-D esters) can be toxic to different organisms (e.g., fish and other aquatic life).

Herbicide resistance is a challenging issue that has emerged in recent years. According to the Ontario Ministry of Food, Agriculture, and Rural Affairs, herbicide resistance is “the genetic capacity of a weed population to survive an herbicide treatment that, under normal conditions, would effectively control that weed population.” There are almost 250 herbicide-resistant weedy biotypes in 47 countries worldwide, and these numbers are steadily growing. Resistance can be reduced, but not prevented entirely, by practices such as using herbicides only when necessary and rotating herbicides among herbicide groups.

In the province of Ontario, Canada, the Ontario Independent Fact Finding Panel on 2,4,5-T conducted a comprehensive study of 2,4,5-T uses by Ontario government ministries and agencies and if exposure may have impacts on workers’ health. The panel found that exposures exceeded the benchmark level for some individual employees involved in ground, backpack, and aerial mixing or loading and application or flagging. Workers whose exposures were much higher than the benchmark were almost all occupationally exposed groups, with the highest levels of exposure to 2,3,7,8-TCDD, a 2,4,5-T contaminant. The panel concluded that workers’ health could be affected but that the risk of developing diseases as a result of 2,4,5-T or 2,3,7,8-TCDD exposure for an individual would likely be very low. Studies of Vietnam War veterans exposed to herbicides and their contaminants

Nearly 50 percent of the world’s labor force is engaged in agriculture and most are exposed to herbicides. As with all pesticide exposures, human contact with herbicides may occur through skin, inhalation, or oral ingestion. (Photos.com)
Herbicides demonstrated associations with heart disease, Parkinson's disease, and numerous cancers, including soft tissue sarcoma, non-Hodgkin's lymphoma, and chronic lymphocytic leukemia.

The International Agency for Research on Cancer (IARC) has thoroughly evaluated the human and animal evidence of carcinogenicity for some herbicides, including 2,4-D, 2,4,5-T, dicamba, MCPA, MCPB, dichlorprop, and mecoprop. These were all classified by the IARC as Group 2B, possibly carcinogenic to humans. However, these assessments were done in the late 1980s and early 1990s. Epidemiological studies published since then add valuable information to these evaluations. For instance, licensed pesticide applicators exposed to glyphosate in the U.S. Agricultural Health Study did not have associations with cancer incidence overall or most cancer subtypes studied; however, there was a suggestive link to multiple myeloma. A Canadian study found a significantly elevated risk of non-Hodgkin's lymphoma among men who reported ever using 2,4-D. These population-based studies are often hampered by small numbers of cancer cases. Follow-up in larger groups of exposed cases is warranted.

Regulations and Exposure Prevention
Concerns about the known or potentially harmful health effects of herbicides in the environment and humans (specifically, children) have prompted numerous jurisdictions worldwide to introduce cosmetic pesticide bans with varying levels of protection on public and private property. In Canada, ornamental pesticide bans began in the early 1990s and now exist in more than 170 cities and towns. For instance, in 2009, the province of Ontario followed the city of Toronto's lead and passed the Cosmetic Pesticides Ban, which prohibits the use of pesticides for aesthetic weed control on lawns across the province.

The city of Toronto evaluated the effectiveness of their pesticide bylaw and found that it improved health and environmental protection by reducing pesticide use and motivating many residents and companies to take more sustainable approaches to lawn and garden care. Its success may be due to an implementation strategy based on public education and enforcement, phased-in penalties, and ongoing review and adaptation.

Strong collaboration with other city divisions was also crucial. In the United States, the city of Takoma Park, Maryland, recently passed a law that generally restricts the use of cosmetic lawn pesticides on private and public property. Pesticides have been banned on school and day care center grounds in New York and Connecticut, and other states have adopted or are considering adopting similar measures to protect children's health.

Alternatives to synthetic herbicides can be used to prevent and control weeds with different degrees of effectiveness. Manual weed removal may be possible in small areas. Natural chemicals and plant-based oils can act as contact herbicides. Larger plots of land could benefit from wholly or partially exercising other options such as integrated pest management and organic agriculture. These and other methods may also reduce crop damage caused by synthetic herbicides, prevent leaching and runoff, and help avert resistance.

Conclusion
Herbicides and associated technologies to prevent and control weeds have evolved greatly over time. Beginning with manual removal, today's methods of weed management integrate innovations in chemistry and genetic engineering with long-standing traditions such as integrated pest management. Nevertheless, herbicide exposure is associated with numerous known and suspected ecological and human health effects. Exposure prevention is a key guiding principle in herbicide bans and related legislation. Further research is needed to fully understand herbicide health effects and the best measures for reducing exposure.

Manisha Pahwa
Occupational Cancer Research Centre
Ann Del Bianco
York University

See Also: DDT; Insecticides; Pesticides; Water Treatment.

Further Readings
History of Cancer

The history of cancer is a story of theories about the causes and effects of the disease as well as of the continuing specific discoveries regarding the disease’s structure, treatments, and methods for diagnosis. Furthermore, this history is also embedded in the more general advances within medicine, such as new methods concerning surgery and discoveries regarding new techniques and instruments. In such a broad sense, the history of cancer may be subdivided into distinct periods, where the first covers the relatively long ancient and medieval periods based on what we by now consider as incorrect theories about the nature of cancer.

A transitional period of theories trying to replace the ancient theories followed but was quickly replaced by a period based on the cellular theory, proposing that both normal and cancerous cells come from cells of common origin. There were a series of new techniques for diagnosis and treatments from the mid-19th century and onward. More recently, further advances within this prolonged cellular period have been made based on new insights into genetics and other scientific fields.

Cancer Before the 19th Century

Archaeologists have found human remains dating several thousand years back from which specimens have been interpreted as consistent with cancer. Such is the case of a female skull from the Bronze Age (1900–1600 B.C.E.) and Peruvian Inca skeletons from ca. 2,400 years ago. When it comes to written evidence, however, the oldest existing cases date from Egyptian papyri, such as the so-called Edwin Smith Papyrus from the 16th century B.C.E. or even earlier. It contains descriptions of eight cases of breast tumors or ulcers. These were removed using a cauterization technique; however, the writing also says that the disease had no actual treatment. Another papyrus describes that the removal of a thigh tumor should be avoided because it could be fatal for the patient in question.

More detailed descriptions exist from the Greek and Roman civilizations. The doctor Hippocrates (460–370 B.C.E.) left a number of detailed descriptions of various diseases, including descriptions of lesions that had affected skin, breasts, stomach, cervix, and rectum. He also classified these into cancers that were in an early stage and others that were “occult.” As for treating early-stage cancers, the options were to cauterize and to apply several ointments. Hippocrates is also credited with the word cancer because he used the term karknoma to describe ulcers or growths that appeared to be malignant tumors. The word means crab in the Greek language, and one interpretation is that Hippocrates might have associated the spreading forms of cancers with the shape of crab claws. Hippocrates’s theory about cancer was to persist for more than 1,300 years and was based on his overall theory of the four types of body fluid, or humors, that a human body had. These were blood, phlegm, yellow bile, and black bile. A person was healthy when the humors were balanced. An excess of the black bile humor, however, was the cause of cancer. The Roman doctor Aulus Cornelius Celsus (25 B.C.E.–50 C.E.) elaborated on the Hippocrates theory and divided cancers into different stages. He called the first stage cacoethes (malignant), and only this stage was receptive to treatment. The doctor and philosopher Claudius Galenus (130–200) introduced the Greek word onkos, meaning a bulk or a mass, for referring to a growth or a tumor that appeared to be malignant, and is thus credited as the originator of the term oncology. Within Arab medicine, there were also a series of doctors who made observations and recommendations regarding cancer, including Avicenna of Baghdad (980–1037), who observed that cancer may destroy neighboring tissues.

Approaching the 17th century, there were a number of theories contesting the humor theory, including hypotheses proposed by Zacetus
Lusitani (1575–1642) and Nicholas Tulp (1593–1674), who published their hypotheses in 1649 and 1652, respectively, that cancer was contagious based on observations of breast cancer cases within the same household. John Hunter (1728–1793) was the first to suggest possible predispositions to cancer like, for example, age, heredity, and even perhaps the climate. Xavier Bichat (1771–1802) contributed to scientific progress in a number of ways but is also known for his misleading theory published in 1800 proposing that blastema, a substance that he thought was formed from blood and lymphatic fluid, was the primary source of all cellular tissues. His view persevered as a universal theory on cancer during several subsequent decades.

One probable cause behind the lack of any significant progress regarding the treatment of cancer during especially the medieval period was that postmortem autopsies had been practiced on a very limited scale, mainly due to religious obstacles. Autopsies were, however, becoming more frequent by the 16th century and were part of the basis for the William Harvey (1578–1657) epoch-making treatise on blood circulation (1628). Later, the doctor and professor Giovanni Morgagni (1682–1771) focused for the first time in his 1769 treatise on the potential of systematic approaches toward pathology.

Nineteenth-Century and Early-20th-Century Breakthroughs

During the 19th century, research took advantage of the findings made possible through the use of the modern microscope. Rudolf Virchow (1821–1902) has often been called the founder of cellular pathology and contributed to the understanding of tumors through a work titled *Cellular Pathology* (1858) as well as three comprehensive, albeit unfinished, illustrated volumes published between 1863 and 1867. According to Virchow’s method, tissues that were removed by the surgeon could be examined thoroughly and a precise diagnosis of the cancer could be made. The pathological method thus provided a scientific basis for the study of cancer, and hospital staff and researchers could understand in a better way the damage that had happened to the patient as well as the options for more precise cancer surgery. This breakthrough meant in addition that a pathologist by way of using a microscope could inform about whether an operation had completely removed the tumor or not. Virchow’s cellular theory is the basis of how cancer overall is understood today, but he built his treatise in part upon some of his immediate predecessors, such as Johannes Müller. Müller developed the blastema theory regarding the origin of cancer in 1838 by way of arguing that blastemas were budding cells and not lymph. He thus showed in part the way toward the understanding that cancer is made up of cells.

Incidentally, significant progress occurred within the field of general surgery techniques from about the same time as these new cellular insights became widely known. Removal of tumors had been an option from ancient times, and continued to be so, but this approach faced a crucial dilemma. During surgery, the patient might die due to loss of blood or of excruciating pain, and the simple means of anesthesia that had been available, such as opium, were of limited reliability. In 1846, John Collins Warren (1778–1856) and William T. G. Morton (1819–1868) used ether as a general anesthetic and performed a public demonstration of its effects when they removed a tumor from the jaw of a patient. Incidentally, the Japanese doctor Seishū Hanaoka (1760–1835) had performed more than 150 breast cancer operations from 1804 onward using a general anesthetic based on herbs, but this was unknown to the West due to Japan’s closure policy of the times. The Warren and Morton operation, however, became quickly known and heralded the age of modern anesthetic techniques. Furthermore, Joseph Lister (1827–1912) in Scotland applied the theories regarding germs proposed by Louis Pasteur (1822–1895) and announced in 1867 the practice of using disinfection during operations. One of the legendary surgeons of the times was William Stewart Halsted, who started to perform a radical form of operation for breast cancer in 1891. Attempting to remove all tracks of the cancer in order to avoid recurrence, Halsted removed the breast and its underlying muscles as well as the lymph nodes under the arm during his operations.

Some time after Virchow’s publications, Stephen Paget (1814–1899) proposed in 1889 a new theory, called the seed and soil theory, regarding the spreading of cancer. It was similar to theories proposed by Karl Thiersch (1822–1895), showing that cancer spreading is due to the spread of the malignant cells and not the work of some kind of unidentified fluid, and by Ernst Fuchs (1851–1930) in 1882, regarding the predisposition of an organ to
be the recipient of specific growths. Paget, however, constructed a more comprehensive theory, and it eventually turned out to constitute the foundation for theories regarding how cancers spread from one organ to another, the process of metastasis. Paget thought that metastatic tumor cells were like a kind of seed that spread throughout the body by way of the bloodstream but settled only in a "soil," an organ, which it finds compatible. Virchow himself incidentally thought, incorrectly, that some kind of chronic irritation was the cause of cancer and that cancers spread like a liquid.

The late 19th and early 20th centuries were also a period of several technological breakthroughs regarding the diagnosis and treatment of cancers. In 1895, the physicist Wilhelm Conrad Röntgen (1845–1923) discovered electromagnetic rays later known as X-rays or Röntgen rays. The first technical manual of X-ray radiology was published, and the first diagnostic radiology units were installed in European and U.S. hospitals already in 1896. Shortly thereafter, two different research groups, including Marie Sklodowska Curie (1867–1934), Pierre Curie (1859–1906), and Antoine H. Becquerel (1852–1908) discovered the radioactivity of uranium. Marie Sklodowska Curie is credited with the isolation of the highly potent radioactive substance that got the name *radium*, and the Curies used the term *radio-active* for the first time in a paper published in 1898.

Radium was thereafter introduced as a treatment for cancers, with skin cancer being the first type. In the first years and decades of therapeutic radiation, the approach was referred to as brachytherapy, meaning that radioactive material was implanted inside or next to tumors. Cancer cells thereby received radiation from a very close range. Later, the approach became refined in a number of ways, including the first electron linear accelerator designed for radiation therapy in 1943, capable of more precise targeting of tumor cells at the same time, so healthy tissue had a better chance of being left unharmed.

**Insights Into Environmental Influences Causing Cancer**

There also have been numerous developments regarding possible external factors influencing cancer in parallel with the research and experiences focusing on clinical diagnosis and treatment of patients. In a book published in 1700, Bernardino Ramazzini (1633–1714) listed a series of possible occupation-related diseases, including a virtual absence of cervical cancer, but relatively high incidence of breast cancer, among nuns. In 1761, John Hill (1716–1775) published “Cautions Against the Immoderate Use of Snuff.” Percivall Pott (1714–1788) described in 1775 how chimney sweeps suffered illness caused by soot, and Katsusaburo Yamagiwa (1863–1930) and Koichi Ichikawa (1888–1948) published in 1915 how they induced cancer in laboratory animals by applying tar to rabbit skin.

During the 1930s, clinicians began to suspect in earnest that there was a linkage between smoking and several types of cancer, and this was subsequently confirmed in 1950. Thereafter, other substances added to the list of carcinogenic substances included asbestos. Its use started to become banned in an increasing number of settings starting in the 1980s. Benzene, a chemical widely used as a solvent and once an ingredient in an after shave lotion, was discovered to be carcinogenic and became classified as such in 1987. In addition, a growing number of studies indicated a link between melanoma and excessive sun exposure (1970s–1990s), and a 2000 study linked excessive household radon exposure to lung cancer. Starting in 1998, the National Health Institute issued treatment guidelines highlighting the obesity–cancer link.

**Some Further Advances in the Treatment and Diagnosis of Cancer**

The first experimental usage of chemicals within cancer treatment used nitrogen mustard, based on wartime observations of the potential effects of the gas. Nitrogen mustard was approved by the Food and Drug Administration (FDA) on March 15, 1949, as the first chemotherapy drug approved for cancer because it was found that it kills cancer cells. It was temporarily effective in managing some cancers, but another avenue of research from about the same time proved to be a broader venture into chemotherapy. Sidney Farber (1903–1973), who was a pediatric doctor, used the substance aminopterin, based on folic acid, a kind of vitamin B. As vividly described in Siddhartha Mukherjee’s 2010 book, aminopterin was synthesized by Farber and Yellapragada Subbarow (1895–1948), and Farber subsequently used it from 1947 onward for children...
with leukemia with remarkable results. From the 1960s onward, it became common to combine two or more drugs within a combination chemotherapy approach. Furthermore, so-called adjuvant therapy, in which both chemotherapy and surgery were used in treatment, was gradually being developed as chemotherapy was expected to function in the most effective way in the cases where tumors were small. Most commonly, surgery would occur first and chemotherapy second, but chemotherapy given before surgery could also be an option in order to shrink down the tumor and allow for easier surgical removal. During the 1980s, several new types of antinausea drugs were marketed in order to alleviate the side effects of chemotherapy.

When it comes to diagnosis, Otto H. Warburg (1883–1970) had discovered already in 1929 that cancer cells use glucose at a higher rate than normal tissues. This principle lies behind the positron emission tomography (PET) scanning technique developed from the 1950s onward. The first and relatively simple version of a PET scanning device was invented in 1950, whereas the first complete scanner was invented as recently as 2001. Building on ultrasound technology developed during World War II, the University of Minnesota reported in 1952 that ultrasonic echography made it possible to distinguish between benign and malignant breast tumors. The first scanner for routine usage started operation in 1958. Geoffrey N. Hounsfield (1919–2004) developed during the 1960s several prototypes of the computed tomography (CT) scanner. CT scanning made it possible to differentiate very subtle differences in tissue densities.

The publication of the structure of DNA in 1953 had a profound impact on both the treatment and diagnosis of cancer. Renato Dulbecco (1914–2012) discovered the interaction between tumor viruses and the genetic material of cells, and he received the 1975 Nobel Prize together with Howard M. Temin (1934–1994), David Baltimore (1938–), who had shown that information in the synthesis of proteins essential to such oncogenesis could be transmitted from RNA, the nucleic acid synthesizing protein within a cell, to DNA. During the 1970s, methods for sequencing DNA were developed and laid the foundation for identifying and targeting mutated genes and DNA damage that causes cancer. Subsequently, in 1976, Michael Bishop and Harold E. Varmus discovered that different forms of cancer all arise from a common genetic mechanism involving specific genes present in normal cells, the cellular origin of the retroviral oncogenes mechanism. A series of discoveries followed, including the discovery of p53, the most frequently mutated gene in connection with cancer, in 1979, and the discovery of the C-erbB2 cancer-causing gene in mice in 1981, followed by discovery of HER2, the human version of this gene, in 1985.

In 1975, Georges J. F. Köhler (1946–1995) and César Milstein (1927–2002) discovered a technique for producing monoclonal antibodies for use against defined proteins. The first commercially available such monoclonal antibody drug was approved by the FDA in 1997 (rituximab, for treating non-Hodgkin's lymphoma). The following year, the first humanized antibody targeting a cancer-related molecular marker received FDA approval. This antibody was for the treatment of HER2-positive metastatic breast cancer. Shortly thereafter, the first drug specifically developed to target the molecular problem that causes a particular type of cancer was approved by the FDA: the 2001 approval of imatinib used in treatment of chronic myeloid leukemia. Still another important event was the 2004 approval of bevacizumab, used for the treatment of metastatic colorectal cancer. Bevacizumab is unique in that it targets the vascular endothelial growth factor (VEGF). VEGF is a factor that causes the growth or proliferation of blood vessels. The drug thereby became the first antiangiogenic agent ever approved by the FDA and is also counted as the first of a new generation of targeted drugs. It was later approved for use in the treatment of, for example, non–small cell lung cancer and breast cancer.

There are some cases where there may be a known genetic predisposition toward certain types of cancer. These include the 1990s discovery of the BRCA1 and BRCA2 genes, genes that cause some breast cancers. The first evidence that the BRCA1 gene existed was provided by the University of California Berkeley in 1990, and it was cloned by scientists at the University of Utah in 1994. The BRCA2 gene was discovered in 1994 at the Institute of Cancer Research in the UK. Other genes linked to cancers that run in families include genes related to cancers of the colon, rectum, kidney, ovary, thyroid, and pancreas and skin melanoma. Such familial cancers are far less common than spontaneous cancers, but the knowledge may be
used to identify, through genetic screening, people who have a higher risk of developing particular forms of cancer.

Terje Grønning
University of Oslo

See Also: Biologic Therapy; Chemotherapy; Future of Cancer; Natural Causes of Cancer; Radiation Therapy; Screening; Technology, New Therapies.

Further Readings

Holden Comprehensive Cancer Center at the University of Iowa

The Holden Cancer Center at the University of Iowa was established in 1980. It became the National Cancer Institute (NCI)–designated Holden Comprehensive Cancer Center in 2000 and is the only NCI-recognized cancer center in the state of Iowa. The Holden Comprehensive Cancer Center encompasses interlinking clinical services, cancer research, and cancer education. The Holden Comprehensive Cancer Center involves more than 300 faculty and physicians from more than 36 departments and six colleges across the University of Iowa campus and the University of Iowa hospitals and clinics. Research in the Holden Comprehensive Cancer Center is split broadly into six programs that include (1) Cancer Signaling and Experimental Therapeutics, (2) Cancer Immunology and Immunotherapy, (3) Free Radical Cancer Biology, (4) Tumor Imaging, (5) Cancer Epidemiology, and (6) Cancer Genomics and Cell Growth. Cancer prevention and cancer and aging represent other areas of focus for researchers in the Holden Comprehensive Cancer Center.

Each of the six programs includes faculty across many colleges and has a strong emphasis on translational research. This research is supported by significant shared resources and core facilities that include (1) Bioinformatics Core, (2) Biostatistics Core, (3) Cancer Center Support Grant, (4) Central Microscopy Research Facility, (5) Clinical Trials Support Core, (6) DNA Core, (7) Flow Cytometry Core, (8) Gene Transfer Vector Core, (9) Population Research Core, (10) Radiation and Free Radical Research Core, (11) Small Animal Imaging, (12) Tissue Procurement Core, (13) Lymphoma SPORE Grant, (14) Biospecimens, (15) Biostatistics and Bioinformatics, (16) Clinical Research, (17) High Throughput Screening Facility, (18) Large-Scale Digital Cell Analysis System, and (19) the Proteomics Core. The Holden Comprehensive Cancer Center specifically promotes interdisciplinary cancer research; provides health care related to the prevention, detection, and treatment of cancer; and educates cancer professionals and the citizens of Iowa about cancer.

As a result of this, outreach is a major component of the Holden Comprehensive Cancer Center’s activities. This includes providing cancer information to patients, families of patients, and physicians and other health care professionals. The Holden Comprehensive Cancer Center has many cancer center support groups that meet in local communities. The Holden Comprehensive Cancer Center has a strong focus on translating research advances in the laboratory to advances in patient care. One way in which the Holden Comprehensive Cancer Center achieves this is through clinical trials. The Holden Comprehensive Cancer Center offers more than 300 active clinical trials. Each trial is carefully monitored and controlled to ensure patient safety and privacy and to ensure data integrity. The Holden Comprehensive Cancer Center also incorporates significant numbers of patients in its active portfolio of phase I and phase II clinical trials.

Aliasger K. Salem
College of Pharmacy, University of Iowa

See Also: Education; National Cancer Institute; Psychosocial Care/Support.

Further Readings
Honduras

The Central American country of Honduras is bordered by the Caribbean Sea and north Pacific Ocean as well as Nicaragua, El Salvador, and Guatemala. The terrain is diverse, ranging from desert-like regions to tropical rain forest with fluctuations in climate from extreme dry and hot weather to torrential rains and flooding with cooler temperatures.

Historically, the land once was inhabited by the Mayan and Lenca tribes until the discovery of Honduras by Christopher Columbus in 1502. Spain began conquest of the territory in 1525 and succeeded in complete takeover from the native population in 1539. The Spanish empire ruled until 1821, when Honduras gained independence from Spain and became part of the Mexican empire. Honduras gained full independence in 1840.

With the original groups consisting of native tribes and the movement of the Spanish empire into the land, the mixing of people created a new heritage of native and European known as Mestizo. Currently, 90 percent of the 7.9 million population is Mestizo, with the remaining population of 2 percent black and 1 percent white.

Of the population, 60 percent live in poverty, making Honduras one of the poorest countries in Latin America. The extreme poverty can be highly attributed to Hurricane Mitch, which devastated Honduras in 1998. More than 5,000 people lost their lives, and damage ranged in the billions of dollars. This disaster placed a major burden on government funds, which led to limited health care resources. This in turn created lack of appropriate means to provide health care and poor quality of care for Hondurans.

In regard to health care in Honduras, a national public health system was established in 1959. During the first decades of the public health system, the capital city of Tegucigalpa was the sole location in which services were provided. Access to care was extremely limited for those who did not have the means or ability to travel. In the 1970s, the government extended care to San Pedro Sula; however, with the locations of both Tegucigalpa and San Pedro Sula in the northwestern part of the country, access to care was still difficult for those living in the east or south. Over the decades, the government has attempted to increase access to care; however, as of 2013, 15 percent of the population does not have access to care.

In considering the state of the health care system, a particular aspect of health care that is at a considerable deficit is that of cancer-related care. Honduras lacks the appropriate resources for the population in regard to cancer awareness, prevention strategies and programs, screening protocols and procedures, means to make a prompt diagnosis, and treatments.

In the Honduran population, cancer rates have been researched but are difficult to determine due to the lack of care and therefore lack of diagnosis. It is understood that stomach, liver, prostate, and cervical cancer have the greatest prevalence in the population. For females, cervical cancer is the leading cause of cancer-related death, while for males prostate cancer is the leading cause. The overall leading cause of cancer-related deaths in Honduras is stomach cancer.

In Honduras, the cancer survival rate is extremely low, with a five-year survival rate below 2 percent. This low survival rate most likely is due to poor awareness, lack of screening, and deficiency in early detection as well as insufficiency of funds to receive appropriate care and poor quality of treatment.

In regard to preventative measures, research of current preventative tactics demonstrates that there are some prevention policies in place. In regard to tobacco smoke, Honduras has created policies to ensure that all public places are smoke free, and health warning labels are in place on all packaging. While these policies are in place, other high-risk behaviors such as obesity and alcohol abuse do not have policies.

Currently in Honduras, there are cancer screening guidelines in place for some types of cancer. There are cervical cancer guidelines in place that recommend Pap tests every three years starting at age 30 years old. Screening coverage of the population is estimated at around 40 percent. For breast cancer, no guidelines are currently recommended,
with limited availability of mammography. For gastrointestinal cancers, no guidelines currently are in place with lack of availability to endoscopy screening. As with most aspects in health care in Honduras, much of the population does not have access to screening resources.

In regard to treatment for cancer in Honduras, as with other health care resources, treatment is difficult to access due to availability and cost. Currently, chemotherapy and radiation therapy are offered; however, affordability of these expensive treatments makes them accessible only to those with financial resources. Additionally, it is estimated that there are as few as five treatment centers in Honduras. This makes access to care difficult for those in rural and remote places.

Due to the lack of resources and poor access to care, Honduran and international organizations have recognized the ongoing deficits in cancer care and have set in place numerous initiatives with the goals of improvement in awareness, prevention programs, screening initiatives, diagnosis, and treatment.

A current Honduran organization involved in cancer initiatives is the Liga Contra el Cáncer, also known as the League Against Cancer. The League Against Cancer is composed of medical professionals and volunteers that provide care free of charge or at low cost. The organization supports a medical center located in San Pedro Sula that provides services including surgery, chemotherapy, and radiation therapy as well as psychological support for patients and families.

On an international level, the American Society of Clinical Oncology has sponsored an international initiative called Health Volunteers Overseas that facilitates cancer care to the Honduran population. Health care providers in the Health Volunteers Overseas include nurses, physicians, and treatment experts who are specialized in oncology care. These specialty professionals work alongside Honduran health care providers to train and facilitate the provision of up-to-date and quality care for patients.

Janice Marie Moreland
Nationwide Children’s Hospital

See Also: Alcohol; Cervical Cancer; Chemotherapy; Cost of Therapy; Liver Cancer, Adult (Primary); Obesity; Prostate Cancer; Radiation Therapy; Stomach (Gastric) Cancer; Tobacco Smoking.

Further Readings

Hong Kong Anti-Cancer Society

The Hong Kong Anti-Cancer Society (HKACS) is a charitable organization that was established to assist in the prevention and treatment of cancer in the southern region of China. In the era of its founding, many Hong Kong–area hospitals lacked the infrastructure to support fully those suffering from cancer and their families. Supported by private donations, as well as by the Hong Kong Council of Social Service, the Community Chest of Hong Kong, and the Union for International Cancer Control, which has its headquarters in Geneva, Switzerland, the HKACS has undertaken to increase the available medical facilities to treat cancer; to support research on cancer treatments and education about the disease’s prevention; and to provide services for cancer survivors and their families.
The Early Years of the Hong Kong Anti-Cancer Society

The HKACS was founded in March 1961 by John Hung-chiu Ho, a highly respected radiologist in the city’s medical community. Ho received his medical training at the University of Hong Kong; after graduating in 1940, he pursued additional study in diagnostic and therapeutic radiology in the United Kingdom, as radiological and oncological sciences were not well developed in Asia at this time. During the 1950s, Ho was active in Hong Kong’s philanthropic circles, raising funds for the cancer wing at Queen Mary Hospital and launching the Queen Elizabeth Hospital’s Institute of Radiology and Oncology. His research evinced that cancer was the leading cause of death in Hong Kong and placed heavy burdens on the region’s medical centers.

Leading the charge against the spread of cancer, Ho, along with a group of cancer sufferers and Hongkongers who shared his concern about community health, established the HKACS. The concerns of the HKACS encompassed the emotional and physical well-being of those afflicted with the disease. Since its early years, the HKACS has sponsored workshops, exhibitions, talks, and other activities to educate the citizenry of Hong Kong on cancer prevention. In addition, it has disseminated information in the form of printed literature, electronic media, and public talks on lifestyle choices that minimize the risk of cancer. Given the link between common forms of cancer in southern China and the consuming of preserved, salted fish, much of the HKACS’s work has centered on nutrition and dietary habits.

In 1966, the HKACS began raising funds for the region’s first medical center devoted specifically to cancer treatments; with the charity’s gift of HK$2.65 million and the political support of Sir David Trench, who was the colonial governor of Hong Kong from 1964 to 1971, Nam Long Hospital opened with 120 beds in 1967. By 1978, the society had increased the number of beds by 33 percent. The HKACS continued to raise money for Nam Long Hospital through the 2010s, even after the Hong Kong government assumed administrative control over the formerly private medical center.

Ho’s contribution to the field of radiology continued after his tenure at the helm of the HKACS began; during the late 1970s, he published a series of journal articles on the causal relationship between infants’ diets and nasopharyngeal carcinoma, which was especially predominant in that part of Asia. The society applied Ho’s research and made combating nasopharyngeal carcinoma part of its platform.

The Hong Kong Jockey Club Charities, which have played a role in the city’s philanthropic community since 1884, have partnered closely with the HKACS since its founding, providing financial support for outreach activities to cancer survivors. Since the 1960s, the HKACS has received more than HK$110 million from the Hong Kong Jockey Club Charities in support of Nam Long Hospital alone. In addition, the Hong Kong Jockey Club Charities have sponsored the integration of Chinese and Western medical treatments for sufferers of cancer.

The Hong Kong Anti-Cancer Society in the 21st Century

Ho led the organization from its founding until his retirement in 2000. Subsequent senior leadership of the HKACS also had close ties to the medical or social welfare fields: Dr. Y. F. Poon, a noted radiologist who has published numerous journal articles on nasopharyngeal carcinoma, served as chairman for the year after Ho’s retirement; Dr. Leong Che Hung, who had helped establish the Hong Kong Academy of Medicine and chaired the Hong Kong AIDS Foundation, the Advisory Committee on Nursing for Hong Kong, and the Hong Kong Hepatitis Research Foundation, was Poon’s immediate successor; and Patricia Chu Yeung Pak-Yu, who became chairperson in 2012, previously had served as deputy director of Hong Kong’s Social Welfare Department as well as the chairperson of the Social Workers Registration Board.

The HKACS has partnered closely with other community organizations that share its mission of eradicating cancer, including the Hong Kong Cancer Fund, the Children’s Cancer Foundation, the Hong Kong Bone Marrow Donor Registry, and the Cancer Crusade Angel’s Service Society of Hong Kong. In 2009, in collaboration with the Hong Kong Baptist University, the HKACS opened the Cancer Rehabilitation Center, which was designed for both inpatient and outpatient care.

By 2014, the HKACS was headquartered in the Wong Chuk Hang district of the city. Under its administrative structure, the responsibilities for programmatic activities have been subdivided among four different committees: the betterment fund subcommittee, which directly supplies cancer...
patients with financial assistance; the detection and prevention subcommittee, which assesses risks of developing cancer and offers consultations; the cancer research subcommittee, which administers more than HK$350,000 annually for competitive research grants on nasopharyngeal carcinoma and female lung cancer; and the cancer education subcommittee, which offers programming on both the prevention and management of the disease.

Leon James Bynum
Columbia University

See Also: Asian Diet; Australia; China.

Further Readings
Fielding, Richard and Cecilia Lai-wan Chan, eds. Psychosocial Oncology and Palliative Care in Hong Kong: The First Decade. Hong Kong: Hong Kong University Press, 2011.
Topley, Marjorie. Cantonese Society in Hong Kong and Singapore: Gender, Religion, Medicine, and Money. Hong Kong: Hong Kong University Press, 2011.

Hospice Care

Over the past 40 years, hospice care has become an integral part of the cancer continuum by improving the quality of life of patients and their families living with advanced cancer. This entry provides a succinct overview of hospice services, a brief history of the development of hospice care, an explanation of the relationship between hospice and palliative care, and a description of hospice care in the context of oncology; this entry concludes with comments on pervasive misconceptions about hospice care.

Hospice can be thought of as both a philosophy of care and a defined component of the health care delivery system. Understood as a philosophy, hospice holds paramount concepts of patient autonomy, enriched quality of life, respect, dignity and compassion for the dying, and effective bereavement. Moreover, hospice is a holistic approach to caring for the dying addressing the biological, psychological, social, and spiritual needs of the patient and family in order to promote living fully through the final stage of life.

As a defined component of the health care delivery system, hospice programs are designed for patients with a life-limiting illness whose physicians have determined life expectancy is less than six months if the disease takes its expected course. Patients who meet the eligibility criteria for admission to hospice also choose to forgo curative or life-prolonging treatments in order to focus on maximizing comfort and enhancing quality of life. Hospice programs must provide services from an interdisciplinary team of specially trained medical professionals, medications, medical equipment, and supplies needed for the care of the terminal diagnosis and bereavement support to the surviving family. Surveys indicate that people prefer to die at home, surrounded by friends and family, free of pain, and with as much control as possible. Hospice programs respond to those wishes.

Hospice services are provided wherever a patient resides, which can include private residences, nursing homes, assisted-living facilities, hospitals, and hospice in-patient units used for acute symptom management and respite care. Most hospice care occurs at a patient’s residence.

In the United States, hospice services are covered by Medicare, Medicaid in most states, and many private insurance companies. Any person can make a referral to a hospice program. While this is typical of a physician or hospital, referrals also can come from a patient, the family, a friend, or a spiritual care provider.

Core Hospice Services

Hospice services include support by a team of specially trained medical professionals who work with a patient and the family to discuss values, identify goals of medical care, and then design treatments, therapies, and interventions to maximize the patient’s quality of life. Because there are many sources of suffering or distress for an individual with a terminal illness, hospice care requires expertise from an interdisciplinary team. The hospice team includes but is not limited to the following.

Physicians. Hospice physicians bring expertise and specialization in pain and symptom management, in educating around disease progression, and in
facilitating goals of care conversations. Hospice medical directors are responsible for decisions around eligibility for hospice services as well as management of the plan of care for each patient. The American Board of Medical Specialties approved hospice and palliative medicine as a recognized subspecialty in 2006. Much as an oncologist brings specialization in the understanding and treatment of individuals with cancer, hospice and palliative medicine physicians bring expertise and specialization in pain and symptom management to individuals living with serious illness.

Nurses. Hospice nurses serve multiple roles for patients and families. Nurses work to implement the plan of care and work with physicians to ensure patients receive adequate relief of pain and suffering. Nurses provide education to the patient and caregiver on disease progression, medications management, supplies, medical equipment, and patient care issues. A patient and family will have access to hospice nurses by phone at all times. The hospice nurse will provide ongoing medical and physical assessments to ensure all the patient's needs are being met. Most hospice nurses have advanced certification in hospice and palliative care.

Social Workers. Hospice social workers oversee the psychosocial support needed by the patient and family. This support can take many forms, including but not limited to counseling, connection to available community resources, assistance with goals of care conversations, procuring volunteer support, assisting patients and families in navigating the health care delivery system, and education on grief and bereavement for the family. Social workers also can assist patients with health care insurance questions and funeral planning.

Spiritual Care Providers. There is variability among hospice providers on the level of spiritual care support provided to patients and families. Most hospice providers employ health care chaplains who assist patients in exploring the spiritual dimensions of their lives, facilitate discussions about connectedness with the transcendent, and address sources of spiritual distress. Hospice chaplains also can pray with patients, read sacred texts to patients, connect patients to a faith community, and officiate funerals. Chaplains do not represent any particular faith tradition or denomination while working in their professional role. Some hospice programs provide spiritual care with the use of volunteer chaplains or ministers.

Certified Nursing Assistants. Certified nursing assistants provide assistance with activities of daily living for hospice patients such as bathing, changing, and dressing. Additionally, certified nursing assistants are specially trained to assist patients in a way that preserves respect and dignity.

Bereavement Support. Hospice providers are required to offer bereavement support to the surviving family for the first 13 months after a patient dies. There is variability among hospice providers in the scope of bereavement services available. While all hospice providers offer grief education, some hospice organizations employ bereavement counselors who provide individual and group counseling services. Bereavement counselors may begin supporting the patient and family prior to death if any members of the family are experiencing anticipatory grief.

Volunteers. Volunteers are a mandated component of hospice care. Hospice providers train community volunteers to provide practical support to patients and families. Volunteer services typically include respite care for the caregiver, companionship visits for the patient, and transportation services. Volunteers also provide administrative support to hospice programs.

Other Providers. Pharmacists, speech therapists, physical therapists, occupational therapists, and dieticians may also be involved in the care of the patient should the patient's condition or goals of care require them.

The hospice team is designed to address all potential sources of pain and distress a patient and family may experience. This team of highly trained medical professionals works with the patient and family to identify goals for care and to develop a comprehensive end-of-life plan of care. Provision of services and presence of each discipline in the home depends on patient and family needs and preferences. The hospice team will update the plan of care as the patient's condition changes and meet every 15 days to formally discuss the plan of care.
In addition to the interdisciplinary team, hospice services also include provision of all medications, medical supplies, and medical equipment related to the terminal diagnosis. In short, hospice providers are experts at providing quality physical, psychosocial, and spiritual care to individuals and their families in the late stage of serious illness.

The hospice approach to caring for individuals with terminal illness has improved end-of-life care. There is a large body of evidence that demonstrates the hospice approach to caring for individuals with a terminal illness results in better pain and symptom management, enhanced quality of life, and improved caregiver well-being.

A Brief History of Hospice Care
Dame Cicely Saunders, a nurse, social worker, and physician in London, England, is widely recognized as the founder of modern-day hospice. Saunders started work to improve care for the terminally ill in 1948 because she believed the medical orthodoxy at the time was doing an inadequate job caring for the dying. Saunders witnessed patients dying in hospitals in both pain and isolation. Saunders's prescription for a better death was specialized medical care from an interdisciplinary team whose members could address a patient's total pain. She started St. Christopher's hospice in the United Kingdom in 1967, caring for almost exclusively patients with cancer diagnoses. For Saunders, it was individuals with advanced cancer diagnoses who could benefit most from the services of a hospice team.

The hospice approach to caring for the dying spread from Europe to Canada and then to the United States, with Connecticut Hospice opening in 1974. From 1974 to 1982, hospice programs developed around the United States. Many programs during this time were started by community volunteers, and the sustainability of the programs relied on donations. During this time, almost all patients served by hospice programs had diagnoses of cancer. In 1982, the United States Congress created the Medicare Hospice Benefit. This benefit established coverage for hospice services, and for the first time, hospice providers had a reliable revenue stream. Since the creation of the Medicare Hospice Benefit, hospice has grown steadily. In 2012, there were an estimated 5,500 hospice programs in the United States caring for approximately 1.6 million hospice patients. As hospice has grown to serve all individuals with a terminal diagnosis, the proportion of patients with a primary diagnosis has declined to approximately 40 percent.

Hospice Care and Palliative Care: What Is the Relationship?
It is often said that all hospice care is palliative care, but not all palliative care is hospice care. While this is true, the saying does little to clarify the distinction.

Palliative care is best understood as specialized medical care for individuals with one or more serious illnesses. Palliative care is active, interdisciplinary care that aims to relieve suffering and improve quality of life for patients and their families with advanced illness.

While the descriptions of hospice and palliative care appear similar, there are important distinctions. Unlike hospice care, palliative care services are available to anyone with a serious illness in need of pain and symptom management without the hospice necessity of having a terminal prognosis. Moreover, palliative care services can be provided concurrently with curative treatments.

While there is some variability in palliative care services based on geography and setting, palliative care is a team approach, which can include a physician, nurse practitioner, nurse, social worker, and chaplain. Palliative care teams are specially trained to manage intractable pain and other bothersome symptoms that include but are not limited to physical pain, dyspnea, nausea, delirium, restlessness, and constipation. Additionally, palliative care teams bring expertise in addressing emotional and spiritual distress. Palliative care providers are experts in communicating effectively with patients and families about prognosis and facilitating family meetings aimed at defining quality of life and goals to ensure that additional treatments are concordant with a patient's values and preferences.

Most palliative care services are provided to patients while in the hospital; however, palliative care may also be available in long-term care facilities, outpatient clinics, and an individual's home. It is important for caregivers of individuals living with serious illness to ask health care providers about available palliative care services in the area.

Similar to hospice care, palliative care services have grown rapidly over the past decade. According to the Center for the Advancement for Palliative Care, more than 65 percent of hospitals had palliative care programs in 2010, a 148.5 percent increase.
over the decade. With an aging population, the need for hospice and palliative care services is expected to grow significantly.

**Hospice Care and Oncology**

Hospice has been widely demonstrated to improve the quality of life for patients living with cancer as well as the well-being of caregivers supporting individuals with cancer. Not only has hospice been shown to be excellent at pain and symptom management, but surprisingly in some instances, hospice and palliative care extend life expectancy. Most notably, Jennifer Temel, M.D., and her research team conducted a randomized, controlled trial of patients with newly diagnosed non–small cell lung cancer. One cohort received standard oncologic care, while the other cohort received standard oncologic care and support from a palliative care team. The group of patients who received support from the palliative care team had better quality of life scores, fewer depressive symptoms, and prolonged survival when compared to the group who received only the standard oncologic care. This research is one example of a large body of research that shows that hospice and palliative care improve the quality of life of the patient, enhance caregiver well-being, reduce pain and bothersome symptoms, and in some cases extend life.

Because of the compelling evidence demonstrating the value of hospice and palliative care for individuals with advanced cancer, many reputable organizations have endorsed a broader utilization of hospice and palliative care. The American Society for Clinical Oncology (ASCO) is encouraging providers working with cancer patients to engage in discussions about palliative care and treatment options. Similarly, ASCO, as part of the Choosing Wisely campaign, recommends that patients with advanced cancer for whom treatment is unlikely to provide benefit avoid anticancer therapy and focus on symptom relief and palliative care. ASCO issued a clinical opinion emphasizing the use of palliative and supportive care at the time of diagnosis of metastatic or advanced cancer, which evidence has shown can increase quality of life and, in some cases, increase survival.

In addition to ASCO’s recommendations to increase palliative care services, the Institute of Medicine identified the need to ensure individuals with advanced cancer receive end-of-life care consistent with needs, values, and preferences as a key part of high-quality care delivery.

**Misconceptions About Hospice Care**

While hospice and palliative medicine have begun to bring end-of-life care into the medical mainstream, some pervasive misconceptions around end-of-life care persist.

*Hospice is only for the last hours to days of life.* While hospice is a benefit designed for the last six months of life, the average length of stay for hospice patients in the United States is approximately 70 days. Half of patients electing the hospice benefit will only receive services for approximately two weeks, potentially limiting the patient’s and family’s ability to take full advantage of the scope of hospice services. Surveys consistently show patients and families often wish they had known about hospice services sooner.

*Hospice is a place.* While hospice can be a place in the form of a stand-alone inpatient unit, most hospice care occurs in a patient’s residence. Hospice services are available in homes, nursing homes,
Hospice care has grown dramatically in the last 40 years, and the result has been an appreciable improvement in the quality of end-of-life care. Research has demonstrated that the hospice approach to terminal illness with an interdisciplinary team supporting patient and family and addressing total pain has multiple benefits including but not limited to better pain and symptom management, increased patient quality of life, improved caregiver well-being, and important support for the bereaved. Because of the multiple benefits of the hospice approach, numerous professional medical societies have recommended a broader utilization of hospice and palliative care services for individuals with advanced cancer. With an aging population, the demand for high-quality hospice and palliative care services is expected to increase.

Hospice care has grown dramatically in the last 40 years, and the result has been an appreciable improvement in the quality of end-of-life care. Research has demonstrated that the hospice approach to terminal illness with an interdisciplinary team supporting patient and family and addressing total pain has multiple benefits including but not limited to better pain and symptom management, increased patient quality of life, improved caregiver well-being, and important support for the bereaved. Because of the multiple benefits of the hospice approach, numerous professional medical societies have recommended a broader utilization of hospice and palliative care services for individuals with advanced cancer. With an aging population, the demand for high-quality hospice and palliative care services is expected to increase.

Robert West
Salli Whisman
Hospice of the Bluegrass

See Also: Alternative Therapy: Mind, Body, and Spirit; Pain and Pain Management; Survivors of Cancer, Families of.

Further Readings
Hospitals

Although the function of the hospital as an institution for health care or as a physical place to confine marginal populations has changed throughout time, its history and tradition has about 2,500 years. We cannot approach its function ignoring the role of religion in society, the hegemonic ideas about illness and disease, or the main purposes for its existence (healing, welfare, recovery, etc.), and the degree of responsibility involved in it. The etymological origin of the word hospital is the Latin term hospes, meaning foreigner, and therefore “guest,” a person who has to be taken in in the context of a hospitable reception. It has the same origin, then, as hospitality. Hospitality concerns both host and guest. It is important to take this into consideration in order to see how this aspect has evolved, depending on historical periods or cultural scenarios.

The Origins of the Hospital: From Ancient Times to the Middle Ages

Probably the generic hospital is an abstraction, and important nuances like location, religious nature, mission, and so on need to be approached. There is no doubt that the launching of hospitals is a response to the presumed needs of a given population. Originally, there was a clear fusion between religion and medicine. For that reason, in ancient cultures, clinics were founded within the temples. That was the case in Greece—dedicated to the god Asclepius—or Egypt. People went there to find medical advice and eventual healing. In other cultures, for example, Indian, institutions for care of the ill were created about the year 400. But the most evident link between religion and medicine appears in medieval Europe, when nuns and monks from religious communities, who followed a model of monastic discipline, provided care to the ill. Hospitals were charitable guesthouses. As some authors critically point out, those institutions were instruments of hope and pious benevolence. They gave care support not only to the ill but also to the homeless, poor, vagrants, prostitutes, disabled, or presumed lunatics. As a matter of fact, traditionally stigmatized groups play a main role in medieval asylums or hospices. People did not go there to look for healing, but sometimes they were captured to be confined. Healing was not a main goal.

Modern Times

In the 16th and 17th centuries, that concept changed, and medical institutions were, if not totally, at least partially secularized in most European countries. And, definitely, from the Enlightenment on, most hospitals were considered as places for science. The high incidence of infections within hospitals, however, extended the common belief that it was a place to die. The Enlightenment meant the implementation of some new rules, for example, the rite of visiting hours for relatives and the existence of reports and mandatory prescriptions. In summary, there is a progressive professionalization of medical caregivers. Surgery is not an open spectacle for large audiences anymore but rather a part of the whole treatment process of a patient. At the same time, voluntary hospital movements began, and many medical institutions were supported by private subscriptions. It was the first step to becoming centers of innovation and teaching and not only places to provide care to the ill and to marginal populations in general.

Throughout the 19th century, it is particularly relevant because new technologies were discovered and because most hospitals were also centers of training for future professionals. Early in the 19th century in England, for instance, it was mandatory that, before becoming a doctor, the future professional had at least half a year of experience in some asylum, dispensary, or infirmary. For that reason, it was important that hospitals could offer not only a room and treatment for the patient but
also good training for doctors and nurses. Thanks to this fact, hospitals transformed into centers of study of anatomy and of experimentation. At the same time, pharmacology was totally implemented at the end of the century. Nevertheless, substances like morphine, quinine, or codeine were discovered before 1840. Treatment used to rely on a change of air together with purgation and bleeding, with the idea of clearing impurities from the body. Hospitals, at that time, were also spas or retirement houses where a combination of care and some light activity was provided. After all, the main cause of morbidity was infection; tuberculosis was endemic, and cholera, in the last decades of the century, was epidemic.

**Toward a Current Concept of Hospital**

As a consequence of all this, hospitals began to generate epidemiological mapping and measurement, especially at the end of the 19th century. Concurrently, new knowledge in histology, pathology, and microbiology, even in hygiene, was developed. The improvement of the microscope and the invention of the ophthalmoscope aided diagnosis, and surgery notably improved thanks to the application of anesthesia and antiseptic procedures. In the first years of the 20th century, after X-ray discovery, many hospitals were better equipped—this does not mean, however, that they were modern in a modern sense. All those factors simply made medical institutions less unpleasant for the ill. People with mental illnesses had their own specialized institutions for confinement and isolation. In most European countries, hospitals were built and paid for with public funds. In the United States, hospitals were operated by different administrations (federal, state, and city) but also by both for-profit and nonprofit enterprises.

At the turn of the century—and the beginning of the 20th—hospitals became more complex in their organization and also in their staff, including trained persons with technical responsibilities. The introduction of the X-ray machine meant a big step forward, but it also introduced an economic variable because radiologists had to be paid for their services. It was expensive technology. Besides, if in the first decade of the century many patients belonged to low social classes, about 20 or 25 years later, middle classes began to be patients in hospitals with the idea that medical institutions not only offered a room to stay in but were also centers for research and, somehow, for scientific advancement. From an epidemiological point of view, the most common diseases at that time, as in earlier decades, were infections of all kinds. From the point of view of clinical patterns, one of the first tests applied in most hospitals in the first two decades of the century was a urine test. Blood counts were implemented much later in common medical practice.

In the 1930s, chronic diseases, such diabetes and dental problems, were not covered by the public health system (in Western countries, including the United States), and costs had to be assumed by the patient him- or herself. The 1950s was an era of expansion, and in the 1960s most intensive care units were completely established. From that point on, the concept of hospital—and its structure—was quite similar to the hospitals of today. Now highly advanced health information systems require a highly qualified sanitary personnel, and allow accessing millions of data points and choosing the optimal (and personalized) treatment for each patient.

**Cancer Hospitals in History**

The first hospital specializing in cancer was founded in Rheims in the 18th century. It remained active for about 20 years. After that, it was forced to close because there was a general conviction that cancer could be contagious. In the mid-19th century, hospitals for cancer patients were very common in England. The first cancer hospital in New York was set up in 1884. Many of those hospitals from the end of 19th century were inspired by philanthropic motivations—more than by a real interest in the patient’s improvement or survival. X-rays and radium (both discovered at the end of the century) increased the enthusiasm of surgeons, who saw the possibility of fewer surgeries and more alternative treatment. Those factors caused a true explosion of cancer institutions at the time of World War I.

From the 1950s on, when the concept of quality of life was established, most hospitals, first in developing countries but now also a large number of hospitals in low-income regions, share a main concern about an integral treatment for cancer patients, ranging from an accurate diagnosis to systematic follow-ups or painless palliative care, including emotional support for patients and their families.

Natalia Fernández Díaz-Cabal

*Free University of Barcelona*
HPV Vaccination

The human papillomavirus (HPV) vaccination is the first primary prevention method in the fight against cervical and other cancers. The vaccine is given in three doses over six months, and it is recommended that children receive the vaccine around 11 or 12 years old. The introduction of the vaccine came with controversy over its timing and appropriateness and produced barriers to adoption. Yet, evidence is growing that it is a successful method for preventing the spread of certain kinds of HPV that cause cancer.

Background of HPV Vaccinations

Research on developing an HPV vaccine began soon after it was discovered that a significant majority of cervical cancers (and, later, penile, anal, vagina, vulva, and head and throat cancers) can be attributed to certain strands of persistent HPV infection. In fact, about 26,000 new cases of cancer each year are attributed to HPV. Specifically, researchers began focusing on the development of a vaccine against HPV types 16 and 18; about 75 percent of cervical cancer diagnoses can be attributed to persistent infections with these types of HPV.

Two HPV vaccines are currently approved for use in the United States. In 2006, the pharmaceutical company Merck received Food and Drug Administration (FDA) approval for Gardasil, the quadrivalent vaccine that targets not only HPV types 16 and 18 but also types 6 and 11, which are known to cause about 90 percent of genital warts cases. The vaccine was, at that time, licensed for use in females ages 9 to 26 years. In 2010, the FDA approved Cervarix from the pharmaceutical company GlaxoSmithKline; this vaccine was licensed for use in females ages 10 to 25. Cervarix is a bivalent vaccine and targets HPV types 16 and 18. Since that time, both Gardasil and Cervarix have been licensed for use in males ages 9 to 26 years old. Both vaccines are given in a three-dose schedule; the second dose is given two months after the first dose, and the third dose is given six months after the first dose. Despite Cervarix being available to patients, about 99 percent of the doses distributed in the United States are the quadrivalent Gardasil vaccine.

For both vaccines, the Advisory Committee on Immunization Practices, a Centers for Disease Control and Prevention (CDC)-sponsored group of medical and public health experts who offer recommendations on vaccinations in the United States, advises that the optimum age for girls and boys to receive the vaccine is at 11 or 12 years old. Early immunization is desirable so that adolescents may develop immunity before they become sexually active and exposed to HPV.

HPV vaccination is considered safe relative to other adolescent vaccines, with similar levels of adverse reactions. Common side effects reported are pain, swelling, itching, and redness at the site of the injection; nausea; dizziness; syncope; headache; and fever—these are considered nonserious adverse events. According to clinical trial and post-licensure monitoring data collected by the Vaccine Adverse Event Reporting System (VAERS), about 92 percent of the adverse events reported by those patients who received the HPV vaccine were classified as nonserious.

Barriers to Vaccination and Behavioral Barriers

Behavioral barriers and controversy over vaccination limited the early diffusion of HPV vaccination in the U.S. population.

There are several reasons why the HPV vaccine has not been adopted quickly. First, many people think young people do not need the vaccine if they are not sexually active, misunderstanding the
need to vaccinate before being exposed to HPV through sexual contact. This leads to low uptake rates (i.e., dose 1). Second, the three-dose schedule of the vaccine complicates adherence. While many people will get the first dose, it can be a challenge to get patients to return for doses two and three at the appropriate time. Third, the vaccine is relatively expensive, with each dose costing about $130 ($390 for all three doses). The vaccine is covered by health insurance, but for those who do not have coverage or who have a deductible, cost is a significant barrier. Various health education and health communication campaigns have been developed to address these barriers, including focusing on education about HPV and the need to vaccinate early and receive all three doses on time and raising awareness about low-cost or free vaccine opportunities through local health departments or through the CDC’s Vaccines for Children (VFC) program.

Public Controversy
Negative publicity about the HPV vaccine’s development and its maker’s lobbying has fueled the public’s perception that the vaccine was approved too rapidly and it might not be safe. In fact, the HPV vaccines went through the same clinical trials and licensing process as all vaccines, and it is continuously monitored for safety by VAERS. Another area of controversy concerns the disease itself—HPV is a sexually transmitted disease, so despite the benefit of preventing cancers, the vaccine is still targeting a disease that is spread through sexual contact. With the recommendation to vaccinate children as young as nine, this has led many religious and political groups to make public comments objecting to policies to require HPV vaccination for school attendance or to give children this vaccine at all. Unfortunately, this controversy has contributed to low uptake rates of the HPV vaccine.

Evidence of Effectiveness
Despite these barriers, epidemiological evidence suggests that the HPV vaccination is successful. Since its 2006 approval, the CDC reports that more than 57 million doses of the HPV vaccine have been distributed, more than 50 percent of adolescents 13 to 17 years old have received dose 1, and more than 35 percent of adolescents 13 to 17 have received all three doses. Despite these relatively low rates of vaccination, the HPV vaccination has already made a difference in HPV infection rates. Researchers with the CDC published findings that, since the introduction of the quadrivalent HPV vaccine in 2006, HPV infection (for types 16, 18, 6, and 11) has dropped by more than half in females age 14 to 19 years. Further research will most likely show rates continuing to drop, given more widespread adoption of the vaccine and with males now being vaccinated as well.

Conclusion
The HPV vaccine represents a real step in the fight against cervical and other cancers caused by certain types of HPV. Within the next few decades, the combination of HPV vaccine combined with regular Pap and HPV testing may make cervical cancer mortality extremely rare. The quadrivalent HPV vaccine also has the potential to prevent 90 percent of genital warts cases, which can cause discomfort and embarrassment to millions of Americans. The Advisory Committee on Immunization Practices (ACIP) recommendations are clear, and despite several barriers to uptake and adherence to the three-dose vaccine schedule, recent research reveals the HPV vaccine is making a difference in not only HPV infections but also cases of cancer and genital warts. Continued HPV vaccination education and promotion is needed to ensure maximum success of this prophylactic innovation.

Katharine J. Head  
*Indiana University–Purdue University Indianapolis*  
Elisia L. Cohen  
*University of Kentucky*

**See Also:** Cervical Cancer; GlaxoSmithKline (United Kingdom); Merck & Co. (United States); Vaccines.

**Further Readings**
The President’s Cancer Panel. “Accelerating HPV Vaccine Uptake: Urgency for Action to Prevent
Cancer treatment in Hungary began in the Middle Ages (5th–15th centuries). After the fall of the Roman Empire, medical knowledge was primarily preserved and practiced from existing Greek and Roman texts in monasteries. However, the medicine practiced relied on a combination of Christianity, astrology, folk remedies, and other nonempirical sources. Civilians stricken with cancer or other diseases often traveled to monasteries from surrounding towns for medical assistance.

Under Ottoman rule (1541–1699), 77 madrasas operated from the dominion’s 39 major towns, where the Koran and Islam, as well as secular subjects like medicine, were taught. The Crusades and subsequent Ottoman rule spread Eastern advances in cancer treatment through Hungary into the Renaissance period, when ancient Greek and Islamic medical texts were translated from Arabic, including Avicenna’s *The Canon of Medicine*.

The regions of Hungary under Habsburg rule (1526–1804) also continued to advance in medical treatments with the rest of central and western Europe. Several institutions of higher learning were founded, including the Jesuit Academy in Kolozsvár in 1581 and the Calvinist College of Debrecen (now the University of Debrecen) in 1531. The first medical work in Hungarian was written ca. 1577 by György Váradi Lencsés, titled *A Complete Guide to Medicine* (*Ars Medica*).

The sunset of Ottoman’s rule and the rise of the Austro-Hungarian empire brought a large multi-ethnic population under its dominion, with tensions between nationalism and cultural supremacism on one hand and ethnic diversity and a robust political environment on the other. Lectures on the history of medicine were intermittently taught in Budapest beginning from 1835. In 1753, Holy Roman Empress Maria Theresa founded what soon became the Hungarian Royal University (now University of Szeged)—including the faculty of medicine and surgery (est. 1775)—where teaching was conducted in German. Semmelweis University, the oldest medical school in Hungary, was founded in 1796.

Austrian and Hungarian physicians performed surgical procedures on cancer patients using anatomical methods and provided state-supported medical education to a multiethnic student body. This approach contrasted sharply with the Prussian approach—partially adopted in the 1870s after the Austro-Prussian War—where surgery was grounded in a more physiological paradigm (including the administration of anticancer agents), a science-oriented medical education system for the elite, and a university that functioned independently from the state.

University- and hospital-centralized treatment has remained the primary approach to comprehensive cancer care in Hungary to this day. In 1952, the National Institute of Oncology (NIO) was established by the Hungarian Ministry of Health through expansion of the Eötvös Loránd Radium and Roentgen Institute, signaling a transition from radiological to comprehensive oncology care. Working in conjunction with the on-site Oncopathological Research Institute, NIO is considered Hungary’s premier center of oncology treatment and research. NIO director-generals have held positions of prestige at the World Health Organization and Union for International Cancer Control, including Drs. János Vikol (1959–1970), Sándor Eckhardt (1971–1992), and Miklós Kásler (1992–present), who led Hungarian participation in the 2004 European Code Against Cancer.

Internationally renowned Hungarians responsible for advances in oncology medicine and research
include Ignaz Philipp Semmelweis (1818–1865, an early pioneer of antisepctic procedures), and Nobel Laureates Drs. George Charles de Hevesy (1885–1966, an early pioneer in the use of radioactive tracers to study metabolic processes) and Albert Szent-Györgyi de Nagyrápolt (1893–1986, discoverer of vitamin C). In the United States, Dr. Szent-Györgyi developed research interests in applying quantum mechanical theories to cancer biochemistry and founded the nonprofit National Foundation for Cancer Research.

Despite its modern health care system, Hungary's cancer-related mortality rate remains the poorest in Europe, with a 2012 annual mortality rate of 458 people out of 100,000 people (followed by 347 per 100,000 in Russia and Ukraine). Hungary has the world's highest mortality rate for lung cancer at 135 per 100,000 people (followed by Poland at 90 per 100,000), primarily because of heavy smoking. Semmelweis University data suggest that breast cancer, which is observed in every seventh Hungarian woman, is diagnosed at advanced stages in 35 to 40 percent of cases at first treatment.

In 2005, Hungary's leading national daily newspaper ran an award-winning article by Viktória Kun highlighting the weaknesses in Hungary's oncology services. Cancer outcomes were reportedly dependent on treatment site, with admission to these sites dependent on personal connections or "gratitude money" payments. While cancer surgeries were performed in hospitals nationwide, patients were sent home postoperatively 65 to 70 percent of the time without follow-up referral to an oncologist and were subsequently lost from the system.

Alternative oncology therapies have been advanced in Hungary. One of only two clinics licensed to perform Gerson Therapy worldwide is located near Budapest. In the 1950s, Dr. Alexander Ferenczi treated post-chemotherapy cancer patients using one kilogram of beetroot a day (now available in freeze-dried powdered form) to successfully support tumor regression. Anthocyanin is reportedly the active ingredient in this remedy. In the early 1990s, Hungarian chemist Mate Hidvegi and his colleagues developed fermented wheat germ extract (FWGE), which is fermented with baker's yeast to concentrate bioactive benzoquinones. Dr. Hidvegi later developed and patented an industrial fermentation process for large-scale production of the FWGE extract, which is now marketed by his company Biropharma Ltd. in granulate and tablet form.

David Keleti
Independent Scholar

See Also: Breast Cancer; Lung Cancer, Non–Small Cell; X-Rays.

Further Readings
Buklijas, Tatjana and Emese Lafferton. “Science, Medicine and Nationalism in the Habsburg Empire From the 1840s to 1918.” Studies in History and Philosophy of Biological and Biomedical Sciences, v.38 (2007).
Huntsman Cancer Institute

Huntsman Cancer Institute (HCI) was established in 1995 through an endowment from Jon M. Huntsman, chairman and founder of Huntsman Corporation, Salt Lake City, Utah. HCI is part of the University of Utah Health Care system and is located in Salt Lake City on the University of Utah campus. Although HCI serves Utah residents primarily, this institution also serves residents of parts of Idaho, Montana, Nevada, and Wyoming in an area referred to as the Intermountain West. HCI utilizes a three-pronged approach to assist, directly or indirectly, people with cancer through research, education, and state-of-the-art patient care.

HCI was one of the first cancer centers to establish high-risk cancer clinics, providing families with unusually high rates of cancer with resources and strategies for risk management. To support their research goals, HCI has a significant amount of research facility space. HCI has 231,118 square feet of on-site research space with an additional 12,746 square feet of research space at their satellite locations, 442,000 square feet of state-of-the-art clinical space, and a new space of 220,000 square feet designated as the Primary Children's and Families' Cancer Research Center. HCI’s affiliations with larger regional and national cancer programs such as Intermountain Healthcare, National Cancer Institute (NCI), and the National Comprehensive Cancer Network (NCCN) enables their patients to participate in larger clinical trials and receive the most advanced medicines and treatment protocols.

HCI has access to unique assets such as the Utah Population Database (UPDB), a collection of millions of genealogic, birth, death, and marriage records linked to health data. HCI has managed the UPDB for nearly two decades, providing critical information helping to advancing the understanding of cancer biology, prevention, and early detection.

In January 2005, the HCI joined with Intermountain Healthcare to create the Huntsman–Intermountain Cancer Care Program. This program combined HCI’s leadership in laboratory, population sciences, and clinical research with Intermountain’s expertise in clinical quality improvement and program development, thus allowing HCI researchers to use data about cancer care and outcomes from throughout the mountain states region. Through this alliance, the spectrum for cancer research from causes, delivery of care, at-risk populations, and prevention is diversified. HCI is designated as an NCI-designated cancer center. Being an NCI-designated cancer center reflects HCI’s high standards for cancer care and research and demonstrates its support for scientific endeavors through investment of significant resources into the development of high-quality research programs, faculty, and facilities dedicated to the prevention, diagnosis, and treatment of cancer. As of this date, there are 68 NCI-designated centers, making HCI part of a unique national network. Membership in this community of NCI-designated cancer centers allows HCI to participate in future NCI strategic plans and initiatives as well as representing its own community in the national dialogue about cancer treatment. HCI is one of 25 institutional members of the NCCN, a nonprofit group of cancer centers whose sole focus is the improvement of the quality, effectiveness, and efficiency of cancer care. Membership in the NCCN gives HCI partnership opportunities with other NCCN member institutions for sharing resources such as clinical content, research, and educational programs.

Education

HCI established the cancer learning center (CLC) as a part of its commitment to provide information about cancer risk, prevention, and care, not only to patients with cancer but to the general public as well. CLC provides reliable cancer information with the goal of reducing patients’ fears about cancer, helping them become informed decision makers, and educating members of the public about cancer risk reduction. Since the establishment of the CLC, it has been recognized as a model program for cancer education, serving patients from almost every state in
the United States. The information is provided free of charge to HCI patients and to the general public. Information requests are accepted via telephone, via e-mail, or in person. Trained health educators have print and online materials as well as HCI doctors and nurses to assist in answering individual questions.

Utah is home to seven Native American tribes or nations, and HCI dedicates special programming designed to meet the needs of Native Americans for cancer education, screening, and care. As a culture that has been greatly affected by cancer, this HCI community outreach program demonstrates respect for Native American culture and tradition while working to assist and educate members of this culture about cancer. To further public awareness and education within the community, HCI presents the Inaugural Cancer Awareness Expo. This exposition is a free-to-the-public event featuring talks by cancer care providers, with booths staffed by lab researchers and free cancer screenings. To date, HCI has offered more than 100 health conferences and hundreds of presentations to schools and community groups.

State-of-the-Art Patient Care
HCI employs almost 1,500 health care providers and staff as well as having a substantial group of volunteers. The University of Utah Health Care System, which includes the HCI, has been ranked in the top 10 percent for three years in a row. HCI offers an extensive number of specialized cancer treatments and a new program, Supportive Oncology Service, which provides additional support for not only the cancer patients but their friends and families as well. HCI’s commitment to quality extends to their research, with the research branch housing 170 faculty researchers. HCI has been awarded $57.5 million in grant funding, and at any given time has more than 200 cancer clinical trials ongoing. Their research has been recognized with awards from The V Foundation for Cancer Research V Scholar Award, the Samuel Waxman Cancer Research Foundation Award, and the Damon Runyon Foundation for Cancer Research Award. HCI also demonstrates a high level of commitment to future generations of cancer researchers and care providers through their postdoctoral fellows, clinical fellows, masters and doctoral cancer-focused programs, and specialized oncology training for nurses.

See Also: American Cancer Society; Association of Community Cancer Centers; Cancer Therapy Evaluation Program; Clinical Trials; National Cancer Institute.

Further Readings

Hypopharyngeal Cancer

The hypopharynx is the area of the neck where the larynx and esophagus meet. The hypopharynx is the bottom part of the pharynx, or throat, which is a hollow tube that is about five inches long. This acts as a passageway for food and air on their way to the esophagus. Hypopharyngeal cancer is a malignant tumor of this portion of the aerodigestive tract. Since the lining of the pharyngeal mucous membrane is primarily composed of squamous cells, more than 95 percent of malignant tumors in this area are squamous cell carcinoma. This type of
Hypopharyngeal Cancer

Cancer poses a high risk of metastasis via the lymphatic system. Hypopharyngeal cancer is relatively rare in comparison to other more common malignancies. Only approximately 2,500 cases are diagnosed in the United States each year, representing about 7 percent of all cancers of the upper aerodigestive tract. The relative male to female incidence in the United States is 3:1. Incidence of the disease is rare in patients younger than 30 years old, and rises after 40 years old. The mean age at diagnosis is 65 years. Because of its rarity and the absence of early symptoms, hypopharyngeal cancer is not usually detected in its initial stages. Most cases are diagnosed in the end stage, in which there is metastasis to other regions of the body. For this reason, this malignancy exhibits one of the highest mortality rates of any head and neck cancer. The prognosis for the end-stage patient is poor, with only 10 percent surviving for five or more years.

There are a number of symptoms that may be indicative of the presence of this cancer. Swollen lymph nodes in the neck are seen as the first sign in about one-half of presenting patients. A persistent localized sore throat that resists treatment, with pain that radiates up to the ears, is suspicious. The specific sore throat pain symptom for cancer is unilateral, rather than the generalized pain from an infectious inflammatory sore throat. In the late stage, blood streaked saliva, difficulty in swallowing, resultant weight loss, or voice changes may be observed. This morbidity is from the intrusive tumor causing pain, bleeding, and, in very advanced stages, airway obstruction from growth into the larynx.

Contributory factors to the development of this malignancy include smoking, chewing tobacco, heavy alcohol intake, and nutritional deficiencies of iron and certain vitamins. Tobacco smoke contains carcinogens, and similar to its causative effect in lung cancer, it alters the RNA or DNA during cell division. This can produce an oncogene, a gene that causes malignancy because of exposure to a carcinogen. Chewing tobacco can cause similar effects in that saliva partially digests the carcinogenic component, and when swallowed, it passes through the hypopharynx. Alcohol damages the lining of the hypopharynx, allowing toxic chemicals to penetrate the underlying membranes. A genetic disorder called Plummer-Vinson syndrome may contribute to this cancer because it causes long-term iron deficiency. Poor nutrition and resultant vitamin deficiencies can be contributory.

There are several ways in which the physician may arrive at a diagnosis of hypopharyngeal cancer. First is physical examination to detect swollen lymph nodes, and direct observation of the inside of the throat with a long-handled mirror. A more thorough modality of direct observation is endoscopy. Here, a lighted tube is inserted through the nose or mouth, allowing observation further down the throat into the esophagus or trachea. A small tissue sample may be excised for biopsy, to be analyzed for the presence of malignant cells. The physician may call for a computed tomography (CT) scan or magnetic resonance imaging (MRI) to gain a more definitive picture of any abnormalities in the body of the patient.

Once the positive diagnosis is made, there are a variety of treatment options, depending on the stage of the disease, comorbidities, and the general health status of the patient. One or more of the triumvirate of surgery, radiation therapy, or chemotherapy may be employed. Traditionally, surgery and radiotherapy were the primary treatment modalities. In recent years, chemotherapy has been added to the mix. In the early stages of the disease, surgery or radiotherapy is usually the treatment of choice, with the goal of eradicating the malignancy and preserving organ function. However, most patients present with advanced disease, including regional or distant metastases. In those cases, initial surgery followed by postoperative radiotherapy and chemotherapy are the preferred options. In some advanced cases, neoadjuvant chemotherapy, that is, chemotherapy administered to reduce the malignancy prior to surgery and radiotherapy, may be employed. Treatment goals include control of the disease, prolongation of survival, or simply to allow the patient to talk, eat, and breathe in as normal a fashion as possible. In summary, treatment may consist of radiation therapy prior to or following surgery, in some cases with chemotherapy. Or the treatment team may elect chemotherapy followed by surgery and/or radiation therapy; chemotherapy given at the same time as radiation therapy; or surgery followed by chemotherapy given at the same time as radiation therapy. Treatment may also include reconstructive surgery to restore eating, breathing, or talking if all or part of the hypopharynx is removed.

Management of this disease can present a vexing challenge to the physician because of its aggressive nature.
nature and its location in proximity to other critical structures, especially the proximity of several large lymphatic vessels that can spread malignant cells to other regions of the body. Because of the low incidence of this malignancy, a preponderance of clinical data on the ideal combination of therapeutic modalities is somewhat limited, although significant progress has been observed in recent years.

Walter Landers
Independent Scholar

See Also: Head and Neck Cancer; Laryngeal Cancer; Laryngeal Cancer, Childhood.

Further Readings

Hypothalamic and Visual Pathway Glioma, Childhood

Optic pathway hypothalamic glioma (OPHG) is a rare type of brain cancer representing 2 to 7 percent of all pediatric intracranial tumors, with 65 percent of tumors presenting in children less than 5 years of age. These tumors occur anywhere along the visual pathway, including the optic nerve or optic chiasm, and may also be found in the hypothalamus, the area of the brain responsible for controlling body temperature, hunger, and thirst. The term *glioma* refers to a tumor with similar microscopic cellular features to normal glial cells, including astrocytes (*astrocytoma*), oligodendrocytes (*oligodendroglioma*), and ependymal cells (*ependymoma*). Further classification of the glioma can be made based on the World Health Organization (WHO) grading system ranging from low grade (I, II) to high grade (III, IV), providing the basis for diagnosis and prognosis as well as treatment options for those patients who possess a specific glioma. OPHG are nearly always low-grade tumors, the majority of which are pilocytic astrocytomas (WHO grade I), although a small proportion are pilomyxoid astrocytomas and rarely grade II tumors. A significant percentage of OPHGs (10–70 percent) occur alongside the genetic disease neurofibromatosis type 1 (NF-1).

Association to NF-1
There is a marked increase in risk of developing an OPHG for children with neurofibromatosis type 1. This rare genetic condition presents with brown spots and tumor growth on the skin, freckling in places on the body (like the armpit) that are not exposed to sunlight, and tumor growth on nerves.

Symptoms
The symptoms of OPHGs generally manifest over months to years and vary depending on the location of the tumor. Those tumors found behind the eye demonstrate a forward protrusion of the eye known as proptosis. Vision loss is relatively uncommon, most likely due to the young age of the patients at presentation. Examination of the eye may demonstrate fluid accumulation, known as edema of the optic disk, or a pale color due to cell death (atrophy) at the optic disk.

OPHGs located at the optic chiasm and the hypothalamus present as large masses, although they are most commonly low-grade gliomas. Those with tumors at the optic chiasm often present with impaired vision and obstructive hydrocephalus, in which the cerebrospinal fluid accumulates due to the inability of cerebrospinal fluid (CSF) to flow into the subarachnoid space. Due to the resultant increase in intracranial pressure, infants may suffer
from symptoms such as vomiting, drowsiness, irritability, constant downward gaze, or seizures.

Those patients with hypothalamic gliomas may also present with a rare condition known as diencephalic syndrome, where the affected infants present with symptoms that include failure to gain weight and grow as would be expected upon age and gender, and they may also display progressive thinness and weakness known as emaciation. These patients may display a cheerful, alert external demeanor that is in stark contrast to their outward appearance.

Dysfunction of the endocrine hormones due to extension of the tumor into the hypothalamus occurs in 10 to 20 percent of patients with OPHGs. The most common problem is precocious puberty, where the patient undergoes puberty far sooner (before the age of 7 or 8) than would be expected. This is due to the disruption in the signaling among the hypothalamus, pituitary glands, and gonads, occurring in 39 percent of children with NF-1 and tumors of the optic chiasm.

The symptoms of patients with OPHGs differ between those with NF-1 and those without. Primarily, patients without NF-1 more commonly present with signs of increased intracranial pressure and hydrocephalus, while those with NF-1 associated OPHGs are more likely to present with precocious puberty.

**Diagnosis**

The use of magnetic resonance imaging (MRI) provides the best diagnosis of OPHG, allowing for full visualization of the entire optic pathway as well as potential involvement of the tumor into the hypothalamus. Computed tomography (CT) imaging is superior for bone detail and the detection of calcification within the tumor, a sign suggestive of a low-grade tumor.

Three typical patterns seen during imaging studies are thickening of the optic nerve and optic chiasm, tumor in close proximity to the hypothalamus contiguous with optic nerve involvement, and tumor in close proximity to the hypothalamus contiguous with optic tract involvement.

A biopsy is a surgical procedure to remove a small sample of brain tissue for examination under a microscope in order to determine the type and severity (malignancy) of the tumor present. Many children with OPHGs do not undergo biopsy in order to preserve the function of the patient’s optic nerve, and this is especially the case if the patient has had a prior diagnosis of NF-1.

**Clinical Course and Prognosis**

The behavior of OPHGs is unpredictable, ranging from spontaneous regression of tumor, aggressive malignant progression, and metastasis or spread of the tumor to other regions of the brain. Due to the fact that most OPHGs in children are generally benign, low-grade tumors, the variation in clinical course is generally a product of the location of the tumor rather than the specific cellular features.

For those tumors of the optic nerve located within the skull or the orbit of the eye, the median survival is greater than 15 years. There is a small risk (5 percent) of optic nerve tumors invading the optic chiasm, and recurrence of tumor may also develop following complete surgical removal of the tumor. The risk of recurrence, however, for those children with NF-1 is twice that of patients without NF-1 following complete surgical removal of the tumor.

**Treatment**

Current standard treatment strategies are controversial, challenging pediatric oncologists, due to the central site of involvement, the variation in clinical course, and the disease modifying effect of NF-1. The initial course of treatment is generally MRI imaging accompanied with ophthalmologic examinations. More active treatment is generally reserved for those patients with progressive decline in vision or significant changes in the nature of the tumor as seen on MRI imaging. Surgical removal of the tumors is rare as the risks of visual deficits, endocrine hormone dysregulation, and vascular complications of the brain increase.

Radiation therapy remains the mainstay of treatment. However, in recent years, the use of chemotherapy has become prevalent for those patients less than 10 years of age. The utilization of chemotherapy to shrink the size of the tumor works to avoid or at least postpone the use of radiation, which is often detrimental to development of a child’s immature brain.

Krishna Subhash Vyas
Christopher Kubajak
*University of Kentucky College of Medicine*
See Also: Brain Stem Glioma, Childhood; Brain Tumor, Cerebellar Astrocytoma, Childhood; Brain Tumor, Cerebral Astrocytoma/Malignant Glioma, Childhood.

Further Readings
Immigrant Populations

Immigrant populations face language, financial, and cultural barriers to obtaining cancer care. Americans show progress in their cancer survival rates in recent years, but foreign-born individuals display more diversity in their rates of cancer survivorship. Other developed countries demonstrate similar diversity with foreign-born populations. This entry addresses the current research on immigrants and cancer.

Patterns of Cancer Trends

P. S. Pinheiro and colleagues reviewed cancer rates of Hispanics and Latinos according to geographic origin (e.g., Mexico, Puerto Rico, and Cuba) in Florida. A Hispanic male cancer rate of 537 per 100,000 came out at a lower rate than the white male cancer rate of 601 per 100,000, whereas the female rates compared similarly and showed a Hispanic female cancer rate of 376 per 100,000 and a white female rate of 460 per 100,000, respectively. Among Florida Hispanics, Puerto Ricans showed the highest rates followed by Cubans and then Mexicans with the lowest rates.

According to I. Olver, F. Marine, and P. Grogan in 2011, the immigrants to Australia come from diverse backgrounds and show a reduced incidence of common cancers (colon, breast, prostate, and melanoma) and less overall mortality in these common cancers. The immigrant population represents 24 percent of the Australian population. However, the immigrant population displays higher rates of lung, stomach, liver, cervix, thyroid, and bladder cancer. These immigrants exhibit a distinct spectrum of cancer with more liver cancer from exposure to hepatitis B and C infections.

In 2012 R. Siegel, D. Naishadham, and A. Jemal demonstrated a lower incidence of cancer in Hispanics for breast, prostate, lung, and colorectal cancer; however, the researchers found an elevated incidence and mortality rate for stomach, liver, uterine, cervix, and gallbladder cancers in the Hispanic population. These higher rates possibly relate to cancer-causing infectious agents, reduced screening for cervical cancer, differences in lifestyle or food intake, and genetic factors. Implementing screening, vaccines, and proven interventions for obesity, smoking, and alcohol intake could reduce the incidence of the higher rates of cancers in Hispanics.

Breast cancer incidence continues to rise globally as it is the leading cause of cancer mortality in low- and middle-income countries. In 2012 O. Beiki and colleagues employed the Swedish nationwide registers to look at socioeconomic and immigration patterns in Sweden. The database encompassed a cohort of women between 1961 and 2007. The incidence in the immigrants produced a low result with an incidence rate ratio (IRR) of 0.88 (95 percent confidence interval [CI] = 0.86 to 0.90) but not for the daughters of the immigrants, who
Immigrant Populations

showed an IRR of 0.97 (95 percent CI = 0.94 to 1.01) in comparison to native Swedes. A further thought-provoking statistic found the case fatality rate of breast cancer to be 14 percent higher if diagnosed after age 50 in the immigrant population compared to native Swedes. The lower risk of breast cancer in the immigrant women compared to their daughters calls for further research on lifestyle factors to ascertain the differences in the two groups.

A cross-sectional survey in a Danish study by G. P. Kurita, P. Sjogren, K. Juel, J. Hojsted, and O. Ekholm found that individuals with non-Western backgrounds described an elevated pain prevalence, higher pain intensities, and more widespread body pain over individuals of Danish background; however, native Danes consumed more opioids at a higher rate than foreign-born individuals. These results indicate diversity exists in treatment of pain in cancer between the immigrant population and Danish population despite higher pain in the immigrant individuals.

A Canadian study by G. M. Carriere, C. Sanmartin, H. Bryant, and G. Lockwood in 2013 found areas of high concentration of foreign-born individuals demonstrating an all-cause cancer rate of 388 per 100,000 compared to individuals in low concentrations of foreign-born of 493 per 100,000. This pattern ensued for lung, colorectal, prostate, and breast cancer but did not emerge for liver, nasopharynx, and thyroid cancers. These results contain evidence suggesting lower cancer risk in foreign-born populations for a majority of cancers except nasopharynx, liver, and thyroid cancers.

D. K. Nguyen and M. Maggard-Gibbons reviewed incidence of gastric cancer in 2013 using the Surveillance, Epidemiology, and End Results (SEER) registry. Analysis of 42,187 patients from 1980 to 2009 in the SEER registry found individuals residing in high-immigration areas and foreign-born patients both demonstrated low rates of mortality, 0.74 and 0.87, respectively. So high-immigration areas and foreign born receive no disparity in cancer-directed therapies and survival after resection, as shown by the SEER registry results.

Research by K. Richardson, S. Jatrana, M. Tobias, and T. Blakely in 2013 found Pacific immigrants in New Zealand demonstrated lower all-cause cancer mortality. The lower rates existed in the group living in New Zealand for less than 25 years compared to a higher rate for immigrants living there more than 25 years. No difference was found for mortality between overseas born and New Zealand born for Pacific immigrants living in New Zealand.

Genetic studies by E. Corona and colleagues in 2013 found that patterns of disease changed with human migration. The researchers studied 102 diseases across 51 populations using the Human Genome Diversity Panel. A genetic-associated risk for pancreatic cancer decreased as individuals migrated toward East Asia. These studies pave the way for further investigation of migration effects on the genetic foundation of disease.

Research in the Netherlands by M. Arnold and colleagues in 2013 uncovered a higher rate of nasopharyngeal carcinoma due to differentiated, nonkeratinizing tumors. This increase of cancer appears to be related to Epstein-Barr virus infection and to an increase in immigration of people from China and North Africa. At the same time, the incidence of nasopharyngeal carcinoma due to keratinizing tumors decreased over the 20 years in nonforeign-born individuals.

S. M. Mousavi, A. Forsti, J. Sundquist, and K. Hemminki in 2013 employed the Swedish Family-Cancer Database to review death from female breast cancer in 12,505 and 137,547 subjects (immigrants in Sweden and Swedes, respectively) diagnosed with breast cancer. This study indicated that immigrant Turks, Southeast Asians, and Chileans displayed the lowest breast cancer risk, at a 0.44 incidence ratio, and immigrant Iraqis had the most-elevated risk of 1.19, compared to the Swedish subjects.

Cervical cancer screening and risk behaviors differ between U.S.- and foreign-born Hispanic women. J. R. Montalegre, R. Zhou, E. S. Amirian, and M. E. Scheurer found that Hispanics represent a heterogeneous group, with many members of the Hispanic group being nonforeign born using SEER data. Their results showed foreign-born Hispanic women with significantly elevated late-stage diagnosis of cervical cancer. The study also demonstrated differences in nativity (birth location) and survival by stage of diagnosis. Foreign born with early stage diagnosis showed poorer survival, with a hazard ratio (HR) of 1.31, whereas foreign born with late-stage diagnosis depicted better survival, with an HR of 0.81. The researchers believe it is inappropriate to lump Hispanics into one single group for cervical cancer studies.
Montealegre and colleagues in 2014 again used the SEER data file to look at missing data on birthplace of foreign-born individuals. Their results showed data missing for cervical, prostate, and colorectal cancer subjects. The researchers used multiple imputations of variables (e.g., diagnosis, treatment, and survival) in the SEER data file to accurately determine foreign-born status. Using the strategy developed by Montealegre and colleagues, nativity-related cancer disparities can be corrected for analysis of vulnerable populations like the foreign born.

Using the California Cancer Registry from 1995 to 2008, C. W. Schupp, D. J. Press, and S. L. Gomez in 2014 evaluated the impact of nativity (birth location) and neighborhood-level enclave (living in a community of Hispanics) on prostate cancer survival in Hispanics in California. The researchers studied 35,427 Hispanic males with invasive prostate cancer. The foreign-born Hispanics demonstrated a significantly lower risk of prostate cancer survival with an HR of 0.82 (95 percent CI, 0.75–0.87); in addition, if the foreign-born Hispanics lived in their ethnic enclave, the survival HR improved even more, with an HR of 0.79 (95 percent CI, 0.71–0.86) compared to U.S.-born Hispanics. These results indicate a better survival in Hispanic immigrants over U.S.-born Hispanics for prostate cancer.

Conclusion

Reviewing the current research in the cancer of immigrants demonstrates some diverse results in risk and screening profiles. Research on immigration populations in multiple countries indicates the need to study subgroups separately. An example is Hispanics from Cuba, Mexico, and Puerto Rico, who represent very heterogeneous groups. Many other developed countries demonstrate similar diversity in their incidence and mortality rates in different types of cancer. Foreign-born individuals frequently demonstrated significantly lower rates of common cancers (colon, breast, and prostate) but frequently significantly higher rates of stomach, liver, cervix, thyroid, and bladder cancer. These studies provide a starting point to study characteristics of the immigrant population to determine what attributes reduce their risk of common cancers.

See Also: Australia; Cuba; Developing Countries; Mexico; New Zealand.

Further Readings


India

India, a country inhabited by more than 1.2 billion people, is facing a tremendous challenge in rising cancer rates, the second-most common disease and one of 10 leading causes of death in India, accounting for the maximum mortality with about 0.4 million deaths per annum. The cancer deaths add up to about 6 percent of all adult deaths in India. The current 2.5 million cancer cases are increasing at the rate of 0.8 million new cancer cases per year. Along with the current high prevalence, cancer mortality is projected to increase to 1.2 million by 2035. India has taken some concrete steps in establishing a robust infrastructure and is a member of many global alliances to curb cancer, but it still needs to allocate significantly more resources to deal with this emerging challenge.

Causes

Apart from the globally prevalent general causes of cancer, some specific reasons are salient in the Indian context. The national cancer registry data indicated that oral cavity, lungs, esophagus, and stomach among men and cervix, breast, and oral cavity among women were the leading cancer sites. Researchers identified tobacco as the most important cause, and its use accounted for about two-fifths of all cancers in India, responsible for 40 to 50 percent of cancers in men and 20 percent of cancers in women. The mainly smokeless tobacco users in India number about 275 million, constituting 35 percent of the adults and 14.1 percent of children in the age-group of 13 to 15 years. In addition, changing dietary habits, increasing carcinogens in the environment, increased alcohol consumption, radiation exposure, and harmful lifestyles constitute the other contributory factors to the increasing cancer incidence. This is underlined by the effect of social factors, like inequalities and inequities that form some major determinants of the Indian cancer burden, with the poor more likely to die from cancer than the rich.

Impact

Apart from the health mortality and morbidity impact, cancer has severe emotional and economic effects on individuals and families. According to 2002 and 2003 estimates, the economic costs of cancer in India add up to nearly $5 billion in direct and indirect costs. Researchers noted that the tobacco consumption costs in India exceed the total budgeted expenditure estimates by the Indian government on essentials like public health, sanitation, and water supply. These economic inequities result in further disparities down the line, where the poor and vulnerable are the most affected by different forms of cancer; for example, the rural poor constitute 90 percent of the oral cancer patients, and women with breast cancer have been mostly detected in low socioeconomic strata. Further, the families of cancer patients incurred increased, unsustainable expenses on detection, treatment, and management of the disease, and 2010 estimates put a quarter of such families in an impoverished condition. These costs also eat away at the family and social capital, thus putting the entire health and social system at risk.

Policies and Interventions

India’s response to cancer is mainly through its National Cancer Control Program (NCCP), launched in 1975 with the triple aims of early detection, primary prevention, and prompt treatment. The NCCP, followed by the subsequent National Program for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases, and Stroke in 2010 and National Rural Health Mission in 2005, has positively impacted cancer health care services and human resources but with poor awareness, detection, and survival outcomes. The program has been drafting and implementing strategies linked to
the Indian five-year plans leading to the establishment of regional cancer centers, oncology wings in select government medical colleges, infrastructure development, and the initiation of a cancer program at the district governance level. India is also one of the first signatories and members from developing countries in the International Agency for Research on Cancer (IARC) that has ratified the World Health Organization tobacco control framework.

But none of the activities of the NCCP have been sustainable or leveraged into long-term results. As of now, the Indian government has revised the NCCP with five new schemes, which recognize new regional cancer centers (RCCs) by providing a one-time grant of $0.8 million, strengthening of existing RCCs with a $500,000 grant and development of oncology wings in government medical installations, increasing district cancer control programs, and involving nongovernmental organizations (NGOs) and civil society in information education and communication (IEC) activities. The current program is a part of the National Program for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases and Stroke, which lumps cancer with all the other noncommunicable diseases. The figures show the minuscule funding and resources pointing at the need for significant funding and policy attention to combat cancer in India. The population-based registries only cover about 7 percent of patients with cancer. The per-capita government cancer spending in India is a scant $641, compared to $2,202 in China and $86,758 in the United States. In addition to increased allocations for strengthening the health system and infrastructure on cancer prevention, diagnosis, and treatment services, protection systems must be developed to help individuals and families cope with adverse financial consequences, social support needs, and other expectations.

Other Challenges
One significant challenge is to map the cancer incidences in the vast population groups and areas in India and increase the coverage of people under the population-based cancer registries. India, with its ancient past and diversity, also poses a complex social environment, attitudes, and beliefs for cancer prevention and other communication strategies. Gender relationships, caste, social hierarchy, and stigma add to the complexities. Other challenges include low health service effectiveness, lack of trust in health service providers, and low medical service use. The large numbers of poor and rural people and health and socioeconomic disparities create further challenges and also underline the affordability of care.

Conclusion
India needs significantly more resources and programs to address the increasing cancer incidences and outcomes in its population. A fundamental need is to recognize cancer as a serious public health challenge and demonstrate strong political and bureaucratic commitment and action. The links of cancer with the socioeconomic fault lines and disparities in India need to be recognized and addressed. A crucial determinant would be how India negotiates the entrenched social inequalities and allocation and distribution of resources. Public health initiatives; legislation; convergent health policies; increased public health spending; leadership at national, district, and block levels; and
communication campaigns focusing on major social determinants of health are key to the strategy.

Lalatendu Acharya
Purdue University

See Also: Asian Diet; Government; International Agency for Research on Cancer.

Further Readings

Indonesia

This southeastern Asian nation, officially termed the Republic of Indonesia, was created in 1949 after the citizens of the country established their independence from Dutch colonial rule. In the ensuing decades, Indonesia was the site of political turmoil concerning governance. However, the nation has stabilized considerably in the past 15 years. Currently, Indonesia is the fifth-most populated country on Earth, with nearly 240 million citizens. Indonesia is a unique nation as it is an archipelago comprised of more than 13,000 individual islands. Researchers presently estimate that cancer is the second-leading cause of death in the country.

Cancer control efforts in the territory of Indonesia date back to 1920, when Dutch administrators of the chain of islands enacted cancer treatment programs there. Various cancer control efforts in the country were spawned from this initial Dutch effort until 1942, when Japanese military forces occupied Indonesia and shut the programs down. After Indonesia gained its independence in the ensuing years, it took until 1962 for the next domestic cancer control program to be initiated in the nation in the form of the Indian Foundation for Cancer Control. Since then, many organizations have been formed with the goal of battling Indonesia’s domestic cancer incidences, such as the creation of the Indonesian Cancer Society in 1977 and the Jakarta Cancer Center Hospital in 1993.

There are currently no nationwide cancer registries in use in the country as the government has not procured the finances or the staff to manage cancer data deriving from the more than 13,000 islands of the Indonesian state. As the country is composed of 27 provinces, 241 districts, 55 municipalities, 3,501 subdistricts, and 66,979 villages, it would be a uniquely monumental effort to compile an accurate and effective national cancer registry. Instead, information regarding Indonesian cancer incidences and trends are garnered from regional hospitals and universities, where most Indonesian cancer patients are referred for treatment. Research and registration efforts in the country are regarded as relatively rudimentary, though cancer treatment facilities in the country have been hailed as proficient and strengthening.

Tobacco usage is currently uniquely high within the male Indonesian population, with nearly 70 percent of all Indonesian males being smokers. Such high usage rates have created the conditions for a robust lung cancer problem in the nation. Furthermore, on average, Indonesian lung cancer patients have been shown to be diagnosed with lung cancer when the disease is in its latest stages, making treatment options poor. As an Indonesian lung cancer patient’s chance of surviving the disease is estimated currently at being around 15 percent, there is much work that needs to be done in order to stem the tide against domestic incidences of lung cancer. Fortunately, the Indonesian government is now taking steps to enact extensive antitobacco legislation as well as to mandate that domestic tobacco companies use less toxic elements in their products. All in all, there is hope that the targeted efforts of the Indonesian government will bring down the incidences of lung cancer in the country.

While it is difficult to estimate the exact amounts of cancer incidences in Indonesia because the nation lacks a national cancer registry, in recent years, researchers estimate that the most prevalent forms
of cancer in Indonesia are bowel cancer, breast cancer, liver cancer, lung cancer, lymphomas, and oral cancer. Lung, bowel, and liver cancers are the most predominant forms of cancer incidences in males in the nation, while cervical, breast, and bowel cancers are the most common types of incidences of cancer in females there. Nationwide, incidences of esophageal cancer have been decreasing over the past several years, and incidences of soft tissue cancer have been steadily declining.

Regarding cancer, the future is positive for Indonesia. The country presently has more than 20 cancer treatment centers where the nation’s nearly 300 oncologists provide their highly specialized services. On top of this, new cancer treatment centers are being created, and new domestic oncologists are being trained every year. As treatment options for Indonesian cancer patients improve, more steps will need to be taken by the Indonesian government in order to further combat the disease, such as by creating an effective national cancer registry.

William M. Peaster
Independent Scholar

See Also: Breast Cancer; Cervical Cancer; Lung Cancer, Non—Small Cell; Oral Cavity Cancer, Lip and.

Further Readings


Mangunkusumo, R. “Frequency of Malignant Tumors in Indonesia, a Pathological Base Observation—for Presentation at the 4th Continuing Medical Education on Early Detection and Prevention of Cancer.” *University of Indonesia* (September 1998).


Infection

There is a strong association between sexually transmitted infections (STIs) and cancers. Specifically, STIs such as human papillomavirus (HPV) and human immunodeficiency virus (HIV) place individuals at increased risk for the development of cancers, researchers say, including cervical cancer, anal cancer, Hodgkin’s lymphoma, liver cancer, leukemia, and lung cancer. A malignancy increases risk of recurrence or second malignancy as compared to those without a history of cancer, according to the National Cancer Institute (NCI). STIs and cancer account for a substantial amount of national health care expenses and lost wages due to illness and represent two of the largest public health burdens in the United States, reports the Centers for Disease Control and Prevention (CDC). Therefore, the link between STIs and cancer is extremely important to the public health and economic health of the nation.

One of the most serious threats to public health in the United States is the HIV epidemic. Approximately 1.1 million people in the United States are infected with HIV. Individuals living with HIV have a higher risk of certain cancers than uninfected individuals due to the deleterious impact that this disease has on the immune system. In fact, the development of cancers such as Kaposi’s sarcoma,
non-Hodgkin’s lymphoma, and cervical cancer denotes a transition from HIV infection to acquired immune deficiency syndrome (AIDS). In addition to these AIDS-defining cancers, those with HIV are at increased risk for anal, liver, and lung cancer, which may be due to individual-level risk behaviors such as smoking and alcohol consumption.

Two of the most common cancers among people living with HIV are Kaposi’s sarcoma and non-Hodgkin’s lymphoma. Kaposi’s sarcomas that develop as a result of progressive HIV are called epidemic Kaposi’s sarcoma. Kaposi’s sarcoma is life threatening because of its potential to affect the lymph nodes and other organs, such as the digestive tract, lung, liver, and spleen. All lesions caused by Kaposi’s sarcoma contain human herpes virus-8 (HHV-8). However, individuals who are infected with HHV-8 may not necessarily develop Kaposi’s sarcoma. People with compromised immune systems are at increased risk of developing Kaposi’s sarcoma. Therefore, people living with HIV are more likely to have HHV-8, which can develop into epidemic Kaposi’s sarcoma.

Non-Hodgkin’s lymphoma impacts the white blood cells and lymph nodes and, as a result, impairs the body’s immune system. Non-Hodgkin’s lymphoma can cause seizures, facial paralysis, confusion, memory loss, and fatigue. There are two types of non-Hodgkin’s lymphomas: aggressive (i.e., fast growing) and indolent lymphomas. Each type of lymphoma can be comprised of either B-cells or T-cells. People living with HIV are more likely to develop an aggressive non-Hodgkin’s lymphoma than an indolent type. Non-Hodgkin’s lymphoma that develops as a result of immune-compromise related to HIV is called AIDS-related lymphoma. Diffuse large B-cell lymphoma, B-cell immuno-blastic lymphoma, and small, non-cleaved cell lymphoma are the main types of AIDS-related lymphomas. These types of lymphoma are considered AIDS defining because their development is a sign of a significantly weakened immune system as indicated by extremely low CD4 cell counts (i.e., white blood cell count lower than 200), which is considered the threshold for an AIDS diagnosis.

Fortunately, both Kaposi’s sarcoma and non-Hodgkin’s lymphoma are treatable. The standard of care for Kaposi’s sarcoma includes radiation therapy, chemotherapy, surgery, and biologic therapy. Radiation therapy usually uses photon or electron beams to kill or stop the growth of cancer cells. Chemotherapy uses a variety of drugs to stop the growth of cancer cells. Usually, chemotherapy drugs are administered orally, intravenously, or intramuscularly. In the case of Kaposi’s sarcoma located in the mouth, chemotherapy agents may be injected directly into the lesion, which is called intralesional chemotherapy. Alternatively, Kaposi’s sarcoma of the skin may be treated with a topical chemotherapy agent such as a gel or lotion. Another type of chemotherapy that is used to treat Kaposi’s sarcoma is liposomal chemotherapy. Liposomal chemotherapy uses fat particles to carry anticancer drugs, such as doxorubicin, to the site of the lesion. When the fat particles build up in the lesion, they excrete the doxorubicin. The method maximizes the effects of the doxorubicin while minimizing damage to healthy tissue. Surgery may also be used to remove the tumor or surrounding lesions, reports the American Society of Clinical Oncology (ASCO).

Local excision, curettage, electrodessication, and cryosurgery are the most common surgical options to treat Kaposi’s sarcoma. Local excision involves cutting cancerous cells and a small amount of normal tissue from the skin. Curettage and electrodessication involves cutting a tumor or lesion from the skin with a sharp tool and then using an electrode to treat the area to stop bleeding and destroy any cancerous cells on the edge of the surgical wound. Cryosurgery uses liquid nitrogen to freeze and kill cancerous cells. Biologic therapy uses the patient’s own immune system to fight cancerous cells. This type of therapy uses substances made by the patient’s body or artificial substances produced in a laboratory to boost, direct, or restore the patient’s immune system in the service of building a defense against cancer. Palliative care, which includes medication, nutritional changes, and other therapies, is used to treat HIV/AIDS-related Kaposi’s sarcoma. Although this does not cure the cancer, it helps relieve pain and other symptoms.

The standard of care for non-Hodgkin’s lymphoma is similar to the treatment for Kaposi’s sarcoma. Treatment usually involves monotherapy or combination therapy, including radiation therapy, chemotherapy, targeted therapy, plasmapheresis, biologic therapy, and watchful waiting. As described, radiation therapy involves the
elimination of cancerous cells through the administration of either high-energy X-rays or radioactive substances to the patient. The site and method of radiation depend on the type of lymphoma. Chemotherapy can also be used to treat non-Hodgkin's lymphoma. Some types of non-Hodgkin's lymphoma may spread to the brain and require central nervous system prophylaxis, which is chemotherapy that kills cancer in the brain or spinal cord. Target therapy uses drugs to identify and kill specific cancerous cells without damaging healthy cells. Two common drugs used in targeted therapy to treat non-Hodgkin’s lymphoma are a monoclonal antibody and a proteasome inhibitor. Monoclonal antibodies identify substances and kill cancerous cells by blocking their growth or keeping the cancerous cells from spreading to healthy cells and tissue. Protease inhibitors block the action of the proteasomes of cancerous cells, impairing their ability to replicate. Plasmapheresis involves removing extra plasma and antibody proteins from the blood when the blood becomes thick due to the excess of plasma and affects circulation. During the procedure, blood is removed from the patient, the blood cells and plasma are separated, and the blood cells are returned to the bloodstream without the plasma. A specific type of biologic therapy called interferon is used to treat non-Hodgkin’s lymphoma. This substance interferes with the division of the cancerous cells and slows cancer growth. Last, watchful waiting closely monitors a patient’s condition without direct intervention. Intervention may be recommended when the patient’s symptoms appear to change or worsen.

Although these treatments are efficacious, they are not without their challenges. There are complexities associated with simultaneous HIV and cancer treatments due to the debilitating nature of HIV infection and chemotherapy on the immune system. The treatment for individuals who are infected with HIV with a comorbid cancer diagnosis depends on the type and stage of cancer but often consists of standard cancer treatments coupled with highly active antiretroviral therapy.

Preparation of a human papillomavirus (HPV) vaccination. HPV is the most common sexually transmitted infection and plays a causal role in several types of cancers, although cervical and anal cancer are the two most common cancers associated with HPV. Recent efforts to reduce cervical cancer led to the development of vaccines protecting against specific types of HPV. (Flickr/PAHO/WHO)
Infection

(HAART) for HIV. However, HAART medications may interact with medications used to treat cancer, which necessitates a need for the management of both diseases and treatments by a doctor who has experience with these diseases.

HAART is used in conjunction with cancer treatments and afterward for people living with HIV. The use of HAART allows for the effective control of the HIV virus, which is advantageous because it decreases the side effects of cancer treatments, decreases the chances of recurrence, and improves the odds of recovery from cancer. Other cancer treatments for individuals living with HIV infection include radiation therapy, chemotherapy, immunotherapy, and target-related therapy. The selected treatment for cancer in individuals with HIV infection will be determined by a skilled and experienced physician who must take into consideration the stage of HIV infection and the severity and type of cancer for which a person has been diagnosed.

HPV is the most common sexually transmitted infection. Prevalence rates range from 40 to 49 percent in the general population. HPV plays a causal role in cervical, vaginal, vulvar, penis, anal, and oral cancers. However, the two most common cancers associated with HPV are cervical cancer and anal cancer. In fact, researchers have found that HPV accounts for all cases of cervical cancers and 85 percent of all anal cancers. Cervical cancer is the second-most common cancer among women worldwide, according to the World Health Organization (WHO), and left untreated, cervical cancer can be fatal. However, due to the increase in the use of Pap tests, the number of cervical-cancer-related deaths has declined by 70 percent. Anal cancer is less common than cervical cancer. Approximately 7,210 new cases have been diagnosed in 2014; however, prevalence rates have increased in past years. Other cancers such as vaginal, vulvar, penile, and oropharyngeal cancers are associated with HPV. It is estimated that HPV accounts for 50 percent of vaginal, vulvar, oropharyngeal, and penile cancers. While these cancers are not as life threatening as cervical cancer, they can result in significant impairments in daily functioning and quality of life, including loss of sexual functioning, fertility, and self-image.

Cervical cancer develops when external and internal tissues of the cervix develop cancerous cells. Cervical cancers first present as precancerous cells called cervical intraepithelial neoplasia, squamous intraepithelial lesion, or dysplasia. These precancerous cells can be detected by a Pap test and treated to prevent the development of cervical cancer. If these precancerous cells go undetected and untreated, they may develop into cervical cancer. There are two main types of cervical cancers: squamous cell carcinoma and adenocarcinoma. Some cervical cancers have properties of both squamous cell carcinomas and adenocarcinomas and are called mixed carcinomas. The majority of cervical cancers are classified as squamous cell carcinomas. Squamous cell carcinomas originate in the cells that cover the surface of the exocervix. Cervical adenocarcinomas start in the endocervix of the cervix and develop from mucus-producing gland cells.

Anal cancer is also closely related to HPV infection. There are several types of anal cancer cells, including carcinoma in situ, squamous cell carcinomas, adenocarcinomas, basal cell carcinomas, and gastrointestinal stromal tumors. Cells that are carcinoma in situ are cells that appear to be cancerous but have not grown into any of the deeper layers of the anus. These cells are analogous to the precancer cells found on the cervix during a Pap test. Squamous cell carcinomas are the most common type of anal cancer and originate in the cells of the lower part of the anus and the anal canal. As the cancerous cells spread to the deeper layers of the anus, they are considered invasive. Adenocarcinomas start in the cells that line the upper part of the anus and rectum. Basal cell carcinomas are found on the skin of the anus and are considered a type of skin cancer. Gastrointestinal stromal tumors are rare and usually found in the stomach or small intestine but can spread to the anus.

Recent efforts to reduce cervical cancer led to the development of vaccines protecting against specific types of HPV associated with cervical, anal, and other HPV-related cancers. These vaccines are currently available and are safe and clinically effective. The Advisory Committee on Immunization Practices (ACIP) recommends that all adolescent females between the ages of 11 and 12 years be vaccinated for HPV and that the vaccines are approved for females. ACIP recommends that males between the ages of nine and 26 years be vaccinated for HPV. However, vaccination rates among the general population and survivors of cancer are unacceptably low.
STI-related cancers pose a health challenge to patients and health care professionals. However, recent medical advancements such as the HPV vaccine and developing cancer treatments are promising. Future research agendas should continue to pursue treatment development and also identify factors that promote STI- and cancer-prevention behaviors. Specifically, research should focus on increasing HPV vaccine uptake to prevent cervical, anal, and other HPV-related cancers. In addition, research should investigate the impact of HAART adherence on AIDS-related lymphomas and sarcomas.

Christopher L. Edwards
Courtney Peasant
Labarron Hill
Mary Wood
Duke University Medical Center

See Also: AIDS-Related Cancers; American Cancer Society; HPV Vaccination; National Cancer Institute.

Further Readings


Insecticides

An insecticide is a substance that is used to kill, repel, or control insects. More than 1 million insect species worldwide can be found in habitats ranging from forests and swamps to deserts and cities. They are extremely adaptable, multiply in numbers rapidly, and are resilient to harsh environmental conditions. Approximately 10,000 species consume agricultural crops. Of these, nearly 700 are responsible for most insect damage to field and stored crops. In 2001, insecticides accounted for 12 percent of all pesticides applied to surveyed crops in the United States, with corn and cotton making up the largest shares of insecticide use. This entry outlines major chemical classes, human exposure, environmental and human health risks, and regulations and exposure prevention.

Major Chemical Classes

Many different insecticides with varying levels of sophistication have been developed since the existence of ancient civilizations. One of the first recorded was sulfur (brimstone), which was burned for use as a fumigant. Other agents included extracts of pepper and tobacco, soapy water, white-wash, vinegar, turpentine, fish oil, brine, lye, and
various readily available ingredients. Some of these substances were more effective than others; for instance, soapy water is still used today as a spray on household plants.

Dichlorodiphenyltrichloroethane (DDT), an organochlorine and once one of the most commonly used agents of this chemical type, was a synthetic agent developed in 1939 as an insecticide and chemical to control vector-borne diseases such as malaria and yellow fever. Organochlorine insecticides are generally characterized by an organic compound containing at least one covalently bonded chlorine atom. These stable structures persist in soil and sediment, can travel long distances in the upper atmosphere, and move slowly into groundwater. They deposit in plants and concentrate in the fatty tissues of fish, birds, and animals. Evidence of DDT’s toxicological effects became apparent shortly after its peak usage, and it subsequently was banned by the U.S. Environmental Protection Agency (EPA).

The most frequently used chemical groups today in the United States are organophosphates, carbamates, and pyrethroids, which primarily elicit neurotoxic insecticidal effects. Although less common, the following chemical classes are among many designed for specific organisms, environments, or circumstances: botanicals (toxicants derived from plants), fumigants (small, volatile, organic molecules used in confined spaces), inorganics (carbon-free compounds, e.g., sulfur), and repellants (usually applied to human skin or building surfaces, e.g., N,N-Diethyl-meta-Toluamide [DEET]). The variety of insecticides reflects the diversity of target species and their habitats as well as attempts to address negative health effects and insecticide resistance.

Transgenic plants were recently developed to incorporate pest-resistant genes from other species into plant genes. For example, the naturally occurring soil bacterium *Bacillus thuringiensis* (Bt) produces Bt toxin, a protein that is toxic to certain herbivorous insects. On its own, Bt is considered to be a biopesticide; when the gene that produces Bt toxin is introduced into crops such as corn, cotton, and potatoes, these crops can then synthesize their own bacterial protein to kill pests. While their use is controversial, biopesticides and transgenic plants are of increasing interest to governments, industry, and communities that are seeking innovative ways to cope with insects in food crops.

**Human Exposure**

Humans can be exposed to insecticides from natural sources, in occupational settings, as part of public health interventions, and from household and commercial uses. Exposure may happen via dermal contact and inhalation, even from historical or current uses in other countries. Contact may also arise from consumption of residues in human breast milk and on food products.

In occupational settings, farmers and farm workers can be exposed from insecticide mixing, loading, and transfer to application equipment. Forestry workers routinely apply insecticides on tree farms. Pentachlorophenol, an organochlorine and fungicide, was commonly applied to lumber as a wood preservative. Workers at wood treatment facilities and lumber mills were exposed along with those who then handled treated lumber. Insecticide-manufacturing workers can come into contact with chemicals during production and transfer to storage facilities.

Public health uses of insecticides remain in parts of the world where the prevalence of insects carrying diseases and the risks of becoming infected and seriously ill are both high. DDT and pyrethroids are sprayed indoors and used to treat bed nets in malaria-endemic regions.

Insecticides and their mixtures are widely available in stores for home, garden, and commercial uses. Examples include products containing carbaryl, malathion, boric acid, and pyrethrum. Topical head lice and scabies treatments containing the synthetic organochlorine lindane were commonly used and are still available by prescription; however, usage has declined since safer alternatives have become available.

The amount or level of exposure to insecticides from any source depends on the route of exposure, as well as the frequency, duration, and intensity of use at either a single point, an interval of time (e.g., growing season), or over a lifetime. Exposure may be averaged or calculated on a cumulative basis. There are various methods to measure human exposure, and the selection of methods depends on numerous factors: chiefly, feasibility and cost.

**Environmental and Human Health Effects**

Insecticides are the most common method of preventing and controlling insects. They have conferred numerous benefits for their ability to protect
food crops and supplies, control vector-borne disease, and mitigate bodily and household pests. However, widespread and long-standing use of these chemicals has had adverse consequences for environmental and human health. DDT exposure has been associated with eggshell thinning in birds, causing substantial declines in certain bird populations in the United States. Lindane has been associated with hormone disruption, nervous system effects, and cancer in humans.

Organophosphates are not as persistent as organochlorines; for example, the half-life of malathion in soil is one to 17 days, compared to two to 15 years for DDT. They do not tend to deposit and accumulate in fatty tissues of living organisms. Nevertheless, they are toxic to humans because they act by inhibiting the enzyme cholinesterase. Short-term exposure is associated with cholinergic effects such as headache, respiratory symptoms, convulsions, and coma. Chronic effects of exposure to low levels of organophosphates may include increased risks of neurological disorders in children in agricultural areas exposed prenatally and in early childhood. Carbamate insecticides have a similar anti-cholinesterase mode of action. The EPA has found that permethrin, a type of pyrethroid, is likely to be carcinogenic to humans by oral ingestion based on evidence in laboratory mammals and supporting structural activity relationship data.

Some individual agents have been evaluated in association with cancer. Canadian men who reported previous exposure to the insecticides malathion, DDT, carbaryl, aldrin, and lindane had significantly elevated risks of non-Hodgkin's lymphoma. Similar results were found in case-control studies conducted in the United States, with increased risks associated with greater numbers of days per year of use of DDT. Significantly higher risks were also observed for carbamate and organophosphate insecticides as groups. Canadian men who reportedly used carbaryl had a nearly 2.7-fold higher risk of being diagnosed with multiple myeloma. An increasing exposure–response trend based on days per year of use was also observed.

Insecticide resistance, including to Bt crops, is a major challenge, and multiple generations of insecticides have been developed in efforts to stay ahead of resistance. Additionally, Bt corn pollen may have unintended adverse effects on nontarget organisms (e.g., monarch butterflies). The human health effects of newer compounds (e.g., transgenic plants) are an area of ongoing research.

Regulations and Exposure Prevention
In 1991, the International Agency for Research on Cancer evaluated the carcinogenicity of aldicarb, chlordane, heptachlor, DDT, deltamethrin, dichlorvos, fenvalerate, and permethrin. Chlordane, heptachlor, DDT, and dichlorvos were classified as Group 2B (possible) human carcinogens based on inadequate evidence in humans and sufficient evidence of liver cancer in animal studies. Aldicarb, deltamethrin, fenvalerate, and permethrin were classified as Group 3 (not classifiable as to its carcinogenicity to humans) based on no human data and inadequate animal evidence. Occupational exposures in spraying and application of nonarsenical insecticides were deemed to be Group 2A (probable) human carcinogens based on limited evidence for lung cancer in humans.

DDT is still used in regions that lack effective pesticide regulation, enforcement, exposure controls, and safe handling practices. The Stockholm Convention on persistent organic pollutants bans DDT for all uses except for malaria control. In September 2006, the World Health Organization declared support for indoor use of DDT in African countries where malaria is endemic. Agricultural uses of lindane were banned by the EPA in 2007 and globally under the Stockholm Convention in 2009.

Reducing workplace exposure can be achieved through setting and enforcing occupational exposure limits, with the use of personal protective equipment as a last resort. Alternative approaches to pest control can be used at work and in other contexts. According to the EPA, integrated pest management (IPM) is “the coordinated use of pest and environmental information with available pest control methods to prevent unacceptable levels of pest damage by the most economical means and with the least possible hazard to people, property, and the environment.” It includes activities such as using mechanical trapping devices, natural insect predators and biopesticides, and monitoring crops for damage.

Conclusion
Insecticides have been used for millennia as agents to prevent and mitigate a diverse array of insect species. The merits of these chemicals need to be
carefully weighed with the known and potential harms to the environment and humans. Carcinogenic effects have been observed for numerous individual chemicals. The development of biotechnologies for creating genetically modified organisms, advancements in IPM, and regulatory actions are some of the important directions for the future of insecticides.

Manisha Pahwa

Occupational Cancer Research Centre

Ann Del Bianco

York University

See Also: DDT; Herbicide; Lymphoma, Non-Hodgkin’s, Adult; Pesticides.

Further Readings


Insurance

Health insurance is an arrangement in which individuals pay an up-front premium in exchange for guaranteed full or partial compensation for health care costs resulting from sickness or injury. Health insurance in the United States includes both private and public insurance programs, including Medicare and Medicaid, that provide health care assistance for people who are unable to afford health care coverage. Health insurance organizations determine the cost of an insurance policy by estimating the overall risk of disease and health care expenses among targeted groups or individuals. Organizations then develop a health insurance policy structure, including the monthly or annual premium, deductibles, co-payments, or payroll deductions that will ensure funds are available to pay for health care benefits for individuals or groups as agreed on in the associated health insurance policy. In recent years, supplemental cancer insurance has emerged within the health insurance industry. Cancer insurance was developed in order to mitigate the high costs of cancer treatments and offer the individuals with cancer insurance policies financial assistance.

History of Health Insurance in the United States

Health insurance in the United States began as a quasi-indemnity policy as most people paid a fixed amount per day in the hospital. Just before the Great Depression, Blue Cross became one of the first companies to offer Americans private health insurance. The Blue Cross system originated as an agreement between hospitals and schoolteachers in Dallas, Texas. These early insurance agreements offered individuals reimbursement of a preset amount of hospitalization costs in exchange for a flat monthly premium. Early health insurance policies were run by hospitals; however, following World War II and partially driven by the favorable treatment from federal tax policies, life insurance companies entered into the health insurance market, and the popularity of private health insurance began to grow.
Interest in universal health coverage has consistently remained a subject of American politics; however, the goal to provide Americans with universal health coverage was not within reach until the passing of the Patient Protection and Affordable Care Act (PPACA) by President Barack Obama and the U.S. Congress in 2010. In association with the Health Care and Education Reconciliation Act, the PPACA has been the most significant overhaul of the U.S. health care system since the passage of Medicare and Medicaid in 1965. The goal of the PPACA is to increase the quality and affordability of health insurance and expand the number of Americans with public and private insurance coverage.

Today, health insurance plans are available to groups and individuals or may be obtained through public programs, such as Medicare and Medicaid. Group health insurance plans may then be further divided into either fee-for-service or managed care. Group health plans are offered through employers, educational institutions, professional associations, religious organizations, or other types of groups. Employer-sponsored health insurance plans are the most common form of individual health insurance. Employer-sponsored health insurance is paid for by businesses for employees as part of the employee’s benefit package. Typically, the employer makes a substantial contribution toward the cost of insurance coverage, while the employee is responsible for the remaining cost of the insurance premium, usually paid for with pre-tax or tax-exempt earnings.

Fee-for-Service and Preferred Provider Organization Plans
Fee-for-service health insurance operates under the traditional health insurance agreement in which the insurance company reimburses the care provider or hospital for all or part of the incurred patient fees. Preferred provider organization (PPO) health insurance is the primary type of health insurance in the United States that utilizes this traditional fee-for-service system. In these types of fee-for-service plans, individuals are granted the freedom to choose a care provider or site for health care services. A PPO will contract with individual health care providers in order to create a network of providers, including specialists and hospitals, available to patients. Individuals are granted the freedom to choose their care provider or site for health care services; however, if they choose a provider that is part of their PPO network, their co-payments are fixed at a predetermined amount and are significantly reduced. This system incentivizes individuals to choose providers within the network.

Managed Care and Health Maintenance Organization Plans
Managed care is a term used to describe strategies employed by health insurance organizations that are intended to improve the quality of health care while reducing its cost. These strategies were pioneered by health maintenance organizations (HMOs) but may also be used by other insurance organizations also seeking to reduce health care costs. The traditional fee-for-service and PPO health insurance plans thrived well into the 1970s until the U.S. Congress passed the HMO Act of 1973 in response to the rising costs of health care across the country. HMOs trace their origins to prepaid group health care practices that began in California during the Great Depression. HMOs are designed to implement tight restrictions on provider authorizations for treatments and patient choice of providers as a way to manage treatment utilization and quality. In recent years, the United States has witnessed dramatic growth in the number of HMO companies and plans as the private insurance market has struggled with cost containment.

HMO health insurance plans place the patient’s health care within the management of the insurance company. Patients usually select a primary care physician (PCP) from a list of providers approved by the insurance organization. The PCP then coordinates the patient’s care and is responsible for referrals to specialist physicians and approvals for diagnostic tests and procedures. People with managed care insurance coverage pay an annual or monthly premium and a co-payment when they receive health care services.

Government-Sponsored Health Insurance Plans
In an address on November 19, 1945, President Harry Truman proposed a system of U.S. public health insurance to include a national system, similar to those that were, at the time, common in many European countries. Truman’s proposal garnered wide public support; yet, the U.S. Chamber of Commerce, the American Medical Association (AMA), and the American Hospital Association (AHA)
fiercely opposed it. Truman saw that the battle for a national health care system would be long and costly, and many labor unions chose to support employer-sponsored coverage instead. Therefore, the national insurance system lost momentum and ultimately failed to pass.

Regardless, private insurance still remained unaffordable or unavailable to many U.S. citizens such as the poor, the unemployed, and the elderly. Therefore, many politicians and private citizens continued to express interest in the creation of a form of federally sponsored insurance for individuals in the population who were unable to afford private health insurance coverage. The 1960 Kerr–Mills Act was the first step toward the formation of public health insurance options; the law provided matching funds to states that assisted individuals with health care costs. In 1965, President Lyndon B. Johnson signed the Medicare and Medicaid programs into law through the Social Security Act, creating the first publicly run insurance program for the elderly and the poor; in 1972, Medicare was later expanded to cover individuals with disabilities, end-stage renal disease, and amyotrophic lateral sclerosis (ALS).

Medicare is the U.S. federal social insurance program that was created under Title 18 of the 1965 Social Security Act for people who meet certain age and disability criteria. Primary eligibility requirements include individuals who are 65 years of age and older, some younger individuals with disabilities, and people with end-stage renal disease or ALS. Medicaid was also created as part of the 1965 Social Security Act under Title 19. Medicaid was designed to serve as a social welfare program as opposed to a social insurance program. The program is for individuals with low income and resources and those who receive federal government aid. Medicaid recipients must be U.S. citizens or legal permanent residents, and poverty alone does not necessarily qualify an individual for Medicaid.

Supplementary Cancer Insurance
Cancer insurance is a relatively new phenomenon within the health insurance industry. Cancer insurance is beneficial for policyholders if they are diagnosed with cancer because it helps to mitigate the costs of cancer treatment and provides some financial assistance. This type of insurance is not meant to replace conventional health insurance but instead is meant to augment individuals’ existing health insurance plans covering the high out-of-pocket costs that are often associated with cancer treatment and care. Even more recently, supplemental cancer insurance has become available for specific forms of cancer, including breast and colorectal cancers. These specific types of cancer insurance are most appropriate for individuals who have a family history of a particular type of cancer and, thus, may be at higher risk.

Emily Hammad
David P. Tracer
University of Colorado Denver

See Also: Cost of Therapy; Disability; Government; United States.

Further Readings

International Agency for Research on Cancer

The International Agency for Research on Cancer (IARC) is an intergovernmental agency constituting the specialized cancer agency as part of the World Health Organization (WHO) of the United Nations (UN). The mission of the IARC is to coordinate and conduct research on the causes of human cancer and the mechanisms of carcinogenesis, and to develop scientific methodologies for cancer control.
It conducts epidemiological and laboratory studies into the circumstance of cancer worldwide. It disseminates scientific knowledge through publications, conferences, fellowships, and meetings. The agency also maintains a series of monographs on the carcinogenic risks to humans posed by various forms of agents, mixtures, and exposures. The IARC devotes particular attention to conducting research in low- and middle-income countries through collaborations and partnerships with researchers in these regions.

The development and establishment of the IARC can be traced to the many years of efforts that were devoted to the registration of persons suffering from cancer. Historical accounts show that early efforts to create a cancer census took place in London in 1728. These early, unsuccessful attempts were aimed at establishing reliable and comparable mortality or morbidity statistics. For more than 100 years until around 1900, nevertheless, demands in England and Germany persisted for improved statistical investigations on the promulgation of the cancer population as an imperative basis for etiological research. In 1900, an undertaking was again made to register cancer patients who were receiving medical treatment in Germany, based on the results of a general survey on cancer in Hamburg. Although the German approach was repeated between 1902 and 1908 in the Netherlands, Spain, Portugal, Hungary, Sweden, Denmark, and Iceland, the attempt to improve cancer registration continued to produce unsatisfactory results because of low participation in all the surveys.

Meanwhile, a cancer registration project had started in the United States, with ideas and recommendations that required compulsory registration of all cancer cases. Yet, the cancer registration that was piloted in the state of Massachusetts in 1927 was unsuccessful as only about one-third of the cancer cases were reported. The registration scheme that began in Mecklenburg in 1937, recording individuals, yielded better outcomes than the institutional approach. Between 1937 and 1938, the Mecklenburg registration format worked fairly well, as indicated by a recorded rate of about 200 new cancer patients per 100,000. Regional political developments caused a discontinuation of similar registration initiatives instituted in Saxony-Anhalt, in Saarland, and in Vienna in 1939. In the United States, similar encouraging outcomes were recorded, as all cases of cancer were documented in 10 urban areas during a calendar year in 1937 and 1938 and again in 1947 and 1948. From the mid-1940s, many individual countries participated in some form in the development of cancer registries.

Perhaps the most paramount momentum for the global establishment of cancer registries resulted from a conference that was held in Copenhagen in 1946 under the leadership initiative of the then director of the Danish cancer registry, Dr. Clemmesen. Following the conference, a group of 12 international leading authorities in the field of cancer control provided the interim commission for the WHO with recommendations for the worldwide establishment of cancer registries. Those recommendations suggested the following:

1. Great benefits would follow the collection of data about cancer patients from as many different countries as possible.
Such data should be recorded on an agreed-upon plan so as to be comparable.

Each nation should have a central registry to arrange for the recording and collection of such data.

There should be an international body whose duty it should be to correlate the data and statistics obtained in each country.

In May 1965, the IARC was established as a specialized cancer research center through a resolution of the 18th World Health Assembly (WHA) as an extension of the WHO. The founding nation members of the IARC were the Federal Republic of Germany, France, Italy, the United Kingdom, and the United States. France provided the building for the agency’s headquarters, located in Lyon, France. Recent member nations joining the IARC include Australia, Austria, Belgium, Brazil, Canada, Denmark, Finland, India, Ireland, Japan, Norway, the Netherlands, Qatar, Korea, Russia, Spain, Sweden, Switzerland, and Turkey.

In the area of governance, the IARC follows the same general rules as all other UN organizations. Particularly, it is governed by a governing council (GC), composed of the representatives of participating states, the director-general of the WHO, and the scientific council (SC). The GC elects the IARC’s director, who usually serves for a five-year term. The director reports to the IARC GC and is responsible for the overall leadership of the agency. The FC membership consists of highly qualified scientists who are appointed for four-year terms by the GC. In 2014, the IARC’s SC was headed by Dr. C. Ulrich as the chairperson, with Dr. J. F. Bishop as the vice chairperson. The Office of the Governing Council had Dr. M. Palmer as the chairperson, with Dr. A. Buzyn as the vice chairperson. The WHO’s director-general was Dr. M. Chan.

IARC activities are principally funded by the regular budget contributions paid by its participating states. The GC approved the biennium 2014 to 2015 budget in May 2013, at a level of 40,424,491 euros. Among the major funding sources for the IARC operations are the European Commission, the United States National Institutes of Health, the World Cancer Research Fund International, and the Bill and Melinda Gates Foundation. Also, the agency receives significant funding support from both governmental and charitable sources in France.

Felix O. Chima
Prairie View A&M University

See Also: International Association of Cancer Registries; Statistics; World Health Organization.

Further Readings

International Association for the Study of Lung Cancer

In 1972, the First International Workshop for the Therapy of Lung Cancer was sponsored by the National Cancer Institute. The international group of people enthusiastically supported Dr. David T. Carr’s suggestion that an international organization be founded. An organizational committee, including Dr. Carr, Dr. Oleg S. Selawry, Dr. Lawrence Broder, and Dr. George Higgins began to develop the association. The International Association for the Study of Lung Cancer (IASLC) was founded in 1974. Initially, 250 individuals accepted membership. Today 4,000 lung cancer specialists are among its members from 80 countries. Worldwide management is the responsibility of IASLC’s Council of Regents, a network of professionals around the world who are responsible for a country or group of countries within a geographical area to ensure effective communication among members and potential members. IASLC works to increase understanding of lung cancer with scientists, the public, and the medical community.
IASLC’s mission is comprised of three key concepts: (1) to embrace all aspects of lung cancer and other thoracic malignancies through the study of their etiology, epidemiology, prevention, diagnosis, and treatment; (2) to provide information and education about thoracic malignancies and lung cancer to IASLC members, the medical community, and the public; and (3) to use all means to eliminate thoracic malignancies and lung cancer as a threat to the individual patient and throughout the world.

The IASLC’s *Journal of Thoracic Oncology* (JTO) was first published in January of 2006. Initially publishing nine issues per year, the journal is now published monthly with multiple supplements. It is a multidisciplinary approach that includes original research, reviews, and opinions. Its audience includes all those involved in the treatment and research of thoracic malignancies and lung cancer, including pathologists, researchers, oncologists, pulmonologists, surgeons, radiologists, and epidemiologists.

The newest strategic plan approved by the IASLC board of directors includes seven mission goals: (1) embrace the study of lung cancer and thoracic malignancies; (2) provide education and information to the public, the medical community, and IASLC members; (3) advance research to reduce the incidence of thoracic malignancies worldwide; (4) commit to long-term, global growth; (5) value the work of volunteers; (6) solicit philanthropic funding to support research and education; and (7) commit to fiscal responsibility and operational excellence.

IASLC is significantly active in creating and maintaining 17 committees. The Awards Committee determines IASLC award recipients. The Career Development Committee recruits mentors to help members progress through their careers. The Communications Committee seeks to increase awareness of IASLC and educate the public. Education programs are planned and initiated by the Education Committee. The enforcement of ethical conduct and rulings on ethical issues are the responsibility of the Ethics Committee. Regular business of the association is monitored and completed by the Executive Committee. The Fellowship Committee selects recipients for the IASLC Lung Cancer Fellowship Award and Young Investigators Award. Fiscal management and risk management is monitored by the Finance Committee. The Membership Committee recommends and reviews levels of membership and strategizes to increase and maintain membership. The Nominating Committee develops a pool of members as candidates for elected positions. The Nurses and Allied Professionals Committee ensures IASLC is meeting nursing and allied health-related needs. Review of lung and thoracic malignancies is the responsibility of the Pathology Committee. The educational and related needs of the public are met by the Patient Advocates Committee. Cancer prevention activities are the responsibility of the Prevention, Screening, and Early Detection Committee. The Publications Committee manages all IASLC publications, including the JTO. The Staging Committee studies and improves patient information and research to improve the cancer staging system. The Tobacco Control and Smoking Cessation Committee aims to reduce the use of tobacco worldwide.

Some of the benefits associated with membership in the IASLC include access to the JTO, free continuing education opportunities, discounted registrations at workshops, eligibility for fellowship and travel awards, a monthly newsletter, and access to the member directory. Regular membership is for all researchers and clinicians at a rate of $250 per year. Allied health professional membership is discounted at a rate of $50 per year for nurses, therapists, patient advocates, statisticians, and pharmacists. Developing country membership also has a rate of $50 per year. Fellows, residents, and trainees may apply for a complimentary, nonvoting membership. IASLC also offers joint membership at discounted annual rates to the Pulmonary Pathology Society ($125) and the International Thoracic Oncology Nurses Forum and National Lung Cancer Forum for Nurses ($30).

Every year, IASLC supports young researchers to encourage innovative research. Three researchers who represent North America, Asia, and Europe are awarded funding for one year. The Prevent Cancer Foundation jointly sponsors the research with grants from Eli Lilly. Additionally, in collaboration with Boehringer Ingelheim, the Chinese Lung Cancer Fellowship Award enables one researcher to come to the United States for one year to research a project. The Lung Cancer Foundation of America also collaborates with IASLC with the Lung Cancer Research Grant, awarded every two years.

IASLC has also partnered with Patient Resource Publishing to produce the *Patient Resource Lung Cancer Guide*. The guide provides details to families
and patients with the information they need upon diagnosis. The information provided includes financial resources, symptom and side effect management, treatment options, and staging and pathology. IASLC also supports a variety of materials published by the American College of Chest Physicians, who in part provide smoking cessation information to practitioners and physicians.

Jessica Anne Hammer

*Independent Scholar*

**See Also:** Environmental Tobacco Smoke; International Cancer Alliance for Research and Education; Japan Lung Cancer Society; Lung Cancer, Non–Small Cell.

**Further Readings**


**International Association of Cancer Registries**

The International Association of Cancer Registries (IACR) was established in 1966 in Tokyo as a global professional body to address both preventive and treatment dimensions of cancer. It aimed to develop standardized measures to estimate the prevalence and incidence of cancer globally to generate comparable data.

**History**

The earliest attempts to estimate the number of cancer cases were made in European countries at the turn of the century. In the United Kingdom, initial attempts to measure cancer prevalence based on mortality and morbidity statistics were undertaken in London, though these attempts were unsuccessful. In 1900, under the auspices of Katz, Germany was the first country to register all cancer patients undergoing treatment. On October 15, 1900, all physicians in the country were sent out questionnaires through the Prussian Ministry of Culture to record the details on prevalence of cancer. Between 1902 and 1908, several European countries, such as Denmark, Hungary, Iceland, the Netherlands, Portugal, Spain, and Sweden, made attempts to collect similar information but, however, were met with limited success owing to poor response and lack of collaboration among physicians. The first population-based cancer registry was set up in Hamburg, Germany, in 1926, and the main thought underlying this registry was not only to address medical dimensions of cancer but also to take into account public health dimensions. As a part of this work, three nurses visited hospitals and medical practitioners at regular intervals in Hamburg and recorded the names of the new cancer patients in the hospitals that were then transferred to the central index in the health department. This data was later compared to the official death certificates. By 1955, the country had 55 cancer registries. In the United States, around 1930, Wood indicated that cancer should be a notified illness and registration of cancer cases should be mandatory. In 1927, the state of Massachusetts started registering cancer cases, and it was a failure as only one-third of cases were registered.

The global importance of cancer registries came after a conference in Copenhagen in 1946 under the initiative of Dr. Clemmesen, the director of the Danish cancer registry in 1946. Twelve international experts recommended establishment of cancer registries to facilitate cancer control to the interim commission for the World Health Organization (WHO). They recommended collection of information on cancer patients across the world; that information should be collected in a uniform fashion to be comparable, and centralized cancer registries should be established in all countries of the world along with an international body that will correlate data and statistics from various registries in each country. The WHO established a subcommittee to work on the registration of cases of cancer and the statistical presentation of these cases. The International Union Against Cancer (UICC) in 1950 organized an International Symposium on Geographical Pathology and Demography of Cancer, which reiterated the importance of enumerating the prevalence
of cancer. In 1965, the IACR was established to standardize data collection methods across all the registries in the world. It was established as a specialized cancer research center under the WHO to generate comparable data globally.

Today, it serves as an organization that has membership of all cancer registries that collect and analyze data on the prevalence and incidence of cancer and study its implications for treatment in defined population groups. There are 200 cancer registries across the world, which cover around 5 percent of the world’s population, with more cancer registries located in developed countries. In developing countries, these registries are located in urban areas, which have more facilities for diagnosis and treatment. Population-based cancer registries cover only a small part of the population and are located in Colombia, India, Italy, and the United States. Few specialized registries for particular age-groups, such as the one on childhood cancer located in Oxford, United Kingdom, exist, and there are specific cancer sites such as the one in Dijon, France, for gastrointestinal cancers.

Role of Cancer Registry
Cancer registries play vital roles in cancer control as they periodically register and record all cancer cases that occur in the population, with specific details of cancer patients along with their clinical and pathological characteristics of cancers collected continuously and systematically from various data sources. Each registry analyzes and interprets the data to discern the information on the incidences and characteristics of cancer prevailing in population groups and variations across time in the occurrence of cancer. Population-based registries are vital in planning, monitoring, and evaluating various health services for the prevention, diagnosis, and treatment of the disease. Hospital-based registries could potentially assist health care providers in following up cases and generate data on the impacts of therapy.

Currently, the IARC series Cancer Incidence in Five Continents estimates that most of the registries are located in North America and Europe and there is a need to establish more registries in developing countries. In spite of variations in the data due to local needs and availability of information, the use of common nomenclature enhances the international comparability of the data.

Another important contribution made by cancer registries is to study disparities among and within nations. Through internationally comparable studies, it is possible to ascertain the dominant forms of cancer in certain spatial areas along with their risk factors and therefore design preventive and treatment pathways.

Within nations, it is possible to study prevalence of cancer among socially and economically deprived sections of the population and address issues of gender, race, ethnicity, and class in the planning of health services. The data collected by registries provide the most important tool for monitoring and evaluating the effectiveness of public health policies to mitigate cancer.

Keerty Nakray
Jindal Global Law School

See Also: Developing Countries; International Agency for Research on Cancer; National Cancer Registrars Association; North American Association of Central Cancer Registries; Organisation of European Cancer Institutes; World Health Organization.

Further Readings


International Cancer Alliance for Research and Education

The International Cancer Alliance for Research and Education, or ICARE, is a nonprofit organization. The group was founded in 1981 in Bethesda,
Maryland, by renowned cancer scientists from all over the globe. The organization was intended to serve cancer think tanks that looked to identify obstructions to innovation in cancer research laboratories.

It is nearly impossible for one physician to care for any number of patients and simultaneously stay on top of every innovative treatment or promising trial that could benefit his or her patients. That's where ICARE comes in. The goal of this organization is to facilitate the communication of cutting-edge, life-saving information about cancer treatment among researchers, physicians, and patients. ICARE supports researchers in attempting to transition research from the lab to the patients through clinical trials. According to the ICARE mission statement, the organization wants to have the best minds in medicine to create the best chance of survival for cancer patients.

ICARE provides information geared toward people suffering with cancer and the physicians who treat those people on a person-to-person basis. Cancer is used broadly, meaning it includes any group of diseases whose characteristics include uncontrolled, rapid growth of cells that may invade and metastasize to other tissues or organs.

Cancer may be categorized by the organ or type of cell involved, whether or not it is malignant, and the course the disease most often takes. ICARE sponsors several programs geared toward patients through collecting, evaluating, and providing information and putting affected patients into contact with doctors and scientists worldwide. The alliance is composed of a network of scientists, physicians, staff, and volunteers, many of whom have felt the effects of cancer on a personal level. The alliance maintains a registry, which is a confidential membership list that allows for continued communication between ICARE and its members.

ICARE has been responsible for initiating many information and research programs that had the potential to up patient survival rates by increasing the flow of information on therapy advances to doctors and patients.

Over the past few years, ICARE has begun to change its scope from a solely informational entity to identifying, starting, and funding cutting-edge research projects aiming to treat tumors in individual patients. Research projects such as these have the potential to hasten the development of new therapies with fewer side effects. This change of scope was kick-started in 2010, when a group of ICARE scientists accepted the challenge of working with individual patients and their physicians to attempt to find treatments as swiftly as possible for clinical problems facing both patients and their doctors.

From 2010 to 2013, ICARE received funding to establish customized medical projects for three individual patients who were suffering from advanced stages of cancer. One was suffering from a rare form of cancer affecting the liver, and both of the others suffered from variations of metastatic melanoma. The project led to the development and consideration of more than 30 new medications or techniques to be used by the doctors of these three individuals.

Currently, ICARE is serving its mission by working with individuals in an investigative program that begins with one patient, one physician, and one researcher. The investigative teams, or I-Teams, participate with patients and their doctors in real-time academic research projects that are personalized to the cancer patient and his or her needs. I-Teams now constitute the majority of ICARE's efforts to achieve its mission.

On the official ICARE Web site, one can find a myriad of links to research for everything from bladder cancer to sarcoma. In addition to providing information on specific types of cancer, ICARE participates in a clinical trial-matching program. ICARE currently provides clinical trial information through its think tanks and symposiums, both of which have full participation from patients, leading physicians in the field, and cancer scientists.

In addition to sharing clinical trial information, ICARE also provides cancer therapy reviews (CTRs). These are published for many different kinds of cancer with the goal of housing all therapy information pertinent to the diseases in one central source. These CTRs contain much more than general descriptions and brochures that patients often receive from other sources. Each CTR provides an overview of the disease, information on staging procedures, the most current treatments and diagnostic tests, and a list of ongoing clinical trials and second-opinion centers, among other things.

ICARE is dedicated to forming a partnership of education and study involving cancer patients,
doctors, and researchers. Knowledge and the sharing of knowledge are key to ICARE’s mission. The objectives of ICARE are to create I-Teams to investigate each type of cancer among the medical, scientific, and patient communities; to provide support for the movement of research from lab to patient; and to facilitate creativity and innovation in cancer research. Patients and their physicians are given easy-to-use, comprehensive information regarding options for treatment and the most cutting-edge medical advances. ICARE is getting involved in the community by reaching out to local high schools, organizations, and small businesses.

ICARE is funded by donations from individuals who believe that targeted research will eventually lead to cures for these diseases. Already, a lot of good has been accomplished. Through ICARE, patients and doctors can research diagnoses and make the most informed decision for treatment based on the trials and research for a myriad of cancer types. Knowledge can be survival in this case, and ICARE provides that knowledge to patients and physicians alike. Through individual treatment studies, matching patients with clinical trials, and facilitating research into these subjects, ICARE makes a large impact on behalf of cancer patients worldwide.

For more information on how to get involved as a volunteer for ICARE or to make a donation, the ICARE Web site is http://www.icare.org. For more information about volunteering, visit http://volunteer.truist.com.

Michael Fox
Independent Scholar

See Also: American Association for Cancer Research; European Association for Cancer Research; Lymphoma Research Foundation of America.

Further Readings

International Committee of the Red Cross

The International Committee of the Red Cross (ICRC) is an international humanitarian organization based in Geneva, Switzerland, founded by Swiss businessman Henri Dunant. In 1859, Dunant witnessed the suffering and dismal medical care received by wounded soldiers during the battle of Solferino, which pitted the Franco–Sardinian Alliance against the Austrian Army. Dunant, with the help of the local community, offered what help and assistance to injured soldiers and civilians he could, regardless of on which side of the conflict they were. Dunant understood that organizing in order to provide appropriate medical attention and humanitarian intervention could save and help heal many of the injured. He began to advocate internationally for a better system in order to achieve this. Today, 189 individual National Red Cross and Red Crescent societies form the International Federation of the Red Cross and Red Crescent Societies, which are associated with the ICRC. Worldwide, the ICRC has more than 10,000 staff in 80 countries. The organization has helped in war conflicts throughout the two world wars and in other modern battleground and war-induced crises as well as in natural catastrophes worldwide.

The ICRC has always aimed to offer protection and assistance to people suffering from crises and catastrophes around the world. In 1862, Henri Dunant published his book Memories of Solferino, which he sent to leaders worldwide. It soon impacted European society. He proposed the idea of developing a network of organizations in all nations capable of helping the injured and other victims in times of war.

Four Swiss citizens joined forces in order to achieve this goal: General Guillaume-Henry Dufour, lawyer Gustave Moynier, and two doctors: Louis Appia and Théodore Maunoir. In 1863, they founded an international aid society to help injured soldiers, which in time would become known as the ICRC. During that same year, the ICRC organized the first international conference in Geneva, in which 16 nations participated, with the end result of providing for the amelioration of the conditions of those injured at war. It was at that point that its emblem of a red cross over a white background was
adopted. The emblem covers situations of armed conflict, medical and religious personnel, military as well as civilians, who may use it to provide the injured with medical attention, equipment, and transportation. This marked the inception of the field of contemporary humanitarian human rights and the Geneva Convention of 1864.

The ICRC of the 1920s, after World War I, moved to implement additional rules to the provisions of the Hague Conventions of 1899 and 1907, which proved insufficient to protect civilian populations in enemy and occupied territories. The Geneva Conventions include four treaties: 1854, 1906, 1920, and 1949. The latter was ratified by 196 countries and proved seminal in setting international standards for humanitarian treatment of people during war. In 1949, after the horrors of the Holocaust had come to light, states agreed to the idea of protecting civilians under enemy control. Additional protocols were added in 1977 and 2005, which extend the ICRC’s mandate to international as well as internal armed conflicts. Among many awards won during its trajectory, the ICRC has been awarded the Nobel Peace Prize in 1917, 1944, and 1963.

The International Red Cross Committee Today
Since its inception, the ICRC’s goal has extended its mandates to provide protection and help not only to soldiers but also to victims of armed conflict, war, and catastrophe. Victims of war include noncombatant people who have been wounded or become prisoners and refugees. During World War I, the ICRC began implementing systems to connect military prisoners with their families. It also began to visit prisoners of war and political prisoners to ensure they were treated humanely and to call for the end of weapons of mass destruction such as mustard gas. Today, the mandate and mission of the ICRC follows the Geneva Conventions of 1949 and its additional protocols, and the original system has extended to help bring together people who have been displaced by catastrophes.

By World War II, the ICRC had persuaded more governments to adopt the Geneva Convention of 1929, which amplified the protections for prisoners of war. The ICRC, however, had not managed to get all countries to agree on international legislation to protect civilians in war-affected areas or under enemy control and thus had been unable to protect the millions of victims of the Holocaust.

Since the post–World War II years, the ICRC continued its mediating and humanitarian labor, working to persuade governments and leaders to support and respect international humanitarian legislation. It also has worked to help with the consequences of armed conflicts on populations, such as helping people in refugee camps, among others. The protection and aid mandates of the ICRC cover four types of population: the injured and sick in battlegrounds, injured and sick at sea, prisoners of war, and civilians under enemy control. Given the disasters that occurred against unarmed civilians during World War II, specifically the bombings of Hiroshima and Nagasaki, the ICRC has long advocated for nuclear disarmament as a humanitarian imperative. It also has been instrumental in bringing war-torn families together and in creating safe refugee camps for those displaced by wars. The Red Cross today is a standard-bearer respected by states and armed combatants worldwide and continues its mission to advocate for peace and for respect of humanitarian and international law.

Trudy M. Mercadal
Florida Atlantic University

See Also: International Cancer Alliance for Research and Education; International Society of Nurses in Cancer Care.

Further Readings
International Myeloma Foundation

The International Myeloma Foundation (IMF) is a nonprofit organization based in North Hollywood, California. The primary aim of the foundation is focused toward finding a cure for multiple myeloma, a rare and incurable cancer of the plasma cells. The IMF works collaboratively with patients diagnosed with myeloma, families, myeloma specialists, and researchers at local, national, and global levels to meet this goal. However, the discussion about IMF cannot be appreciated unless myeloma is discussed.

Myeloma: A Rare and Incurable Cancer

Myeloma, also known as multiple myeloma, stems from the plasma cells, which are formed within the bone marrow. There are many individual variations in terms of symptoms, prognosis, and treatment options associated with myeloma; however, a diagnosis of multiple myeloma can potentially lead to a range of symptoms, depending on the severity of the disease process, which can include fatigue, pain, bone fractures, weight loss, and kidney problems. The term *multiple myeloma* is used as there are many areas of the body that can potentially be impacted by the disease process due to the fact that it stems from the bone marrow sites. It is also a disease that potentially can have a significant psychological impact on the person affected as well as his or her surrounding family and friends.

There are a number of treatment regimens available at different stages of the disease, all with varying side effects, and the treatment options available for myeloma have increased over the years and have extended the lives of many people living with myeloma. Such treatments can offer hope and a level of optimism in the face of a disease that may trigger uncertainty about the future.

Origins and Key Functions

According to the IMF Annual Report of 2013, the IMF has, since its founding, developed collaborative networks with approximately 350,000 members in 120 countries worldwide. The IMF originated in 1990 when a patient diagnosed with myeloma, Brian Novis, his partner, Susie Novis, and the hematologist providing their care and support, Dr. Brian G. M. Durie, decided to set up the foundation in recognition that there were gaps in the provision of information and support for people affected by myeloma.

Following an impressive and productive commitment to the founding and development of the IMF, Brian Novis died in 1992. Since then, Susie Novis and Dr. Durie have continued to advance the mission of the foundation in their respective roles as president and chairman and IMF board of directors to develop it into the flourishing and influential organization that exists today.

The IMF, in its mission statement and award-winning multilingual Web site, highlights a number of key areas that are central to their work, which include research, education, support, and advocacy.

Patient and Family Support

Given the significant impact of receiving a diagnosis of myeloma on the patient and his or her family members, there is a need for timely and accessible information and support. The IMF plays a key role in delivering such support through the provision of patient and family support seminars, which take place around the world. As of 2013, the IMF supports 245 support groups worldwide. Patients and family members have opportunities to attend seminars and hear about the latest, cutting-edge research and treatment interventions from highly skilled researchers and specialists working in the field of multiple myeloma. The seminars aim to educate and support people affected by myeloma so that they can increase their understanding of the disease and treatment options.

In addition to seminars, being a member of the IMF provides both patients and their families support through a toll-free information line when the need arises to clarify questions and obtain crucial information throughout the different stages of the disease process.

The IMF Web site provides comprehensive, current information about a variety of topics relevant
to myeloma and explains the key roles and functions of the IMF. Recognizing the importance of technology for disseminating information, the IMF has also developed a Myeloma Post app, which offers a further medium for provision of information and support. Beyond the efforts already identified, the IMF has a presence on social media, including Facebook and Twitter. These social media channels of communication have proved particularly effective during myeloma awareness week, observed in March each year, to both provide support and raise awareness.

The opportunities to access information relating to developments around myeloma and potential treatment options through seminars, the website, the app, Facebook, and Twitter or via the information line can potentially empower patients and their families and enable them to take active roles in their treatment through informed decision making.

**Research**

Working collaboratively worldwide and capitalizing on the cutting-edge technology that is available, there are a number of research initiatives in which the IMF has been involved. These have ranged from supporting research through funding to engaging in relevant research with partners around the world. The IMF has been involved in funding research initiatives since 1994 and, according to its 2013 annual report, has awarded 115 research project grants since 1994.

**Bank on a Cure**

Working internationally with key partners, the IMF has been involved in research called Bank on a Cure aimed at gaining a deeper understanding of the link between different DNA patterns and myeloma. It is anticipated that obtaining and analyzing samples of DNA from patients with myeloma will provide important information about potential causes of myeloma and provide specific information about which treatments can be tailored to individuals depending on their genetic analysis.

**The Black Swan Research Initiative**

The Black Swan Research Initiative (BSRI) focuses on research aimed at identifying a cure for myeloma. The name of the initiative originates from the discovery of the black swan in 1697, where up until that point in time, it was assumed that only white swans existed. Similarly, although there is currently no cure for myeloma, it is envisioned that there could be a cure in the future. According to the IMF, the BSRI is the signature project of the IMF and is a multipronged research project based on the growing understanding of how myeloma develops in the body as well as the ability to assess, measure, and quantify the disease development in the body and to measure and quantify the response to treatments. The BSRI is also dedicated to using treatments that will leave patients with the most minimal level of residual disease. The ultimate goal is to reach no residual disease, which should lead to a cure. Currently, the BSRI is working to define a cure as MRD-Zero, the eradication of minimal residual disease. This is important research as myeloma is currently a relapsing and remitting disease.

**Advocacy**

The IMF plays an important role in advocating for people with myeloma and their families and has also set up a number of advocacy initiatives focusing on raising awareness of multiple myeloma. The IMF has set up the first and only existing international
cohort of patients and people working in the area of myeloma in an attempt to work toward ending insurance coverage disparities, which ultimately lead to unequal access to treatment.

The setting up of the Myeloma Action Team, founded in 2013, builds on strengthening community networks and empowering advocates to influence policy development and federal legislation, particularly in relation to lobbying for access to treatment for people with myeloma who need it.

Conclusion

As has been discussed, the IMF plays crucial roles in driving the agenda for action and reflection on myeloma. Over the time of its existence, it has made great strides to improve the nature and quality of services for myeloma patients and their families. The collaborative relationships between myeloma patients, their families, myeloma specialists, researchers, the IMF, and service providers are perhaps some of the most innovative and unique types of collaborative relationships that can be found within medical and health contexts. Thus, it cannot be disputed that the foundation has achieved significant milestones. It must be acknowledged, however, that the future lies in such efforts being harnessed and sustained through financial, academic, and other human resources and from within communities and beyond. Having started from humble beginnings, the IMF has emerged as a global entity that plays a crucial role in empowering patients and their families and in providing a sense of hope in the face of an uncertain disease process.

Kathleen Nthakomwa-Cassidy
Coventry University

See Also: Insurance; Multiple Myeloma/Plasma Cell Neoplasm; Plasma Cell Neoplasm/Multiple Myeloma.

Further Readings

International Psycho-Oncology Society

There is more to oncology than just treating cancer. There is a spiritual and emotional response to this by both the patients and their families. Patients have a higher chance of improvement and healing if these needs are also met. That is what the International Psycho-Oncology Society (IPOS) tries to foster by providing education and serving as an advocate for the goal of providing psycho-oncology to cancer patients.

In terms of education, IPOS sponsors the Psychosocial Academy. The lessons are provided by leaders in the field, and several workshops are offered throughout the year to address the most important issues faced both in research and in practice. The Psychosocial Academy provides numerous different courses: research methods, demonstrations of hypnotic and mind–body regulation for symptom management, the genetics of cancer, helping children cope with a parent that has the illness, end-of-life and palliative care, and more.

Among the goals of IPOS are educating doctors, patients, and families of patients. They press for further research and education in the emotional and mental effects of cancer on individuals and their families. They also seek to bring about more understanding of the importance of psychosocial resources to victims of cancer. Two main realms of the psychosocial view of cancer are the reaction of patients, families, and staff to the cancer diagnosis and treatment in all stages as well as the social and behavioral patterns that have an impact on tumor progression and the survival rates of patients. The ultimate goal is to provide cancer patients and their families all over the world with the best psychosocial care at every stage of the disease.

Cancer patients who learned relaxation coping skills before going through treatment had an easier time dealing with symptoms of treatment such as nausea and pain. The relaxation techniques used in the study included hypnosis and muscle-toning treatments. These techniques also are used to reduce problems in the body. If these techniques were learned before treatment, they also served to lower the anxiety of patients undergoing more
potent treatments to slow or destroy cancer. Individuals going through cancer treatment often feel out of control and hopeless, so these techniques give them something they can control and may help them to feel more connected to their treatment.

Some of the most common maladies caused by cancer treatment include nausea, pain, blood pressure, and pulse rate. The emotional needs of the patient can entail the need to control hostility, mood, and other common behavioral threats that can get in the way of a healthy lifestyle. The relaxation techniques patients were taught did more for anxiety than any other side effect regardless of the type of treatment the patient was undergoing. Counseling was also shown to be beneficial in terms of reducing distress, self-image, locus of control, tiredness, and sexual dysfunction. Structured counseling also showed benefits with depression and distress. Behavioral exercises and hypnosis were effective with symptoms such as anxiety, pain, nausea, and vomiting.

In a study of women with breast cancer, an experimental group was included in sessions aimed at reducing stress, helping with mood, changing health behaviors, and encouraging maintaining the cancer treatment and care. The results of the experimental group showed significant progress. Patients were more likely to improve behaviors such as smoking cessation, dietary habits, and social support. Their immune responses were also improved markedly just like their psychological and behavioral progress. The improvements were physiological as well as psychological.

Other studies have implied that these group therapies may not prolong life but argue that the quality of patients’ lives were improved. Patients had better moods and were better with pain management, showing the greatest results in women who had psychological distress or poor pain management skills at the time they entered the study. According to some studies, women with metastatic breast cancer that regularly attended an intensive support group lived 18 months longer on average than the control group. Those findings encouraged use of psychosocial treatment, but they have been criticized in tests that could not replicate such a trend.

There are concerns that the medical community will not acknowledge these results and use such treatments in the care of cancer patients. Quality-of-life results have been ignored in the past in cases where there was no physically measurable improvement in health. According to one researcher, the treatment should not be invalidated because it does help cancer patients. Even if it does not prolong life, it was instrumental in helping patients deal with pain, depression, and other quality-of-life improving metrics. Whether or not such psychosocial techniques prolong the lives of patients has been debated by different studies, but the benefits in pain management, depression, anxiety, and social support are clear.

One trend that these studies consistently show is that highly distressed breast cancer patients who go through these group therapies show positive changes. These highly distressed patients develop coping skills that alleviate their emotional and psychological symptoms. These studies alone suggest that doctors should give this methodology more consideration, especially in the treatment of highly distressed patients.

According to other studies, connected to written treatment manuals for leading these groups of breast cancer patients, a difference should be made between first-time cancer patients and women whose cancer is recurrent. It was more beneficial for these women to be in the respective groups that they belonged to. First-time cancer patients are dealing with different emotions and different struggles than women who have battled cancer already.

There are other forms of psychosocial treatments that are being researched, including individual therapy, acupuncture, meditation, and yoga. As these alternative therapies are being explored, physicians and counselors are keeping the needs of the patients in mind. These treatments give them a place to express their fears and stress, connect with other women who relate to them, and provide other intangible benefits that the patients consider important or encouraging. These metrics keep such alternative treatments from being ruled out as lacking any benefit, although spiritual and emotional benefits may be more difficult to discern.

Michael Fox
Independent Scholar

See Also: Alternative Therapy; Mind, Body, and Spirit; Breast Cancer; Pain and Pain Management.
International Society for Cutaneous Lymphomas

The International Society for Cutaneous Lymphomas (ISCL) is a nonprofit association with worldwide operations. It was founded in December 1992 at the World Congress of Dermatology in New York. The association is headquartered in Geneva, Illinois. The founding members of the association were Perter Heald from Yale Dermatologists Associates, New Haven, Connecticut; Gunter Burg from the University of Zurich, Switzerland; and Eric Vonderheid from Johns Hopkins University, Baltimore, Maryland. The objectives of ISCL are to increase knowledge of lymphoproliferative and related disorders of the skin and to foster collaboration among clinicians, scientists, and regional or national groups by sponsoring a database of different lymphoma problems and other common issues relating to the diagnosis and control of lymphoma as it develops. In summary, these objectives of the association can be stated as to foster communication and stimulate interactions among regional and national groups and individuals interested in cutaneous lymphomas. ISCL was formed after the realization that there were several regional groups that worked toward improving health care for persons with cutaneous lymphomas. ISCL was meant to create a global central point for coordination of the activities of the various groups.

Today, the association still works toward the realization of these objectives. The leadership of ISCL has been made up of Youn Kim, MD, from Stanford University Medical Center California, United States, as the president; Maarteen Vermeer, MD, PhD, from Leiden University Medical Center, The Netherlands, as the secretary; and Larisa Geskin, MD, of the University of Pittsburgh Medical Center, Department of Dermatology, Pittsburg, Pennsylvania, United States, as the treasurer. Under the executive arm of ISCL is the board of directors, which is made up of 18 members. The current members of the board are Marie Beylot-Barry of France; Kwang Hyun Cho of Seoul, Korea; Francine Foss of New Haven, Connecticut; Robert Gniadecki of Copenhagen, Denmark; Joan Guitart of Chicago, Illinois; Emmilia Hodak of Petah Tiqva, Israel; Richard Hoppe from Stanford, California; Werner Kempf from Zürich, Switzerland; Thomas Kupper from Boston, Massachusetts; Pablo L. Ortiz-Romero from Madrid, Spain; Pierluigi Porcu from Columbus, Ohio; H. Miles Prince from Melbourne, Australia; Pietro Quaglino from Torino, Italy; José Antonio Sanches, Jr., from São Paulo, Brazil; Professor Rudolf Stadler from Minden, Germany; Makoto Sugaya from Tokyo, Japan; John A. Zic from Nashville, Tennessee; and the Web site chair, which has been occupied by Elise A. Olsen from Durham, North Carolina.

To reach its global consumers, ISCL has a Web site through which interested persons can register as members. The majority of those who register are persons who are suffering from cutaneous lymphomas, persons looking for information about the diseases, or persons who wish to provide useful information about the disease. As a result, there are four membership categories:

General membership is available or can be granted to any physician or scientist actively involved in the care of patients with lymphoproliferative skin disorders or who are engaged in research in this or a related area. Associate membership can be granted to an allied health care professional, an individual, or an entity that grants financial support to the society or an individual involved in a cutaneous lymphoma patient support group who is interested in, and supports, the purposes of the society. Honorary membership is sought as a privilege position in the ISCL and is granted to any individual, who, as determined by the board of directors, has made an outstanding contribution to the society and to the field of cutaneous lymphoproliferative disorders.
As such, this membership is more of an appreciation for exceptional work in the field of cutaneous lymphoma. Resident membership may be granted to any physician in good standing who is in a residency program or postresidency fellowship and is interested in the field of cutaneous lymphoproliferative disorders.

Applications to become a member of the association are reviewed by the executive committee of the ISCL. As a member of the ISCL, one is entitled to serve on committees and attend the meetings of the association. However, it is only general and honorary members who have the power to vote as well as hold offices. The society holds meetings often as well as invites its members to attend meetings related to dermatology and cutaneous lymphoma.

To achieve its objectives of disseminating information to the various groups and individuals interested in cutaneous lymphoma, the ISCL publishes materials that are useful to its members. These will be from the members and researchers of the ISCL or from third-party sources. In addition to these publications, the meetings that ISCL members are eligible to attend contribute greatly toward the realization of the association’s objectives. ISCL also works in association with other cutaneous societies, for example, the Cutaneous Lymphoma Task Force (EORTC), the Japanese Association for Cutaneous Lymphomas, and the Latin American Cutaneous Lymphoma Group. The operations of the association are mainly through members’ contributions or donor contributions.

For improved care of cutaneous lymphoma patients, research is important for the establishment of new, better, and innovative care as well as management strategies for the disease. To realize this, the ISCL has several research projects as well as clinical trials in the United States. Some of these include the phase I dose-finding and preliminary efficacy study of Istodax in combination with Doxil for the treatment of adults with relapsed or refractory cutaneous T-cell lymphoma and analysis of cutaneous and hematologic disorders by high-throughput nucleic acid sequencing, among others that are ongoing.

Michael Fox
Independent Scholar

See Also: International Society for Experimental Hematology; International Society for Preventive Oncology; International Society on Thrombosis and Haemostasis.

Further Readings

International Society for Experimental Hematology

The International Society for Experimental Hematology (ISEH) was established in 1959 by a group of scientists who wanted to create a forum for the presentation and discussion of preclinical data in experimental hematology. Over time, ISEH remains committed to the promotion of the scientific knowledge and clinical application of basic hematology and immunological disorders. This society works through scientific programs, research, and publications. ISEH was incorporated in the United States in 1972. Currently, it has 800 active members, and it has operations in more than 40 countries spread
all over the globe. The society has an annual scientific meeting, and this attracts more than 500 participants within the four days in which the meeting runs. Through this annual meeting and an official monthly journal—Experimental Hematology—ISEH provides essential delivery of quality education, training programs, and discussion forums and promotes basic research in the field of hematology.

The members of the society present their significant breakthroughs in research through the forum. This has seen the presentation of high-profile research, such as on cloning and characterization of many new hematopoietic growth factors or the initial presentation on the work of Dr. Don Thomas that led to his award of the Nobel Prize in Medicine. The ISEH was the first to successfully describe a number of in vitro controls and to study the use of stem cells as needed; in vitro LTC-IC, CFU-C, CAFC, CFU-S assays; and in vivo transplant functions. Others work with the means of purifying cells in the body for managing several of the different health-related functions that the human body may have when certain treatments are to be managed. In recent times, studies have been made with the intention of managing different solutions for signals within blood cells, protein problems, and other commonplace issues. This all can work to see how well different solutions are to be managed in the best possible cases.

The mission of ISEH is the promotion of scientific knowledge and clinical application of basic hematology, stem cell research, immunology, cell and gene therapy, and all the related aspects through research, discussions, publications, support of investigators, and organization of scientific meetings. To achieve this objective, ISEH undertakes the following: sponsoring of international meetings while emphasizing the highest-quality science, sponsoring fellowships and awards to promote education and training, publication of a first-rate scientific journal, and any other activity that might be approved by the board.

ISEH leadership is the board of directors and has included Paul Frenette, M.D., from the Ruth L. and David S. Gottesman Institute for Stem Cell and Regenerative Medicine Research, United States, as the president; David Traver, Ph.D., from University of California San Diego Division of Biological Sciences, United States, as the president elect for 2017; Timm Schroeder, Ph.D., from the Swiss Federal Institute of Technology, Zurich, Switzerland, as the vice president; Jean-Pierre Levesque, Ph.D., from Mater Medical Research Institute, Australia, as the treasurer; R. Keith Humphries, M.D., Ph.D., from the British Columbia Cancer Research Center, University of British Columbia, Canada, as the editor; Margaret Goodell, Ph.D., from Erasmus Medical Center Cell Biology Department, United States, as the immediate past president; and the following directors—Andrew Elefanty of Monash University, Jonas Larsson of Lund University, Sarah Ellis of Peter MacCallum Cancer Centre, Hartmut Geiger of Ulm University, Trista North of Beth Israel Deaconess Medical Center, Emery Bresnick of University of Wisconsin, Conny Bonifer of University of Birmingham, Koichi Akashi of Kyushu University School of Medicine, and Patricia Ernst of Dartmouth Medical School.

ISEH activities range from a number of activities, among them knowledge, innovation, and exchange. To promote knowledge, ISEH offers comprehensive programs and publications in training and education. The members of the society provide the tools for expansive understanding and cutting-edge methodologies from around the globe. To enhance innovation, the society provides the latest scientific information. Its members are at the forefront of advances in experimental hematology with regard to the study of commonplace problems relating to hematologic functions and stem cell issues as well as gene problems that may come about. Transplant and gene therapy procedures are also studied in most cases. Last, ISEH does exchange programs to connect clinicians and researchers from around the world. This is best done through ISEH membership within an inclusive, international forum, which creates many opportunities for conversations between young scientists and leaders in the research field and industry.

The members of ISEH are professionals in varying positions; scientists—42.6 percent, students—19.4 percent, clinicians—16.5 percent, postdoctoral fellows—16 percent, and industry representatives—5.5 percent. The membership plans include active members who pay an annual fee of $175, which has the option of a two-year subscription at $329. This membership plan is for scientists engaged in the study of hematology and stem cell research. The other is the associate or member in training, which requires an annual fee of $65. This plan is open for students in universities or colleges as well as postdoctoral fellows.
ISEH has two major publications: *Experimental Hematology* and *Connections Newsletter*. *Experimental Hematology* is the society's official journal. It is committed to publishing the latest research reports, reviews, letters to the editor, and abstracts of the annual meeting of the ISEH. *Connections Newsletter* covers details on new developments in the field at large.

As a mark of success and achievement for not only the society but also its members, ISEH has a number of awards that are meant to recognize distinguished scientists in the field through their exemplary work. The awards available are the Donald Metcalf Award, McCulloch and Till Award, New Investigator Awards, and travel grants for young investigators.

Michael Fox
Independent Scholar

**See Also:** American Society of Hematology; International Society for Cutaneous Lymphomas; International Society for Preventive Oncology.

**Further Readings**


---

**International Society for Preventive Oncology**

The International Society for Preventive Oncology (ISPO) is a World Health Organization (WHO)-associated group that has been in operation for nearly 50 years. ISPO is the forum of an international membership, and it studies interactive etiologic factors in cancer development and their impact on prevention, detection, and management of neoplastic diseases.

The ISPO mission statement is made up of scientific objectives and activities. The scientific objectives are to foster primary prevention of cancer through identification and control of cancer causes and to identify high-risk individuals and secondary prevention through detection and management of occult cancer and precursor lesions. In addition, ISPO seeks to promote continuing education in areas of the role of lifestyle, including sexual practices, nutrition, and tobacco, as cancer-causing factors and their impact as well as genetic influences, predictive markers, novel therapies, and other commonplace points that could be utilized in many forms.

In addition to the scientific objectives, ISPO has activities in which it seeks to disseminate information on a global scale on the latest advances in basic and clinical oncology. This is done through the society’s continuing education programs and educational initiatives, which include publications and international meetings and workshops. ISPO publications include the bimonthly, multidisciplinary journal *Cancer Detection and Prevention*, which publishes reviews on oncology and how to treat conditions while preventing serious complications from developing. International meetings and workshops foster education in oncology through investigators exchanging information on the newest approaches for identification of the multiple interacting factors in the etiology, prevention, detection, and management of serious issues.

Some of the international meetings and workshops that have been held by the society include the Seventh International Symposium on Biotechnology in Preventive Oncology in 2004 in Nice, France, with the topic predictive oncology and intervention strategies, the Sixth International Symposium on Biotechnology in Preventive Oncology on February 9, 2002, in Paris, France, and the Fifth International Symposium on Biotechnology in Preventive Oncology, held from October 28 to 31, 2000, in Geneva, Switzerland, with the topic on prognostic indicators for managing oncology and other commonplace solutions for taking care of patients who may be struggling with issues relating to cancer.

The past president of the society has been H. E. Nieburgs, M.D., who was the founder of ISPO. ISPO has Nieburgs's address as the society's mailing address. L. Santi, M.D., from Genoa, Italy, has been president, with G. de Thé, M.D., from Paris, France, as
Persons interested in oncology can apply and become members of the society. Such persons include primary care physicians, hematologists, immunologists, pathologists, epidemiologists, experimental oncologists, social scientists, and educators as ISPO supports the needs for health care professionals who need assistance with managing cancer prevention while educating people about how such solutions are to be utilized. Active members of the society are eligible to hold offices, vote in the biennial elections of the society, and serve in the various standing committees. To ensure members are well informed and up-to-date with information on cancer, the society provides continuing education through the society’s scientific activities, and members can attend the ISPO's workshops, international meetings, and regional symposia at a reduced fee. For one to be a member, a membership fee is required, which includes a yearly subscription to the "Cancer Detection and Prevention" journal and free online access to the journal.

The membership of ISPO consists of active, associate, junior, life, and honorary members. An applicant wishing to become a member of the society should be sponsored by two members of the society or by two individuals who are accepted to the society. Recommendation letters are required and can be sent accompanied with the application or separately to the secretary general. Also, the application should be sent with the initial fee, and it is considered to be the annual fee for the first calendar year. Active members are limited to physicians and other professionals at the doctoral level. Associate membership includes those persons of unusual proficiency and scientific attainment without a doctorate degree. Junior membership includes physicians and scientists in training.

"Cancer Detection and Prevention" is the journal founded by ISPO. The journal reflects the society's viewpoint that human cancer is a preventable disease and use of the information that has accumulated over time has the potential to eradicate morbidity and mortality of patients with neoplastic diseases. However, in 2008, the ownership of the journal was transferred to Elsevier Science, Ltd. Even with the ownership transfer, the publication of the journal has remained bimonthly.

The society is managed through membership fees, which are submitted annually. In addition, donor contributions are used, even though they are not common. ISPO has been presented with an award for outstanding contributions to the understanding of cancer that may provide practical applications for improved cancer control.

Michael Fox
Independent Scholar

See Also: American Society of Clinical Oncology; European Society of Surgical Oncology; International Psycho-Oncology Society.

Further Readings

International Society of Nurses in Cancer Care

The International Society of Nurses in Cancer Care (ISNCC) was founded in 1984. According to its Web site, it is comprised of more than 60,000 cancer nursing members, which include national and regional societies and oncology institutions in addition to individual cancer nurse practitioners, researchers, and educators. The ISNCC “is a nongovernmental member of the World Health Organization (WHO) and is affiliated with the International Council of Nurses (ICN) and the Union for International Cancer Control (UICC).”

The ISNCC mission, as professed on its Web site, is to “maximize the influence of nursing to reduce the global burden of care,” and its vision is to “lead the global nursing community in cancer
control.” The ISNCC employs “strategic directions,” according to Kathryn Godfrey, for the purpose of obtaining its vision by “building and sustaining stakeholder relationships, influencing health policy, advancing and applying knowledge, developing and engaging cancer nurse leaders.” It is well regarded as an international institution that has a positive influence on the health care field through developing the “knowledge and skills of international cancer nurses.”

Three types of memberships are available: individual, association, and full membership. Individual memberships are available to nurses and other healthcare professionals who have an interest in cancer nursing. On the association member level, national specialist nursing groups, institutions, and organizations in the field of cancer nursing are eligible for membership. According to the ISNCC Web site, “This network is an invaluable international resource of nurses working in clinical practice, education, research and management to advise them on cancer nursing and the nurse’s role in cancer care. Oncology institutions, charities and related organizations are eligible to be associate members.” Full membership is available to oncology nursing societies providing resources for “working in clinical practice, education, research and management to advise them on cancer nursing and the nurse’s role in cancer care.”

Aims of the Society
The ISNCC focuses on the specific areas of charity, education, and science and enacts specific strategies to aid in all areas. Toward that end, the ISNCC provides a forum so that cancer nurses can improve care through discussion of strategies and innovations that advance clinical practice. The ISNCC also offers support for increasing the role of cancer nurses as leaders in the field internationally. Finally, the organization also emphasizes enhancement of health and well-being of people at risk for or living with cancer.

Through an array of committees developed and supported by ISNCC, members are encouraged to participate in the society in various capacities that advance ISNCC’s efforts to promote charity, education, and science. For example, ISNCC embraces its charitable focus within the organization through an International Conference on Cancer Nursing (ICCN) scholarship that ensures nurses from low- and middle-income countries are able to participate in the conference. Additionally, according to ISNCC’s position statement on Cancer Nursing Education, “investing in cancer nursing education is crucial to prepare adequate numbers of nurses to address the growing global burden of non-communicable diseases.” Furthermore, ISNCC takes a position that nursing is responsible for its own knowledge base and works to achieve its scientific goals through its annual conferences as well as through its Scientific Planning Committee, whose purpose is to “develop the overall conference program for the biennial International Conference on Cancer Nursing (ICCN) requiring international input and collaboration.”

Conferences
ISNCC holds the biennial International Conference on Cancer Nursing (ICCN). Recent hosts include Toronto, Canada; Singapore; Atlanta, Georgia; and Prague, Czech Republic.

At the 15th International Conference on Cancer Nursing in 2011, then president of ISNCC Professor Sanchia Arnada told delegates, “ISNCC is the voice of cancer nurses in the international arena. This conference is a unique experience where we learn from our colleagues in many different countries where sometimes the most remarkable innovations are those that are borne of the ingenuity of nurses with little support but great commitment.”

Developing Global Partnerships
A central goal of the ISNCC is to collaborate with other associations globally in order to develop mutually beneficial relationships. With each of its associates, Godfrey describes, the ISNCC “develops a Memorandum of Understanding (MOU)” for the purpose of “collaboration, mutual recognition, and shared, culturally sensitive approaches to the work of both organizations.” Collaborations are aimed at developing “communication with each other about eventual strategies to develop and promote oncology nursing and multidisciplinary cancer care.” Presently, the ISNCC “has MOU agreements with three international organizations—the Multinational Association of Supportive Care in Cancer (MASCC), the European Oncology Nursing Society (EONS), and the Oncology Nursing Society (ONS) USA.” ISNCC disseminates information to its cancer nursing members through the official Web site
and The International Cancer Nursing News, the quarterly publication that is available in both print and digital formats. Newsletters typically feature a message from the president, a research column, and an education column. More than 11,000 individuals and organizations subscribe worldwide.

Catherine A. Dobris  
Indiana University–Purdue University Indianapolis  
Rachel Diana Davidson  
University of Wisconsin, Milwaukee

See Also: Cancer Communication; Careers; Caregivers.

Further Readings

International Society of Paediatric Oncology

The International Society of Paediatric Oncology (SIOP), founded in the late 1960s, has grown into a worldwide organization with more than 1,000 members from allied health professions, scientists, and other researchers. Members aim to improve treatment for childhood cancers with a vision that no child should ever die from cancer. SIOP’s visional goals include providing access to state-of-the-art treatment for pediatric patients; ensuring that all persons involved in childhood cancer have access to information through continued professional development, networking, and meetings; supporting caretakers of children with cancer with the best palliative and curative therapies; and advocating for long-term follow-up care for survivors. SIOP sponsors continental and regional meetings to promote good practice and the exchange of information, including an annual congress.

SIOP has six continental branches, and each addresses particular issues relevant to its specific region of the world. The regions include North America, Latin America, Europe, Africa, Asia, and Oceania. SIOP encourages all health care professionals to join their organization, to attend meetings and the annual congress, and to use the organization to develop regional networks.

The management and development of strategies and policies fall within the responsibility of the board of directors. The board of directors are elected by members of SIOP. SIOP has six primary committees: scientific committee (SC), psychosocial committee, publication committee, pediatric-psycho oncology committee (PPO), nurses committee, and the committee on developing countries (PODC).

The primary task of the SC is to organize the scientific program for the annual SIOP meeting. The annual meeting consists of two and one-half days of meetings: the expert sessions, eight keynote lectures, 10 symposia, 24 oral paper presentations, and one large poster session. Nurses, parents, and survivors have their own programs, while other programs are combined. Annually, the Schweig Guth prize is awarded to a young investigator for the best original scientific work and for the three best abstracts presented in clinical studies, studies in developing countries, and basic or translational studies. The official committee, scientific program advisory committee (SPAC) invites experts to speak and proposes topics for the annual meeting. The SC subcommittee groups include the following: pathology, basic science, radiation oncology, epidemiology, nursing, psychosocial, surgical, and psycho-oncology.

The psychosocial committee was formed in 1991 based on directives from the SIOP board, who recognized the importance of psychosocial issues in the care of children with cancer.
The committee has published 11 journal articles addressing psychosocial interventions as a part of pediatric oncology and therapeutic trials. The topics have included critical commentary, school and education, care of long-term survivors, communication of the diagnosis, therapeutic alliance, terminally ill children, siblings, burnout, refusal and noncompliance, informed consent, and alternative therapies. These 11 articles have been translated from English into Japanese, Greek, Portuguese, Spanish, and Italian.

The publication committee was created to review manuscripts prior to publication if they use the SIOP logo or SIOP data, originate from the board or committees, sanction SIOP treatment or management guidelines, or publish SIOP’s position on advocacy or policy. The committee determines if the article is appropriate to use the SIOP name, if the content is accurate and draws appropriate conclusions, and if it is a duplication of other articles. The committee can also offer a full editorial and scientific review if the authors request it.

The PPO, established in 2007, educates and provides support about the impact of childhood cancer on the children’s well-being and their families from a developmental perspective. The PPO strongly advocates for the inclusion of psycho-oncology in pediatric cancer treatment, rehabilitation, and counseling. The purposes of the PPO include support of the exchange of research data on psycho-oncology pediatric issues; support of the integration of data into practice; and integration of data into current research and theory.

The nursing committee promotes information exchange among nurses who care for pediatric oncology patients and their families. The committee promotes and develops standards of care that are globally relevant and initiates research in pediatric nursing oncology.

The PODC committee, established in 1998, has the goal to develop pediatric oncology in developing
countries. The committee has 12 core members and more than 60 consultants. The primary activities of the PODC committee are symposia and workshops, sponsorship of local meetings, educational programs, scholarships, exchange programs, clinical trials, and collaborative research.

SIOP created a “Standards of Care and Training” document in 2002. The purpose of the document was to outline that every child has a basic right to life and that parents should be supported in obtaining these rights for their children. The document sets guidelines for parents that outline what they should expect in terms of care and treatment. The document is intended to provide guidance for any professional in the position to advocate, provide care, or improve standards of care. It is also intended for patients and their families. A key source of information for the “Standards of Care and Training” document is the United Nations Convention on the Rights of the Child. In part, the convention concludes that access to information is available that promotes health, health care should conform to established standards, working parents should benefit from child-care facilities, children have the right to the highest standard of health and to treatment facilities that support this, every child has the right to social insurance, and every child has the right to education.

Jessica Anne Hammer
Independent Scholar

See Also: American Academy of Pediatrics, Section on Hematology/Oncology; Mesothelioma, Childhood; Salivary Gland Cancer, Childhood; Unknown Primary Site, Cancer of, Childhood; Visual Pathway and Hypothalamic Glioma, Childhood.

Further Readings

International Society on Thrombosis and Haemostasis

The International Society on Thrombosis and Haemostasis (ISTH) is a worldwide nonprofit organization to encourage the understanding, prevention, diagnosis, and treatment of thrombotic disorders and other commonplace problems that entail bleeding. ISTH was established in 1954, when a small group of investigators used seed money from the National Heart, Lung, and Blood Institute to form the International Committee on Thrombosis and Haemostasis (ICTH). The members of the group were well-known in the world of blood studies and the overall analysis of how the bloodstream functions. With time, interests in the group grew, and ICTH began consideration to expand the scope of the mission. Attendance to the yearly meeting of the ICTH grew, and they no longer could accommodate the meeting in the small, meant-for-committee rooms.

All through the 1960s, members of ICTH delved into expansion plans by clarifying and planning the mission, structure, and function and amending the leadership of a larger group. The vision behind the plans was to have a society that would be open to all researchers, clinicians, educators, and others who are in the fields of vascular biology. ICTH was built primarily on blood coagulation and hemorrhagic disorders. The new organization was designed not only to focus on the primary area as ICTH but also to include fields relating to platelet studies and understanding many problems that relate to serious issues all around the body. At the turn of the decade in 1969, in the 15th annual meeting in Bath, UK, members of ICTH finally came to vote, unanimously approving the creation of the ISTH.

Currently, the impact and contributions of ISTH are dedicated toward the understanding, prevention, diagnosis, and treatment of thrombotic and bleeding disorders. These activities are available in six continents with more than 3,800 members in more than 94 countries; the organization is now the leading thrombosis- and haemostasis-related professional organization in the world.

The governing body of ISTH is the council. The functions of the council are authorization and
exercising all corporate powers of the society and overseeing all of its activities. The executive committee is a subset of the ISTH council, and its function is to provide executive direction to the activities of the society in between council meetings. These governing bodies, just like every other organization, are guided by set laws and bylaws. ISTH bylaws empower the council to establish committees that recommend to the council policies, programs, and actions related to their areas of expertise and responsibility. The committees also implement recommendations that the council approves. Any ISTH member can be added to the council if consulted properly. Council members serve six-year terms and may serve up to two nonconsecutive terms with at least two years elapsing in between those said terms.

Every two years, members of the ISTH society elect five of their peers to the council. This replaces about a third of the elected members of the council. The Council also has ex-officio voting members who are members by virtue of holding another office with the ISTH, as mandated by the society’s bylaws. Office bearers have been Nigel Key from the United States as the chair, Nuala Booth from the UK as the treasurer, and Ingrid Pabinger from Austria as the secretary, who is also the chair elect.

ISTH is the leading global community of specialists in bleeding and clotting disorders. Given this fact, the society offers benefits that inspire, drive, and connect researchers in the translation of science to advance clinical practice to improve the lives of millions of people worldwide. As a member of ISTH, one is guaranteed to stay up-to-date on the latest scientific advances and emerging trends in thrombosis and haemostasis. This ensures every member of the society deepens and broadens in expertise.

One of the missions of ISTH is to ensure its members as well as any other persons interested in thrombosis and haemostasis have advanced knowledge and understanding through effective and consistent provision of quality information. To realize this, the organization has a number of publications. The Journal of Thrombosis and Haemostasis (JTH) is a key guide that is used in this field. Its authors, reviewers, and editors volunteer their time and expertise to contribute and disseminate important scientific information to the international research community. The society’s Scientific and Standardization Committee (SSC) prepares reports on the field to determine how well they are able to function as needed. As a service to the scientific community, these official SSC communications are made available as open-access documents: They are available on the society’s Web site. Most of the standards developed by SCC are adopted by the World Health Organization as international standards. ISTH’s quarterly e-newsletter highlights global thrombosis and haemostasis news, reports on the work of the society’s committees, and publishes other information that helps facilitate the participation of members in the many activities in the field. The other sources of information from ISTH include registries and databases, meeting materials, monographs, and member obituaries.

ISTH meetings include the ISTH congress, which meets every two years, and SCC meetings, held annually. The SCC and the congress are held jointly. All people associated with the field can attend these meetings in order to get a better idea of how the industry is working and what is being done in order to treat such problems as they come about.

Michael Fox
Independent Scholar

See Also: International Society for Cutaneous Lymphomas; International Society for Experimental Hematology; International Society for Preventive Oncology.

Further Readings
Intraocular Melanoma

Eye-related cancers can develop on the eyelids, on the ocular surface, or inside of the eye. Melanoma is the most common intraocular malignant tumor in adults and can significantly affect vision-related quality of life and survival. This entry discusses the pathogenesis, epidemiology and risk factors, diagnostic methods, and treatment options for intraocular melanoma.

Melanomas arise from melanocytes, which are cells responsible for tissue pigmentation. These tumors are therefore often pigmented in appearance. Within the eye, melanocytes are most abundant in the uvea. The uvea is a layer of highly vascular and pigmented tissue that is located underneath the sclera, the white portion of the eye. The iris is the most anterior segment of the uvea. Moving toward the back of the eye, it continues as the ciliary body, which is responsible for movement of the lens and production of intraocular fluid (aqueous humor). The majority of the uveal tract is posterior to the ciliary body, called the choroid. The choroid has the highest blood flow in the entire body and plays an important role in sustaining the functions of the retina. Intraocular melanomas can arise from any of these tissues, but the most common are choroidal melanomas. Iris and ciliary body melanomas are relatively rare and have the better and worse prognoses, respectively.

Uveal melanomas represent approximately 3 percent of all melanomas, and the incidence in the United States is about five per million per year. It predominantly affects adult Caucasians: approximately 98 percent of cases occur in white patients, and the average age of diagnosis is about 60 years. It appears to affect both men and women equally. Uveal melanoma is generally a sporadic event, but rare cases of familial uveal melanomas have been reported. Diet and smoking do not appear to be risk factors, but those with light skin color, light eye color, and propensity to sunburn may be at higher risk.

Patients are diagnosed either on routine eye examination or when they present with visual symptoms, such as blurry vision, flashing lights, and visual field defects. Vision loss can also occur if the tumor involves the center of the retina or if there is associated retinal detachment. The most important step in the management of intraocular melanomas is an examination by an ophthalmologist with experience in ocular oncology. Uveal melanomas usually appear as pigmented masses, but some may contain minimal or no pigmentation, and some may be diffuse with minimal elevation. Small tumors can be difficult to distinguish from benign lesions, and close observation is a reasonable option for indeterminate lesions. Other diagnoses that may mimic choroidal melanomas include nevi, hyperplasia of the retinal pigment epithelium, hemorrhage, choroidal hemangioma, choroidal osteoma, and choroidal metastasis.

An important ancillary imaging study is ultrasonography, which can characterize the tumor and measure its dimensions. Ultrasound measurements are routinely used to track the growth or regression of intraocular tumors. Fluorescein angiography also may aid in diagnosis. Fluorescein is a synthetic dye that is injected into a vein, and photographs are taken using special filters that allow visualization of retinal and choroidal vasculature and associated lesions.

Management of intraocular melanoma used to be limited to enucleation (removal of the eye), but most patients are now treated with radiation therapy in order to preserve the eye and vision as much as possible. Eyes with large melanomas are
Intraocular Melanoma

at high risk for complications after radiation and have a poor visual prognosis; therefore they may still be managed by enucleation. Enucleations are performed under general anesthesia by ophthalmologists. Implants are placed into the orbit (eye socket), and prostheses are designed and fitted several weeks after the surgery. Many advances have been made in optimizing the cosmetic appearance and movement of prostheses.

The Collaborative Ocular Melanoma Study was a seminal clinical trial in the 1980s and 1990s that randomized patients with medium-sized choroidal melanomas to either enucleation or radiation therapy using I-125 brachytherapy. The study showed that survival rates did not differ significantly between the two groups. Brachytherapy is a form of radiation treatment where a short-range radiation source is implanted in close proximity to the target. Ophthalmic application of brachytherapy involves a plaque embedded with radioisotope seeds. The exact location, size, and shape of the melanoma are first determined by an ocular oncologist, and plaques are chosen to most effectively treat the tumor. The plaques are implanted in the operating room, and the patient wears a lead shield during the treatment period. The plaque is then removed in the operating room after several days. Brachytherapy is currently the most commonly used treatment modality due to its wide availability.

Proton beam irradiation is another type of radiation treatment that is offered at several specialized centers. Unlike conventional external beam irradiation, proton therapy uses charged particles that allow precise targeting of tumors while minimizing radiation exposure of adjacent tissues. A property of proton therapy called the Bragg peak results in a sudden drop-off of radiation after a highly concentrated, uniform dose is delivered to the target, thereby sparing any distal tissues, such as the optic nerve or other areas of the retina. In preparation for proton therapy, radiopaque rings are sutured onto the eye in the operating room to allow accurate tumor localization. Individualized face masks and bite blocks are created, and patients are asked to gaze at a fixation light during the treatment. Most tumors show regression in a few months and continue to regress thereafter.

Tumors that involve or are close to the optic disc (part of the optic nerve that exists inside the eye) or fovea (part of the retina responsible for central vision) carry poor visual prognosis due to damage by the tumor as well as by the radiation that needs to be directed at these vital structures. Approximately half of patients treated with either brachytherapy or proton therapy will develop radiation retinopathy, and about a quarter will develop radiation optic neuropathy. Radiation retinopathy is a slowly progressive condition caused by vascular damage from radiation. Retinal hemorrhage, swelling, exudation, and growth of abnormal vessels can occur, which may worsen vision. Depending on the manifestation and severity, laser treatments or injections into the eye may be helpful. Radiation optic neuropathy is caused by radiation damage to the optic nerve. The nerve can appear swollen or pale and have hemorrhages. There are no established treatments for radiation optic neuropathy.

Choroidal melanomas can metastasize through blood vessels, most commonly to the liver. Tumors that are large, involve the ciliary body, have certain appearances under the microscope, or carry specific genetic alterations are more likely to metastasize. Recent advances have allowed for profile needle biopsy samples based on analysis of DNA or RNA to categorize the tumors into those high and low risk for metastasis. Unfortunately, advances have not yet been made in the treatment of eye-related cancers can develop on the eyelids, on the ocular surface, or inside of the eye. Melanoma is the most common intraocular malignant tumor in adults. (Flickr/Dan Foy)
of metastatic disease. Up to half of patients with uveal melanoma will die from metastasis. However, genetic testing can now identify high-risk patients for clinical trials that may lead to effective therapies in the future.

Yoshihiro Yonekawa
Ivana K. Kim
Harvard Medical School

See Also: Melanoma; Proton Therapy; Radiation Therapy.

Further Readings

Iran

The western Asian nation officially termed the Islamic Republic of Iran was created in 1979 as a result of the Iranian Revolution. Historically, the territory that makes up the modern state of Iran has been the site of numerous civilizations, empires, and cultures. Currently, Iran has a population of nearly 80 million citizens. The national language is Persian, while the national tender is the rial. In the past 50 years, the country has instituted the domestic infrastructure to meet the cancer challenges of its citizens resolutely.

Data regarding cancer incidences in Iran was first compiled in 1960 by Professor Abdollah Habibi, and contemporary researchers in the country now consider Professor Habibi’s reporting to have provided a prototype for the domestic cancer registries that were to arise within the country in the years to come. The first true national cancer registry in Iran was established in 1969 as the collaborative effort of Tehran University and the International Agency for Research on Cancer because researchers wanted to analyze the seemingly unusually high amount of esophageal cancer incidences in the nation's Mazandaran territory. Since the initiation of the national registry in 1969, domestic and international researchers have been able to accurately analyze incidence trends in the country.

Cancer is presently estimated to be the second-leading cause of death in Iran. While the nation has a robust cancer registry system in place to track cancer incidence rates, the country does not have a system in place to accurately track the mortality rates related to specific cancers. Researchers believe that more than 50,000 new incidences of cancer are occurring in Iran each year. In recent years, increased levels of obesity in the country have correlated with higher rates of intestinal cancers, while researchers have found lung cancer rates to be relatively low when compared to the population of domestic smokers in Iran.

Cancer care in Iran is regarded as well structured and effective. If an Iranian is diagnosed with cancer there, he or she is referred to local health centers, where they are further referred to advanced regional treatment facilities. Treatment is free of charge up until a patient is referred a third time, at which point personal health insurance is enacted. At present, there are efforts by the Iranian government to provide insurance to all nonurban Iranian citizens who would otherwise likely struggle to pay for more advanced levels of treatment. Somewhat ironically, cancer treatment in urban Iranian areas can be regarded as slightly chaotic, though the levels of treatment capabilities at the urban facilities are some of the best in the nation.

Currently, the most prevalent forms of cancer in Iran are breast, bladder, lung, ovary, and prostate cancer. Bladder, lung, prostate, and stomach cancers are the most common forms of cancer incidences in males in the nation, while breast, ovary, and stomach cancers are the most prevalent incidences of cancer in females there. Nationally, incidences of lymphomas, nasopharynx, and skin cancer have been consistently trending upward over the past several years, while incidences of bladder, bowel, and lung cancer have been consistently increasing.

Unfortunately, many citizens of Iran have had cancer throughout the nation’s history. The famous Iranian pop musician Toofan Ataee passed away as a result of lung cancer in 2012. Mahasti, another popular Iranian pop musician, succumbed to her fight with lung cancer after battling the disease for
several years. Moreover, the critically acclaimed Iranian playwright Ostad Mohammad died in 2013 from complications arising from liver cancer.

With regard to cancer, Iran’s future is bright. The nation is home to several facilities capable of excellent cancer care such as the Cancer Institute of the Islamic Republic of Iran, which was first established in Tehran in 1949. Since then, the institute has become one of Iran’s leading cancer research and treatment facilities as it is fully equipped to deal with the nation’s cancer incidences, having departments dedicated to chemotherapy, experimental research, genetic studies, pathology, radiology, and surgery. Not only is the facility capable of world-class cancer care, but it is also the site of Iran’s nationwide cancer registry center. This facility, among the many other capable cancer treatment centers in Iran, is a positive indication signaling that the nation has the proper means to adequately tackle domestic cancer incidences in the coming decades.

William M. Peaster  
Independent Scholar

See Also: Bladder Cancer; Breast Cancer; Lung Cancer, Non–Small Cell; Prostate Cancer.

Further Readings


Iraq

Iraq is located in southwest Asia, bordered by the Islamic Republic of Iran on the east, Kuwait on the south, Saudi Arabia on the southwest, Jordan and Syria on the west, and Turkey on the north. The population as of 2012 was just over 32 million living in an area of 168,754 square miles (437,072 square kilometers). Iraq has two major ethnic groups: Arabs and Kurds. The history of health services in Iraq was not well documented until the beginning of the 20th century; however, it was likely to have been similar to other Middle Eastern countries, with limitations in terms of up-to-date medical services and a basic reliance on herbal medicine. Iraq has seen major advances in health care systems and preventative measures in the 20th century, and by the 1980s, the health system in Iraq was considered one of the best in the Middle East. However, since then, continuous unrest has led to a level of deterioration in all sectors in Iraq, including health care.

Iraq established a population-based cancer registry in 1976. The last registry was issued in 2011 and includes updated reports up to 2009 (according to the official Ministry of Health [MOH] Web site). Iraq has four pediatric oncology centers: two in Baghdad,
one in Basrah, and one in Mosul. Iraq also has five radiotherapy centers in service; two in Baghdad, the other three centers in three different governorates, and three more that are yet to start administering services to patients. Additionally, there are 23 oncology centers distributed in 18 governorates that provide chemotherapy for cancer patients. All these public oncology and radiotherapy centers are part of the free central health care system in Iraq.

In spite of the continuous effort to improve the quality and size of services available, these might not be sufficient to accommodate the number of cancer patients in Iraq. According to the last report by the Iraqi MOH, there were 15,251 new cancer cases reported in 2009, representing an incidence rate of 46.16 per 100,000 people and increasing from 44.46 in 2008. The most prevalent types of cancer reported among Iraqi patients were breast cancer, lung cancer, brain and central nervous system carcinoma, bladder carcinoma, and leukemia.

An important factor in controlling cancer globally is providing means for early diagnosis of cancer and for palliative therapy for cancer patients. A program for early detection and downstaging of breast cancer was established in Iraq in 2000 in collaboration with the World Health Organization (WHO). The program involved approximately 20 centers and clinics distributed in all Iraqi governorates. Mobile mammography units have been implemented to perform breast cancer screening services in Baghdad, Basrah, and Mosul. More are planned to be employed in other Iraqi cities and governorates. Palliative therapy, however, does not meet the current requirements for the increasing number of reported cancer patients.

Several studies have been conducted recently by Iraqi researchers looking at the rate of specific types of cancer or incidence among specific populations or cities. Overall, the studies have concluded that the incidence rates of the types of cancer studied are in general comparable to those reported for other Middle Eastern countries.

A recent study reported that the incidence of cancer was increasing in the city of Fallujah, Al Anbar governorate, and was higher than other cities during the year of 2011. This increase is claimed to be caused by depleted uranium used in armor-piercing munitions dropped in the war of 1991 and of 2003. Iraqi studies have shown that the level of this material is higher in regions where cancer incidences are high. However, other studies have argued against this hypothesis and reported acceptable levels of depleted uranium to be present in Iraqi soil.

Given the current state of increased exposure of the Iraqi people to hazardous pollution and the increased rate of tobacco smoking, cancer incidences are expected to rise.

Aliasger K. Salem  
*College of Pharmacy, University of Iowa*

Ali Al-Jumaili  
*Sean Geary*  
*University of Iowa*

See Also: Iran; Saudi Arabia; Syria.

Further Readings


---

### Ireland Republic of

Ireland is an island in the Atlantic Ocean found to the west of the island of Britain. Ireland’s human occupation stretches back at least to the Mesolithic, and Stone Age monuments and mounds still are widely scattered across the landscape. The island of Ireland is divided into 32 counties. The Republic of Ireland is a political unit that is constituted of 26 of the counties; the remaining six counties are part of the United Kingdom of England, Scotland, Wales, and Northern Ireland. Prior to the 20th century, the 26 counties also were part of the United Kingdom of
Britain and Ireland, but a bloody War for Independence concluded in 1922 with a treaty that granted home rule for most of the island. Medical care in the Republic has tended to follow a British model for the last two centuries. Medical care, including cancer treatments, has been controversial for decades, although charitable funding and research into cancer treatments has been outstanding.

Ancient Times
In ancient times Ireland was home to tribal people who generally are known today as Celts or Gaels; included among their gods was Dian Cecht, the god of medicine and herbs. The first recorded mortal physician in Ireland was Maelodar O’Tinnri, who died in 860 C.E. Cancer was known in ancient times as tuthle, aile, teine-buirr (fiery swelling), or úrphasiú. Ancient Celtic medicine in Ireland was based upon a combination of herbal medicines, such as bilberry (fraochán), which contains the antioxidant anthocyanidin (which blocks cell proliferation), and other anti-cancer constituents. Bilberry still is used in some modern anti-cancer remedies. Druids, Celtic priests, were reported to harvest mistletoe (drualas), which is toxic in large quantities, to make a hallucinogenic drink. Mistletoe also has been used for a cancer treatment, and some modern drugs, such as Iscador, Plenosol, Helixor, and Isorel, have contained mistletoe extracts.

The Middle Ages
In the middle ages noble Irish families would have hereditary personal physicians attached to their houses, who would possess their own medical books, for example the Book of the O’Lees, from 1443, the Book of the O’Hickeys, or the Book of the O’Shiels. These books were compendia of the medical knowledge of their days in both Latin and Irish (Gaeilge). According to Belfast-based archaeologist Robert M. Chapple’s blog from March 26, 2014, an American student named Lauren Jean is investigating The Culture of Medicine in Late Medieval Ireland in the original medieval Irish, and it promises to reveal exciting information about medieval Irish medicine, including cancer treatments.

Folk Beliefs
Herbal remedies for cancer still figure in modern folk medicine, as does the belief in holy wells. In 2014 the Irish language television channel, TG4, ran a series of programs titled Garraí Glas (Green Garden), hosted by Síle Nic Chonaonaigh, on the modern usage of herbal medicines, including their use by GPs such as Frieda Ní Chatháin, who supplements her pharmaceuticals with herbs from her “physic garden,” and herbalist Darach O’Murchú, who recommends sorrel for its anti-cancer properties.

Other folk beliefs in cures for cancer and other diseases have a pre-Christian provenance. Nonetheless, such practices as visits to sacred wells, followed by leaving personal objects behind, persist to this day. Lawrence J. Taylor reports that pilgrimages to holy sites such as Lourdes, Medjugorje, or local shrines were considered to be especially powerful. Taylor also reports that blessings by alcoholic priests were sought for cancer cures in rural County Donegal (sober priests’ cures were considered less powerful). Cancer cures also were sought from lay women, known as “healers,” at prayer meetings.

Cancer Statistics
Since 1994, the Republic of Ireland has maintained a National Cancer Registry, which uses
information gathered from hospitals, health care centers, cases reported by medical personnel and laboratories, and death certificates as its sources. According to Cancer in Ireland 2013, which is the National Cancer Registry's latest annual report, cancer cases show a 3 percent annual increase, with most diagnoses occurring in those over 65 years of age. Cancer deaths are increasing at an annual rate of 1 percent. Whether this increase is because more people are living beyond the age of 65 today than in the past is not discussed in the report.

Female breast cancer is the most common type of cancer reported, perhaps because of the Breast-Check screening program, at 32 percent of cases, closely followed by prostate cancer at 31 percent of cases reported to the Registry. Much less common are colorectal/bowel cancer at 13 percent, and lung cancer with an 11 percent incidence rate. Nonetheless, lung cancer is the most common cause of death by cancer in Ireland, at 20 percent of all deaths. The National Cancer Registry reports that this is 50 percent above the European average.

Even so, the five-year long-term survival rates have improved considerably (now at more than 100,000) since 1994, when the National Cancer Registry was started: up from 42 percent to 60 percent in men and up from 52 percent to 62 percent in women. This may be credited, in part, to the 2004 government-issued ban on smoking in enclosed work spaces, such as public houses, taxis, retail establishments, or offices. The five-year long-term survival rates for testicular, prostate, and thyroid cancer now top 90 percent. This may be credited to an increase in treatment rates: chemotherapy (medical oncology or haemato-oncology) rates have increased by 13 percent since 2000, radiation treatments (radiation oncology) have increased by 4 percent, and surgical intervention, known as surgical oncology, has risen by 2 percent.

The Republic of Ireland's Health Services Executive (HSE), which replaced the Regional Health Boards, operates a National Cancer Control Programme (NCCP) with eight self-sufficient Regional Cancer Centres joined together in a network that consists of two centers within each of the four HSE regions. The East Dublin North East region contains Beaumont and Mater University Hospitals; the East Dublin Mid Leinster region holds Saint James's Hospital and Saint Vincent's University Hospital. Cork University Hospital and Waterford regional Hospital are in the NCCP South region, while Galway University Hospital and Mid-Western Regional Hospital are in the NCCP West region. Each of the Centres is set up to serve more than 500,000 people. The executive board of NCCP consists of Susan O'Reilly, Director, Mary Hynes, Deputy Director, Arnold Hill, Maccon Keane, Jerome Coffey, Marie Laffoy, Deirdre Murray, and Majella Byrne. Their goal is to prevent cancer, increase survival rates, and improve the quality of life for patients. NCCP reports that 20,000 people contract cancer each year, of which 7,500 die.

**Charities and Community Services**

CROSS (Cancer Research of the Oesophagus and Stomach) at Saint James's Hospital not only funds cancer research through Trinity College, but also funds the education and training of researchers, for example scholarships for Masters of Science degrees in translational oncology. Another charity, ARC, founded at the Mater Hospital in Dublin in 1994, offers psychological counseling as well as holistic and complementary treatment methods free of charge in ARC Houses. Throughout Ireland cancer support services may be accessed by telephone or online. Some of these services include transportation to medical centers or appointments, drop-in centers where anyone may come for information or counseling, social work or at-home nursing caretakers, and a variety of other support systems, including hospice for terminal patients.

Michael J. Simonton
Northern Kentucky University

**See Also:** Alternative Therapy: Herbs, Vitamins, and Minerals; History of Cancer; Irish Cancer Society; United Kingdom.

**Further Readings**

ARC Cancer Support Center. http://www.arc
cancersupport.ie (Accessed March 2014).
Cancer Research of the Oesophagus and Stomach (C.R.O.S.S.) at St. James’s Hospital Department of Surgery. http://www.hse.ie/eng/services/list/5/nccp
Ireland (Ohio) Cancer Center

The Ireland Cancer Center was the first cancer-focused medical center at the University Hospitals Cleveland in Cleveland, Ohio, a multidisciplinary hospital facility founded in partnership with the city’s Case Western Reserve University. In 2011, a major university-led fund-raising drive led to renovations and new facilities construction that resulted in the center’s reopening as the newly named University Hospitals Seidman Cancer Center.

History

The genesis of Cleveland’s University Hospitals cancer center dates back to 1940, when its original cancer-focused treatment centers were founded as a faction of the Cleveland Cancer Consortium.

Advanced patient facilities were first constructed at the center in the 1970s, when the Ohio state legislature granted $14 million toward plans for their design and development. The state legislature was set in motion to secure funding for the center’s initial construction thanks in large part to the political efforts of then-Ohio Governor James Rhodes. Rhodes worked in concert with prominent Cleveland-based businessman, philanthropist, and University Hospitals Case Medical Center board member R. Livingston Ireland. Ireland’s efforts helped expand numerous arts-based programs throughout the city.

Governor Rhodes was convinced the city should move ahead with the project when he received an impassioned letter from Ireland regarding the necessity of such a facility for the residents of Cleveland and future generations of Ohioans touched by the disease. Ireland himself was stricken by bone cancer at the time he penned his letter. He ultimately succumbed to the illness in 1982. The center was renamed in Ireland’s memory in 1984.

It was in that same year the Ireland Cancer Center underwent a long-proposed merger between Cleveland’s University Hospitals Case Medical Center and Case Western Reserve University. The alliance created one of the most expansive clinical and laboratory research facilities in the American Midwest.

Reopening as Seidman Cancer Center

The Ireland Cancer center received national accolades on numerous occasions for its pioneering efforts in cancer treatment, patient care, and research. The center was recognized as Northern Ohio’s first officially designated clinical cancer center in 1987 by the National Cancer Institute (NCI.)

In 1996, the Ireland Cancer Center received a $500,000 grant from the National Institute of Health to commence the United States’ first major research program dedicated to Kaposi’s sarcoma, a form of cancer often associated with acquired immune disease syndrome (AIDS). By 1998, the seven-building facility’s success in both research and patient care had earned it the NCI’s highest designation, that of comprehensive cancer care center.

In 2011, the grand opening of the University Hospitals brand-new Seidman Cancer Center encompassed the 120-bed Ireland Cancer Center into a
state-of-the-art 150 bed facility. The 375,000-square-foot facility was completed at a cost of $240 million. The new institute was named in honor of Ohio philanthropists Jane and Lee Seidman, who donated more than $40 million to the new center’s construction as part of the university’s strategic fund-raising drive known as University Hospitals Vision: 2010.

**Facility Highlights**

The 375,000-square-foot facility conducts clinical cancer research while simultaneously providing patients and families with the latest in advanced diagnostic and therapeutic care techniques. The Seidman Center’s breadth of technological advances includes gamma knife radiosurgery and intraoperative radiation therapy technologies.

The center is also just the fourth in the world to utilize specialized scanners that combine positron emission tomography (PET) and magnetic resonance imaging (MRI) for clinical purposes, a technology that exposes patients to considerably lower amounts of harmful radiation than previously used methods.

In addition to its advanced MRI technology, the University Hospital Seidman Cancer Center is also home to a cellular therapy laboratory that allows doctors and specialists to conduct immediate evaluation and analysis of samples derived from patients undergoing treatment for leukemia and other blood cancers as well as bone marrow transplants.

In July 2014, the Seidman Cancer Center was awarded more than $4 million in support across a three-year grant from the U.S. Department of Health and Human Services (HHS) to create a new national care standard dedicated to improving clinical care for patients in the late stages of complex cancer. The program was founded in an attempt to provide in-depth insight to patients regarding their methods and options for treatment in less-technical, nonmedical terminology. Such information is relayed to patients via individually assigned health care professionals known as navigators.

The Seidman Cancer Center is also home to an expansive Clinical Trials Unit, which offers more than 300 programs offering cancer patients the latest in experimental treatments.

The facility’s clinical trials unit is also dedicated to a myriad of studies concentrating on cancer prevention and control as well as to investigations focused on the genetic traits of the disease. Much of the Seidman Center’s clinical work is carried out in conjunction with the Case Western Reserve University School of Medicine.

**Other Innovations**

The Seidman Center’s Cleveland headquarters also houses the Mary and Al Schneider Healing Garden. The garden, which is located on a one-third acre parcel of land at the hospital’s center, is a four-season garden custom designed to promote feelings of relaxation and well-being among both patients of the hospital and the general public. The garden’s labyrinth path features expansive water sculptures and displays meant to represent earth, air, fire, and water.

In addition to an expansive garden, the Seidman Center is also home to an expansive collection of contemporary art. The collection, which is comprised of more than 300 paintings, drawings, and pieces of sculpture, is also meant to comfort and uplift both the hospital staff and its patients. Among the facility’s most prominent works are paintings by the Spanish painter Joan Miró.

John Pritchard
Independent Scholar

**See Also:** Association of Community Cancer Centers; Chao Family Comprehensive Cancer Center; Ohio State University Comprehensive Cancer Center.

**Further Readings**


“UH, CWRU Win Grant to Study Form of Cancer.” *Crain’s Cleveland Business*, v.17/44 (1996).

Irish Cancer Society

The Irish Cancer Society is a registered charity that was founded in the Republic of Ireland in 1963 by Professor Austin Darragh to provide information about treatments and cures for cancers after he learned that 100 Irish people died each year from a wholly curable form of skin cancer. Since that time, the Irish Cancer Society, located at 43-45 Northumberland Road, Dublin 4, Ireland, with local offices throughout the country, has become the leading disseminator of information regarding cancer cures and treatments as well as a major contributor to research, treatments, and support for patients and student physicians in the field of oncology on the order of 30 million euros since its beginnings (adjusted from the pre-21st-century currency, the Punt).

Ninety-four percent of the Irish Cancer Society's funding comes from the public, and special events to raise funds are national events that are supported on radio, television, and in print media. Among these fund-raising events since 1988 are Daffodil Day (influenced by Daffodil Day in Canada), which has Dell Computer Company as a major partner and supporter and involves buying daffodils and Daffodil Day merchandise on March 28 to raise funds. Daffodil Day brings in about 12 percent of the funds raised by the society. In 2014, the Irish Cancer Society and Today FM radio sponsored a Shave or Dye event that encouraged shaving or dying hair in support of chemotherapy patients and to raise funds. In October 2013, Irish senator and former presidential candidate David Norris shaved his beard for the first time in 40 years in support of the charitable fund-raiser. The Irish Cancer Society also held fund-raisers called Get the Girls to support breast cancer awareness and treatment; Relay for Life, a 24-hour walking fund-raiser; and Movember, a moustache-growing contest to help in the fight against prostate cancer.

Criticisms of the Irish Cancer Society are difficult to come across, although on January 23, 2014, it was revealed that a fund-raising lottery held by the society had lost 420,000 euros between 2009 and 2013. Nonetheless, the society continued to hold the lottery because the government of the Republic of Ireland had compensated the organization 1,200,000 euros from the Department of Justice's charitable lotteries scheme, according to an Irish Times report.

Sponsored Programs

Fund-raisers help the Irish Cancer Society to endow research scholarships, fellowships, and other programs. As of 2012, the Irish Cancer Society provided more than 1 million euros (5 percent of their annual budget) to patients who were in need of financial help, according to Kathleen O’Meara on Radio Télfís Éireann's (RTÉ) Morning Ireland program. Collaborative cancer research centers are the first of their kind in the world, according to the society. Their first project, the largest the Irish Cancer Society has ever funded, is a 7.5 million euros venture called BREAST-PREDICT, and it will collect tumor samples from every breast cancer patient in Ireland as part of a five-year study to determine how best to treat individual patients, based upon their responses to various treatments, and to predict if drugs taken before the patients’ cancer diagnoses may affect their treatments. Most of the funding is predicted to come from the Get the Girls campaign. The principal investigators on this project are William Gallagher of University College Dublin, John Crown of Dublin City College, University College Dublin, Saint Vincent's University Hospital, Walter Kolch of University College Dublin, Bryan Hennessy of Beaumont Hospital, Des Higgins of University College Dublin, Michael Kerin of the National University of Ireland–Galway, Jochen Prehn of the Royal College of Surgeons in Ireland, Rosemary O'Connor of University College Cork, Kathleen Bennett of Trinity College Dublin, and Leonie Young of the Royal College of Surgeons in Ireland. Experts around Ireland will conduct clinical research with direct patient contact; lab researchers will determine if particular...
treatments are or are not effective; and demographic experts will analyze population trends.

Although breast cancer research has been an important focus of the Irish Cancer Society, some of the other projects funded by it include Amanda Tivnan's research into drug-resistant brain tumors and Clare Butler's development of drugs for the treatment of colorectal cancer. Other researchers working with colorectal cancers under funding by the society include Sudipto Das, Mary Clare Cathcart, Aideen Ryan, Catriona Dowling, and Nicholas Clarke's male-oriented research into population screening for colorectal cancers. The society reported in 2013 that Irish men are more likely to die of all cancers that both men and women can get than are Irish women, sometimes at as much as three times the rate at which women will die. Some of the reasons include lifestyle factors, but diagnoses at later ages also figure into the problem. One cancer that only men can get is prostate cancer, and prostate cancer research also has been extensively funded by the Irish Cancer Society under Maria Prencipe, Ciaran Morrison, William Watson, Caitriona O'Driscoll, Laure Marna, James Evans, Therese Kinsella, Silvin Knight, and Mark Tangney. Research also has been funded for esophageal, ovarian, and lung cancers, as well as leukemia.

Public Outreach

As part of the Irish Cancer Society's public outreach programs, it maintains an informational Facebook page in which it has posted warnings against ultraviolet (UV) radiation exposure with daily charts of UV indexes per hour from 6 a.m. through 6 p.m. around the country in Dublin, Cork, Galway, and Limerick. It also posts anticancer advice on being sun smart, how to reduce the risk of bowel cancer, the benefits of physical activity to reduce the risk of cancers, and advertisements and notifications of lectures, informational meetings, workshops, and other events. Even Podge and Rodge, RTE's cantankerous puppets, have supported the Irish Cancer Society by making a video (www.cancer.ie/bottomline) in which Podge insists that Rodge get a colonoscopy to determine the cause of his abdominal discomfort symptoms. Joan Kelly, who is nursing services manager at the society, believed that, by treating the subject with humor, it might not be so embarrassing for people. On April 22, 2014, the RBS Six Nations Rugby trophy was on display for public viewing and photography at the society's Northumberland Road headquarters, which further raised awareness of the Irish Cancer Society and its mission among yet another segment of the population.

Michael J. Simonton
Northern Kentucky University

See Also: Ireland, Republic of; United Kingdom.

Further Readings


Islet Cell Carcinoma
(Endocrine Pancreas)

Pancreatic cancer ranks as the fourth-most common cause of cancer-related death in men and women, and the number of cases diagnosed each year continues to increase. At this time, approximately 90 percent of patients diagnosed with pancreatic cancer are considered incurable and undergo an average survival rate ranging from six
to 12 months. Based on the rapid deterioration of a pancreatic cancer patient and the lack of effective treatment strategies, an early detection method is imperative, which in turn may significantly improve patient outcomes.

Pancreatic endocrine tumors are rarely occurring neoplasms that involve the exocrine pancreas cells (also known as islet cells or islets of Langerhans), which are responsible for generating chemicals that regulate specific activities of cells and organs, including the production of insulin for the maintenance of blood sugar levels. Pancreatic endocrine tumors rarely cause any symptoms, thus making it very difficult to diagnose. Furthermore, the details of its molecular pathogenesis remain elusive. In an effort to shed light on this fascinating, yet dreadful disease, clinicians and researchers have embarked on molecular and genetic investigations to establish its mechanisms of development.

A few years ago, Giorgio Malpeli and colleagues conducted an investigation on gene silencing, mainly focusing on the Ras Association Domain Family 1 (RASSF1) gene, which is a putative tumor suppressor gene that has been localized to chromosomal region 3p21.3. The protein product of the RASSF1 gene has been reported to suppress tumor growth using in vitro as well as in vivo systems. RASSF1 has been regarded as a major component in the inhibitory effects of Ras on cell proliferation by regulating downstream agents, thus inactivating the entire Ras signaling pathway. The investigation was based on the fact that the RASSF1 gene harbors two CpG islands, one extending into the regulatory segment that occurs in gene types A, D, E, F, and G, whereas the other one is present in the regulatory segment of the RASSF1 type C gene. The research study thus evaluated the possible role of methylation of the RASSF1A gene in regulating transcription in pancreatic endocrine tumors.

Approximately 20 primary pancreatic endocrine tumors, as well as matched healthy pancreases, were used as controls in the genomics study. In addition, the methylation status of the RASSF1 gene of three pancreatic endocrine tumor cell lines was assessed using methylation-specific polymerase chain reaction, together with pyrosequencing. Reverse transcription-polymerase chain reaction was also performed on 13 tumors. The results of the study showed that the RASSF1A gene of 16 of the 20 primary pancreatic endocrine tumors were methylated, whereas 13 of the 20 normal pancreases showed the same particular epigenetic modifications. Despite similar findings in both tumor and normal tissues, pyrosequencing showed that the amount of methylation in the pancreatic tumor tissues were almost sevenfold higher than that observed in the normal tissues. In addition, an inverse correlation between the degree of methylation and the level of RASSF1A expression was observed. Although this study was unable to confirm that the RASSF1A gene could serve as a specific biomarker for this specific neoplasm, its elevated expression in relation to its methylation status may provide additional hints on the mechanism of pathogenesis of pancreatic endocrine tumors. The findings of this study have thus paved the way for future studies in the area of molecular pathology of cancer.

Another study involving methylation was conducted by Albertas Dauksa, who examined the significance of employing these specific epigenetic marks as predictive biomarkers in pancreatic tumors. In this particular study, methylation levels at specific sites within CpG-rich domains of the promoter sequences of various pancreatic endocrine tumor-related genes were assessed. The genes examined were ACIN1, APC, BCL2, CD44, DAPK1, p16, RARbeta,
Using blood collected from a total of 30 patients diagnosed with pancreatic endocrine tumors, methylation levels of selected CpG sites were assessed. The results of the investigation showed that several CpG areas were significantly highly methylated, whereas sites consisting of repeat sequences showed a slightly lower degree of methylation relative to that of the control. Furthermore, a positive correlation between the degree of methylation and risk for pancreatic endocrine cancer was observed. Interestingly, the study also detected potentially useful correlations such as that between elevated methylation levels in TNFRSF10C and ACIN1 and a lower survival rate for a patient. This promising and significant finding could be applied eventually in the clinics, although a larger-scale study should be conducted initially to further strengthen and validate this correlation. Should this be achieved in the near future, then a simple blood test could assist clinicians in detecting pancreatic endocrine tumors as well as predict the survival time of a patient.

A recent study conducted by MingZhou Guo further strengthened the usefulness of epigenetic modifications in detecting and assessing neoplasms involving exocrine as well as endocrine pancreas. By extracting the DNA from a total of 48 paraffin-embedded pancreatic tumors, the levels of methylation were examined using nested methylation-specific polymerase chain reaction (PCR). The tissue samples used in the study consisted of acinar cell carcinomas (12 cases), adenocarcinoma (18 cases), and islet cell tumors (18 cases). This study was able to describe a methylation signature involving various pancreatic tumor-related genes. Thus, the pattern of methylation of specific genes involved in pancreatic cancer in a decreasing order was as follows: APC gene (50 percent), BRCA1 gene (46 percent), p16INK4a gene (35 percent), p15INK4b (35 percent), RAR (35 percent), and p73 gene (33 percent).

In addition, the majority (94 percent) of the pancreatic tumors showed methylation in at least one of the studied genes, whereas 69 percent of the neoplasms showed methylation in two or more of the genes investigated in the study. Another significant finding of this particular study was that the patterns of methylation of these genes in pancreatic adenocarcinomas could be distinguished from those of pancreatic endocrine tumors. This difference could therefore be applied in the clinics, specifically in diagnosing the type or subtype of pancreatic cancer. For decades, pancreatic cancer has been considered as a very difficult neoplasm to detect, diagnose, and predict in terms of its progression. These molecular signatures involving methylation in specific genes may therefore help in resolving the major challenges experienced by clinicians, particularly oncologists.

Rhea U. Vallente
PreventionGenetics, LLC

See Also: Pancreatic Cancer; Pancreatic Cancer, Childhood; Pancreatic Cancer, Islet Cell.

Further Readings

Israel

The Middle Eastern nation, officially termed the State of Israel, is one of the newest states on the global stage, having been established in 1948, when the local populace declared its independence after British forces retreated from the territory. As of 2014, Israel is the only country in the world that bears a Jewish majority population. Though the nation of Israel is young, it has quickly established itself in recent decades as a major cultural and intellectual player on the world stage, especially with regard to the field of medicine. Presently, the nation has one of the top 50 economies in the world and is composed of a population of more than 8 million citizens.

Though cancer is currently the most common source of mortality in Israel, survival rates are rising fortunately in the country. In 2012, more than 10,000 Israelis passed away as a result of cancer.
Members of the Israel National Cancer Registry, the Israel Cancer Association, and the Health Ministry’s National Center for Disease Control all work closely together in order to track domestic trends in the disease and to garner more effective ways to combat it. Such institutions provide invaluable statistics with regard to cancer in the country; this information allows Israeli specialists to deduce information about the disease that they would not be able to otherwise, such as the fact that women and Jews in the country are at a higher risk for the disease than their male and Arab counterparts.

In the past several years, promising cancer research has been conducted in the country. For instance, the Israeli researcher Dr. Sarit Larisch has discovered that cancer cells lack the protein that regulates cellular destruction when a cell is no longer functioning properly. Dr. Larisch’s research has opened up possibilities for new diagnosing methods based on the particular protein he has been studying. Moreover, the Israeli scientist Dr. Aaron Avivi discovered as recently as January 2014 that certain mole rats discharge a substance that has been found to obliterate cancer cells.

As of late, the most prevalent forms of cancer in Israel are bowel, breast, lung, and prostate cancer. Bowel, lung, and prostate cancers are the most common forms of cancer incidences in males in Israel, while breast, bowel, and lung cancers make up the most common forms of cancer incidences in females there; altogether, the top three most common cancers observed in both genders of the Israeli population account for over half of all cancer cases in the country. Moreover, Israel has some of the highest rates of cancer incidences in the entire Middle Eastern region, especially with regard to bowel cancer. Incidences of non-Hodgkin’s lymphoma and bladder cancer have been consistently increasing in Israel over the last decade, while incidences of esophageal cancer have been decreasing, making the country have one of the lowest rates of esophageal cancer in the world.

Sadly, and in line with the fact that cancer is a global disease, many Israeli citizens have experienced cancer during the nation’s relatively short history. For example, Israel’s popular, strong-willed, and first female prime minister, Golda Meir, succumbed to her battle with lymphatic cancer in 1978 at the age of 80. Lily Sharon, the wife of another one of Israel’s prominent prime ministers, Ariel Sharon, died in the year 2000 after losing her own bout with lung cancer. More recently, the beloved Israeli comedian and television entertainer Sefi Rivlin passed away in 2013 after struggling for a few years with lung cancer.

There are numerous cancer centers in Israel where some of the nation’s most talented doctors work together to stem the tide of the disease. For example, Dr. Tamar Peretz, who oversees the Department of Oncology at the Sharett Institute of Oncology in Jerusalem, is an internationally acclaimed physician who contributes her oncological expertise to the treatment of thousands of domestic and international patients every year. The D.R.A. cancer center located in Haifa, Israel, is home to some of the nation’s most highly trained specialists, such as Dr. Abraham Kuten. Dr. Kuten oversees the Oncology Department at the D.R.A., where he and his staff utilize novel and innovative treatment plans to attack each of their patients’ cancers with a unique and personalized approach. Dr. Kuten and his staff have helped to establish the D.R.A. cancer center as one of the most preeminent cancer treatment facilities in the whole world.

William M. Peaster
Independent Scholar

See Also: Breast Cancer; Lung Cancer, Non–Small Cell; Prostate Cancer.

Further Readings


---

**Italy**

The Republic of Italy is a parliamentary democracy located in southern Europe, bordered to the north by France, Switzerland, Austria, and Slovenia, and is part of the Italian peninsula. As a highly industrialized and densely populated nation, Italy is the fifth-largest economy in Europe and the ninth largest in the globe in terms of gross domestic product (GDP). The health care system in Italy is widely considered one of the best in the world and represents a national health service funded in large part by general tax revenues. Home to some of the world’s oldest universities, Italy has a tradition of supporting research, including that involving cancer. A variety of private organizations also support cancer research and are involved in conducting basic research and finding ways to reduce the risk of cancer to Italians.

**Background**

Significant politically for more than 3,000 years, Italy has a rich history that affects its current culture. After the collapse of the Roman Empire, which by the 2nd century C.E. controlled most of the known world, Italy developed a series of city-states, independent but interrelated. The Renaissance, which began in Italy, was a result of the great wealth accumulated by merchants in the region and a desire for knowledge. After several hundred years during which foreign powers such as Spain, Austria, and France exerted control over the Italian peninsula, the conclusion of the Napoleonic Wars resulted in returned independence to the Italian city-states. The growing sense of nationalism in Europe, however, increased pressure for a unified Italy, which came about after a series of revolutions, resulting in the establishment of the modern Italian state in 1870.

Siding with the Allies during World War I, Italy waged battle against the German and Austrian-Hungarian empires, incurring more than 650,000 casualties as a result. The conflict also resulted in the near bankruptcy of Italy, leaving the embattled monarchy susceptible to the fascist dictator Benito Mussolini. During his 21-year rule in Italy, Mussolini promoted a corporatist economic system where workers and business owners theoretically set economic policy with the state. After Italy’s defeat during World War II, Italy became a republic, and with help from the Marshall Plan, rebuilt its economy. The Italian economy grew rapidly during the 1950s and 1960s, a period known as the Italian miracle, during which the previously agrarian nation became rapidly industrialized. Postwar Italy established a social health insurance system that administered sickness funds for those afflicted by disease or other medical conditions. Financial instability plagued the system, and in 1978, the Italian government established the Servizio Sanitario Nazionale (SSN), a national health care system that provides all citizens and residents access to medical services through a mixed public–private system.

SSN pays all family physicians, who must offer office hours five days a week and are limited to a total of 1,500 patients. The SSN assigns patients doctors, although each patient is free to change doctors if dissatisfied, provided the doctor chosen has free slots. Prescription medications, which can be obtained only with a doctor’s authorization, are
subsidized by the SSN, and the co-payment is based upon the patient’s income. Hospital stays and visits to specialists require a co-payment if ordered by a family physician, while all surgeries are free, regardless of the patient’s income level.

Cancer Care and Research
Italians enjoy the world’s fourth-highest life expectancy and generally enjoy very good health. Concerns about certain diseases and medical conditions exist, of course, and are the focus of government policies regarding health care and research. At 278.6 per 100,000, Italy has the 21st-highest rate of diagnoses for cancer for men and women in the world, although this rate trails many other industrialized nations such as France, Canada, the Netherlands, and the United States. Italy’s death rate from cancer, at 124.2 per 100,000, ranks 57th highest on the globe. Certain policy decisions made by Italy’s leaders have been intended to reduce the risk of cancer. Nearly 70 percent of Italian men, for example, smoked cigarettes during the late 1960s, a rate that had been reduced to 25 percent by 2012, largely through increases in tobacco taxes, public health campaigns, and prohibitions on where one could smoke. Similar programs to increase air and water quality are also believed to have had a positive effect on cancer rates.

In certain areas of Italy, cancer rates are much higher than in other parts of the country. The government’s compilation and monitoring of cancer rates have assisted in identifying these areas. In an area within the province of Campania, for example, there is a region comprised of the area around the towns of Acerra, Marigliano, and Nola known as the Triangle of Death because of cancer rates that greatly exceed that of Italy as a whole. In this region, for example, the incidence of cancer of the bladder, central nervous system, and liver greatly exceeds that of Campania and Italy as a whole. This discrepancy is believed to have been caused by the illegal dumping of toxic wastes and has caused reform efforts to attempt to reduce the level of dioxins and other substances in the area as a result of this activity.

A variety of universities and other institutions conduct research on cancer, its causes, and potential treatment options in Italy. The European Institute of Oncology and the Istituto di Candiolo, for example, are two organizations that engage in cancer research. The European Institute of Oncology was founded in 1994 in Milan to conduct basic research, train physicians and other health care providers, and provide patient care to those facing cancer. In keeping with these goals, the European Institute of Oncology works to improve prevention and diagnosis services, provide health education and training, and investigate the best research and treatment options. The Istituto di Candiolo is located in Torino and is a collaborative effort of the Fondazione Piemontese per la Ricerca sul Cancro-Orlus (FPRC), which provides funding, and the Fondazione del Piemonte per l’Oncologia (FPO), which operates it. The Istituto di Candiolo works to make a significant contribution to the fight against cancer. It strives to do this through improving understanding of the basic causes of the disease and by providing world-class diagnostic and therapeutic services to patients. The institute, which collaborates with the University of Torino, is especially interested in the interaction between molecular biology and medicine. These and other institutions are working in collaboration with others around the globe to improve understanding of cancer and the best ways to prevent and treat it.

Stephen T. Schroth
Towson University

See Also: Austria; Drugs; Education; France; Future of Cancer; Hospitals.

Further Readings
Japan

In 2011, Japan’s Ministry of Health, Labor, and Welfare announced cancer, heart disease, and pneumonia are the top three causes of death in Japan, accounting for 28.5, 15.5, and 9.9 percent of total deaths, respectively. Cancer has been the leading cause of death in Japan since 1981. Because cancer incidence and mortality rates generally increase with age, peaking at 80 to 94 years, Japan is particularly vulnerable to cancer-related deaths as it is experiencing population aging that is unprecedented in the world. Its proportion of people age 65 and more is the highest in the world: 23 percent in 2009. By 2030, one in three people in the population will be more than 65 years old, and one in five will be more than 75 years old. Between 1930 and 1950, the leading causes of death in Japan were tuberculosis, pneumonia, and cerebral vascular disease. Postwar economic recovery and significant reductions in stroke and other major diseases have contributed to these changes in cancer trends. Many of the common cancers in Japan often are associated with an infection. For example, stomach cancers often are associated with a *Helicobacter pylori* infection, which has the highest prevalence among those born during World War II and the 1950s. During this time, the overall cancer mortality rate rose but began to decline in the early 1960s. In the 1960s, gastric and liver cancers were the top two common cancers among Japanese men, and gastric and uterus cancers the top two among Japanese women. Currently, the overall cancer incidence is increasing.

The availability and affordability of alcohol and cigarettes and the Westernization of dietary practices and lifestyle have contributed to some of the top common cancers in Japan: liver, lung, and the digestive system (e.g., stomach and colorectal). While gastric cancers continue to have the highest incidence rate among men, there is a declining trend, especially in the younger population. For women, the most common cancer is now breast cancer.

Ovarian cancer occurs more often in industrialized countries, except Japan. While some researchers noted the possibilities of genetic factors, others found that second and third generations of Japanese women who moved to the United States share a similar occurrence rate as the U.S. general population, suggesting the importance of environmental factors. Several studies have identified that Japanese individuals’ increased cancer risk is associated with increased acculturation to the West. The unique cancer trends in Japan often are shaped by dietary practices, social trends, health behaviors, and beliefs and attitudes.

**Risk Factors and Common Cancers: Diet**

Traditional Japanese diet and changes in diet have diverging impacts on cancer. Traditional Japanese
diet is rich in isoflavone, which is found mainly in soybeans and soy products, such as tofu (bean curds) and natto (fermented soybeans). Frequent intake of isoflavone is associated with a reduced risk of breast cancer and of localized prostate cancer. Despite the prevalence of a Westernized diet, the amount of isoflavone intake in Japan is high compared to other Asian countries. Frequent consumption of cooked or raw fish is believed to reduce lung and prostate cancer risks. Green tea, a common beverage in Japan, has been demonstrated to reduce gastric cancer among Japanese women.

Traditional Japanese cuisine, however, includes foods that are high in salt. In addition to soy sauce and miso soup, there are many salt-preserved foods, such as umeboshi (pickled plums), taku-an (pickled daikon radish), and salt-cured vegetables and fish. Habitual salt intake is a strong risk factor to developing gastric ulcers and gastric cancer among individuals infected with *Helicobacter pylori*.

In Japan, only about 15 percent of the calories in the diet come from fat, whereas in the United States, 35 percent of calories are from fat intake. A high-fat diet can lead to high production of estradiol, a form of estrogen, resulting in increased risks for breast cancers. The Westernization of diet has brought increased consumption of red meat and fat, which are associated with increasing trends in colorectal and prostate cancers in Japan. This change was noticeable around the Meiji period (1868–1912), bringing sukiyaki (Japanese hot pot with beef) and tempura (battered and deep-fried seafood or vegetables) to the public diet. It is noteworthy that the highest quintile of red meat consumption by Japanese individuals would be considered a moderate level of consumption by Western standards. Based on a 1955 to 1993 National Nutritional Survey in Japan, Westernized dietary habits are associated with increased mortality by colorectal and prostate cancers in Japan. In contrast, traditional Japanese dietary habits are associated with increased mortality by stomach cancer.

**Social Trends**

The changes in social trends in reproduction and fertility provide insights into the increased mortality by breast cancer in Japan. In the 1900s, the mean age of menarche was 16 years old, and Japanese society encouraged early marriage and large families. With some short-term fluctuations, a Westernized diet contributed to lowering the age of menarche to 13 years old in the 1960s and 12 years old in 2009. The mean age of menopause has been around 50 years old during that time, due to the complex influences from both an increase in life expectancy and expanded stressors. Along with the tendency to put off marriage and the downward trend in the birthrate, the mean age of birth of the first child increased from 25 to 28 between 1975 and 2005. In short, the decreased age at menarche, late child-bearing, fewer pregnancies, and the increased use of postmenopausal hormone therapies are all factors that are prevalent in Western countries and that are associated with an increased risk for breast cancer; the same trends have been affecting the Japanese population.

**Health Behaviors**

A 2011 national survey found that 34.1 percent of Japanese men and 9.0 percent of Japanese women smoke, among which 10 percent consume more than 21 cigarettes a day. The number of these heavy smokers has decreased, but the overall number of smokers has not changed significantly. In Western countries, smokers have a 10 times higher risk of developing lung cancer compared to nonsmokers. Despite the lack of strict laws and restrictions on tobacco products and consumption, Japanese smokers have a four times higher risk of developing lung cancer compared to Japanese nonsmokers. The phenomenon is also known as the Japanese smoking lung cancer paradox.

Some studies indicate that this is because (1) Japanese smokers’ risk for developing cancer is not as high as those in Western countries and (2) nonsmokers are at a higher risk of having cancers in Japan. Cramped offices and rooms within a limited national space bring smokers and nonsmokers in close physical proximity, causing passive exposure to tobacco smoke. Smoking has been determined to be the cause of approximately 40 percent of Japanese individuals diagnosed with lung cancer. The other 60 percent have been determined by other factors, such as eating habits, secondhand smoke, and alcohol consumption.

Drinking has been an important communicative component in Japanese business culture. Comparisons between individuals in Western countries
and Japan have revealed that approximately one in two Japanese people has an atypical allele of a group of enzymes (aldehyde dehydrogenase 2 gene [ALDH2]). Because these enzymes catalyze the acetaldehyde metabolism less, resulting in a high blood level of acetaldehyde after drinking, Japanese individuals with ALDH2 heterozygotes are more susceptible to subsequent risk in developing breast and esophageal cancers compared to people in the West. Japanese drinking culture is always harmful because alcohol consumption appears to be a moderator for certain cancer risks. Alcohol consumption among smokers increases the risk of developing distal colon cancer, whereas alcohol intake among nonsmokers decreases the risk of both cancers’ incidence and mortality.

Beliefs and Attitudes
In 2012, approximately 27 percent of the Japanese population had been screened for cancer. Although the cancer-screening rate in Japan has increased over time, it is still low compared to other economically developed countries. Misconceptions about cancer seem to contribute to a low cancer-screening rate. Based on the National Cancer Center’s report of 2006, the understanding of cancer risk factors in the Japanese general population tends to be governed by cancer-causing bacterial and viral infections, occupational exposure to hazardous substances, air pollution, and food additives or pesticide chemicals rather than major lifestyle factors, such as diet and alcohol consumption. Although the belief in cancer-causing bacterial and viral infections stems from the long-term prevalence of gastric cancer, such understanding seems largely influenced by the mass media and other sources rather than health professionals. In dealing with life-threatening diseases like cancer, medical professionals and patients’ family members in Japan tend to avoid disclosing a diagnosis to the patients, believing such information may overwhelm the patients and diminish their willingness to participate in treatments.

Sachiko Terui
Elaine Hsieh
University of Oklahoma

See Also: Japan Lung Cancer Society; Japanese Cancer Association; Stomach (Gastric) Cancer.

Further Readings

Japan Lung Cancer Society

The Japan Lung Cancer Society (JLCS) has been in operation since 1960, when it was first referred to as the Society for the Study of Lung Cancer (SSLC). The purpose of this group was to initiate a 35-year lung study group Showa. The aim of the initial group was simply to study cancer, given the disease at the time had very little known about it. The SSLC was renamed officially the Japan Lung Cancer Society in 1966; therefore, some literature will quote the establishment of the JLCS as being 1966. The aim of the society was and still is to promote diverse research on lung cancer and its related fields as well as helping to diffuse knowledge and understanding of the disease among society. In 1984, JLCS became a full member of the Union for International Cancer Control (UICC). In 2007, the establishment was pronounced as being a nonprofit organization.

To achieve the set objectives of the society, JLCS has a number of activities; the society holds various meetings and congresses for members, produces official publications and books that include the society’s journal and proceedings, research work, study, education on matters and issues concerning lung cancer, and close contact, cooperation, and coordination with related academic organizations at home and internationally.

Individuals can register as members of the society. In 2014, the society had 7,404 regular members, 85 associate members, 12 honorary members, 149
special members, 12 groups for supporting members, 65 subscription members, and 15 honorary presidents.

While the guiding objective of the society is to promote diverse research on lung cancer and its related fields, as well as helping diffuse knowledge and understanding of the disease among society, the society has a business objective, whereby the object is to measure the dissemination of knowledge as well as the progress of research in this area and to contribute to the promotion of human health and welfare widely. The headquarters of JLCS is at Nihonbashi, Chuo-ku, Tokyo 3-chome, No. 8, No. 16, Buyo Building, Fourth Floor.

JLCS activities are mainly organized and run by committees. The society therefore has a number of committees that are headed by different individuals at the leadership position of committee chair. These include the general administration committee with T. Goya as the committee chair, the finance committee with I. Yoshino as the committee chair, the editorial committee with the chair as T. Tamura, the scientific committee with the chair as K. Nakagawa, the mass screening committee with T. Kondo as the committee chair, the subcommittee for mass screening by sputum cytology with M. Sato as the committee chair, the subcommittee for mass screening by chest X-ray with the chair as C. Konaka, the future planning committee with Y. Hasegawa as the committee chair, the collaborative activities committee with N. Ikeda as the committee chair, the subcommittee for promotion of smoking cessation with H. Nomori as the chair, the subcommittee for data management with Y. Takiguchi as the committee chair, the international affairs committee with the chair as H. Asamura, the bylaws and constitution committee with the chair being M. Noguchi, the election management committee with S. Miyoshi in the chair position, the committee for evaluation of guideline proposals with K. Hayakawa as the chair, the subcommittee for pharmacotherapy and multidisciplinary treatment with N. Yamamoto in the chair position, the subcommittee for diagnosis with K. Kasahara in the chair position, the subcommittee for surgical treatment with Y. Ichinose in the committee chair position, the subcommittee for radiotherapy with the committee chair being K. Hayakawa, the subcommittee for pleural mesothelioma with T. Nakano in the chair position, the subcommittee for thymic tumor with M. Okumura as the committee chair, the ethical behavior committee with A. Gemma as the committee chair, the COI committee with the committee chair being S. Negoro, the biomarker committee with T. Mitsudomi as the committee chair, the lung cancer registry committee with K. Yokoi as the committee chair, the committee on guidelines for management of lung cancer with T. Mitsudomi as the committee chair, the diagnostic imaging committee with K. Eguchi as the committee chair, the TNM classification committee with T. Mitsudomi as the committee chair, the committee for cytologic diagnosis with H. Akita as the committee chair, the working group for cytologic criteria of mesothelioma with T. Kamei as the committee chair, the committee on classification of bronchoscopic findings with H. Isobe as the committee chair, the committee on surgical records with the chair being H. Date, the committee on pathological diagnosis with M. Noguchi as the committee chair, and the committee on criteria for therapeutic effectiveness with the committee chair being H. Senba.

In 2005, the guideline committee of the JLCS revised the role of chemotherapy and of chemotherapeutic agents with a clinical practice guideline for lung cancer in Japan, which had been published in 2003 by an expert multidisciplinary panel. The guideline covers points on standard diagnostic functions and how to adapt different methods for treatment based on the stage that the patient is in at a given time. This often includes a full analysis of what can be done. The revisions will renew the decision trees for standard treatment procedures and molecular-targeted therapies based on the new TNM classification and add parts to the treatments for malignant mesothelioma and the management of bone metastases with bisphosphonates.

In addition, JLCS has a journal as the major form of publication that it uses to provide information related to lung cancer to the entire world. The journal can be accessed online as well as in print form through subscription and through purchase.

Michael Fox
Independent Scholar

See Also: Japanese Gastric Cancer Association; Lung Cancer, Non–Small Cell.
Further Readings

Japanese Cancer Association

The Japanese Cancer Association is the premier organization devoted to the diagnosis and cure of all cancers. The stated purpose for the association is to promote cancer research and cure.

The history of the association is as follows: Lecture meetings about cancer started in 1908. The loosely knit organization was called the Japanese Foundation for Cancer Research. Yearly meetings were conducted until 1935. In about 1935, the members of the foundation agreed that cancer research in other settings had advanced quickly and that a new association should be born to cover all of these activities. They saw they needed to call in more qualified medical personnel. The association was formed in March 1941.

Japan, the Country, and Its People

The Japanese people (Nihonjin, Nipponjin) occupy the islands of Japan. Japanese people comprise 98.5 percent of the total population there. Their culture and art are unique anywhere in the world. They live in a colorful world of multicolored clothes and accessories like the umbrella. Yet, this tiny place has an incidence of cancer that just about trumps any in the world. The atom bombs dropped on Hiroshima and Nagasaki still are having their effects felt. Nowhere in the world can cancer and its causes be studied so thoroughly.

Nevertheless, the people are polite to a fault and generous beyond belief. There is no better place to have an organization like the Japanese Cancer Association than on the front lines of a country where carcinoma is the leading cause of death.

Cancer Registration System in Japan

The association is involved with the registration system, an invaluable tool in studying incidents of cancer deaths in the country. Currently, cancer is the number one killer among the population. In 2012 there were 360,963 deaths from cancer, with lung cancer the most common type of fatal cancer for men, and colon/rectum cancer the most common type for women. Cancer registration and investigation began in the late 1950s and first focused on the cities of Hiroshima and Nagasaki, the places bombed by the Allies in 1945.

The registration system has been criticized for collecting invaluable data on cancer deaths but then doing nothing about it in a statistical way to track the deaths to locations, types of cancer generic to certain areas, and generally not putting the data to its full use. More surveillance services may be needed, and the registry system may need to become more standardized.

Diabetes and Cancer

The Japanese Cancer Association has joined with the Japanese Diabetes Society to explore the link between diabetes and cancer. They found a link between the two diseases as late as the 1980s. There is substantial evidence that demonstrates that diabetes increases cancer risk, notability colorectal, liver, and pancreatic cancers. Diabetes promotes oncogenesis, the mechanism that turns normal cells to cancer cells.

Diabetes includes insulin resistance associated with hyperinsulinemia (making one insulin resistant), hypoglycemia (low blood sugar), and inflammation. Risk indicators for diabetes causing cancer are aging, male sex, obesity, physical inactivity, inappropriate diet (red meat intake and little fresh vegetables), alcohol drinking, and smoking. There is no substantial evidence that anti-insulin medications can cause cancer.

It has been shown recently that diabetes can be a cause of breast cancer, in which the Japanese Cancer Association is involved. Hyperinsulinemia is common in type 2 diabetes. Again, the condition and its insulin-resistant properties have been shown to cause or worsen breast cancer. The high rate of death persists as the cancer metastasis sets in. Metastasis is the spreading of cancer into other parts of the body.
The Journal
The association publishes Cancer Science, a monthly medical journal focused on cancer research. First published in 1907, the journal continues today to publish current, relevant articles on oncology and translational and clinical cancer research. Journal Citation Reports evaluates the journal as having a 2012 impact factor of 3.479, making its ranking 69 out of 196 journals in the world category on oncology. The impact factor is a number representing how many times the journal quotes or refers to previous articles. Journals that have a higher ranking are considered more important than others.

The purpose of the Japanese Cancer Association is to spread the word about cancer and its most up-to-date treatments. The journal has a significant role in fighting the battle against cancer. Original research articles are put to press as fast as possible to keep the medical community (and the public) aware of the deadly disease and the treatment thereof. The latest breakthroughs in the field are available every month giving readers an overall picture of cancer appearing in its various manifestations in the human body. The publication is limited to cancer, its research, and treatment and is not cluttered by information that is not useful in real time.

All of the volumes published are available for order at http://onlinelibrary.wiley.com/. Each issue has 10 to 12 pertinent articles essential to medical practice wherever it may be. It is not just for oncologists as all specialties can benefit; cancer is capable of invading the body anywhere. Cancer often is missed as an initial diagnosis because it may be hiding behind ordinary symptoms such as come with a cold or flu. Each volume gives early detection clues to better care for patients.

Awards
The Japanese Cancer Association has proved its excellence by winning the most highly regarded awards in the field: the Tomizo Yoshida Award, Mataro Nagayo Award, Japanese Cancer Association Incitement Award, JCA-Mauvernay Award, and JCA-CHAAO Award.

The Japanese Cancer Association is applauded the world over for its innovative force in ridding the world of one of its biggest scourges.

Kenneth B. Alexander
Independent Scholar

See Also: Japan Lung Cancer Society; Japanese Gastric Cancer Association; Japanese Society for Therapeutic Radiology and Oncology.

Further Readings


Japanese Gastric Cancer Association

In 1962, the Japanese Research Society for Gastric Cancer was established. The society’s aim was to research and provide information about gastric cancer. The society did a thorough job in regard to its mandate and played an important role in the promotion of basic and clinical research on gastric cancer. However, it was a closed association organized by 352 leading institutions in Japan. In 1997, the society was changed to an open association composed of individual members. The change saw the organization rebranded as the Japanese Gastric Cancer Association (JGCA). This is a global organization that offers plenty of services for members in all parts of the world.

Even though the organization changed its name from Japanese Research Society for Gastric Cancer to JGCA and even its systems and operations to allow foreign and international members, the aim of the organization has not changed in principle. The only change to the aim is in terms of scope. Initially, the objective was supporting many studies on gastric cancers and other issues in the body with the intention of managing different foreign controls and to take a look at how people from different parts of the world are studying the functions of cancer. The goal now is to create an international
approach to supporting the research needed for managing cancer in all of its dangerous and potentially fatal forms.

The major activities of JGCA with regard to realization of the set objectives are as follows. These are all activities designed with the intention of ensuring that all cancer patients receive the help that they deserve in all stages in their lives based on the treatments that they might require.

The Japanese Gastric Cancer Congress is a meeting that is held annually. The 2014 event was the 86th congress of the society. The theme of the congress was *Total Control of Gastric Cancer: Wisdom and Practice*. Each congress is chaired by the congress president, and the 86th congress was chaired by Wasaburo Koizumi, professor and chair from the Kitasato University School of Medicine Department of Gastroenterology. The congress started March 20 and ended on the 22nd of the same month in 2014. The congress is held annually, and the recommended time is February; it is organized most often by the congress president. English abstracts, English presentations, and English discussions are accepted from international members.

*Journal of Gastric Cancer* is published by the society's editorial committee; *Gastric Cancer* is a key journal that provides people with information in the English language on cancer research and how it is being utilized in a number of critical ways for the enhancement of society as a whole. It has a global audience, and at its initial publication and circulation, the journal received approximately 3,000 in readership and later expanded to 5,000. Even though it is not possible to provide the exact readership of the journal because of the online access option, 7,000 members have subscribed. The journal provides people with critical pieces of information that are relevant to the needs that people have when it comes to studying at large and seeing how certain functions are to work.

A new manual was also produced as a means of analyzing cancer treatments and how they are operational for many requirements. This has helped to take a look at the ways the body is able to handle different problems that it might get into and how it may requires assistance in some way.

The JGCA is also functional with the intention of registering gastric cancer patients. This is to ensure that there are enough data around with regard to the treatments that different patients might require at given times. The solutions that are of use may be essential and critical as there are more than 10,000 bits of patient data being collected each year.

In addition to the above activities, JGCA is involved with or undertakes other activities to foster the promotion of basic and clinical research on gastric cancer. For instance, JGCA is working with the International Gastric Cancer Association (IGCA) and the World Health Organization (WHO) to help with studying gastric conditions and various aspects relating to cancers in these parts of the body as a means of checking on how the body can respond to such issues at large. All the members can get information from these international organizations. All members contribute to the activities of JGCA, particularly in election of the council members every two years and approval of various activities and decisions.

The various activities and operations of the association are under committees. JGCA has a number of committees, and each committee is under a committee head. Some of these are the manual committee and the registration committee.

For an individual to join the society, a registration fee is required together with an application. The membership fee is 12,000 yen. There is no difference between the amount paid by Japanese members and those from the international community. The application form for anyone interested in joining JGCA is available online. The majority of the members are professionals interested in JGCA and in the gastric cancer profession, namely clinicians, educators, researchers, and students. The membership fee indicated is required to be sent together with the filled-in membership application form, and it is an annual fee.

Michael Fox
*Independent Scholar*

**See Also:** Japan Lung Cancer Society; Japanese Cancer Association.

**Further Readings**

Japanese Society for Therapeutic Radiology and Oncology

The Japanese Society for Therapeutic Radiology and Oncology (JASTRO) has been in operation since 1988. At its establishment, it was a membership group that featured persons working in health care, the field of oncology, and other general functions. The society's office is located in Tokyo, Japan. The aim of JASTRO is to promote communication and cooperation in studies to determine how radiotherapy works.

JASTRO has an executive and a board of directors, which are responsible for running the society. The members of the board include people from many different schools from cities all around Japan. These include people from the University of Tokyo, Keio University, the Yamanashi Faculty of Medicine, and the Osaka Medical Center, among several other critical organizations. There are many board members and auditors who work together, with the key leaders being Yasumasa Nishimura of Kinki University as the president of the society and Kenji Nemoto of Yamagata University as the secretary general.

At the inception of JASTRO, little was known about cancer as a disease. This inadequacy of reliable information required research into the field so as to understand cancer better and improve treatment. Hence, the purpose of JASTRO became to communicate, cooperate, and promote general and professional research relating to the identification of cancer through many techniques like radiotherapy to analyze patients. To realize this purpose, the society has undertaken various projects, each appropriate for the promotion, advancement, and realization of a specific aspect in the society's aim. These include to hold academic conferences, symposia, and lectures: Individuals among them, clinicians, researchers, educators, or students in the field of therapeutic radiology and oncology, hold conferences and present research work and findings. So far, the society has successfully held 26 meetings. The 2014 meeting focused on analyzing the overall functions in the industry.

Members of the society are required to make publications of their research work. One of the major and popular publications made by the society is the Journal of JASTRO. The journal was published on a quarterly basis, at least up to 2008. However, from 2009, only a single publication was made per year. The journal has surpassed volume 21.

JASTRO has several associations with both local and international societies, organizations, and bodies for the aim of furthering their scope and knowledge in terms of cancer management and treatment.

To encourage study, research, education, and training concerning radiotherapy, the members of the society are required to actively engage in research work in the field of cancer and especially therapeutic radiology and oncology.

JASTRO has several commendations for excellent achievements in the research of cancer therapeutics. These are in the form of awards to those who excel in the field.

In addition to the projects already mentioned, the society undertakes various other projects to further their purpose. These are mainly projects that might be passed by the board.

JASTRO has a community in the form of members. An individual who meets the membership requirements can apply. The majority of members are researchers, clinicians, students in the field of cancer therapy, and honorary individuals. For admission into the society, a person who wishes to join must get a recommendation and submit a proper form for entry. The application should then be sent together with the membership fee for the applicable year, which must be approved by the board of directors.

JASTRO has various membership types. A member can enter, but an honorary member may also join. An associate member like a technician or nurse may also come in. Other supporting members may join provided that the organization endorses the applicant.
Jet and Rocket Fuels

In 2013, the society had 2,006 active members, 1,452 associate members, 24 honorary members, and 34 supporting members, totaling to 3,516 members. The society has 1,013 board certified radiation oncologists. Among the members are gold medalists and honorary members. JASTRO distinguished service gold medal members are Ritsuko Komaki and Hirohiko Tsujii.

The society has three awards: the Umegaki Award, awarded to Norio Katoh and Keiiti Zingu in 2013; the Abe Award, won by Takahumi Toita in 2012; and the Excellent Educational Lecturer Award, awarded to Yusuke Demizu, Norihiro Aibe, and Takayuki Ooguri in 2013.

Michael Fox
Independent Scholar

See Also: American Society for Radiation Oncology; European Society for Therapeutic Radiology and Oncology; Radiation Therapy.

Further Readings

Jet and Rocket Fuels

An often under-recognized risk factor for cancer and other health issues, jet or rocket fuels are comprised of a plethora of noxious and potentially carcinogenic compounds that can be linked to a plethora of health problems. Studies examining compounds found commonly in rocket fuel have suggested links to cancer, endocrine problems, and other health concerns for many years, beginning all the way back in the 1950s. This entry investigates the health risks associated with rocket and jet fuel exposure, common routes of exposure, issues surrounding its usage, and legal and illegal dumping across parts of the United States, its composition, and how that has exposed many individuals to contaminants, often unknowingly.

Rocket Fuel and Its Composition
Rocket fuel in its typical composition today consists of many different chemical compounds, some 2,000 approximately, not all of which have been formally identified. Many of these are either known carcinogens or at least noxious to human, aquatic, or animal life, including benzene, perchlorate, and halon. Moreover, upon combustion, many other dangerous chemicals are formed, such as the class of carcinogens called polycyclic aromatic hydrocarbons. Nitrogen dioxide is another commonly produced high-temperature combustion by-product, which is primarily associated in studies with potentially damaging the lungs. Other types of petroleum derivatives and by-products such as perchlorate, toluene, xylene, kerosene, and others are commonly used in rocket fuel or are produced through combustion. Accordingly, these chemicals are given off in exhaust trails from commercial and military planes as well as private jets and planes.

Common and Historical Routes of Exposure: The Example of Perchlorate
Elevated levels of these and many other chemical compounds are frequently found in air around airports in particular, causing local, knowledgeable residents much concern due to the mounting evidence suggesting certain types of cancer, respiratory problems, endocrine problems, and other health issues are strongly linked to exposure to such compounds. Additionally, these chemicals can settle onto crops, waterways, into livestock feed, and really anything in the proximity of highly traveled airspace. However, that has not been the only or necessarily the primary way some individuals have gotten exposed to, in some cases, high doses of rocket fuel.

Following World War II, there was much focus on developing new types of rocket fuel to compete with the burgeoning powers of the Soviet Union in the Cold War. Thus, highly combustible yet stable-enough compounds such as perchlorate began to be used and added in the manufacturing of such fuels in selected locales across the United States. At that time, concerns over communist invasion generally outweighed concerns about environmental
impact or public safety, and also at this time, perchlorate was not considered very dangerous, and thus, waste materials from rocket fuel manufacturing and usage were simply dumped at various sites across the United States, especially in the desert southwest region. To explicate, perchlorate, dubbed powdered oxygen, is combusted inside a rocket engine with aluminum powder and a rubberlike polymer to stoke an intense burn. To propel a rocket, the solid fuel must be ground and molded into a particular shape.

Over time, the fuel breaks down, requiring continual replacements. That’s why, for more than 40 years, tons of perchlorate were routinely flushed from rockets and missiles onto the ground and into water supplies. In fact, literally millions of tons of this contaminated wastewater were dumped into unlined pools, holes, and ponds and onto the ground, allowing it to seep into underground aquifers, rivers, and ultimately municipal water supplies, which have been historically ill equipped to filter it out. Unfortunately, due to a myriad of factors such as poor testing, pushback from manufacturers, and unclear advisory standards for exposure, more legal and illegal dumping continued from the late 1940s all the way into the late 1970s, before the Environmental Protection Agency (EPA) and other regulatory bodies (after the passage of the clean water bill) began asserting greater authority and regulatory control on manufacturers, pushing them to start cleanup efforts. However, unfortunately by that time, much of the damage had already been done from nearly 30 years of dumping into ground pits, unlined pools, and so on. To date, the EPA has cataloged at least 75 perchlorate releases across 22 states that exceed safety standards and require years of cleanup efforts. Of course, this does not include all of the additional chemical exposure the vast majority of the country gets from airplane traffic crisscrossing all states.

One of the most troubling routes of potential exposure is through the consumption of produce that has absorbed rocket fuel metabolites, such as perchlorate, from contaminated water. One preliminary study conducted by the Environmental Working Group in the San Bernardino Valley east of Los Angeles found that lettuce grown in a known area of perchlorate contamination in well and city water from years ago showed levels 65 times that of what was found in the water samples. Essentially, this means that plants are concentrating the perchlorate and thus subjecting those who consume the produce to drastically higher levels of the contaminant beyond what they may already be getting through the water.

**Health Risks Associated With Rocket Fuel Exposure**

In the human body, perchlorate affects production of thyroid hormones, which according to the EPA, can cause thyroid ailments such as Graves’ disease and thyroid cancer in adults. Fetuses and newborns are at even greater risk, susceptible to neurological and other developmental damage. The EPA worries that even the smallest traces of perchlorate are dangerous to newborns and fetuses because thyroid hormone production is crucial to normal brain development. Animal studies as far back as 1957 have illustrated how this can be readily passed from mother to newborn in utero, as such was the case in a 1957 Harvard University study on guinea pigs, where the transmission of perchlorate via the placenta to newborn guinea pigs was witnessed.

Of course there are many other chemicals noxious and carcinogenic to human health in rocket fuel. Polycyclic aromatic hydrocarbons (PAHs) are known to be extremely carcinogenic even in tiny quantities. Exposure to NO₂ (i.e., nitrogen dioxide) induces pulmonary injury in a multitude of ways.
NO$_2$ is converted to NO, HNO$_3$ (nitric acid), and HNO$_2$ (nitrous acid) in the distal airways, where it exerts toxic effects on type I pneumocytes and ciliated airway cells. NO$_2$ also initiates free radical generation in the terminal bronchioles, resulting in protein oxidation, lipid peroxidation, and subsequent cell membrane damage. NO$_2$ furthermore alters macrophage and immune function, causing impaired resistance to infection. Benzene has hematological, immunological, and lymphoreticular effects and is classified in EPA Group A as a human carcinogen. Children and fetuses may be at increased risk to benzene toxicity because their hematopoietic cell populations are expanding and their dividing cells are at a greater risk than quiescent cells. Furthermore, based on studies of benzo(a) pyrene in animals, women may be at increased risk of reproductive dysfunction following exposure to high levels of benzene types of compounds.

Individuals with impaired pulmonary function may be more susceptible to the respiratory irritant effects of the many volatile petroleum hydrocarbons found in or given off via jet fuels. Acute inhalation or aspirating such aromatic petroleum hydrocarbons can lead to pulmonary irritation and even hydrocarbon pneumonia, which is an acute hemorrhagic necrotizing disease. Furthermore, these aromatic and aliphatic hydrocarbons found in petroleum products, including jet fuel, are metabolized through the cytochrome P-450 pathways in the liver, which are then transformed into metabolic metabolites. Some of these (such as intermediary metabolites of benzene and other PAHs) are known to cause cancer from chronic exposure as well as peripheral neuropathy. At this time, there are no known, proven clinical treatments to interfere with these mechanisms of action.

The comprehensive listing below illustrates the sheer magnitude of many potential health issues linked to persistently elevated levels of jet fuel and jet exhaustion: asthma, brain cancer, conjunctive irritation, coughing, delayed hypersensitivity, distorted perceptions, drowsiness, dyspnea, headache, EEG changes, emphysema, flushing, hallucinations, heart disease, high blood pressure, Hodgkin’s disease, lacrimation, liver damage, lung disease, lung structured damage, lung tightness, lymphoma, mental depression, muscle weakness, myeloid leukemia, nausea and vomiting, pulse rate decrease or increase, pulmonary irritation, respiratory system damage, skin and eye irritation, systemic irritation, and wheezing.

Last, according to researcher Dr. Hitomi Suzuki, the compound 3-nitrobenzathrone, given off in the exhaust of jet fuels, may be the most hazardous compound ever to be tested for carcinogenicity. Researchers such as Dr. Suzuki and others have remarked that there are also very likely synergistic effects increasing the carcinogenicity of isolated compounds in jet fuel when interacting with the sun and the atmosphere when given off as exhaust, causing even further concern for those who live especially close to airports. Studies as far back as the early 1990s have drawn this conclusion, for instance, when the EPA conducted a study looking at cancer cases in the proximity of Midway airport in Chicago. This study concluded that nearly 99 percent of the cases of cancer reported in the vicinity of Midway airport were directly linked to aircraft emissions.

**Past Exposure, Cleanup, and Continued Insidious Exposure**

Limiting exposure to items such as perchlorate and other chemicals found in jet fuel is hampered by the fact that, for many years, such compounds were freely dumped into the Earth in unlined pits and such, allowing it to seep deeply into underground aquifers and rivers and, in some cases, out of the reach of remediation efforts by companies trying to make right their previous environmental faux pas. Limiting exposure from commercial and private jet planes is obviously very limited for the public by not being able to control what is released into the air across the country, thus leaving a potential considerable route of exposure largely unmitigated for many people. Last but not least, while the EPA has released public statements agreeing that perchlorate is dangerous and must be regulated in public water supplies at a deemed safe level (which is based on review of extant scientific literature as of 2012), this has not translated into mandatory meaningful action on a large scale as of yet. This is because the EPA has not posed any regulatory requirements on public water supplies and systems at this time, even though some 4 percent of public water supplies routinely test positive for perchlorate contamination.

Eric Wood

*Hawthorn University*
See Also: Leukemia, Chronic Myelogenous; Lung Cancer, Non–Small Cell; Thyroid Cancer.

Further Readings

Jimmy Fund

The Jimmy Fund was introduced in 1948 to collect donations for improving the survival rates for children and adult cancer patients through the support of cancer research and patient care. The Jimmy Fund is associated with the Dana-Farber Cancer Institute in Boston, Massachusetts. The organization emerged when a child patient of Dr. Sydney Farber, founder of the Dana-Farber Institute and the father of modern chemotherapy, took part in a broadcast at the hospital bedside of an inspirational 12-year-old cancer patient, Einar Gustafson. He was dubbed the original Jimmy to protect his privacy. Gustafson’s cancer went into remission, and he returned to his home in Maine, where he lived out of sight until 1998, the 50th anniversary of the Jimmy Fund, when people were shocked that he had survived pediatric cancer. He died at the age of 65 of a stroke and remains a beacon of hope for all cancer patients. His story established the mission of the fund to sustain research and care that improves cancer survival rates because most doctors believed that his long-term prognosis was not strong.

The Jimmy Fund, a nonprofit organization, began as a grassroots effort that included events like lemonade stands, bake sales, and various runs and walks. In 1953, the Major League Baseball team the Boston Red Sox became a proud partner of the Jimmy Fund along with the Massachusetts Chiefs of Police Association, Pan-Mass Challenge, and Variety Children’s Charity of New England. The Jimmy Fund serves as the official charity of these key Massachusetts institutions. Today, there are countless national fund-raising events held each year to raise money for the Jimmy Fund.

The Dana-Farber Cancer Institute boasts an equal commitment to both patient care and research in cancer advances. Dana-Farber is associated with several areas of Harvard University, including the Medical School and the Stem Cell Research Institute. Dana-Farber services more than 300,000 patients and sponsors in more than 700 clinical trials a year. It is continually ranked as the number-one cancer hospital in New England and number five in the United States by U.S. News and World Report. It is affiliated with Brigham and Women’s Hospital, Boston Children’s Hospital, and Massachusetts General Hospital.

In 2013, the Jimmy Fund and the Boston Red Sox celebrated their 60th year together, making it the oldest and most effective partnership between a sports team and cancer charity in the United States. The Jimmy Fund has raised millions of dollars for research and patient care for the Dana-Farber Cancer Institute. The fund reports that 89 cents of every dollar collected goes directly to patient care and cancer research. One of the fund’s largest fund-raising events is the WEEI and New England Sports Network (NESN) Jimmy Fund Radio Telethon, which has been held for the last 13 years. The radio and television telethon runs for two days in mid-August. Celebrities who have donated to the Jimmy Fund include Matt Damon, the late George Steinbrenner (the Yankees’ owner), Donald Trump, and countless others.

The Boston Marathon Jimmy Fund Walk continually raises the most money of any one-day walk in the United States, raising close to $95 million toward the fight against cancer since 1989.

The Jimmy Fund is an impactful and inspirational not-for-profit organization strategically paired with several long-time Massachusetts historical
institutions including the Boston Red Sox. It continues to be a thriving fund-raising organization with the sole purpose of supporting the Dana-Farber Cancer Institute. The patient stories of those helped by the amount of positive research and clinical trials to emerge from the Dana-Farber Cancer Institute highlights the real promise of the Jimmy Fund to one day eradicate cancer.

Diane Ferrero-Paluzzi
Iona College

See Also: Chemotherapy; Childhood Cancers; Dana-Farber Cancer Institute; History of Cancer; Massachusetts Medical Society; United States.

Further Readings

Johnson & Johnson (United States)

Three brothers (Robert Wood Johnson, James Wood Johnson, and Edward Mead Johnson) started the Johnson & Johnson Company in 1886 in New Brunswick, New Jersey. Their product line involved medical supplies. The company published “Modern Methods of Antiseptic Wound Treatment” and facilitated the growth of routine sterilization for surgical methods in the United States and globally. By 1901, Johnson & Johnson placed the first “Handbook of First Aid” in the company’s first aid kits. The company developed many over-the-counter medications to meet the health needs of individuals in the early 1900s. Johnson & Johnson truly represented a company ahead of their time with the publication of education material along with the items sold. When the company provided supplies and money to Galveston, Texas, after a hurricane in 1900, the practice of disaster relief by private enterprise began.

Fast-forward to 1957; Johnson & Johnson introduced Tylenol as the first prescription aspirin-free pain reliever. Then in 1968, RhoGam became the first product to treat babies with hemolytic anemia caused by the mother’s Rh-negative blood. With the company’s past history of breakthrough treatments, it brought a new method, GeneSearch Breast Lymph Node Assay, to market in 2007 as the first gene-based test to uncover the extension of breast cancer into the lymph nodes. Johnson & Johnson continuously stayed abreast of the needs of the consumer.

Under the leadership of Robert Wood Johnson, the concept of a global market changed. He realized after World War I that the company needed to stop working through sales agents in other countries. The company needed to get to know local economies worldwide and open locally managed Johnson & Johnson companies capable of understanding local needs in order to truly serve the populations in each setting worldwide. The company expanded to New Zealand, Australia, Canada, and the United Kingdom after World War I.

More recently in the millennium, Johnson & Johnson developed a program for cancer prevention, called the chief executive officer (CEO) Cancer Gold Standard. The company leadership felt that employers perform a major responsibility in the battle against cancer by supporting a workplace conducive to a healthy environment and safe health practices. Consequently, Johnson & Johnson outlined a program to reduce health risks by detailing activities to prevent cancer, to detect the disease early, and to guarantee access to the most suitable treatments for their employees.
The company took the leadership role by integrating the Cancer Gold Standard Program into their prevailing health promotion practices. The guidelines in the program highlight tools to monitor progress in their cancer prevention and treatment initiatives. Since execution of the program in 2013, Johnson & Johnson has collated and interpreted data analysis of health care eligibility, claims, and health risk assessment to uncover progress in their own institution.

Organizations can join the Cancer Gold Standard group. The Gold Standard outlines how business leaders and CEOs can alter the course of cancer. Companies in the CEO Cancer Gold Standard Program can collectively as a group impact formulators of policy, payers, and the establishment at large in altering behaviors and generating a belief in health and wellness to reduce cancer or adverse outcomes of the disease.

Why support a program about cancer? The cancer statistics tell a compelling tale of risk and death. In the United States, the risk of developing cancer over a lifetime remains at slightly less than one in two for males and a little more than one in three for females. Cancer comes in second as the most frequent cause of death in the United States. The collective cost entails direct medical costs, lost productivity, the price of disability claims, and the burden of cancer on the individual and family. The number one preventable activity contributing to cancer development remains tobacco use, with heavy alcohol use as a second influencing factor. A few other controllable aspects associated with cancer include inadequate diet, insufficient exercise, and infectious diseases.

What does the Cancer Gold Standard Program entail? The primary tenet of the Cancer Gold Standard Program remains the concept of health and safety of the workforce. By advocating wellness, lessening the health risks of the workforce, and alleviating the complications of chronic illness, R. Fabius and colleagues describe companies adhering to these concepts as realizing a reduction in health care costs, an increase in productivity, and elevated levels of performance.

The Gold Standard Program uses five pillars to describe the areas of emphasis in its agenda. The first pillar entails prevention, with the five subcategories of nutrition, physical activity, healthy weight, vaccines, and a tobacco-free workplace. The second pillar favors screening for breast, cervical, and colorectal cancer as early detection is known to provide better outcomes. The third pillar promotes participation of employees in cancer clinical trials as new, more effective cancer treatments can be discovered. The fourth pillar advocates access to quality treatment when cancer diagnosis occurs and linkage to educational resources on cancer survivorships. The fifth pillar focuses on health education and health promotion, so employees understand the rationale for the first four pillars.

Support for the CEO Cancer Gold Standard Program continues to rise. Just in 2014, many companies became accredited by the program to support the healthy lifestyles and battle against cancer. Companies come from all the different niches in society. Some of the companies include Bayer Healthcare, Amgen, Latham & Watkins (a global law firm), Boehringer Ingelheim Pharmaceuticals, North Dakota State College of Science, Texas A&M Health Science Center School of Rural Public Health, Putnam Hospital Center (Carmel, New York), Georgia Regents Medical Center, and Carroll Hospital Center (Westminster, Maryland).

Johnson & Johnson continuously shows its commitment to healthy issues within the company. Its actions motivate other organizations to change and pursue avenues of not only reducing the risk of cancer but also supporting innovations in the treatment of cancers. Because research indicates that fully half of all cancers are preventable, Johnson & Johnson uses the best evidence available to pursue health prevention and to engage in promotion of treatment like gene-based therapy.

Sharon A. Takiguchi
Independent Scholar

See Also: Breast Cancer; Cancer Communication; Gene Therapy.

Further Readings
The country of Jordan has a population of 6.2 million people. It spends 8 percent of its gross national product (GNP) on health care. There are high frequencies of leukemias and lymphomas in this region, especially in children: 33.2 percent leukemia and 18.1 percent lymphoma. The country lacks resources in cancer research. Prior to the 1980s, in order to obtain treatment, wealthy patients had to travel to another country. Those who lacked the financial means to go abroad were treated using Jordan’s limited resources, most with poor results.

In 1997, the Al-Amal Center, which means the “Center for Hope,” opened. While the center was established to provide care to those living in Jordan, many still traveled abroad for treatment because the technology was years behind that of the United States or Europe. For example, in 1998, King Hussein flew to the United States be treated for lymphatic cancer at the Mayo Clinic in Rochester, Minnesota. The type of non-Hodgkin’s lymphoma that King Hussein had generally responds to treatment, but treatment was not available in Jordan. King Hussein died on February 1999. In 2002, the Al-Amal Center was renamed the King Hussein Cancer Center (KHCC), after King Hussein. This is the only cancer center in Jordan.

When Mahmoud Sarhan was hired as the Director for the KHCC, he founded the bone marrow transplantation program (BMT). This program is now one of the largest in the Middle East, with a success rate that rivals those in the United States and Europe. The center performs matched allogeneic and autologous transplants, and uses umbilical cord blood collected from the placentas after birth in healthy pregnancies. Currently, stem cells, such as those harvested from umbilical cord blood, are used in the treatment of acute leukemia, chronic leukemia, high-risk solid tumors, Hodgkin’s and non-Hodgkin’s lymphoma, multiple myelomas, and myelodysplastic syndromes, in addition to numerous blood, immune, and metabolic disorders. Internationally, 34 percent of hematopoietic stem cell transplants are done using umbilical cord blood.

In 2007, the first national breast cancer program, the Jordan Breast Cancer Program (JBCP), was established. The objectives of this program were to reduce morbidity and mortality from breast cancer using awareness campaigns, early detection, and access to screening for Jordanian women when the survival rates are best. In 2010, the KHCC formed an alliance with the American University of Beirut Medical Center to create a joint cancer research program. On October 31, 2013, Leeds Teaching Hospitals NHS Trust signed a formal Memorandum of Understanding. This agreement created a partnership in which Leeds will share its expertise and innovations and allow development of cancer treatment in the Middle East. Leeds Cancer Centre, located at St. James’s University Hospital, is one of the largest providers of oncology services in the United Kingdom, and is a leader in cancer research and treatment. Healthcare UK was instrumental in bringing Leeds and the KHCC together. Additional partners include St. Jude’s Research Hospital and the University of Texas MD Anderson Cancer Center.

There are over 3,500 new cancer patients each year, with more than 110,000 outpatient visits. The KHCC has 200 oncologists and consultants, 617 trained oncology nurses, and 82 pharmacists, and it performs 120 bone marrow transplants each year. The facility has six operating rooms and 18 intensive care beds, with 6 for pediatric patients. The KHCC is actively involved in academics and research. The Academic Affairs Office promotes education and training at the center. There are five parts to this office: the Education Center, Training Center, Life Support Center, International Affairs Center, and Library & Education Recourse Center, and two committees, the Ranking and Promotion Committee and the KHCC Regional and International Scientific Activities Committee. Two research projects that came from Jordan are on cancer-related outcomes in colorectal cancer and type II diabetes, and the prevalence of biallelic mismatch repair gene alterations in pediatric high-grade glioma and supratentorial primitive neuroectodermal tumor. Additional research projects include treatment of tobacco dependence, BRCA1/2 breast cancer mutations, and breast cancer molecular subtypes.

The number of patients diagnosed with cancer is on the rise in Jordan, and the current infrastructure does not support the current demand, let alone the growing cancer population. Combine this with more patients coming to Jordan for treatment from other countries, such as Palestine, Iraq, Yemen, and Sudan, and cancer patients will
be turned away for lack of facilities. To meet this
demand, the KHCC is expanding to double the
current capacity. This expansion will include an
inpatient tower and an outpatient building, costing an estimated $186 million. The expansion is
scheduled to be completed the middle of 2015.

The Inpatient Tower will consist of 13 floors, containing 182 single-occupancy rooms, an expanded
diagnostic imaging and radiotherapy unit, an
expanded bone marrow transplant unit, and intensive care units, including a specialty pediatric unit, and medical floors specializing in both adults and pediatric patients. The 10-floor outpatient building will house the first public umbilical cord blood
bank in Jordan. The Khalid Shoman Educational
Center and Auditorium will also be located here. This will focus on the education of health care providers, and will include a skills lab, lecture room, medical library, and an interactive lounge. The
Women’s Health Center and the dedicated space for pediatrics is designed to cope with the rising num-
ber of women and children diagnosed with cancer. Finally, the Cell Therapy and Applied Genomics
Department will continue research in laboratories
studying stem cells while increasing the research
capacity of the center.

Justina D. Higgins
Independent Scholar

See Also: Bone Marrow Transplants; Breast Cancer;
Lymphoma, Non-Hodgkin’s, Adult; Surgery.

Further Readings
American Cancer Society. “Stem Cell Transplant
(Peripheral Blood, Bone Marrow, and Cord Blood
org/acs/groups/cid/documents/webcontent/003215-
Radiotherapy and Chemotherapy Patients With
Than Oil and Uprisings: Current Development in
Cord Blood Banking in the Arab World.” Baker
files/Research/1ab9cf18/STP-Poster-ISSCR2013-
Kaposi’s Sarcoma

Kaposi’s sarcoma (KS) is a tumor of lymphatic endothelial cells caused by human herpes virus 8 (HHV8), also known as Kaposi’s sarcoma-associated herpes virus (KSHV). KS lesions typically present as palpable cutaneous violaceous papules that are nonpruritic but may also involve visceral organs such as the gastrointestinal and respiratory tracts. Rapid tumor progression is associated with substantial morbidity and mortality. Clinical familiarity with KS is crucial as KS is the most common acquired immune deficiency syndrome (AIDS)-associated cancer in the United States and accounts for up to 50 percent of all cancer diagnoses in certain African countries.

Since the discovery of HHV8 in 1994, overwhelming evidence has accumulated to demonstrate that KS is a direct consequence of HHV8 infection. KS lesions, regardless of source or clinical subtype, have been shown to contain HHV8 proteins. Recent evidence suggests that a widely expressed 12-transmembrane light chain of the human cystine–glutamate exchange transporter system and the C-type lectin DC-SIGN serve as receptors for HHV8 in vivo. Once the virus has infiltrated the host’s cells, multiple HHV8 gene products have exhibited the potential to transform cells in vivo. These gene products are homologous to human genes involved in the regulation of apoptosis, cell proliferation, and angiogenesis and may be directly responsible for the carcinogenic properties of KS. The latency period between HHV8 infection and the clinical manifestation of KS is variable but is clearly dependent on immune system functionality. Immunosuppressed organ-transplant recipients develop KS within one to two years, whereas human immunodeficiency virus (HIV)-infected patients present with KS after five to 10 years, traditionally with CD4 at less than 200 cells/mm³.

Histologically, early KS is a highly vascular neoplasm consisting of proliferating spindle cells of endothelial origin that surround dense, irregular, vascular-like spaces that leak red blood cells, hemosiderin-laden macrophages, and lymphocytes. In more-developed solid tumors, the spindle cells are arranged in more compact bundles and interlacing fascicles. Though KS was previously considered a monoclonal proliferation of endothelial cells, new studies comparing viral HHV8 DNA suggest a partially multifocal process, where each tumor arises independently from a distinct clone.

Four clinical variants of KS have been described, distinguished by epidemiology, sites of involvement, and rates of progression.

Classic KS predominantly affects men of Mediterranean and eastern European origin, commonly in the seventh decade of life. Lesions start as unilateral or bilateral firm, blue-red macules on the skin of the distal extremities. With time, lesions
grow and coalesce to form nodules or plaques and may assume a brown color. The overlying skin typically becomes hyperkeratotic, which clinically manifests as thickened skin in the affected region. Classic KS may follow a benign course for years to decades after the development of sentinel lesions. In approximately 10 percent of patients, the tumor may disseminate to involve lymph nodes, mucosa, or viscera such the gastrointestinal tract. Symptoms directly attributable to disseminated lesions are rare. In most cases, patients affected by classic KS die from other causes prior to the full spread of the disease.

Endemic African KS was recognized in sub-Saharan Africa in the 1950s, several decades prior to the outbreak of the AIDS pandemic. Though endemic KS may present worldwide, it is most prevalent in central Africa, where it accounts for up to 10 percent of all malignancies in men. Like classic KS, endemic KS is also more common among males but follows a more aggressive clinical course with extensive infiltration of subcutaneous tissues.

Immunosuppression therapy associated KS affects organ-transplant recipients and others receiving immunosuppressive therapy, particularly if they belong to ethnic groups at increased risk of KS. The prevalence of immunosuppression therapy-associated KS rose precipitously in the 1980s, corresponding with the rising use of calcineurin inhibitors as first-line immunosuppressants. Clinical course may be slow or rapidly progressive, based on the type and dose of immunosuppressive drug being employed. Cyclosporine has been known to induce earlier onset of the cancer and more aggressive clinical course relative other immunosuppressive agents, such as glucocorticoids. Immunosuppression therapy-associated KS affects the skin in 85 percent of cases, but isolated visceral involvement has been reported in a minority of cases.

AIDS-related KS, first described in 1981, is the most common AIDS-associated cancer in the United States. HHV8 is frequently sexually transmitted among people who are also at risk of sexually contracting the HIV infection, while immunosuppression caused by AIDS provides an opportunity for the development of KS lesions. AIDS-related KS follows a more rapid course than classic KS and exhibits prompt multifocal dissemination. Initially small, purple-red macules rapidly transform into plaques, papules, and nodules, which are often present at multiple locations at the time of presentation. AIDS-related KS has a predilection for the face, trunk, and mucous membranes, with the oral mucosa representing the most frequent initial site of involvement. Untreated, lesions may coalesce to involve large parts of the body, with the potential to cause significant functional impairment. Involvement of extracutaneous sites occurs more rapidly than with classic KS and most frequently involves the lymph nodes, the gastrointestinal tract, and the lungs.

Definitive diagnosis of KS requires biopsy and microscopic examination of lesions. Typically, specimens are taken by punch biopsy of cutaneous lesions, but bronchoscopy and esophagogastroduodenoscopy may be utilized to sample the respiratory tract and gastrointestinal lesions, respectively. Diagnosis is confirmed by the presence of spindle cells on microscopy and the detection of KSHV protein latency-associated nuclear antigen (LANA) in tumor cells.

KS treatment modalities are determined based on the clinical subtype, the extent of disease, and the organ systems involved. In classic KS that is confined to a limited number of cutaneous lesions, the elimination of lesions by surgical excision, liquid nitrogen, or laser, photodynamic, or radiation therapy is typically the first step in management. Intralesional injections of the chemotherapeutic agents vinblastine or interferon-alpha have also proven effective. In addition, isolated KS lesions may be targeted with topical retinoids, such as 9-cis-retinoic acid, though this approach is associated with local erythema and irritation at the site of application.

Rapidly progressive or widespread classic KS that involves visceral organs is targeted with chemotherapeutic agents such as doxorubicin and bleomycin. Immunosuppression therapy-associated KS has shown excellent response to a reduction of immunosuppressive therapy. Interestingly, complete remission of advanced KS lesions may also be induced by the replacement of calcineurin inhibitors by rapamycin. Experience with AIDS-related KS has demonstrated that KS confined to the skin is often controllable by the initiation or adjustment of HAART therapy. For advanced AIDS-related KS, the addition of chemotherapeutic agents, namely liposomal anthracyclines
and paclitaxel, have proven to be to be an effective and well-tolerated treatment regimen.

Kourosh Beroukhim  
*David Geffen School of Medicine at UCLA*  
Navid Ezra  
*Indiana University School of Medicine*

See Also: AIDS-Related Cancers; Chemotherapy; Radiation Therapy.

Further Readings

Kazakhstan

Kazakhstan, located in the middle of central Asia, lays on the ancient Great Silk roads. Its vast territory covers 2,724,900 square kilometers and is the world’s ninth-largest country. Kazakhstan is ethnically and culturally diverse in part due to the forced migration of numbers of settlers from the Russian empire, who began colonizing the territory of present-day Kazakhstan during the 19th century and the first third of the 20th century, and partly due to mass deportations of many ethnic groups to the country during Joseph Stalin’s rule. Kazakhstan has a population of 17 million, with 131 ethnicities, including Kazakh, Russian, Ukrainian, German, Uzbek, Tatar, and Uyghur, and approximately 63 percent of the population is Kazakh. According to the World Bank, Kazakhstan is an upper middle-income country with a gross domestic product (GDP) of $203.5 billion in 2012, and gross national product (GNP) per capita was $11,780.

Epidemiology of Cancer
The prevalence of noncommunicable chronic diseases is increasing globally owing to improvements in sanitation, housing, and education. Further, with reduction in mortality due to infectious diseases, life expectancy has increased and, consequently, so has the prevalence of age-related diseases, such as cancer and cardiovascular and metabolic diseases. In Kazakhstan, the life expectancy at birth for males was 63 and that for females was 72 years of age.

Cancer is the second-leading cause of mortality in Kazakhstan, and approximately 17,000 people die each year from cancer. While the number of patients with malignant neoplasm has increased by 6 percent between 2006 and 2011, cancer mortality during this time has declined from 113.7 per 100,000 in 2006 to 101.6 per 100,000 in 2011. The observed changes are likely to be due to a combination of better reporting systems, early detection, and improved treatments.

In Kazakhstan, the leading causes of death from cancer among adults in 2011 were breast cancer (11.6 percent), lung cancer (11.4 percent), and skin cancer (10.7 percent) followed by gastric cancer (8.8 percent), cervical cancer (4.8 percent), esophageal cancer (4.4 percent), hematological malignancies (4.4 percent), colorectal cancer (4.4 percent), and rectum (4.1 percent). Among men, highly prevalent cancers were tumor of the trachea, bronchus, and lung (20.4 percent), stomach (12.0 percent), and skin (9.6 percent) followed by prostate tumors (6 percent), esophagus (5.3 percent), hematological malignancies (4.9 percent), rectum (4.6 percent), colon (4.1 percent), and bladder (3.7 percent). Among women, breast cancer (21.4 percent) was the most prevalent cancer followed by skin (11.6 percent), cervix (8.8 percent), stomach (6.2 percent), ovary (5.7 percent), uterus (5.5 percent), colon (4.6 percent), hematological malignancies (3.9 percent), and lung cancer (3.9 percent). Among children, approximately 350 to 400 under 15 years are diagnosed with cancer annually. The most prevalent cancers are cancers in the lymphatic and hematopoietic systems, central nervous system, and bone and soft tissues.

The distribution of cancer mortality varies widely by region. Among 14 Kazakhstani provinces, the industrial regions in east Kazakhstan, north Kazakhstan, and Pavlodar regions have the highest mortality from cancer. Elevated levels of environmental pollutants, such as coal dusts, hard metals, silica exposures, and asbestos, have been implicated. Particularly, the Semipalatinsk nuclear testing site located in east Kazakhstan had been
used for numerous underground and atmospheric explosions between 1949 and 1989 during the former Soviet Union era. Multiple studies have been conducted to investigate the health impact on local residents as well as the ecosystems. Some studies have reported elevated risks of esophageal cancer and thyroid abnormalities. In addition, detailed reports on the effects of radiation on the ecosystems have been published.

**Cancer Screening Programs**

The Kazakhstani government has implemented several programs to reduce the burden of cancer, modernizing oncological clinics and introducing new diagnostic and treatment tools for cancer. The main goal was to screen and diagnose these cancers at early stages through screening programs in order to improve five-year survival rates and reduce treatment costs.

**Medical Care**

Over the past decade, the amount of funds spent on medication for cancer patients has increased by 17-fold to 13.7 billion Tenge in 2012 (approximately $76 million). At the same time, only about 70 percent of the medication needs are met so that it is difficult to provide sustained treatments. Although the Kazakh federal government pays for the specialized drugs that can target tumor cells only, only 51 percent receive the drug, and 46 percent are detected at early stages (stages I–II) of cancer.

At the health policy level, the Kazakhstani health care system fully supports cancer patients as patients are guaranteed free medical care, including the provision of medical services in foreign clinics. Currently, guidelines are being developed for cancer centers, diagnostic laboratories, clinical practices, and patient management. The main goals of the cancer care strategies in Kazakhstan are to (1) improve preventative primary health care, (2) develop the infrastructure to provide accurate diagnosis and treatment, and (3) improve the infrastructure for oncology service. To combat these cancers in children, for example, two institutions were established under the auspices of the Ministry of Healthcare, including the Treatment Center at the Kazakh Research Institute of Oncology and Radiology and the Bone Marrow Transplant Center at the Scientific Center of Pediatrics and Pediatric Surgery. These centers are to develop and introduce the state-of-the-art cancer treatments that will meet the international standards for Kazakhstans.

To provide better translational use of various biological markers (e.g., hormones, molecular profiling, etc.) to clinical practice for Kazakh populations, research is being carried out.

Joseph H. Lee  
*Sergievsky Center/Taub Institute, Columbia University*  
Ainur Akilzhanoyna  
*Nazarbayev University*

**See Also:** Russia.

**Further Readings**


---

**Kenya**

Kenya is situated in eastern Africa. It is bordered on the north by Ethiopia, on the east by Somalia, on the east and south by the Atlantic Ocean, and on the west by Tanzania and Uganda. It is the sixth-most populous country in Africa and 31st most in the world, with a population of more than 43 million. The two official national languages are English and Kiswahili, and there are 67 living indigenous languages still spoken by respective ethnic groups in Kenya. The most widely spoken ethnic languages include Kamba, Kigiryama, Kikuyu, Kimiiru, Kipsigis, Lubukusu, Maasai, Nandi, Somali, and
Each ethnic group has its own rich traditions of ethnomedicine. For example, a traditional healer who uses medicinal plants for treating ailments is known as *mundu mugo* in Kikuyu and *mganga* in Kiswahili.

There are many traditional medicinal preparations used in Kenya for treating cancers that incorporate local plants. *Prunus africana* is used as an herbal remedy for benign prostatic hyperplasia. (Wikimedia)

Turkana. There are serious deficiencies of modern pharmaceutical supplies, as opposed to traditional preparations, and in modern medical services for cancer and similar conditions in Kenya. For example, there are only about 1,800 licensed pharmacists in Kenya; of these, about 600 work in the public sector. According to the World Health Organization's (WHO's) "Health System Response and Capacity," as of 2010, there was no general availability of radiotherapy in the public health system in Kenya, although chemotherapy was generally available.

Kenya is a signatory to the Single Convention on Narcotic Drugs, the Convention on Psychotropic Substances, and the UN Convention against the Illicit Traffic in Narcotic Drugs and Psychotropic Substances; consequently, laws exist to control narcotic and psychotropic substances and precursors. Therefore, the annual consumption of controlled substances is thus highly regulated to curtail abuse. Accordingly, the annual consumption of morphine is 0.575 milligram per capita (mg/capita), fentanyl is 0.000074 mg/capita, and pethidine is 1.215 mg/capita. These factors create a serious lack of access for many individuals to appropriate palliative care for cancers and other conditions, which makes the experience of living with and dying from cancer very different in Kenya from that in the developed world.

Due in part to the shortage of medical services and supplies, health problems are endemic in Kenya. The 10 leading causes of morbidity, in rank order, are malaria, respiratory diseases, skin diseases, diarrhea, intestinal worm infestation, accidents, pneumonia, eye infections, rheumatism, and urinary tract infections. The average number of cancer cases annually is 132.8 per 100,000 population.
Cancers account for a substantial amount of disability and suffering among impacted populations. According to the WHO’s “Disease and Injury Country Estimates,” the age-standardized disability adjusted life-year estimates for 2004, the 10 most prevalent cancers in Kenya were led by esophageal cancer at 182 per 100,000 population; stomach cancer at 95 per 100,000; breast cancer at 93 per 100,000; cervical and uterine cancers at 85 per 100,000; lymphomas at 79 per 100,000; prostate cancer at 64 per 100,000; liver cancer at 63 per 100,000; mouth and oropharynx cancers at 59 per 100,000; trachea, bronchial, and lung cancers at 48 per 100,000; and leukemia at 45 per 100,000.

Modern pharmacological supplies, as opposed to traditional preparations, are generally, if available at all, in short supply in Kenya. Both prescription and over-the-counter products are often unavailable. Consequently, health problems are endemic and limit development. For example, an estimated 1.2 million people live with human immunodeficiency virus (HIV) in Kenya, which ranks the country eighth highest in Africa and ninth highest in the world. Debate continues on the relative risks in Africa for respective cancer types for those infected with HIV.

The mortality rate for tuberculosis is 140 per 100,000 population, and that for malaria is 154 per 100,000. Furthermore, according to the WHO’s “Global Health Observatory Data Repository,” in 2008, the age-standardized estimates of deaths from all cancers were 119 per 100,000 population for males and 113 per 100,000 population for females. As a consequence, life expectancy is only 47.2 years, which ranks Kenya the 33rd highest country in Africa and 204th in the world. There is a clear and urgent need for improved cancer awareness, early detection programs, and health services infrastructure in Kenya.

Victor B. Stolberg
Essex County College

See Also: Developing Countries; Ethiopia; Somalia; Tanzania; Uganda.

Further Readings

Kidney (Renal Cell) Cancer

Renal cell carcinoma (RCC) accounts for the vast majority of all kidney tumors and is responsible for many cancer-related deaths each year. While some cases arise from hereditary genetic abnormalities, a large portion arises sporadically, with several well-known modifiable risk factors including tobacco use and obesity. Not unlike other cancers, early detection is paramount to increasing overall survival and a potential cure via tumor removal. Despite most often being diagnosed incidentally through the use of imaging, patients with RCC can present with a wide range of signs and symptoms.

In addition to their function as the body’s filter, the kidneys serve to metabolize certain drugs and
act as endocrine organs, producing hormones such as vitamin D and erythropoietin (EPO), a hormone that signals the bone marrow to produce more red blood cells. The kidneys receive their blood from the renal arteries, which branch directly off of the aorta (the largest artery branching off of the heart that delivers oxygenated blood to the rest of the body). Blood leaves the kidneys via the renal veins, which drain directly into the inferior vena cava (a large vein that delivers blood from the lower body back to the heart). The portion of the kidney responsible for filtration consists of microscopic tubules lined by specialized cells with various functions. It is within these cells that RCC arises.

RCC accounts for 85 to 90 percent of cancers that arise within the adult kidney and 2 to 3 percent of all adult cancers, making it the seventh- and ninth-most common cancers among men and women, respectively. It is responsible for approximately 14,000 deaths each year in the United States. RCC affects men more often than women, at a ratio of approximately two to one, and occurs most commonly in the sixth and seventh decades of life. Geographically, RCC occurs more often in North America and Europe, with markedly lower rates in Asia and South America.

Cigarette smoking is a well-established risk factor for development of RCC, increasing risk by 54 percent in men and 22 percent in women. Furthermore, studies have shown a direct relation between incidence and number of packs per day. There is also evidence to suggest that long-term smoking cessation (greater than 10 years) may reduce the elevated risk of developing RCC. Strong evidence indicates that hypertension (persistently elevated blood pressure) is a risk factor. Obesity is yet another risk factor for RCC, with an increase in incidence directly related to body mass index (BMI). It is estimated that, for every five-unit increase in BMI, there is a 24 and 34 percent increase in incidence in men and women, respectively. Other risk factors with convincing data include chronic hepatitis C infection, acquired polycystic kidney disease (which develops in 35 to 50 percent of patients with kidney failure in need of long-term dialysis), and several inherited genetic disorders. Potential risk factors with less convincing data include occupational exposures (asbestos, gasoline, and trichloroethylene) and diabetes mellitus. An inverse relationship has been found between alcohol use and incidence of RCC.

Greater than 90 percent of all RCCs arise sporadically from random genetic mutations. The remaining cases of RCC are due to inherited conditions, most notably von Hippel-Lindau (VHL) disease. VHL disease is an autosomal dominant disorder that results from a deletion of the VHL tumor suppressor gene on chromosome 3. Lack of both copies of this gene leads to formation of multiple tumors, including hemangioblastomas (tumors of blood vessels in the central nervous system), RCC, and pheochromocytomas. The majority of sporadic clear cell RCCs (the most common subtype of RCC) also result from random mutations or deletions of the VHL gene. Clinical factors associated with an inherited RCC include tumors occurring in both kidneys, age of onset less than 40, and first-degree relatives with RCC.

RCC is associated classically with the triad of flank pain, hematuria (blood in the urine), and palpable abdominal mass. However, these manifestations only occur together in fewer than 10 percent of cases. Indeed, with the increasing use of imaging, the majority of RCCs diagnosed nowadays are discovered incidentally, appearing as a mass on imaging obtained for another purpose. Of the patients not diagnosed incidentally, hematuria and flank pain are among the most common complaints. Other signs and symptoms include anemia (low red blood cell count), weight loss, fever, and night sweats.
Kidney Cancer, Childhood

Rarely, RCC may present as a paraneoplastic syndrome (signs or symptoms resulting from abnormal production of hormones by tumor cells). Hypercalcemia (elevated calcium levels in the blood) can be caused by tumor secretion of parathyroid hormone related protein (PTHrP), which acts like endogenous parathyroid hormone to increase blood calcium concentration. Erythrocytosis (elevated red blood cell count) may result from tumor production of excessive EPO. RCC has a tendency to metastasize to the brain, lungs, bones, and liver. Interestingly, this tumor also has a tendency to invade into the renal vein and inferior vena cava, with potential to restrict blood flow from the organs that are drained by these vessels (i.e., testes and legs).

Diagnostic imaging typically begins with a renal ultrasound and may be confirmed by computed tomography (CT) scan. CT scanning must include the chest and abdomen so as to assess for evidence of metastasis. Finally, a biopsy of the tumor is used to evaluate the specific subtype.

The treatment of RCC varies depending on several factors including tumor size, presence of metastases, and the presence of various comorbidities specific to each patient. For tumors that are confined to the kidney and are less than seven centimeters in size, the preferred treatment is a partial nephrectomy (removal of only the portion of the kidney containing the tumor). These cases have five-year survival rates greater than 90 percent. Tumors confined to the kidney measuring greater than seven centimeters require nephrectomy (removal of the entire kidney). For tumors that have grown large enough to extend beyond the tissues of the kidney but have not yet metastasized, radical nephrectomy (removal of the entire kidney). For tumors that have grown large enough to extend beyond the tissues of the kidney but have not yet metastasized, radical nephrectomy, with removal of invaded tissue, is the standard of care. With lymph node involvement, the five-year survival rate decreases to 32 percent. With distant metastases, patients require systemic chemotherapy, and possible nephrectomy, and survival beyond five years is exceedingly rare. Depending on symptoms, prognosis, and accessibility, metastatic tumors to the lungs also may be surgically removed. Radiation therapy is typically reserved for the control of large, symptomatic metastatic tumors, particularly to the brain and bones.

See Also: Obesity; Pheochromocytoma; Tobacco Smoking; Wilms’ Tumor.

Further Readings

Kidney Cancer, Childhood

Kidney cancer refers to a number of different cancers that begin in the kidney. While in adults most kidney cancers are either renal cell carcinoma or transitional cell carcinoma, in children the overwhelming majority of kidney cancers are Wilms’ tumor. However, other kidney cancers can present in children, including the aforementioned carcinomas and clear-cell sarcoma of the kidney.

The kidneys are the two bean-shaped organs in the body that assist in metabolism, principally by filtering out waste products. Kidneys produce urine, for instance, by excreting urea and ammonium waste products, which empty into the bladder via a ureter. Proper kidney function is required to regulate electrolytes, blood pressure, and the acid–base balance of the body, all of which are critical to human health. Kidneys also produce some of the body’s hormones. All of these functions are jeopardized by kidney cancers.

Wilms’ tumor rarely manifests in adults but is the most common kidney cancer in children, occurring primarily in 3-year-olds. It is named for German surgeon Max Wilms, who first described it in the early 20th century. Sidney Farber of the Dana–Farber Cancer Institute was the first to develop a treatment for Wilms’ tumor that sent the cancer into remission, combining surgery, radiation therapy, and an antibiotic, and since then, five-year survival rates have climbed to 90 percent.
Wilms' tumor is a nephroblastoma that is almost always unilateral, consisting of the blastema, mesenchyme, and epithelium. Cartilage, fat, bone, and fiber may be found in the spindled cell stroma that surrounds a bundle of abortive tubules. The tumors are classified as either favorable or anaplastic, with anaplastic tumors being more poorly developed and differentiated than described here.

The first signs of Wilms' tumor are usually a painless abdominal lump discovered by the child's pediatrician during a physical examination. Other symptoms may include abdominal swelling or pain, fever, nausea, or high blood pressure, and in a minority of cases, there is blood in the urine. The tumor is diagnosed with imaging informed by the assumption that most childhood kidney cancers will be Wilms' tumors. Because a needle biopsy poses the danger of releasing malignant cells into other parts of the body, it is usually not performed until after surgical removal, which sometimes leads to other kidney cancers being misdiagnosed initially as Wilms' tumors.

Certain conditions predispose the patient toward Wilms' tumors, such as Beckwith–Wiedemann syndrome (BWS), an overgrowth disorder present from birth. While most BWS children do not develop cancer, they are hundreds of times more likely to develop Wilms' tumors as well as similar tumors in the pancreas and liver. This risk seems to apply only to childhood cancers, especially in the toddler years. Perlman syndrome, another overgrowth disorder, which begins with fetal overgrowth, also predisposes toward Wilms' tumor as well as dysmorphic facial features and macrocephaly. Denys-Drash syndrome is a rare disease almost always caused by an abnormality in the WT1 gene, leading to Wilms' tumors, gonadal dysgenesis, and nephropathy. WAGR syndrome is another genetic syndrome that predisposes children to develop Wilms' tumors, aniridia (a lack of colored iris in the eye), genitourinary anomalies, and retardation.

Rhabdoid tumor was originally considered a variant of Wilms' tumor, is highly aggressive, and has a poor prognosis. It nearly always occurs in children under two years old. A substantial minority of patients with rhabdoid tumors also have malignant brain tumors.

Other types of childhood kidney cancer include renal cell carcinoma, which originates in the lining of small tubes in the kidney called proximal convoluted tubules and is the most common adult kidney cancer as well as one of the deadliest genitourinary cancers; transitional cell carcinoma, which can occur in the kidney, bladder, or accessory organs, and is usually caused by environmental carcinogens; angiomylipoma, a benign kidney tumor that can impair kidney function or cause blood vessels to hemorrhage; renal oncocytoma, an epithelial kidney tumor made up of oncocyes, cells abundant in mitochondria, developing in the intercalated cells of the kidney’s collecting ducts, and usually asymptomatic unless they become both malignant and metastasized; squamous cell carcinoma of the kidney, which is especially uncommon in children; clear-cell sarcoma of the kidney, which develops from mesenchymal tissue and often includes a cyst; Bellini duct carcinoma, which originates in the kidney’s duct of Bellini, another name for the collecting duct and which appears physically similar to bubble wrap; and mesoblastic nephroma, which is largely similar to Wilms' tumor but develops in the fetus.

See Also: Kidney (Renal Cell) Cancer; Unusual Cancers of Childhood; Wilms’ Tumor.

Further Readings
Kidney Cancer Association

The Kidney Cancer Association (KCA) was founded in 1990 by medical doctors and a small group of patients in Chicago, Illinois. It is a non-profit and is tax exempt under the U.S. Internal Revenue Service code. Members currently include patients, family members, researchers, physicians, and other allied health professionals. It is the first international charity dedicated to eliminating suffering and death from renal cancers. Members are found in more than 100 countries. The KCA funds, promotes, and collaborates with multiple institutions, including the American Society for Clinical Oncology, the National Cancer Institute, and the American Urological Association, on research projects. Advocacy for patients and families, including education and continuing medical education, are also key to the KCA at the state, federal, national, and international levels. The KCA’s vision is a world without kidney cancer. Their mission is the elimination of suffering and death from renal cancers. KCA’s three primary goals are advocacy, research, and education.

Kidney cancer occurs two times more often in males and represents about 3 percent of the total diagnoses of cancer. In 2005, 12,660 people died from kidney cancer. Currently, there are more than 100,000 kidney cancer survivors in the United States. The most common kidney cancer is renal cell carcinoma (RCC). If caught early and treated (typically with surgery), chances of its return are low. However, early stage RCC has few symptoms. Usually, it is found incidentally. Thirty percent of RCC cases are advanced when first diagnosed. Approximately 15 to 25 percent have metastatic disease by the time it is diagnosed. Painless, bloody urine is the most common symptom of kidney cancer. Some 40 to 50 percent will have this symptom. Often, blood in the urine will be present one day and then not the next. Other symptoms that are common to kidney cancer include an abdominal mass, back pain or pressure, flank pain or pressure, weight loss, fever, anemia, and high blood pressure.

The subtypes of RCC include clear cell RCC (the most common and associated with a gene mutation), chromophobe RCC (rare and usually successfully treated as it metastasizes very late), renal oncocyotoma (a benign tumor that can grow quite large and invade local tissue), collecting duct carcinoma (which is aggressive and associated with sickle cell trait), sarcomatoid RCC (which is typically metastasized throughout the body and therefore has a poor prognosis), and unclassified RCC.

Most kidney cancers are treated through surgical procedures. A nephrectomy entails removing the affected kidney. A radical nephrectomy entails removing the affected kidney, some healthy tissue around the border, and adjacent lymph nodes. In this case, the adrenal gland also may be removed. Nephron-sparing surgery is a procedure that removes the tumor and a small border of healthy tissue but does not remove the entire kidney. When surgery is not an option, treatments can include freezing the cancer cells (cryoablation), heating the cancer cells (radiofrequency ablation), biological therapy (immunotherapy), targeted therapy (drugs), and radiation therapy.

KCA promotes research in private and public institutions. Financial grants are competitive and provided from funds named in honor for their founder, Eugene P. Schonfeld, Ph.D. Funds are raised by KCA members, donations, and the Penn State Football Team’s Lift for Life fund-raisers. The Young Investigator Award provides funds to promising researchers who are transitioning from fellowship programs to faculty appointments. Awards are based on fund availability and individual merit. Other awards include the Eugene P. Schonfeld Medical Research Awards, ASCO Conquer Cancer Foundation Award, Andrew C. Novick and P.H.M. de Mulder/AUA Urology Care Foundation Research Scholar Award, ASCO Cancer Foundation Young Investigator Award, AUA Foundation Research Scholar Award, David A. Stulberg Career Investigator Award, and Senior Career Investigator Award.

From October 2012 to October 2013, KCA provided greater than 60 education and support opportunities for caregivers, survivors, and patients. Two national meetings were held in Houston, Texas, and San Francisco, California. KCA also has hosted an online Facebook group for survivors and caregivers. There are more than 85,000 people around the world who have joined the group. KCA launched a peer-to-peer Web site two years ago for caregivers, survivors, and patients, called Kidney-Cancer.me. They have developed three educational
applications for smartphones, iPads, iPhones, and android platforms. KCA also sponsored the European Kidney Cancer Symposium. Hundreds of allied health professionals attended in Budapest, Hungary. Furthermore, more than 200 attended the International Kidney Cancer Symposium in Chicago. KCA also mails information packets to families and patients. More than 100 countries are represented in KCA membership. Approximately 20,000 monthly newsletters are e-mailed, and hundreds watch Kidney Cancer News, a monthly video magazine featured on KCA’s homepage.

KCA has increased its outreach to global patients by translating their publications into 13 languages. Their goal is to add at least one new language each year. KCA has also increased its outreach to global medical professionals by sponsoring two international symposiums per year. One meeting is held in Chicago and the other in a different European country every year. KCA’s Nurse Advisory Board has completed a review of the more than 100-page publication We Have Kidney Cancer, and distribution is now global. KCA has also partnered with EmergingMed, which has resulted in patient referrals to clinical trials. Patient advocacy remains an important goal and is accomplished by identifying new opportunities for collaboration with other voluntary health organizations. Collaborative relationships continue with the following organizations: Friends of Cancer Research, Cancer Leadership Council, the National Coalition for Cancer Research, Foundation for NIH, Patient Advocate Foundation, and the National Cancer Comprehensive Network.

Jessica Anne Hammer
Independent Scholar

See Also: American Brain Tumor Association; Association of Pediatric Hematology/Oncology Nurses; European Association for Cancer Research; International Association for the Study of Lung Cancer.

Further Readings

Research at Kimmel Cancer Center
The mission and values of KCC focus on providing a respectful and multidisciplinary approach to research, teaching, prevention, and the treatment of cancer. The core values, as outlined on the KCC Web site, are that KCC members are focused on working toward perfection and building excellent teams. Outstanding teams at KCC are to be built through treating other team members with respect, dignity, integrity, always giving hope, and supporting and recognizing others’ achievements.

Research at KCC is supported through KCC’s shared resources. Some of the shared resources include bioimaging; biostatistics; cancer genomics; informatics; proteomics; laboratory animal research; translational research; and X-ray crystallography and molecular characterization. KCC also

Kimmel Cancer Center

The Kimmel Cancer Center (KCC) at Thomas Jefferson University is located in Philadelphia, Pennsylvania. It was founded in 1991. At that time, it included 30 cancer researchers and presently has grown to approximately 150 physicians and scientists. Through KCC’s affiliation with the Thomas Jefferson University Hospital system, the center collaborates with 22 hospitals and partners as well as 400 members to provide research in oncology, treatment of cancer, education, and information.

In 1996, the National Cancer Institute (NCI) designated the KCC as an NCI-designated cancer center, which is the highest ranking bestowed on organizations dedicated to research, treatment, and prevention of cancer. KCC also has received recognition as a top treatment center. The Jefferson University Hospital system, which is affiliated with KCC, was rated by U.S. News and World Report as the 17th-best hospital for 2013 and 2014. KCC, in particular, was listed on Becker’s Hospital Review as one of 70 health institutes with a great oncology program.

has four basic science research programs: cancer cell biology and signaling, molecular biology and genetics, the biology of prostate cancer, and the biology of breast cancer.

The Biology of Prostate Cancer (BPC) is one of the newer programs at KCC. The BPC is a collaborative interdisciplinary research program that involves 10 departments and three institutions. Research in the program has generated more than 343 publications in five years. The program strives to advance new strategies for detection, diagnosis, and treatment of early to advanced forms of prostate cancer through research on hormone action in malignant tumors as well as predictive markers for rational therapy delivery. Of primary interest is translational research or research that can be moved to clinical trials so that patients can receive cutting-edge treatment. Through the KCC Web site, patients can access information on current clinical trials to which they can apply.

**Patient Care**

KCC strives to provide high-quality oncology treatment to patients including minority populations. To that end, KCC includes 10 multidisciplinary centers including a Brain Tumor Center, Breast Cancer Center, Liver Cancer Center, Lung Cancer Center, and Senior Adult Oncology Center. In addition, the Bodine Center for Cancer Treatment provides advanced radiation oncology services, which include the ability to use 3-D images to guide in radiotherapy treatment of cancer. Other service centers include a Breast Imaging Center, Prostate Diagnostic Center, and Integrative Medicine Center at Jefferson, Myrna Brind.

In terms of support for cancer patients and their families, oncology social workers assist families in the maintenance of their disease. Oncology social workers can support families through providing couple and family counseling associated with the cancer diagnosis and treatment; referrals to specialists to help with psychological stress and anxiety; assistance with telling children about the cancer diagnosis; and information to help with financial concerns and opportunities. Financial counselors at KCC can also provide assistance to families.

Nutrition, dietetics, and survivorship are also part of the support given families through KCC. KCC’s outpatient oncology dietitian can work with families to develop nutrition plans that can help alleviate symptoms from cancer treatments. The survivorship program includes a Celebration of Life yearly event and a new Cancer Survivorship Program. The Celebration of Life event is comprised of a health fair, stories of survivors, guest speakers, and an art exhibit. The Cancer Survivorship program includes biannual conferences with guest speakers and breakout sessions where patients and families can work through what happens after they are diagnosed with cancer. The conferences are free.

**Education and Training**

KCC, as part of the Jefferson University and Jefferson Hospital system, includes pre- and postdoctoral training to health care practitioners. Specific training programs include a Hematology and Medical Oncology Fellowship Program and Radiation Oncology Residency Program. Continuing education is offered as well as pharmacy, biomedical sciences, nursing, population health, and health professions training through programs at Thomas Jefferson University.

**Conclusion**

The Kimmel Cancer Center is an NCI-designated cancer center that provides multidisciplinary treatment of, education about, and research on cancer. The mission of KCC is to provide cutting-edge treatment with a focus on the comfort and support of patients and their families. To achieve this, KCC strives to promote the building and maintenance of excellent teams focused on members who support and treat each other with respect.

Anne Hubbell

*New Mexico State University*

**See Also:** Association of Oncology Social Work; Caregivers; Diet and Nutrition; Experimental Cancer Drugs; Insurance; National Cancer Institute; Prostate Cancer; Survivors of Cancer; Survivors of Cancer, Families of; Technology, New Therapies.

**Further Readings**

Kyrgyzstan

Kyrgyzstan, officially known as the Kyrgyz Republic and formerly known as Kirghizia, is a country located in central Asia. It is a parliamentary republic in spite of many of its ongoing internal troubles. The official language is Kyrgyz, and it is closely related to the other Turkic languages; however, the country is under a strong cultural influence from Russia and is rather Russified. The majority of the population (64 percent) is nondenominational Muslims.

The country's population is estimated at 5.6 million as per the 2013 estimates. Of the total population, 34.4 percent are under the age of 15, and 6.2 percent are over the age of 65 years. The country is rural, and approximately one-third of the population lives in urban areas. The country is among the poorest of the post-Soviet countries. In 2004, the poverty rate was officially estimated at 40.8 percent, although Western estimates place it at around 84 percent. Kyrgyzstan is considered to have considerable coal, gold, mercury, and uranium deposits and some oil and gas reserves. However, the country’s economy is primarily agricultural, with cotton, tobacco, wool, and meat being the primary agricultural products, although only cotton and tobacco are exported in any significant quantities. In 2005, the agricultural sector contributed 37.1 percent of the gross domestic product (GDP), and more than 50 percent of the labor force is in the agriculture sector.

The country’s health care system has suffered increasing shortages of health and medicine, especially in the post-Soviet era. The country has to import nearly all its pharmaceuticals. Health care in Kyrgyzstan has been state run and in deteriorating status, but the entry of private health services has helped to supplement it. A national primary-care health system, the Manas Program, was adopted in 1996 to restructure the Soviet system that Kyrgyzstan inherited. The number of people participating in this program has expanded gradually, and province-level family medicine training centers now retrain medical personnel. A mandatory medical insurance fund was established in 1997.

Due to the poverty status of the country, cancer diseases in the country are poorly addressed. In 2005, it was reported that the use of outdated radiotherapy equipment to treat Kyrgyz cancer patients significantly reduces their chances of survival. In addition to use of outdated equipment, the country has a single specialist oncology unit. The National Oncology Center’s equipment was left from the Soviet period, and it has already exceeded its expiration date. However, the high cost involved, lack of parts, and a dearth of qualified technicians all mean it cannot be replaced or at least repaired.

Recently, the number of patients with malignant tumors has increased drastically in the country. The majority of cancer cases require radiotherapy, and the 60 percent of cancer-related mortality is due to inadequate medical care. In addition, Kyrgyzstan has very few specialists capable of servicing the machinery.

The prevalence of cancer in Kyrgyzstan is at its all-time high, with the major type being stomach cancer. According to statistics, stomach cancer has a rate of 21.32. Other high-ranking cancer types in the country are breast cancer, with a rate of 15.55, lung cancer with a rate of 15.18, liver cancer with a rate of 8.56, colon–rectum cancer at 8.18, cervical cancer at 6.47, esophagus cancer at 5.31, pancreas cancer at 4.75, oral cancer at 3.9, and ovary cancer closes the top 10 at 3.39. Other types of cancer that are high rating include leukemia, lymphomas, uterine cancer, bladder cancer, skin cancers, and other neoplasms. Stomach cancer rating in the country is at position 11 in the global standings, which makes it one of the major types of cancer in Kyrgyzstan.
As per data provided by the World Health Organization (WHO) in 2011, breast cancer deaths in Kyrgyzstan reached 356, or 0.84 percent of total deaths. For lung cancer, deaths in Kyrgyzstan reached 579, or 1.36 percent of total deaths in 2011.

In Kyrgyzstan, the breast cancer incidence rate is nine per 100,000 women per year in the entire country. Death due to breast cancer is at the rate of 8.5 per 10,000 women. Cancer services are not covered by the health insurance fund, and treatment often is not affordable or available. The country does not have breast cancer as a priority disease and does not have mammography screening. In 2007, the Breast Cancer Early Detection and Advocacy Program was begun. The program seeks to advocate for training coupled with public events that serve to raise awareness for women's health in Kyrgyzstan.

According to health specialists in the country, both local and those working for nongovernmental organizations, the number of cancer cases is on the rise. On the other hand, access to proper treatment is not widely available, particularly in rural areas. As per the health ministry of Kyrgyzstan, each year, there are more than 4,000 newly registered cases of cancer, with more than 3,000 people dying annually from the disease. However, given the shortcomings in the registration process, the number of people suffering from cancer in the country is definitely much higher. The sharp rise and high prevalence of cancer in Kyrgyzstan is due to poverty, lack of awareness about how to reduce risks, and unhealthy lifestyles, including heavy smoking and drinking.

In addition to the above challenges, there is a lack of places where proper testing for cancer can be carried out; the only places where people can get treated or be diagnosed for cancer are in Bishkek, Tokomak, or Osh. Due to late or poor diagnosis, the number of deaths from cancer is high and keeps on increasing annually. Part of the problem is also the high cost of treatment, which also drives up mortality cancer rates.

In an effort to increase diagnosis, there were mobile cancer diagnosis units that used to operate in rural parts of Kyrgyzstan. These units ran tests every month or so in remote areas, therefore increasing early detection. However, due to limited resources, the program can be run only once in every six months. The result is that many Kyrgyz citizens go undiagnosed.

There are several organizations, initiatives, and societies that deal with cancer matters with the majority being specific to cancer types. Some of these are for prostate cancer: Kyrgyzstan American Urological Association, Kyrgyzstan National Prostate Cancer Coalition, Kyrgyzstan Prostate Cancer Charity, and Kyrgyzstan Prostate Cancer Foundation. Lung cancer, on the other hand, has Kyrgyzstan British Lung Foundation, Kyrgyzstan International Association for the Study of Lung Cancer, and Kyrgyzstan Roy Castle Lung Cancer Foundation, among others.

Michael Fox
Independent Scholar

See Also: Moldova; Nicaragua; Paraguay.

Further Readings
Laos

Laos People’s Democratic Republic is located centrally within southeast Asia. It lies between China, Vietnam, Cambodia, and Thailand. Laos has gained some popularity in recent years as a tourist destination, and its economy is growing; however, it is still a developing country, and life expectancy in the area is still relatively low at around 60 for men and 65 for women. Traditional herbal medicinal practices are the most common in Laos as Western medicine is not readily available, especially to those people living in rural areas.

One of the largest reasons for the higher mortality rate and lower life expectancy among the people of Laos is because of lacking information about preventative care and self-screening. This is particularly indicative of the attitudes to self-screening in women in developing countries in southeast Asia.

Because of the statistics surrounding the disease, cervical cancer has become a topic of interest in recent medical studies regarding southeast Asian women and their knowledge and awareness about the disease. In 2010, a study about cervical cancer in rural Laos concluded that the majority of women have a limited understanding of the disease and prevention practices in general.

A proactive program to prevent cervical cancer is on the rise in Laos. Thousands of women die each year from cervical cancer, which has called to action the necessity of vaccination among young girls. In the fall of 2013, thousands of Laos’s schoolgirls were given the human papillomavirus (HPV) vaccine.

Because the HPV vaccine is so expensive, it has been difficult for lower-income countries to provide; however, the GAVI alliance is working to make this a possibility for women in Laos and other southeast Asian countries.

In addition to concerns regarding women’s health and cervical cancer, liver cancer is also rampant in Laos. Though incidents of liver cancer are low in Europe and North and South America, the staggering majority of liver cancer incidents are localized to low-income countries in southeast Asia. Currently, Mongolia leads the world in liver cancer incidents, but Laos follows closely behind.

Research by the National Cancer Institute attributes many of the liver cancer incidents to the prevalence of Hepatitis B throughout the region as well as the consumption of raw fish containing parasites. The prognosis is generally poor for those afflicted with liver cancer, partly because symptoms of the disease are not apparent until later stages, when the cancer is more difficult to treat. Liver cancer in these areas is a large issue that is attracting international attention. While the greatest incidence of liver cancer and seafood infestation occurs in regions of northeast Thailand, it is also a major area of concern in Laos as well.
Fish in these regions are infected by the parasitic worm known as *Opisthorchis viverrini*. This worm latches onto a human host after the consumption of infected fish. The worm infestation leads to a recurring infection of tissues that eventually leads to cancer. Studies on the subject have concluded that almost a quarter of those who come into contact with the parasite develop cancer.

Cancer, though, in general in Laos, has a higher mortality rate than in other countries due to lack of screening. While there are options for modern medical treatment in Laos, many people still turn to traditional medical practices.

In 1976, the Traditional Medical Research Center opened in Laos and is dedicated to the study and practice of traditional herbal medicine to treat diseases and ailments. Traditional medicine is especially popular in rural areas of Laos and is deeply rooted in cultural beliefs and traditions.

More than 75 percent of households in Laos turn to traditional medical practices largely because they have found them effective for treating many types of illnesses. In addition to perceived efficiency of these treatments, many people find that it is difficult and more cumbersome to gain access to modern medical care. For instance, the cost of treatment and pharmaceuticals is definitely significant, but people of rural villages must also consider the cost of travel to these medical centers where they can obtain care.

Even for those who are willing to pay for the cost of modern medical care, they generally have low expectations, given that the prognosis is typically grim especially for cancer patients who are typically not diagnosed until later stages in cancer development.

While cancer treatment in Laos is available, it is still limited, and people must often travel to outside countries in order to receive treatment. Recent studies show that cancer treatment is on the rise since the 1990s and that, each year, more people seek treatment. Overall, cancer in Laos and other developing countries is an area of major concern. The introduction of the HPV vaccine and the opening of discourses regarding preventative care are the first steps toward an intervention plan to tackle this issue.

**See Also:** Breast Cancer; Cervical Cancer; Liver Cancer, Adult (Primary); Thailand.

**Further Readings**


---

**Laryngeal Cancer**

Laryngeal cancer involves malignant cells occurring in the larynx. The larynx opens and closes to let a person breathe, talk, and swallow. The larynx is composed of three parts: the supraglottis (an area above the vocal chords); the glottis (located in the middle of the larynx and containing the vocal chords); and the subglottis (which connects the vocal chords and the windpipe).

Symptoms of laryngeal cancer may include hoarseness, persistent sore throat, difficult or painful swallowing, and possibly pain in the ear or a lump in the neck. Approximately 95 percent of laryngeal cancer involves squamous cell carcinomas that occur in the lining of the throat rather
than in the muscle or cartilage cells. Approximately 5 percent of laryngeal cancer involves the less-aggressive, slower-moving, verrucous carcinoma.

Some of the tests and procedures that can be used in determining whether laryngeal cancer is present include biopsy, a head and neck exam possibly involving fiber-optic laryngoscopes (narrow, flexible tubes inserted in the mouth or nose), examination of the larynx under general anesthesia, chest X-rays, barium swallow, bone scan, or a magnetic resonance imaging (MRI), positron emission tomography (PET), or computed tomography (CT) scan. Such tests may show precancerous conditions called dysplasia, but although dysplasia may lead to cancer, in the vast majority of cases, it does not.

Although it is the most common source of cancers in the larynx, accounting for approximately 60 percent of all cases, cancer in the glottis is slower to spread than cancer in the subglottis and the supraglottis. The supraglottis is the originating site of approximately 35 percent of laryngeal cancer, and the remaining 5 percent originates in the subglottis.

Laryngeal cancer accounts for approximately 30 percent of all cancers of the throat and between 2 and 5 percent of all cancers overall. Approximately 13,000 people in the United States were diagnosed with cancer of the larynx in 2013, and approximately 3,630 deaths from laryngeal cancer were reported.

Men are affected by laryngeal cancer far more than women, and people over the age of 65 are much more likely to develop it than younger people. African Americans have a much higher rate of laryngeal cancer than Caucasians.

The primary behavioral risk factors for laryngeal cancer are smoking and alcohol. However, not all people who drink or smoke heavily will develop laryngeal cancer.

The single most effective way to prevent laryngeal cancer is to never smoke or to stop smoking. For people who already have laryngeal cancer, quitting may reduce the chance of recurrence of the cancer and may also reduce the chance of another different type of cancer developing (such as lung, esophagus, or oral cancer). Stopping smoking can also improve the effectiveness of cancer treatments. Some people find it effective to join a group or to seek professional help in quitting smoking. Others use nicotine replacement therapy.

Secondary risk factors that may contribute to the development of laryngeal cancer include poor nutrition, human papillomavirus, chronic gastric reflux, a weakened immune system, and certain forms of chemical exposure.

Treatment for laryngeal cancer depends on the specific location of the cancerous cells and the stage of the cancer. Like many other forms of cancer, the earlier that laryngeal cancer is diagnosed, the more effective treatment becomes. Likewise, the survival rates for laryngeal cancer vary according to the stage at which the cancer was first detected. It is always wise to get a second opinion before commencing treatment.

If laryngeal cancers are detected in stage 0 (the earliest stage), they can almost always be cured by either surgically removing them or vaporizing them. In stages 1 and 2, most laryngeal cancers can be treated successfully with radiation therapy, though surgery is sometimes another option. In stages 3 and 4, treatment can include the total or partial removal of the larynx through surgery, chemotherapy, and radiation therapy, or any combination of those treatments. Surgery often includes a neck dissection and the removal of lymph nodes. With any surgery, there are risks and possible side effects, so it is always important to discuss these with the treating physician.

Sometimes, a surgeon may need to create a stoma—a new airway through an opening in the front of the neck. This opening then becomes the place where air enters and leaves the trachea and lungs. The new airway is kept open by a metal or plastic tube, known as a trach tube. For some patients, the stoma is permanent. However, for others, the stoma is only necessary until the patient recovers from surgery. In those cases, the tube is removed several days after surgery, and the stoma closes up.

If a person has a permanent stoma, it is important to learn how to care for it, including removing and cleaning the trach tube, cleaning the patient’s airway, and caring for the nearby skin. Some people with permanent stomas experience self-image issues and are encouraged to seek counseling or professional help if necessary.

Another problem that might arise after surgery is trouble swallowing. Because diet is an essential ingredient of treating laryngeal cancer, it may be necessary to insert a temporary feeding tube.

Learning to speak again is an important part of the rehabilitation process for some people with
Laryngeal cancer. A speech–language pathologist becomes an essential member of the treatment team in this situation. Whether people need speech exercises or more invasive treatment (such as an electric larynx or a tracheoesophageal puncture), the speech therapist will work with the patient to maximize recovery. Another approach might involve the speech therapist teaching the patient esophageal speech.

After surgery, patients need regular checkups. These may occur every month for the first year, and they are important because cancer is most likely to recur in the first two years after medical treatment. Some patients find complementary therapies (such as stress-reduction classes or acupuncture to help relieve pain) useful in dealing with cancer. They are often used alongside regular treatment, but they will not cure cancer. Sometimes, ruthless people promote more radical, “alternative” treatments that have not been tested, have been proven not to be helpful, and some of which are even harmful. Therefore, it is always important to be careful and to discuss all treatment options with qualified specialists.

Clinical trials involving chemoprevention and radiosensitizers for laryngeal cancer are now being explored. People with laryngeal cancer may wish to consult their physicians and specialists about the value of such trials.

Mark D. Sherry
University of Toledo

See Also: Chemotherapy; Laryngeal Cancer, Childhood; Radiation Therapy; Surgery; Tobacco-Related Exposures.

Further Readings

Laryngeal Cancer, Childhood

The renewed global health focus of noncommunicable disease such as cancer has great impact on the diagnosis, treatment, and outcomes of the world’s bottom billion poor. In childhood, the pediatric population poses extreme challenges to the primary prevention of disease, halting it before it even starts. Pediatric laryngeal cancer is rare, and therefore, studies about the etiology, pathology, diagnostic workout, and treatment protocols are lacking and not standardized. Among many other risk factors, secondhand smoking, indoor burning and cook stoves, poor air hygiene, and various environmental exposures may increase the number of new cases of laryngeal cancer in childhood. Opportunities to reduce global morbidity and mortality of laryngeal cancer in the pediatric population are discussed in this very brief entry.

Definitions and Basic Anatomy
Laryngeal cancer is the development of uncontrolled growth of cells in the larynx or voice box. As with all morphologic disease, anatomical reference aids understanding. The larynx is a tube-shaped organ in the neck that is important for breathing, talking, and swallowing. It is located at the top of the trachea. The front walls come out from the neck to form the Adam’s apple. The larynx contains the vocal folds responsible for speech and song that vibrate to make sound. During breathing, the larynx opens like a valve to allow air to pass into the lungs. During swallowing, the vocal folds come together with the epiglottis protecting the airway and preventing food from entering the lungs.

The larynx is divided into the supraglottis (composed of the epiglottis, aryepiglottic folds, false vocal cords [vestibular folds], and ventricles or saccules); the glottis or true vocal cords, plus their undersurfaces, and the anterior and posterior commissures; and finally the subglottis, which extends from approximately 10 millimeters below the true vocal cords to the inferior margin of the cricoid cartilage.

Cancers in the throat refer to tumours that develop in the pharynx or larynx. Cancers of the throat include the nasopharynx (the upper part of the throat behind the nose), the oropharynx (the
middle part of the pharynx), and the hypopharynx (the bottom part of the pharynx). Cancer of the larynx is also called pharyngeal cancer. When cancer or tumors develop in these areas, voice changes can be heard, and the airway can slowly become compromised. Laryngeal and hypopharyngeal cancers are two of the main types of cancer in the head and neck.

**Epidemiology**
In general, cancers in the head and neck in childhood are rare, comprising an estimated less than 0.1 percent of the population, making global prevalence and incidence difficult to describe and calculate. The Web site Cancer.net does offer some surveillance information, and the editorial board has approved data purporting that, in the United States, laryngeal cancer is one of the most common head and neck cancers across pediatric and adult populations. Globally, it is predicted that laryngeal cancer is rare, with less than 0.1 percent of head and neck cancers in childhood with distribution between the sexes at 40 percent female and 60 percent male, report several researchers.

**Risk Factors**
Radiotherapy, laryngeal papilloma, gastroesophageal reflux, human immunodeficiency virus (HIV), immunosuppression, exposure to drug use during pregnancy, active and passive smoking, alcohol use, poor oral hygiene, and a family history of cancer are leading risk factors for children to get cancer in the larynx, describe A. Ferlito, A. Rinaldo, and G. Marioni. The authors of this cited research observed that risk factors as previous radiotherapy, intrauterine exposure to ionizing radiation, smoking, and tobacco were lacking in the clinical histories of some affected patients. Therefore, pediatric laryngeal cancer is more likely a genetic disease with specific chromosomal damage.

**Pathology**
The most common type found in childhood is rhabdomyosarcoma, closely followed by squamous cell carcinoma, and very rare are adenoid cystic carcinomas. Clear-cell carcinoma, adenoid carcinoma, synovial sarcoma, malignant fibrous histiocytoma, non-Hodgkin's lymphoma, chondrosarcoma, Ewing's sarcoma, fibrosarcoma, malignant schwannoma, mixed sarcoma, mucoepidermoid carcinoma, and primitive neuroectodermal tumor are also cancers found in the neck with varying prevalence and incidence across age-groups in the pediatric spectrum, according to R. H. Ossoff, G. F. Tucker, and C. M. Norris.

**Clinical Features and Diagnostics**
Some leading presenting clinical signs and symptoms that pose an index of suspicion for laryngeal cancer in children are shortness of breath, or dyspnoea, hoarseness of the voice, and dysphagia. Delayed diagnoses because hoarseness is presumed to be secondary to puberty voice change, voice abuse, and recurrent respiratory infection can delay appropriate diagnosis and potential initial treatment.

Advanced diagnostic techniques include the combination of computed tomography (CT) and magnetic resonance imaging (MRI) and have more accuracy to visualize in a three-dimensional format the extent of the disease and exact location. Ultrasound is less sensitive but very easy to use with little risk to the patient. Finally, visualization of the larynx via bronchoscopy and direct biopsy offers direct diagnosis for confirming uncontrolled cell growth in tissues, reports D. A. Schwartz and colleagues.

**Treatment: Trends and Opportunities**
Rhabdomyosarcoma is treated with radiotherapy and chemotherapy (vincristine sulfate, actinomycin, cyclophosphamide, and Adriamycin); researchers have found that, if positive metastasis to the neck lymph nodes are observed, then neck dissection may be required with or without radiotherapy, depending on the extent of the disease. However, for squamous cell carcinoma, organ preservation therapy does include chemotherapy with radiotherapy, partial laryngectomy, and rarely total laryngectomy, with laser surgery in combination with radiotherapy showing some results as well. Conversely, with non-Hodgkin's lymphoma in the head and neck, radiotherapy of synovial sarcoma may be chemosensitive to ifosfamide (a synthetic analog of cyclophosphamide, which inhibits DNA synthesis and protein synthesis) in combination with radiotherapy, and neck dissection is not indicated, observes J. Kaur and colleagues.

**Risk and Prevention**
Causal links between laryngeal cancer in children and exposure to a specific carcinogen or genetic determinants are not yet described in the literature definitively. Avoidance of exposure to asbestos,
dusts, paint fumes, and a myriad of household chemicals may reduce the risk of laryngeal cancer in children. A diet high in vitamins A and E may reduce risk of laryngeal and hypopharyngeal cancer as some data support its anticarcinogenic properties. Prevention of cancer and early diagnosis remain the best tools in the fight against uncontrolled cell growth.

John Michael Quinn
University of Illinois at Chicago

Thomas Moors
London Medical School

Rohit Kumar
University Hospitals of South Manchester

See Also: Esophageal Cancer; Head and Neck Cancer; Laryngeal Cancer.

Further Readings


Latitude

As the controlled environments and modern medicines of industrialized countries have curtailed early deaths from classic infectious disease, cancer and other degenerative diseases have increasingly become significant sources of mortality. Cancer risk advances steadily in the post-reproductive years after which there is less pressure to strictly limit, and correct, mitotic copy errors. Latitude and cancer show a number of correlates, ranging from obvious to arresting. Some of these correlations are culturally explained, such as the relationship between access to essential medicines and healthcare services, which differ from country to country along a rough latitudinal gradient; others are biologically explained, such as ecologically derived racial differences in cancer’s age of onset.

The Special Case of Cancer
Cancer incapacitates and kills in great numbers: As reported by the World Cancer Research Fund, cancer afflicted 14.1 million in 2012, with the World Health Organization estimating 8.2 million deaths in that same year. Despite medical advances, humans continue to be pathetically at the mercy of cancer, such that we cannot foresee what it would be like if we powerfully checked its progress. Though, as with other afflictions, cancer is fought by physicians and pharmaceuticals, it is more correctly apprehended as a predictable by-product of age than as a chance product of illness. Precancerous and even cancerous uprisings are commonplace, though they are
arrested and neutralized by genetic elements that copyedit and correct errors and immune cells, such as macrophages, that phagocytose, or ingest, cancer cells. Unlike acquired immune deficiency syndrome (AIDS) and Ebola, which are of recent origin, or smallpox and rheumatic fever, which periodically stalk populations, cancer has been with the human race in perpetuity. Cancer has its own hieroglyph, was treated by Galen, described in millennia-old papyrus scrolls, and found in Paleolithic hominid bones. Cancer is a perpetual and pervasive part of the human condition because it is part and parcel of multicellularity; it is simply cell division gone awry. Animals from dinosaurs to dogs suffered from cancer; in fact, among large and long-lived multicellular organisms, cancer is only vanishingly rare in plants. This is because plants lack the Weismann Barrier, a division between the soma or body of the organism and its germ line. Though many plants reproduce sexually, any cancer that they acquire can be passed onto their offspring. Thus, any cancerous uprisings among plants have been ruthlessly and relentlessly selected against. On the other hand, even as individuals suffer, animal populations, having a Weismann Barrier with its insulation of sperm and egg cells from bodily cancer, can tolerate and even thrive in the midst of cancer.

Still, cancer deaths, judging by rates of paleo-oncological studies reported by Shi-Ming Tu, were relatively rare as a result of the low mean age of death among pre-industrialized societies. Industrialization, bringing with it modern medicine and bounteous provisions, limited early deaths, making old age common. It is only in the modern era, with so many other mortal threats checked, that cancer has become a prime killer. Cancer disproportionately afflicts the aged because with age comes neglect. Old age brings with it a relaxation of the aforementioned policing mechanisms, such that undetectable cancerous cells, surviving, proliferating, and vascularizing, are increasingly likely to become life-threatening cancerous growths. This explains why rates of childhood cancer are so low. Fitness is greatly undermined when cancer strikes
prior to, or during, the reproductive years, as it then limits the number of offspring produced. Yet, post-reproductive cancer does not greatly reduce fitness and so is not readily selected against by evolution. Most women, for example, reach menopause between 45 and 50, and this is precisely when cancer rates among women rise precipitously. Graphic illustrations of cancer incidence provided by the United Kingdom Cancer Research Foundation show menopausal-age women in a transitional state between extremely low cancer rates of the young and uniformly high cancer rates of the sexagenarians, septuagenarians, and octogenarians.

Latitude and Life History Evolution
Cancer comes when it does because of the balance struck between investment in survival and investment in reproduction. While survival is, of course, important, so is reproduction, and consequently, the former is to some extent sacrificed to the latter. Among men, this is most conspicuously illustrated by the prostate, a reproductive gland whose cancer proneness and metabolic activity are strongly and positively correlated. Among women, this is most conspicuously illustrated by the breast, a mammary gland whose cancer proneness comes of cyclical restructuring of its tissue.

More metabolically active prostates make males more fecund, while more metabolically active breast tissue makes the offspring of females more fit. Thus, it is adaptive to be metabolically active. Alternatively, more metabolic activity and cell turnover equate to more chances for cancerous divisions. Though the exigencies of reproductive fitness have certainly curtailed our longevity, as a species, *Homo sapiens* are very long-lived and invest much in gestation, growth, and survival. In the parlance of life history evolution, a branch of evolutionary biology that studies why organisms age, mature, and die when they do, humans are highly K selected. This means that humans, growing slowly, lavishing much parental care on offspring, and maintaining flexibility throughout adulthood, will invest much in maintenance, hence our extremely long lives. Nevertheless, there may be subtle differences among human populations on life history traits, with ecological variables, including latitude, playing a mediating role. Those persons historically occupying southern climates may have faster life histories, acquiring, and dying from, cancer earlier in life.

Paradoxically, if one looks at global distributions of cancer, they are lowest precisely in these southern climates. However, this is because these cancer rates are confounded by life expectancy. Africa, for example, reports an extremely low rate of cancer because its inhabitants have an extremely short life expectancy, which makes sense when recalling the aforementioned relationship between age and cancer. Infectious diseases like Ebola, trypanosomiasis or sleeping sickness, and malaria claim most lives prior to the onset of degenerative diseases, such as cancer. Scrutinizing diverse industrial countries such as the United States removes this confound, showing the true relationship: Cancer rates among Americans of African descent are highest, as reported by the Centers for Disease Control and Prevention, for the years between 1999 and 2010. Why might this be so? The answer comes from juvenile mortality rates. Across species, as biologist David Reznick explains, high juvenile mortality predicts rapid maturation, aging, and death. Humans inhabiting equatorial habitats are exposed to many more parasites and infectious agents, making life precarious. This, in turn, favors a shift away from long-term investment in bodily maintenance, leaving persons of post-reproductive ages more immediately susceptible to developing cancer.

Latitude, Infectious Disease, and Cancer
The relationship between infectious agents and cancer, however, not only is mediated historically through the action of evolution but also is directly demonstrable in the present. Though only the human papilloma virus has received popular attention for its ability to cause cancer, the discoverer of this link, Harold zur Hausen, reports that upward of 20 percent of cancers are associated with infectious agents. As a consequence, studying the epidemiology of infectious disease becomes relevant to understanding the distribution of cancer. Sometimes this linkage is direct, as in the case of cervical cancer; other times, it is indirect, as in the case of the bacteria *Helicobacter pylori*, which causes stomach ulcers and can ultimately promote stomach cancer. Further still, as described by Claudia Cornwall, sometimes geography, susceptibility, genetics, bacteria, and viruses combine to promote complex pathways to cancer. Dr. Denis Burkitt, recognizing regional variation in lymphoma distributions, conducted a geographical biopsy. This geographical
biopsy found that what came to be called Burkitt’s lymphoma was almost exclusively restricted to malarial regions. There is, in fact, a complex interaction between the Epstein-Barr virus and malaria in causing this kind of lymphoma. Similarly, the research of Lawrence Kingsley, an epidemiologist, and Patrick Moore, director of the University of Pittsburg’s Cancer Virology Program, found that skin cancer can arise through concomitant infections of Kaposi’s sarcoma-associated herpesvirus and AIDS. In this case, the virus inhibits normal cell death and induces abnormal cell proliferation.

While relationships can be complex, infectious agents sometimes simply undermine immunity. Psychoneuroimmunology, a hybridized discipline studying the interaction between psychological states and immune function, has repeatedly shown that stress can undermine the immune system’s ability to battle disease, including cancer. A classic study of rats showed that subjects stressed by shock but given a coping mechanism subsequently fought off injected cancer better than those rats shocked without a coping mechanism and controls. With this in mind, it is important to recall that cold is a stressor. And in fact, cold shows a relationship with cancer, which seems to be nonspecific, in that prolonged exposure to cold decreases immune function, which limits the body’s ability to fight cancer. Alternatively, heat is also a stressor. As detailed in the work of Quan Liao and colleagues, heat seems to have a more direct relationship to specific forms of cancer, such as pancreatic cancer, by inhibiting apoptosis or programmed cell death. Similarly, Philip Cornford and associates discuss the increased rate of prostate cancer that comes of prolonged exposure to heat with the resultant expression of heat shock proteins.

Conclusions
Latitude and cancer have other ties worthy of mention. First, as one progresses north, melanin formation and pigmentation decrease, thus allowing more ultraviolet light to penetrate the skin surface, which in turn continues to allow vitamin D synthesis. This has consequences for skin cancer, especially for those fair-skinned persons who migrate to equatorial climates, far from where their ancestors originated. Further still, latitude predicts differences in culture, economics, health care, and technology, all of which can relate in some way to cancer. Industrialized countries, principally found in northern latitudes, have not only fewer infectious diseases but technologies and treatments able to quickly detect, manage, and even eradicate certain cancers. On the other hand, these same high-latitude societies may have higher rates of teratogens and toxins produced by modern manufactures and industrial waste. According to the National Cancer Institute, for instance, American farmers have elevated rates of leukemia, non-Hodgkin’s lymphoma, multiple myeloma, and soft tissue sarcoma, as well as cancers of the skin, lip, stomach, brain, and prostate, possibly as a consequence of exposure to fertilizers, pesticides, fuels, and engine exhaust. On balance, however, industrialization may cure more cancer than it causes. In conclusion, the relationship between skin color and skin cancer aside, latitude and cancer, upon a superficial glance, seem as two unrelated variables. Upon closer inspection, it becomes clear that latitude mediates the relationship between cancer and a host of other variables.

Steven Charles Hertler
College of New Rochelle

See Also: Breast Cancer; Prostate Cancer.

Further Readings

Lead
Lead is a chemical element that has widespread occurrence and extensive usage within society.
Historically, lead has been utilized in a range of industrial processes, recreational endeavors, and household practices that have been accepted and engrained within the lifestyles of many people. However, lead has also been associated with increasing morbidity and mortality of a number of health conditions. Of primary concern, however, is its association with different types of cancer, including lung, stomach, bladder, lymphatic brain, and the nervous and hematopoetic system. This entry seeks to highlight some of the research that has been conducted, along with the challenges and weaknesses associated with the research, and also highlight agencies that have been instituted to monitor and evaluate lead usage and its applications. The link between lead exposure and cancer is clearly a concern, and more research is needed to better define the possible relationship. This entry also highlights the need for more extensive and focused research on lead and cancer that will utilize longitudinal research with adequate controls.

Lead is a naturally occurring metallic element that has had great utility in society. It can be readily combined with other substances in order to produce a variety of compounds that have been very useful. Some of these compounds are leaded gasoline, tetraethyl lead, lead oxide, and lead chloride. Lead compounds have made considerable contribution to the development of society over the years. The products have been used in industrial processes for the production of machinery, ammunition, motor vehicle batteries, gasoline, matches, brass and bronze, dyes and paints, cable coverings, and building materials such as water pipes, plumbing fixtures, and lead sheeting. It has also been extensively used in the visual and creative arts in photography, crafts, and ceramics as well as in the production of medicines and cosmetics. M. C. Rousseau and colleagues reported that lead metal consumption worldwide was approximately 8 million tons, mainly from the production of lead batteries, pigments, building materials, ammunition, and cable sheathing. Even with the application to different areas of national development and the tremendous economic contribution, there have been expressions of concern regarding the possible contribution of lead to cancer.

Cancer is an abnormal malignant condition that can occur within any tissue of the body. It is characterized by uncontrollable replication of cells, which may result in invasion and the damage of surrounding tissues by the neoplasm with possible metastases to other body structures. Cancer usually occurs because of an alteration or damage to the deoxyribonucleic acid (DNA). DNA is the nucleic acid that encodes the genetic instructions for the development and functioning of cells. Two of the substances that have been incriminated in causing damage to the DNA and subsequent malignancy are lead and lead products.

Based on the extensive usage of lead products and the natural occurrence of lead, it is believed that individuals may be at increased risk of exposure in a number of different ways. People may be exposed by breathing or swallowing air or water within the environment. Lead may also be available directly from automobile exhaust or from soil or other materials that have been contaminated with exhaust. Much lead still exists in society from being deposited in the soil decades ago. Another source of exposure is lead-based paints, which may be found in older structures such as houses and bridges. Drinking water is another potential source of lead exposure based on the historic use of lead pipes, fixtures, and solder. Exposure to lead also may be recreational as in the smoking of cigarettes or exposure...
to ceramics and the creative arts. Exposure to lead also may occur through agricultural practices based on the inclusion of certain pesticides. Even with the development of preventative guidelines in restricting lead exposure, there are still increasing health risks, particularly in older residential housing facilities based on poor disposal practices and changes in land use of previously industrial sites.

Exposure to lead has been identified as a primary occupational hazard that is associated with cancer. The occupations that have been identified are battery manufacturers, cable splicers, and lead refinery and foundry workers. Persons in the automotive industry such as radiator repair workers and battery and gasoline workers are also at increased risk. Miners, painters, and construction and demolition workers are also at increased risk. There is also excessive exposure for gun and ammunition makers as well as brass and bronze workers. Extensive research conducted among many of these professional groups has failed to provide conclusive evidence on the contribution of lead to cancer.

**Research on Lead and Cancer**

Although extensive research has been conducted on lead and cancer in laboratory animals and among humans, the reports have been inconclusive. Some of the possible reasons are based on the fact that lead is naturally occurring within the environment through water, soil, or air pollution and that there are diverse sources for exposure, including industrial, recreational, agricultural, and household. Now these research findings may appear inconclusive based on the fact that there is an increasing likelihood of exposure to lead products by respondents in the research. The inconclusive findings also may have resulted from the lack of adequate standards and control measures being incorporated within the research methodologies. Another reason for an inconclusive report on the relationship between lead and cancer is that, to date, there has been no confirmed report of lead as a carcinogen. There is therefore a great need for further and more extensive research that will utilize a longitudinal approach and the incorporation of adequate standards and controls in the methods.

**Implications of Lead Exposure and Cancer**

Lead exposure is believed to have an impact on cancer of certain organs of the respiratory, gastrointestinal, and urinary systems in addition to the brain. Research on the relationship of occupational exposure and lung cancer mainly among battery workers and smelter workers revealed a small increase in cancer risk. One of the weaknesses of the research was that it was conducted among workers who had high levels of occupational exposure to lead. Additionally, the research failed to address other contributing factors such as exposure to other heavy metals and the impact of smoking. Research done on stomach cancer revealed that there was an increased risk of stomach cancer with high lead exposure. However, as in previous research, adequate controls were not in place, and specific control variables that are associated with increased risk of stomach cancer were not considered. Further research investigating lead and other cancers such as of the brain, kidney, bladder, colon, and rectum also revealed inconclusive results.

To date, research has not conclusively confirmed lead and lead products as being carcinogenic. The National Toxicology Program (NTP), based on extensive research on both laboratory animals and humans, reported that lead and lead products are reasonably anticipated to be carcinogenic. The International Agency for Research on Cancer (IARC) reported based on evidence obtained from research that inorganic lead compounds are probably carcinogenic. The Environmental Protection Agency (EPA) also reported that, based on its research, lead and inorganic lead compounds are probable human carcinogens. It further reported that there was inadequate evidence to classify organic lead compounds as carcinogenic. Currently, after extensive research, it is still inconclusive to what extent lead and its products are carcinogens, thus causing cancer. Recognizing that the pervasive nature of lead and lead products in society may present some challenge to obtaining a conclusive result, development of continued research incorporating proper standards and adequate controls can result in more-conclusive results. Based on the fact that lead is classified as an occupational hazard, government policies and legislation to control exposure and safeguard health would be supported.

**Corporate Strategies to Regulate and Control Lead Exposure**

Although there has been inconclusive proof of the specific contribution of lead and lead products to
cancer, several strategies have been instituted in order to protect society from undue exposure. One such measure was the ban on lead additives in motor vehicle gasoline and lead soldering on food cans. There is also the continued monitoring of public and household water supplies by the EPA and bottled water by the Food and Drug Administration (FDA). The Consumer Product Safety Commission (CPSC) also monitors lead levels in consumer products, particularly paints and children's toys. The Occupational Safety & Health Administration (OSHA) also has established guidelines to regulate and monitor lead exposure within industries and the workplace. Employers are also made responsible to provide protective equipment such as respirators, gloves, and medical monitoring of employees who are working in at-risk environments.

**Conclusion**

Lead and its compounds are very pervasive in society. They exist within a wide range of social, agricultural, and industrial environments. Historically, lead and lead products have contributed significantly to development and industry in many spheres of society. However, it is believed that lead and lead products also contribute to increasing morbidity and mortality of different types of cancer. To date, the reports from extensive animal and human research by leading environmental and cancer experts are still inconclusive regarding the carcinogenic effect of lead and its impact on cancer. Weak relationships were identified between lead and lung and stomach cancers, respectively. However, in this research, the workers were exposed to very high levels of lead without adequate controls being considered. The quest to determine the link between lead exposure and cancer continues to be a great concern. It is therefore necessary to have more extensive research on lead and cancer that utilizes robust research design with adequate standards and controls being incorporated. In the meantime, the government and other related agencies such as the NTP, IARC, EPA, FDA, CPSC, and OSHA continue to monitor lead within society.

Fay Williams
Northern Caribbean University

**Further Readings**


---

**Leukemia, Acute Lymphoblastic, Adult**

Acute leukemia is a hematological condition that is strongly associated with significant morbidity and mortality, mainly due to the disease itself and the aggressive treatment utilized. Although extensive studies have been conducted in its diagnosis, progression, and treatment, information on the social and psychological aspects of acute leukemia have not been well established. Information generated from research investigations on these behavioral components may thus improve the standard of care for patients diagnosed with acute leukemia.

One of the most recent and significant studies conducted on acute leukemia, which includes acute lymphoblastic, acute myeloid, and promyelocytic leukemia, involves posttraumatic stress. This condition directly reflects the emotional state of an individual in response to an intense or traumatic incident. The symptoms of posttraumatic stress include emotional detachment or numbness; a
general avoidance of things, events, and people that remind an individual of the incident; and hyperarousal. Previous studies have observed a direct correlation between the degree of trauma and the subsequent level of posttraumatic stress. Interestingly, the incidence of posttraumatic stress symptoms is higher in cancers that are of acute onset or follow a fluctuating disease progression compared to cancers that more slowly progress. For example, patients diagnosed with solid tumors are more likely to develop posttraumatic stress when the treatment that they receive is more aggressive than other cases due to the advanced stage of their cancer or the rate of progression.

In Canada, Gary Rodin conducted a research study on the psychological impact of acute leukemia and its corresponding treatment in terms of posttraumatic stress symptoms. A total of 205 patients (58 percent male) with various types of leukemia, including acute lymphoblastic, promyelocytic, and acute myeloid, were included in the investigation. These adult patients were also classified according to their treatment stages, namely, newly diagnosed and thus just about to start or have recently received treatment, patients who recently relapsed, and patients who failed in a specific treatment regimen. To collect information from patients regarding stress in relation to acute leukemia, the study participants were asked to complete the Stanford Acute Stress Reaction Questionnaire as well as undergo assessment using various psychosocial measurement tools such as the Memorial Symptom Assessment Scale and the CARES Medical Interaction Subscale.

The results of the study showed that 86 percent of the study population was recently diagnosed with acute leukemia, and 94 percent were currently undergoing active treatment for said disease. In addition, 14 percent of the patients were determined to have acute stress disorder based on the criteria of the Stanford stress questionnaire. On the other hand, 18 percent of the study participants were described as having subsyndromal acute stress. The most common posttraumatic stress symptoms in the acute leukemia patients were physical signs of distress, difficulty in interacting with their physicians, poor spirits, and attachment anxiety. The research study thus highlighted the association between acute leukemia in adults and traumatic stress, wherein a more-advanced stage of acute leukemia results in more mental suffering, notwithstanding the aggressive treatment given to the patient. These findings also indicate the importance of mental health interventions for adult patients with acute leukemia.

Another topic of social and psychological concern in adult acute lymphoblastic leukemia is the fear that the disorder could be linked to advanced parental age. The first observations of this association were reported at least 50 years ago, and subsequent research studies have supported this association. However, not all epidemiologic studies on acute lymphoblastic leukemia showed this specific correlation. Furthermore, the association between the development of acute lymphoblastic leukemia and advanced parental age were based on pediatric cases, not adult cases. To revisit this long-standing association, Gunnar Larfors recently conducted a case-control study on the incidence of pediatric and adult acute lymphoblastic leukemia in relation to parental age. The investigation involved reviewing five Swedish health registries for cases involving acute lymphoblastic leukemia. To avoid multiple entries of the same cases, because several health registries were included in the study, the unique identification number of each Swedish citizen was employed in the review.

The comprehensive epidemiological studies included 2,660 pediatric and 4,412 adult cases of acute lymphoblastic leukemia, which were then compared to 28,288 age-matched healthy controls from a Swedish population-based register. Conditional logistic regression was employed to estimate the relative risk for acute lymphoblastic leukemia in each cohort. The results of the study showed that there was a small increase in the risk for acute lymphoblastic leukemia in children based on advanced parental age, whereas the adult cases showed no association to advanced parental age. Interestingly, a lower risk for adult lymphoblastic leukemia was observed with higher numbers of siblings. The information generated from this study could decrease the incidence of social and mental health issues (i.e., anxiety and depression) that emerge upon receiving a diagnosis of acute lymphoblastic leukemia.

In another vein, Suzanne Danhauer and colleagues recently completed a research study on the positive changes involving the psychological conditions of patients diagnosed with adult acute
Leukemia, Acute Lymphoblastic, Childhood

Childhood acute lymphoblastic leukemia (ALL) is the most common cancer of childhood, comprising about 30 percent of all childhood cancers. The majority of children diagnosed with ALL are between 1 and 5 years old. Standard risk ALL is also the most curable of childhood cancers, with a more than 90 percent cure rate. However, even today, 25 percent of children who are in remission for ALL will suffer a relapse. The development of a cure of ALL, or childhood leukemia, is one of the great medical stories of the 20th century. Childhood acute lymphoblastic leukemia was the first cancer in which chemotherapy was successfully used and in which a multimodal approach using chemotherapy combinations and radiation was taken. In the history of cancer treatment, the development of a cure in childhood ALL has served as the prototype or paradigm for approaching cancer treatment in adults as well.

Acute lymphoblastic leukemia is cancer in which the bone marrow makes too many immature lymphocytes (a type of white blood cell). It is a cancer of the blood and bone marrow. ALL usually progresses very quickly if not treated. In a child with ALL, the stem cells that produce infection-fighting cells are out of control—they do not work like normal lymphocytes and aren’t able to fight infection. As the number of leukemia cells increases in the blood and bone marrow, there is less room for healthy white blood cells, red blood cells, and platelets. This can lead to infection, anemia, and easy bleeding.

Although the causes of childhood ALL are not known, there do seem to be certain risk factors. Possible risk factors include being exposed to X-rays before birth, being exposed to radiation, past treatment with chemotherapy, certain changes in genes, and having certain genetic conditions (Down syndrome, Bloom syndrome, Shwachman syndrome, and neurofibromatosis type 1, ataxia-telangiectasia).

The following are often symptoms of childhood ALL: fever; easy bruising or bleeding: petechiae (pinpoint dark red spots under the skin caused by bleeding); bone or joint pain; painless lumps in the neck, underarm, stomach, or groin; pain or feeling
of fullness below the ribs; loss of appetite; weakness; and feeling tired or looking pale.

The diagnosis of childhood ALL is made after a physical exam and history, complete blood count with differential, blood chemistry studies, and a bone marrow aspiration and biopsy. Cytogenetic analysis is also critical to look for certain changes in the chromosomes in the lymphocytes. The Philadelphia chromosome is one such change.

There are certain factors that affect prognosis and treatment options in cases of childhood ALL. Staging is not a factor as ALL is systemic or stage IV. The age at diagnosis, gender, and race are important. The number of white blood cells in the blood at diagnosis is critical as well as whether the leukemia cells began from B lymphocytes or T lymphocytes. Additional factors include whether there are chromosomal changes, whether there are leukemic cells in the cerebrospinal fluid, or whether the child has Down syndrome. How quickly and how low the leukemia cell count drops after initial treatment are also key factors. Treatment options relate to prognosis. These options take into account whether the child has standard-risk or high-risk ALL, the child's age, whether the leukemia cells are pre-B or T cell, whether there are chromosomal changes, and how fast and well the leukemia cells drop after beginning treatment. For leukemia that relapses after initial treatment, prognosis and therapy depend upon how long between the diagnosis and relapse and whether the leukemia comes back in the bone marrow only or in other parts of the body.

The first reported case of childhood leukemia was of a little German girl named Maria in 1846. According to the family physician, the child had a short history of fever, fatigue, and bruising. The 5-year-old girl died, and an autopsy was performed that showed a grossly enlarged spleen and liver. The blood of the child was thick and white, the Weiss blood that would later be termed leukemia.

Until the 20th century, leukemia was often thought to be an infection rather than the cancer that it really was. In the 1940s, Dr. Sidney Farber at Harvard Medical School sought to find a way to combat leukemia. Knowing that leukemia was a disease of the bone marrow, Farber sought to develop a drug that would stop the development of leukemic cells. This idea was not an entirely new one because researchers knew that accidental exposure to poison gas had suppressed bone marrow in exposed soldiers. In the mid-1940s, a folate was used as an antagonist in 16 children, of whom 10 went into remission. Although the children later died from their disease, the study proved that remission was possible. Farber’s report was published on June 3, 1948, in the New England Journal of Medicine and met with great controversy. Many physicians felt that using these drugs on children was torture because death would ultimately result.

During the 1950s, further progress against childhood leukemia was made with the development by Gertrude Elion of Purinethol or 6-mercaptopurine. This drug is still used today in continuation and maintenance therapy in children with acute lymphoblastic leukemia. Prednisone also was used as a treatment, although the side effects were difficult, and the remissions it produced were short lasting. The development of a series of clinical trials at the National Cancer Institute under Emil Frei and Emil J. Freireich were a turning point in the approach toward achieving long remissions. The trials began the process of cooperative groups trials of drugs and drug combinations to rely on statistical evidence to determine better therapy.

The development of total therapy led by Dr. Donald Pinkel at St. Jude Children's Research Hospital for the first time in the late 1960s brought about long-term remissions or cures for about 50 percent of children with acute lymphoblastic leukemia. The addition of cranial radiation became the gold standard that was later replaced in the early 2000s with only chemotherapy injected into the spinal fluid. Pinkel's Total Therapy consisted of a four-drug induction therapy and subsequent intensification and maintenance therapy. This therapy is still the backbone of ALL therapy today in children, with the major addition being stem cell transplant and the importance of tailoring therapy for chromosomal differences.

Robin L. Rohrer
Seton Hill University

See Also: Childhood Cancers; Leukemia, Acute Lymphoblastic, Adult; Leukemia, Acute Myeloid, Childhood.

Further Readings
Leukemia, Acute Myeloid, Adult

Acute myeloid leukemia (AML) pertains to a hematopoietic stem cell disorder that is characterized by the continuous clonal proliferation of myeloid progenitor cells without entering the subsequent differentiation stage. This endless cycle of proliferation results in the accretion of immature cells of different stages as well as in the decrease in the generation of normal components of the hematopoietic system, including fully differentiated cells such as erythrocytes, granulocytes, and platelets.

The incidence of AML currently stands at four in every 100,000 persons annually; therefore, AML is considered as a rare disorder, although it is responsible for a significant fraction of cancer-related deaths. In the United States, it has been estimated that approximately 14,590 individuals will be diagnosed with AML, and around 10,370 of these individuals will die from this disorder. A positive correlation between AML risk and age has been earlier established, and the average age of an AML patient at diagnosis is 67 years. Based on this information, AML is therefore considered as an elderly disease.

The diagnosis and treatment of AML has significantly improved in the last 40 years. The series of clinical trials conducted in the past several decades has resulted in the establishment of a standard of care for AML, with a 75 percent success rate in entering remission and a 50 percent survival rate. However, most of the clinical trials involved patients who were less than 60 years old, and therefore, this standard of care for AML is optimal for this specific age-group and remains ineffective and harmful to the majority of elderly patients. Reports have shown that elderly AML patients have poor tolerance to most chemotherapeutic drugs administered as well as show higher treatment-related mortality rates and major cytogenetic aberrations. Furthermore, the average survival of elderly AML patients who have undergone chemotherapy is only four to six months.

Recent research studies have thus focused on developing new drugs that could be better tolerated by elderly AML patients. To achieve this goal, the novel drug should utilize a mechanism of action that is different from that of the common chemotherapeutic drugs that have been administered in the last few decades. In addition, this novel drug should also be capable of enhancing antileukemic activity as well as be safe enough for administration.

In 2012, a research group led by Hagop Kantarjian presented the results of their phase II clinical trial using oral sapacitabine, a cytosine nucleoside analog, in elderly patients diagnosed with AML who were never treated (86 patients) or recently underwent a first relapse (19 patients). Approximately 105 elderly AML patients with ages ranging from 70 to 91 years old (average age: 77 years) were randomly assigned to any one of three treatment schemes: 200 milligrams (mg) of sapacitabine twice a day for seven days (Arm A), 300 mg sapacitabine twice a day for seven days (Arm B), and 400 mg of sapacitabine twice a day for three days and then once a week for the next two weeks (Arm C).

The results of the study showed that the survival rate of patients belonging to Arm A was 35 percent, for Arm B 10 percent, and Arm C 30 percent. In addition, the overall response rate of Arm A was
45 percent, Arm B 30 percent, and Arm C 45 percent. Arm C showed a higher number of complete remissions than Arm A and Arm B. The 30-day mortality was estimated as 13 percent, whereas the 60-day mortality measured 26 percent. The most frequent adverse events included pneumonia, anemia, and neutropenia. Observed severe adverse events included complications of myelosuppression. The findings of the phase II clinical trial indicated that sapacitabine was well tolerated by elderly AML patients and that the 400 mg dose showed a more effective response. The toxicity profile of sapacitabine on elderly AML patients was also classified as favorable, and the drug was also easier to administer to elderly patients. These promising findings have thus paves the way for a phase III clinical study on sapacitabine, which is currently in progress.

Another promising drug for the treatment of elderly patients with AML is decitabine, which, similarly to sapacitabine, is a cytosine analogue. Decitabine was initially synthesized 50 years ago and is currently distributed by Eisai Pharmaceuticals in Tokyo, Japan, using the brand name Dacogen. Earlier research studies using decitabine showed that the drug possessed antileukemic properties, as observed in experiments using cell lines. In addition, in vitro investigations have shown that decitabine was more potent than cytarabine. Its cytotoxic effects were attributed to its capacity to disrupt DNA synthesis by destroying the DNA structure. Based on its capacity to halt a specific biochemical activity, decitabine was first administered at high doses of 1,000 mg/m²/cycle, either as a single agent or in combination with other pharmaceuticals such as anthracyclines. However, this initial attempt at using decitabine resulted in significant hematological toxicities.

In the 1980s, preclinical studies on decitabine showed that the drug could induce differentiation when administered at low doses. Its mechanism of action involved the reversal of DNA methylation-induced gene silencing. Upon entry into a cell, the cytosine analogue is phosphorylated and then activated by an enzyme called deoxycytidine kinase, resulting in the triphosphate molecule, aza-deoxycytidine triphosphate. This product then competes with and exchanges cytosine in the CpG islands of the DNA strand. CpG islands frequently occur as clusters within the promoter regions of genes. This cytosine replacement thus inhibits subsequent methylation events involving the promoter regions. The molecular pathogenesis of AML involves the suppression of tumor suppressor genes by methylation, and thus, the inhibitory action of decitabine reverses this condition by promoting the expression of specific genes that prevent the abnormal proliferation of progenitor hematopoietic cells.

Various clinical trials using decitabine have been conducted, and some are currently in progress. At least seven clinical trials ranging from phase I to III have been completed using various doses and durations, which in turn have resulted in complete remissions ranging from 13 to 64 percent, whereas the observed survival rates were not significant. Researchers are also currently focusing on identifying specific subgroups within the elderly AML population that would largely benefit from this novel drug.

Rhea U. Vallente
PreventionGenetics, LLC

See Also: Leukemia, Acute Lymphoblastic, Adult; Leukemia, Acute Lymphoblastic, Childhood; Leukemia, Acute Myeloid, Childhood.

Further Readings

Leukemia, Acute Myeloid, Childhood

Childhood acute myeloid leukemia (AML) is a cancer of the blood and bone marrow that is diagnosed in children as young as infancy. It is a disease more
commonly found in adults and is particularly difficult to treat. Whereas great progress has been made in the treatment of childhood acute lymphoblastic leukemia, only about 25 to 50 percent of children with AML will have a long-term remission. AML is also called acute myelogenous leukemia, acute myeloblastic leukemia, acute granulocytic leukemia, and acute nonlymphocytic leukemia. In normal bone marrow, blood cells are produced that later make blood stem cells or immature cells. These cells eventually become mature blood cells. A blood stem cell may become a myeloid stem cell or a lymphoid stem cell. A lymphoid stem cell becomes a white blood cell.

In AML, the myeloid stem cells usually become a type of immature white blood cells called myeloblasts (or myeloid blasts). The leukemia cells can build up in the blood and bone marrow, so there is less room for healthy white blood cells, red blood cells, and platelets. When this happens, infection, anemia, or easy bleeding may occur. The leukemia cells can spread outside the blood to other parts of the body, including the central nervous system, skin, and gums.

There are subtypes of AML based on the type of blood cell that is affected. The treatment of AML is different when it is a subtype called acute promyelocytic leukemia (APL) or when the child has Down syndrome. AML may occur after treatment with certain anticancer drugs or radiation therapy.

Possible risk factors for AML include having a brother or sister, especially a twin, with leukemia, being Hispanic, being exposed to cigarette smoke or alcohol before birth, having a history of aplastic anemia or myelodysplastic syndrome, and past treatment with ionizing radiation or chemicals such as benzene. Having certain genetic disorders increases risk, including Down syndrome, Fanconi anemia, neurofibromatosis type 1, Noonan syndrome, and Shwachman–Diamond syndrome.

Childhood AML may produce the following signs: fever with or without an infection, night sweats, shortness of breath, weakness or feeling tired, easy bruising or bleeding, petechiae, pain in the bones or joints, pain or feeling of fullness below the ribs, painless lumps, or an eczema-like skin rash.

The diagnosis of AML in children is determined by a physical exam and history, complete blood count and differential, peripheral blood smear analysis, blood chemistry studies, chest X-ray, and bone marrow aspiration and biopsy. Cytogenetic analysis is also performed for chromosomal abnormalities.

Certain factors affect the prognosis of the child with AML, and treatment options depend on these characteristics. Key among these factors are the age of the child at diagnosis, the race or ethnic group of the child, whether the child is greatly overweight, the number of white blood cells in the blood at diagnosis, whether the AML was caused by previous anticancer treatment, and the subtype of AML. Other factors are whether the child has Down syndrome, whether the child has leukemia in the central nervous system, and how quickly the leukemia responds to initial treatment.

There is no standard staging system for childhood AML. There are different types of treatment for children with AML. The majority of children are treated in clinical trials. Induction therapy is the first phase of treatment. The goal is to kill leukemia cells in blood and bone marrow. This hopefully puts the leukemia into remission. Consolidation and intensification therapy is the second phase of treatment. The goal of post-remission therapy is to kill any remaining leukemia cells that may be active but could begin to regrow and cause a relapse.

Until the 20th century, leukemia was often thought to be an infection rather than the cancer that it really was. In the 1940s, Dr. Sidney Farber at Harvard Medical School sought to find a way to combat leukemia. Knowing that leukemia was a disease of the bone marrow, Farber sought to develop a drug that would stop the development of leukemic cells. This idea was not an entirely new one because researchers knew that accidental exposure to poison gas had suppressed bone marrow in exposed soldiers. In the mid-1940s, a folate antagonist was used in 16 children, of whom 10 went into remission. Although the children later died from their disease, the study proved that remission was possible. Farber's report was published on June 3, 1948, in the New England Journal of Medicine and met with great controversy. Many physicians felt that using these drugs on children was torture because death would ultimately result.

During the 1950s, further progress against childhood leukemia was made with the development by Gertrude Elion of Purinethol or 6-mercaptopurine. Prednisone also was used as a treatment, although the side effects were difficult, and the remissions it produced were short lasting. The development of a
series of clinical trials at the National Cancer Institute under Emil Frei and Emil J. Freireich were a turning point in the approach toward achieving long remissions. The trials began the process of cooperative group trials of drugs and drug combinations to rely on statistical evidence to determine better therapy.

Although the differences between AML and ALL were not clearly known until the late 1950s, similar therapies were used. However, by the 1960s, it became clear to physicians and researchers that AML was not as sensitive to chemotherapy, and therefore, more and more toxic therapies were developed. The majority of children today with AML will receive very intensive in-hospital therapy in preparation for a bone or stem cell transplant if possible. Maintenance therapy has proven ineffective in AML, and drug toxicity is considerably higher than in ALL treatment.

Robin L. Rohrer
Seton Hill University

See Also: Bone Marrow Transplants; Childhood Cancers; Leukemia, Acute Lymphoblastic, Childhood; Leukemia, Acute Myeloid, Adult.

Further Readings

Leukemia, Chronic Lymphocytic

Chronic lymphocytic leukemia (CLL) is the most common malignancy involving B-lymphocytes that is associated with clinical heterogeneity. It is the most common type of adult leukemia occurring in Western countries. The standard treatment for CLL is chemotherapy, which could employ either a single agent or a combination of agents. Single-agent chemotherapy usually involves chlorambucil, fludarabine, and bendamustine; examples of combination chemotherapy are fludarabine with cyclophosphamide, cladribine with prednisone, and chlorambucil plus prednisone. CLL may also be treated with monoclonal antibodies such as rituximab and alemtuzumab or with a combination of chemoimmunotherapeutic agents such as fludarabine and rituximab; fludarabine, cyclophosphamide, and rituximab; or pentostatin, cyclophosphamide, and rituximab, and so forth. Based on the wide range of treatment options for CLL, it is therefore helpful to understand the cost of treatment of CLL from the point of view of the general public and evaluate the burden of the disease.

According to Carl Rudolf Blankart and coauthors, the burden of disease is relatively lower for CLL compared to other chronic illnesses such as diabetes or chronic obstruction pulmonary disease (COPD). This claim was based on a research study involving a total of 4,198 CLL patients for whom direct medical costs such as inpatient and outpatient care, medications, home nursing care, medical equipment or aids, service fees collected by nonphysicians, and finally, rehabilitation were calculated. Other nonmedical costs associated with CLL include expenses related to sick leave, traveling expenditures to visit the doctor, and fees for patient transport (i.e., use of an ambulance). The data was then compared to a control group consisting of 150 randomly selected individuals who matched each combination of age and sex of the CLL population.

Their study also showed that, aside from the direct medical costs of CLL, there are also indirect costs such as losses in productivity, which could be calculated by multiplying the patient's gross income by the number of days that have been used for sick leave. In addition, there are also drugs that are often prescribed to CLL patients other than those of chemotherapeutic value. These include antibiotics, which are immediately administered to chemotherapy-treated patients because they are at higher risk of contracting microbial infections due to the deterioration of the humoral and cellular immune systems of CLL patients.

For the point of view of the society, the burden of disease varies in CLL because this malignancy
afflicts various age-groups. Younger CLL patients generally spend less money for treatment compared to older patients because most physicians utilize the watch-and-wait approach on these individuals. The watch-and-wait approach also does not entail expensive therapeutic regimens (e.g., chemotherapy) or even hospitalization. The economic burden of this malignancy therefore varies across the age continuum.

The results of the study showed that the direct, nonmedical cost of CLL is twofold higher than the direct medical expenses of the disease. Furthermore, the cost of treating each CLL case is also twofold higher than the cost of treating any other common disease, despite the well-known fact that treatment is conducted only during the later phases of the disease. With the continuous improvements in medical technologies, the increase in size of the aging population, and the elevated incidence of CLL, it is thus highly likely that the cost of treatment of this particular disease will further increase over time.

In a more recent study led by Thitima Kongnakorn, the cost-effectiveness of various first-line drugs for the treatment of CLL was assessed. Because of the availability of various treatment options for CLL, a physician may choose from a group of chemotherapeutic drugs, antibodies, or combinations of two chemotherapeutic drugs or an antibody with a chemotherapeutic drug. A discrete event simulation representing the progression of CLL was developed to assess the cost as well as health outcomes that were associated with the administration of bendamustine, chlorambucil, or alemtuzumab for a CLL population that has never been treated (treatment naive).

Specific characteristics using information generated from a previous bendamustine trial were assigned to every simulated CLL patient in the cohort. Every simulated patient was then cloned to generate three identical cohorts. Every cohort was then assigned one of three treatments, namely, intravenous bendamustine at a dose of 100 mg/m²/day for the first two days of a 28-day cycle for a total of six cycles; intravenous alemtuzumab at a dose of 30 mg three times a week for a total of 12 weeks; or oral chlorambucil at a dose of 0.8 mg/kg/day for the first and 15th day of every 28-day cycle, for a total of 12 cycles.

To generate a simulated CLL patient population, data collected from previous clinical trials were used; these included risk equations in calculating for the progression-free survival rate as well as survival during post-disease progression. The response rates and the incidence of adverse events were also estimated. The cost of the disease and survival in terms of life years, as well as quality-adjusted life years, were calculated for the lifetime of each patient.

The results of the study showed that bendamustine was the dominant therapeutic scheme relative to alemtuzumab because it provided more benefits to the CLL patient, which included longer life years and higher quality-adjusted life years. In addition, the total cost of using bendamustine as the sole therapeutic drug for CLL was lower than that of alemtuzumab. However, bendamustine was more expensive than chlorambucil, although better health outcomes such as longer life years and quality-adjusted life years were observed. These observations thus indicate that bendamustine was the most cost-effective therapeutic regimen when compared to alemtuzumab and chlorambucil. Although the price of chlorambucil was the lowest of the three drugs assessed in the study, the shorter life years of each CLL patient were indicative of additional health issues, which in turn would result in more direct medical and nonmedical costs.

It is interesting to note that, when the study led by Thitima Kongnakorn was completed, the marketing and distribution of alemtuzumab was stopped and immediately became available to health care providers at no cost when specific requirements had been fulfilled. Although the study might have been conservative in its operation, and several limitations have been cited, the investigators successfully presented CLL from a socioeconomic perspective. This approach also could facilitate the review of the effectiveness of other CLL drugs based on medical and nonmedical costs.

Rhea U. Vallente
PreventionGenetics, LLC

See Also: Clinical Trials; Leukemia, Chronic Myelogenous; Leukemia, Hairy Cell.

Further Readings
Leukemia, Chronic Myelogenous

Chronic myelogenous leukemia (CML), also known as chronic granulocytic leukemia (CGL) and chronic myeloid leukemia, is a cancer that starts inside bone marrow due to uncontrolled growth of immature blood stem cells called myeloid cells. As a result, there is clonal proliferation of immature and mature granulocytes (neutrophils, eosinophils, and basophils). The diseased cells accumulate in the bone marrow and blood and affect normal blood cell growth. It is called chronic as it has slower rate of progression than acute leukemia.

Epidemiology, Causes, and Risk Factors

CML typically affects older adults and rarely occurs in children, though it can occur at any age. In Western countries it accounts for 15 to 20 percent of all leukemia affecting adults. It is mostly seen in middle-aged people but can occur in young as well as in elderly populations.

In most cases, no obvious cause for CML can be isolated. It is not a hereditary disorder as chromosomal mutation is not transmitted from parents to offspring. It is mostly diagnosed in people around 65 years of age, and it is seen more commonly in men than women with a ratio of 1.4:1.

Radiation exposure, such as radiation therapy for certain types of cancer, is a risk factor. Ionizing radiation exposure, like in Hiroshima and Nagasaki nuclear bombing survivors, has showed a 50 times increase in incidence of CML.

Pathophysiology

CML is known to be caused by a specific genetic mutation in hematopoietic cells in more than 90 percent of patients. It involves reciprocal translocation between the long arms of chromosomes 22 and 9 (t [9;22]) resulting in a shortened chromosome 22, called a Philadelphia (Ph) chromosome, which has part of the bcr gene from chromosome 22 fused with the abl gene on chromosome 9. The abl oncogene encodes a tyrosine protein kinase, and the resulting bcr–abl fusion gene produces protein with strong tyrosine kinase activity, which supports cancer by allowing affected blood cells to grow out of control and damage the bone marrow. The bcr–abl protein also inhibits DNA repair, resulting in further accumulation of genetic abnormalities. The presence of the bcr–abl rearrangement is the hallmark of CML and is considered diagnostic in a patient with clinical manifestations of CML.

Phases of Chronic Myelogenous Leukemia

Chronic myelogenous leukemia is grouped into three phases mainly on the basis of aggressiveness of the disease, clinical signs and symptoms, and laboratory findings. It is found by the proportion of the diseased cells to the healthy cells in blood or bone marrow. The more the number of leukemic cells, the worse the stage of disease. CML usually starts with the chronic phase and slowly progresses to the accelerated phase, and without treatment it turns into the phase of blast crisis.

The chronic phase is the earliest phase involving proliferation of mature cells as a result of genetic mutation, and patients may have few or no symptoms but are diagnosed when blood tests are done for other reasons. About 85 to 90 percent of the patients are diagnosed in this phase. This phase can last for months or years. Treatment at this stage of the disease usually gives the best response.

The accelerated phase is a more dangerous phase as it represents accumulation of more genetic abnormalities in addition to the presence of the Philadelphia chromosome, resulting in more rapid growth of leukemic cells.

Untreated CML leads to the blast crisis phase. It is a severe and aggressive phase of CML with proliferation of immature cells. The symptoms of blast crisis are similar to those of acute leukemia. Bleeding and infection may occur due to bone marrow failure.
Signs and Symptoms
Around 90 percent of the patients with CML are diagnosed during the chronic phase, which is most often asymptomatic. In these cases, it may be diagnosed as an incidental finding of raised white blood cell count on a routine laboratory test. It can also present with symptoms like the following:

- Fatigue
- Decreased exercise intolerance
- Joint pain (especially hip pain)
- Low-grade fever
- Unexplained weight loss
- Decreased appetite
- Pain or fullness below the ribs on the left side (due to enlarged spleen)
- Right upper quadrant pain due to liver enlargement
- Abdominal fullness and night sweats

Some patients are diagnosed in the blast phase in which the symptoms are mostly due to increased growth of immature cells in bone marrow and include the following: fever; petechiae (small red or purple spots due to bleeding into the skin); bruising; bone pains; and fullness under the lower left ribs from a swollen, enlarged spleen.

Diagnosis
The workup for CML consists of several things. A completed blood count (CBC) with differential shows a raised white blood cell count, usually more than 20,000/μL, with very low levels of leukocyte alkaline phosphatase in most cells. Eosinophil and basophil counts are almost always increased. There is also a decrease in the number of mature red blood cells. A bone marrow analysis is the diagnostic test for CML, and the characteristic finding is the presence of the Philadelphia chromosome, detected by cytogenetics. In a few patients with CML, 9:22 translocation, that is, the Philadelphia chromosome, is not detected by routine cytogenetics due to other added complex chromosomal abnormalities. In these patients, fluorescent in situ hybridization (FISH) or polymerase chain reaction (PCR) for the bcr–abl fusion are utilized for diagnosis. Bone marrow also shows hypercellularity with an increased number of granulocytes, their immature forms, and prominent megakaryocytes. It may also show fibrosis depending on the aggressiveness of the disease.

After making the diagnosis of CML, it is very important to find out its phase so that management can be done accordingly as presence of the accelerated phase means the disease is progressing, and conversion into blast crises is about to happen. Mostly World Health Organization (WHO) criteria are utilized, and if any of the following is present, then the patient is considered in the accelerated phase:

- 10 to 19 percent myeloblasts in the blood or bone marrow
- Greater than 20 percent basophils in the blood or bone marrow
- Platelet count less than 100,000 and unrelated to therapy
- Platelet count greater than 1 million and unresponsive to therapy
- Cytogenetic evolution with new abnormalities in addition to the Philadelphia chromosome
- Increasing splenomegaly or white blood cell count that is unresponsive to therapy

In a patient with CML, the presence of any one of the following defines blast crisis:

- Large clusters of blast cells in the bone marrow on biopsy
- Development of a chloroma (solid focus of leukemia outside the bone marrow)
- Bone marrow fibrosis
- Greater than 20 percent myeloblasts or lymphoblasts in the blood or bone marrow

Complications
CML can cause a variety of complications due to excess proliferation of diseased white blood cells as well as due to a decreased number of normal blood cells. Also, treatment with chemotherapeutic agents leads to various complications.

As the number of red blood cells decrease with disease progression, anemia results, which manifests as fatigue. Medicines used for treatment of CML also cause anemia and its symptoms.

A low number of platelets known as thrombocytopenia can result in easy bleeding and bruising, including frequent or severe nosebleeds and bleeding from the gums. CML can cause bone pain or
joint pain as the bone marrow expands when excess white blood cells build up. When more than the normal number of blood cells are in circulation, they get stored in the spleen and can cause it to become swollen or enlarged.

Patients may feel fullness in the belly or pain in the upper left side of the abdomen. In CML, white blood cells are increased, but they are not functional, and as a result, patients are more prone to infections and fever. If a patient shows no response to any treatment, then CML can result in the patient’s death due to progression of the disease’s blastic phase.

T reatment
Treatment of CML focuses on remission of blood cell counts as well as on remission at the molecular level. Loss of the Philadelphia chromosome is called a cytogenic response, and it is also desirable that normal chromosome returns to 0 percent Ph-positive cells. The blast crisis phase is very difficult to treat. This is because there is a very high count of immature white blood cells (leukemia cells).

The only proven curative treatment for CML is a bone marrow transplant or an allogenic stem cell transplant. Besides this, there are three major mainstays of treatment in CML:

- Tyrosine kinase inhibitors
- Myelosuppressive therapy
- Interferon alfa-2b therapy

Tyrosine Kinase Inhibitors. Imatinib mesylate is used for the treatment of chronic and accelerated leukemia and blast crises. Basically, it is the standard treatment of choice and first line of treatment in every patient with CML as it inhibits the progression of CML in a large number of patients (65–75 percent), which allows regrowth of the normal bone marrow stem cells and formation of mature blood cells. As few leukemic cells persist in almost all patients, the treatment with imatinib should be continued lifelong.

Dasatinib and nilotinib can be used for the treatment of the chronic phase in patients with imatinib-resistant CML. Studies have shown that it reduces the progression to the accelerated or blast phase. Bosutinib can be used for the treatment of chronic and accelerated as well as blast phases of CML.

Ponatinib is a tyrosine kinase inhibitor (TKI) used for chronic or blast phase T315I-positive cases for patients on whom imatinib, dasatinib, and nilotinib have no effect. In these patients, ponatinib has shown good treatment results. It is also effective in appropriate patients in whom no other TKI therapy is tolerated or indicated.

Myelosuppression. Hydroxyurea (Hydrea) is used along with TKIs to control high white blood cell count. Busulfan is a myelosuppressive agent that is also used to induce hematologic remission to achieve normal blood cell counts.

Omacetaxine is a protein translation inhibitor used for treatment of chronic- or accelerated-phase CML with resistance or intolerance to two or more TKIs and other chemotherapeutic agents.

Interferon-Alfa. Interferon-alfa was used as a first-line agent for treatment of CML, but nowadays, its main use is for the treatment of refractory cases in combination with newer drugs. It is also used for the treatment of CML in pregnant women.

Bone Marrow and Stem Cell Transplant. This is the only known cure for CML, but it is mostly considered in patients who show resistance to imatinib and other TKIs or those who do not achieve normalization of blood cell counts. Transplantation is mostly done in the chronic phase and after staging of patients as it has significant morbidity and mortality.

Prognosis
It depends on the phase of CML at diagnosis and extent of hematologic and cytogenetic remission as a response to treatment. Use of TKIs has affected survival rates drastically, especially in patients who achieve cytogenic response. Survival rates used to be three to five years from the time of diagnosis, but now the five-year survival rate is more than 90 percent.

This improvement is also due to earlier diagnosis and better supportive care. Patients who are diagnosed in the blast phase usually do not respond well to treatment, and their longevity is three to six months.

Ghulam Ishaq Khan
Columbia University
Qurratulain Muhammad Iqbal
Heart and Vascular Institute
**Leukemia, Hairy Cell**

Hairy cell leukemia is a unique lymphoid cancer that is characterized by an enlargement of the spleen (splenomegaly) and a reduction in the number of cells in peripheral blood (peripheral cytopenia). This form of leukemia is caused by five somatic mutations, one of which is the heterozygous mutation defined as V600E occurring in the BRAF gene. The biological significance of the other four somatic mutations remains unknown at this time. Previous studies have shown that the V600E BRAF mutation is present in patients with hairy cell leukemia but not in patients diagnosed with peripheral B-cell lymphoma or acute leukemia. The identification of the V600E mutation in the BRAF gene has helped in making an accurate diagnosis of hairy cell leukemia as well as in distinguishing this cancer from hairy cell leukemia-mimicking conditions, which include B-cell chronic lymphoproliferative disorder, splenic lymphoma, and splenic marginal-zone lymphoma.

The V600E mutation identified in hairy cell leukemia patients also occurs as a mutational hot spot in other cancers, such as papillary thyroid cancer and melanoma. However, the involvement of BRAF in hairy cell leukemia is mainly due to the inhibition of the mitogen-activated protein kinase (MAPK) pathways, in which the BRAF protein serves as a component. Polymerase chain reaction and Sanger sequencing of the BRAF gene have shown that the V600E mutation involves a T>A substitution at position 1860 of the DNA strand, which in turn results in an amino acid change from Val to Glu at position 600 of the polypeptide chain (V600E).

Previous studies have shown that, although the V600E BRAF mutation also occurs in other cancers, its frequency in hairy cell leukemia is significantly higher than those reported for other malignancies. For example, the research study led by Enrico Tiacci reported that the V600E mutation was detected in 100 percent of the mononuclear cells that were isolated from the peripheral blood of patients diagnosed with hairy cell leukemia. On the other hand, other studies have reported that the frequency of the V600E BRAF mutation in melanomas was approximately 50 percent, whereas that of papillary thyroid carcinomas was around 40 percent. There are also reports that describe the frequency of the V600E BRAF mutation in Langerhans cell histiocytosis as approximately 57 percent, whereas several articles have indicated that various solid tumors have a markedly lower frequency for the same mutation.

Despite the extensive assessment of mutations in hairy cell leukemia and the claims that the frequency of the V600E BRAF mutation is 100 percent, there are also reports that contradict these findings. Michelle Lavin and Paul Browne recently published a case report involving a patient with hairy cell leukemia that showed all the symptoms of the disorder, including the clinical, cytochemical, and immunophenotypic features yet did not harbor the V600E BRAF mutation. The patient described in the case report initially presented in 1981 with severe pancytopenia, splenomegaly, macular hemorrhage, and bone marrow infiltration, which were suggestive of a lymphoproliferative disorder. The patient then underwent splenectomy, which resolved the symptom of pancytopenia. Analysis of the splenic specimen indicated a diagnosis of hairy cell leukemia.

The patient remained in remission until October 2009, when the patient suffered a relapse, which
was detected using a bone marrow aspirate. Analysis of the bone marrow specimen showed the classical immunophenotypic features of hairy cell leukemia, which included the presence of CD11c, CD19, CD20, CD22, CD25, CD103, CD200, and FMC7 markers and the absence of CD5, CD10, CD23, and CD79b markers. However, allele-specific polymerase chain reaction indicated the absence of the V600E \textit{BRAF} mutation. A five-day treatment using subcutaneous cladribine resulted in the remission of clinical and immunophenotypic symptoms.

Three years later, the patient again developed another relapse, as indicated by the presence of neutropenia. In addition, the patient presented the same clinical and immunophenotypic features as the previous relapse. Allele-specific PCR was again performed, which continued to indicate the absence of the V600E \textit{BRAF} mutation. A five-day treatment using subcutaneous cladribine resulted in the remission of clinical and immunophenotypic symptoms.

The case report also emphasizes the need to exercise caution in the diagnosis of a lymphoproliferative disorder. The absence of the V600E \textit{BRAF} mutation coupled with the occurrence of splenomegaly and severe pancytopenia may also indicate splenic lymphoma as well as splenic marginal-zone lymphoma. Thus, it would be most beneficial if the rest of the clinical, immunophenotypic, and cytochemical features of hairy cell leukemia were assessed in order to make a differential diagnosis of the condition despite the absence of the V600E \textit{BRAF} mutation.

Furthermore, the mere presence of a V600E mutation does not immediately indicate that a patient has hairy cell leukemia because this DNA variant also occurs in other types of neoplasms, such as solid tumors, acute lymphoblastic leukemia, Langerhans cell histiocytosis, and B-cell lymphoma. The burden of disease may also change in the absence of the V600E as additional tests and regular follow-up visits may be required in order to monitor the condition of the patient over time.

Rhea U. Vallente
PreventionGenetics, LLC

See Also: Genetics; Leukemia, Chronic Lymphocytic; Leukemia, Chronic Myelogenous; Leukemia & Lymphoma Society.

Further Readings
Leukemia & Lymphoma Society

The Leukemia & Lymphoma Society (LLS) of America is the largest voluntary organization dedicated to blood cancer. Their mission is twofold and includes curing leukemia, Hodgkin's disease, myeloma, and lymphoma while improving the quality of life of patients and their families. Rudolph and Antoinette de Villiers started an education and fund-raising organization in 1949 in the name of their son, Robert Roesler de Villiers, who died from leukemia when he was 16 years old, in the year 1944. The organization first changed its name to the Leukemia Society but was renamed in the 1960s as the Leukemia Society of America. The organization finally became the Leukemia & Lymphoma Society of America in the year 2000.

The LLS's key priorities aim to help blood cancer patients live longer and better lives. The key priorities include research; patient services; public policy; revenue, marketing, and field management; information technology; human resources; and finance. LLS's research aims to fund academic research and other special projects that advance the diagnosis and treatment of blood cancers. They specifically seek to support unmet research areas, including venture capitalists and pharmaceutical companies.

LLS aims to be the key source of information for patients and families through education and improved access to the latest treatment options and clinical trials. Public policy that efficiently reviews new treatments and accelerates the discovery of new treatments is a key priority of LLS.

Patients should also have quality care supported by their insurance coverage.

LLS's public policy initiative also includes supporting funding access for research of blood cancers. This leads to their next priorities—increasing public awareness of nonprofit research organizations and developing revenue growth for future research. Information technology is key to superior platforms that support research. LLS strives to hire, inspire, and train the best candidates for all positions. It seeks to expand diversity among all personnel. The final key priority is to reduce the time spent on preparation for researching and spend more on actual research by consolidating the forecasting and budgeting needs spent prior to research. LLS has four primary programs for research.

The Specialized Center of Research supports collaboration across boundaries among universities, national organizations, and labs. The Translational Research Program aims to speed up the process from promising findings in the laboratory to actual treatments and prevention measures. The Career Development Program offers stipends to new investigators so that they may devote themselves to blood cancer research. The Therapy Acceleration Program assists with bringing treatment to more patients in a faster manner by funding and supporting researchers so that they may get closer to the final product stage. LLS also offers research grants. While a number of them are not currently accepting applications (i.e., Translational Research Program, Specialized Center of Research Program, the Screen to Lead Program, the New Idea Award, the Quest for Cures, and the MPN Challenge Grant), two opportunities are being made available: the Career Development Program and the Therapy Acceleration Program.

The Career Development Program offers the opportunity to participate in basic clinical or translational research. This award changes with the various stages of the researcher's career. At the scholar level, the award is $110,000 per year for five years. The researcher must be highly qualified and demonstrate original research. Substantial support for the research also should be provided by a national organization, and the researcher should be at the independent faculty level or equivalent.

The Scholar in Clinical Research award is $110,000 per year for five years and is awarded to the...
researcher who is conducting original research that typically includes early-stage clinical trials that address prevention, diagnosis, or treatment of blood cancers. Equivalent support for the research also should be available from another organization. The Special Fellow award is $65,000 per year for two to three years.

The researcher must have completed at least two years of postdoctoral research but not more than four and one-half years. This research award aims to support the transition of the researcher from faculty to an independent research program. The Special Fellow in Clinical Research also awards $65,000 per year for two to three years. The researcher must hold a Ph.D. or M.D. (or equivalent) and must have completed at least two years of specialized clinical training in hematology or oncology. Evidence that the researcher's career will focus on preventing, diagnosing, or treating hematologic malignancies is required. The Fellow awards $55,000 per year for three years and is used to encourage researchers who have less than two years of postdoctoral research training.

The Therapy Acceleration Program is an initiative to speed up the development of blood cancer diagnostics and treatments. The primary focus is on projects that can change the standard of care for blood cancer patients. This program assists companies and clinical researchers alike. There are three divisions within the program: Academic Concierge, Biotechnology Accelerator, and Clinical Trials. The Academic Concierge Division supports development of projects that have clinical promise through partnering with companies that can manufacture treatment materials and with service providers that can participate in clinical studies. This department also assists in assembling the documentation required by the Food and Drug Administration (FDA) before any clinical trial can start.

The Biotechnology Accelerator Division invests in projects that demonstrate safety and efficacy for blood cancer patients that are new and novel approaches. The company seeking funding must demonstrate the therapeutic potential of the drug, capability of management and scientific staff, financial strength, freedom to operate, and well-designed strategies. The Clinical Trials Division helps patients gain access to clinical trials within the community. LLS plans to introduce a network of phase I II sites that will use new strategies to increase enrollment, most especially for underrepresented populations.

Jessica Anne Hammer
Independent Scholar

See Also: American Brain Tumor Association; Carcinoid Cancer Foundation; European CanCer Organisation; International Society for Cutaneous Lymphomas; Lymphoma Research Foundation of America.

Further Readings

Libya

Lying on the southern shores of the Mediterranean, Libya is a vast north African country, roughly the size of Alaska, yet with a population of only 6 million citizens. In terms of natural resources, Libya is a wealthy country, having the 10th-largest proven oil reserves in the world as well as substantial reserves of natural gas.

However, despite its oil wealth, Libya has serious economic problems. The economy is overly reliant on oil, which makes up about 97 percent of exports. Furthermore, the economy is heavily distorted, with about 70 percent of Libyans being employed by the state. Youth unemployment is high, at around 21 percent. Other chronic problems include mismanagement, corruption, and insufficient investment in infrastructure, education, and health care. Thus the country’s wealth does not reflect the rundown condition of many of its health care facilities.

Politically, the country is in turmoil with some describing it as being on the verge of becoming a failed state. Having barely recovered from the revolution in 2011, which toppled Col. Muammar Qaddafi, the country’s long-standing dictator, the
country’s frail democratic institutions have struggled to maintain control.

Nowadays, many Libyans pursue an urban sedentary lifestyle, with an attendant rise in diseases such as diabetes, hypertension, and other negative health factors, such as obesity and smoking. Yet, the country enjoys free public health care, a relatively high life expectancy, a low infant mortality rate, and an effective national immunization program. Since the early years following independence in 1951, many infectious diseases such typhoid, cholera, and malaria have been brought under control. Cancer, however, appears to be on the rise, possibly due to increased longevity among Libyans, or perhaps due to better diagnosis, or possibly other factors such as environmental pollution or lifestyle changes.

There is a lack of definitive nationwide statistics; however, in 2003 the population-based Benghazi Cancer Registry published its first data, revealing that the most common cancers among male patients were lung cancer at 19 percent, followed by colorectal at 10 percent, head and neck at 9 percent, and bladder cancer at 9 percent. Among women, the most common cancers were of the breast at 26 percent, followed by colon at 9 percent, uterus at 7 percent, and non-Hodgkin’s lymphoma at 5 percent. The overall cancer incidence for that year was reported as 118 and 95 per 100,000 for men and women, respectively.

In Sabratha, the National Cancer Institute published hospital-based data in 2007 that revealed the most common cancers among Libyan men were lung cancer at 17 percent, closely followed by colorectal cancer at 15 percent and prostate cancer at 14 percent. Over a quarter of cancers among Libyan men were tobacco related, a fact that underlines the need for an effective cancer prevention strategy.

Among Libyan women, the most common cancers were breast cancer at 35 percent, followed by colorectal cancer at 11 percent and lymphoma at 10 percent. Breast cancer patients in Libya tend to be relatively young (70 percent are younger than 50 years old), with more advanced tumors at diagnosis that exhibit a relatively aggressive course.

There are five cancer treatment facilities throughout the country, two of which are dedicated oncology centers, the National Cancer Institutes at Sabratha and Misrata. The other three facilities are the Oncology and Hematology Departments of Tripoli Medical Center, Benghazi Medical Center, and Tripoli Central Hospital. These three hospitals also have radiotherapy facilities. The country’s only working positron emission tomography (PET) scanner is at Tripoli Medical Center.

In general, the quality of care provided to cancer patients is still inadequate. While the latest chemotherapy drugs and biological therapies are generally available, the supply can be unreliable, with not infrequent shortages.

Furthermore, there are long-standing systemic problems in the health sector as in other sectors of the Libyan economy, which include a lack of investment, mismanagement, corruption, poor training, and emigration of many of the country’s brightest doctors. In particular, the country has a weak primary health care infrastructure.

As a result of these shortcomings, many Libyan citizens have shunned the public (and indeed also the private) health care sector, preferring instead to travel to neighboring countries such as Tunisia and Egypt for medical treatment. Other favored destinations include Jordan and Turkey, whereas the more well-off travel to western Europe for treatment.

An effective national cancer prevention strategy potentially would have a great impact on cancer incidences, particularly as the population of Libya is so young (half the population is under 24 years old), and therefore, modifiable risk factors (such as smoking and diet) can be altered. A World Health Organization (WHO) report issued in 2013 estimated the prevalence of smoking to be 49 percent among Libyan men and 1 percent among Libyan women.

However, a formal national cancer screening program does not yet exist, and patients are all too often diagnosed at a late stage, when the tumor has already spread to nearby tissues or distant organs, making curative treatment generally unfeasible.

This delay in diagnosis is compounded by several social and cultural factors, principally a reticence to seek medical advice. In what still is a conservative society, elderly individuals in particular may feel embarrassed to discuss certain medical complaints. Another reason is the lack of confidence that some have in the health care system, preferring to use herbal or alternative medicines.

In recent years, attempts have been made to raise public awareness through media campaigns especially about breast cancer and lung cancer.
Liver Cancer, Adult (Primary)

Liver cancer, also known as hepatic cancer, is a malignant tumor that grows on the surface or inside the liver. They arise either from the liver itself or from structures within the liver, including blood vessels or the bile duct, and are called primary liver cancer. These cancers are one of the most frequently diagnosed cancers globally and the second-leading cause of cancer death worldwide. Cancers of other organs of the body, like the lungs, kidneys, and intestines, that spread to the liver are known as metastatic or secondary liver cancer. They are more common than primary liver cancer.

Types of Primary Liver Cancer

Primary liver cancers in adults are mainly of two types. Hepatocellular carcinoma (HCC) is the most common type of primary liver cancer, accounting for approximately 75 percent of all primary liver cancers, and is also known as malignant hepatoma. It is formed by liver cells that become malignant. Cholangiocarcinoma is the cancerous growth that arises from the cells of the biliary duct system. There is also a variant type of HCC that consists of both HCC and cholangiocarcinoma.

Causes of Hepatocellular Carcinoma

HCC usually results secondary to cirrhosis, which is commonly caused by alcoholism or viral infections. Causes of liver cancer are viral infections like hepatitis B virus and hepatitis C virus (these infections are the main cause of liver cancer, accounting for more than 70 percent of HCC in the developing world), cirrhosis by any cause, alcoholism (the most common cause of cirrhosis in the developed world is alcohol abuse), aflatoxin B1 (it is a poison present in fungus grown on improperly stored nuts and grains), Wilson’s disease, chronic inflammation of the liver, hemochromatosis, alpha 1 antitrypsin deficiency, diabetes type 2, and obesity.

Epidemiology

Liver cancer is one of the leading causes of death worldwide. According to 2010 data, liver cancer resulted in 754,000 deaths, of which around 50 percent are as a result of Hepatitis C. HCC, the most common form of liver cancer, shows a specific
pattern, with 50 percent of HCC cases diagnosed mainly in China. HCC is more common where hepatic viral infections are more prevalent, which includes east Asia and sub-Saharan Africa. HCC is more common in men than women and seen in people age 50 or older.

**Signs and Symptoms of Hepatocellular Carcinoma**

Hepatocellular carcinoma is associated with weight loss, fever, anemia, back pain, abdominal mass, jaundice, itching, abdominal pain, and vomiting.

**Pathophysiology**

Viral infections cause HCC due to long-term inflammation, fibrosis, and especially, the resulting cirrhosis is the main cause of malignancy. Hepatitis B virus can cause HCC even without causing cirrhosis as viral genetic material when combined with hepatic cells can induce HCC. Chronic alcoholism also increases risk of HCC directly by affecting hepatocytes' genetic material and indirectly by causing cirrhosis. Basically, cirrhosis of any cause can lead to HCC, whether it is due to hemochromatosis (which is an iron overload disease with iron deposition in the liver, pancreas, and other body organs), primary biliary cirrhosis, or Wilson's disease (copper deposition disease). Aflatoxins are poisons produced by the fungi *Aspergillus flavus* and *Aspergillus parasiticus*. These fungi usually are present in improperly stored grains, nuts, and certain vegetables. In patients with hepatitis B infection, aflatoxin exposure increases more than three times the risk of HCC than without aflatoxin exposure.

**Diagnosis**

Different sorts of imaging techniques are used along with some blood tests to aid in the diagnosis of HCC, and these include a liver function test, an ultrasound of the abdomen, a computed tomography (CT) of the abdomen, magnetic resonance imaging (MRI), and alpha-fetoprotein (AFP); high levels of this tumor marker in the blood along with a more than two-centimeter mass in the liver on ultrasound is about 95 percent suggestive of HCC.

**Treatment**

There are various treatment options for HCC with pros and cons for every modality. Surgical resection of the mass is often the treatment of choice for patients with noncirrhotic livers as there are more chances of complications, especially liver failure, if the liver is cirrhotic. After resection of the tumor, the recurrence rate is more than 70 percent, and its reason could be new tumor formation or by metastatic spots spread from previous tumor mass. Liver transplantation is considered only in patients who are eligible for surgery and transplant. Around 30 percent of patients can undergo liver transplantation due to its strict criteria and late diagnosis of HCC. Percutaneous ablation is a nonsurgical treatment modality for HCC and can be done in various ways: chemical ablation through ethanol or acetic acid injection directly into the liver or radiofrequency ablation, which uses extremes of temperature to destroy the tumor. Microwaves, lasers, and cryotherapy can also be used to treat HCC, but radiofrequency ablation gives the best results with cures, but it has its own limitations. Usually, local chemotherapeutic agents are used in the treatment of HCC in which cytotoxic drugs, like doxorubicin or cisplatin, are administered into the arteries supplying the liver, which are then blocked by gelatin sponges. This procedure is known as trans-arterial chemoembolization. For the last few years, a new drug, named sorafenib, has been in use in various parts of the world for the treatment of unresectable HCC. It acts by inhibiting several kinase inhibitors, including tyrosine kinases, raf kinases, and intracellular serine or threonine kinases. It has many serious side effects, which is the reason it is used very cautiously in specific HCC cases. It gives better results when used along with doxorubicin. Radiotherapy is used mainly as targeted radiation to the tumor. Combined therapy with chemoembolization rather than only radiotherapy gives better results.

**Prognosis of Hepatocellular Carcinoma**

Prognosis of HCC depends on many factors, which include resectability of mass, spread of tumor, as well as success of treatment. Duration of survival after diagnosis is usually three to six months in the case of a tumor that cannot be completely removed. But nowadays, in these patients, there is improvement in survival due to new medications, especially sorafenib.

**Prevention of Hepatocellular Carcinoma**

The most successful prevention against HCC is hepatitis B vaccination. Other forms of prevention
include screening of high-risk individuals, screening of blood products before use for donation, and safe injection practices. All these measures decrease the risk of HCC as they decrease spread of hepatitis B and C, which are the most common causes of HCC. Controlling other risk factors, like reducing alcohol intake, weight reduction, and better control of diabetes, are also important ways to decrease incidence of HCC.

**Cholangiocarcinoma Overview**

It is also considered as primary liver cancer as it arises from the epithelial lining of the bile ducts, which drain bile from the liver into the intestine. It is a rare cancer as well as slow growing as compared to HCC.

**Epidemiology**

Cholangiocarcinoma is a relatively rare cancer, but its incidence is increasing since the last few decades. It is more common in Asian countries, especially Thailand, than in the Western world due to the presence of chronic parasitic infections. It is more common in men than women, and its risk also increases with age.

**Pathophysiology**

According to most schools of thought, it is considered as a carcinoma of epithelial cells of the biliary tract lining and develops through stages of hyperplasia, metaplasia, dysplasia, and then carcinoma. More than 90 percent of cholangiocarcinomas are adenocarcinomas.

**Risk Factors**

In most patients diagnosed with cholangiocarcinoma, there may be no risk factor, but in some patients, any one of these factors can be found: primary sclerosing cholangitis (PSC), an inflammatory disease of the bile ducts (according to studies, in patients with PSC, there is a lifetime risk of cholangiocarcinoma of up to 15 percent); congenital liver malformations including choledochal cyst, Caroli’s syndrome, biliary papillomatosis, and Lynch syndrome II; parasitic infections, such as liver flukes like *Opisthorchis viverrini* (usually seen in Thailand, Laos, and Malaysia) or *Clonorchis sinensis* (found in Japan, Korea, and Vietnam); patients with chronic liver disease, whether in the form of viral hepatitis (e.g., hepatitis B or hepatitis C), alcoholic liver disease, or cirrhosis of the liver due to other causes; human immunodeficiency virus (HIV) infection; hepatolithiasis, the presence of intrahepatic stones; and thorotrast exposure, which is a form of thorium dioxide that was used as a contrast medium in radiography.

**Types of Cholangiocarcinoma**

These types are according to the site of the tumor: intrahepatic, referring to tumors occurring in the bile ducts within the liver; extrahepatic, a tumor occurring in the ducts outside the liver; perihilar, when tumors occur at the site where the bile ducts exit the liver; and a Klatskin tumor, which occurs at the junction where the left and right hepatic ducts meet to form the common bile duct.

**Signs and Symptoms**

Prominent signs and symptoms of cholangiocarcinoma include fever, weight loss, abdominal pain, jaundice (yellowish discoloration of the skin and sclera in the eyes), generalized itching, sweating, hepatomegaly, tenderness in the right upper quadrant, ascites, and changes in the color of stool or urine.

**Diagnosis**

Cholangiocarcinoma is diagnosed through a combination of blood tests, imaging, endoscopy, and pathological examination of a specimen. A liver function test usually shows increased levels of conjugated bilirubin, alkaline phosphatase, and gamma glutamyl transferase in the blood. This whole pattern is called obstructive as it shows obstruction in the flow of bile. Serum CA 19-9 (carbohydrate antigen) and CEA (carcinoembryonic antigen) levels are also found to be elevated in most patients. Endoscopic retrograde cholangiopancreatography (ERCP) usually shows common bile duct stricture and dilation of the proximal common bile duct. Biopsy is the definitive diagnosis for cholangiocarcinoma. It can be done either by ERCP or laparoscopy. Other methods include ultrasound of the liver and biliary tree, a computed tomography (CT) scan, and magnetic resonance cholangiopancreatography (MRCP).

**Treatment**

Treatment of cholangiocarcinoma varies as to the stage at which the disease is diagnosed. It is
Liver Cancer, Adult (Primary)

a very deadly disease if the tumor is not removed completely from the body. Only in patients with early disease does the curative option of surgery work. These patients usually have no local or distal metastasis or lymph node involvement as well as no involvement of the portal vein. Distal cholangiocarcinomas are generally treated surgically with a Whipple procedure. Intrahepatic cholangiocarcinomas are treated with partial hepatectomy, whereas perihilar cholangiocarcinomas are usually not operable. If surgery is possible, patients are usually treated with an aggressive approach, often including removal of the gallbladder and potentially part of the liver.

Most patients with cholangiocarcinoma are diagnosed when it has already spread locally to other nearby organs or metastasized to distant parts of the body. At this stage, the disease is usually inoperable; therefore, adjuvant therapy with radiation, brachytherapy (internal radiotherapy), and chemotherapy are utilized to control the disease. These therapies are used in cases when whole tumor masses cannot be removed and tissue margins are positive after surgery. Chemotherapeutic agents usually in use are 5-fluorouracil with leucovorin or a combination of gemcitabine with cisplatin, irinotecan, or capecitabine.

A new medicine, erlotinib, a tyrosine kinase inhibitor with possible good results, is still under study. Another important modality under study is photodynamic therapy, which has shown improved survival as well as quality of life. In this technique, light is applied endoscopically directly to the tumor, resulting in the release of toxic reactive oxygen species, causing killing of tumor cells.

**Prognosis**

Prognosis is related to the extent the tumor can be removed from the body. Most of the patients with cholangiocarcinoma present at a nonresectable stage and therefore have bad prognoses. Their five-year survival rate is 0 percent with average duration of survival of less than six months. In patients with no lymph node involvement, the five-year survival rate is better and more than 50 percent. Patients who have distal cholangiocarcinomas with no lymph node involvement usually have long-term survival rates ranging from 15 to 25 percent. Patients with intrahepatic cholangiocarcinomas after treatment by partial hepatectomy show a 22 to 60 percent survival rate, and it varies according to the involvement of the lymph nodes. Patients with perihilar cholangiocarcinoma, if diagnosed at an operable stage, usually show a five-year survival rate of 20 to 50 percent. The prognosis can be worse for patients with cholangiocarcinoma along with primary sclerosing cholangitis, as in these patients, cancer is diagnosed usually at a late stage.

Ghulam Ishaq Khan
*Columbia University*

Qurratulain Muhammad Iqbal
*Heart and Vascular Institute*

See Also: Chemotherapy; Liver Cancer, Childhood (Primary); Surgery; Technology, Imaging.

**Further Readings**


Primary liver cancer is rare in children, representing only about 1 percent of all childhood cancers. In contrast, adult primary liver cancer is the fifth-most common adult cancer worldwide. Fortunately, primary liver cancer is much more curable in children than it is in adults.

Hepatoblastoma and hepatocellular carcinoma are the two most common types of pediatric primary liver cancer, representing 43 and 23 percent, respectively, of primary childhood liver cancer. The liver is a common site of metastasis, and in children (as in adults) metastatic liver cancer is more common than primary liver cancer.

Other rare pediatric liver cancers include undifferentiated embryonal sarcoma of the liver (UESL), infantile choriocarcinoma of the liver, and epithelioid hemangiendothelioma.

Hepatoblastoma

Hepatoblastoma typically is seen in very young children of 3 years or less. In fact, it represents 90 percent of liver cancers in children under the age of four. The incidence of hepatoblastoma has been slowly increasing over the past four decades. From 1975 to 1983, it was 0.8 per year per million children, whereas from 2002 to 2009, the incidence doubled to 1.6 per year per million children.

One possible reason may lie in the growing number of babies who are born with very low birth weights. Low birth weight is a known risk factor for hepatoblastoma.

Other risk factors for hepatoblastoma include a number of genetic syndromes that are characterized mostly by excessive or uneven growth. These are seen in about 15 percent of hepatoblastoma patients and include Beckwith-Wiedemann syndrome and hemihyperplasia.

Familial adenomatous polyposis (FAP) is another known risk factor. This condition is thought to be due to a genetic mutation. In adults, familial adenomatous polyposis patients are at very high risk of developing colon cancer. Thus, hepatoblastoma survivors who have FAP need to be screened for colon cancer in adulthood.

Other rare genetic disorders associated with hepatoblastoma include Trisomy 18, Aicardi syndrome, and the glycogen storage diseases (which also predispose to hepatocellular carcinoma). Parental smoking is now known to increase the risk of hepatoblastoma in children.

The cell of origin of hepatoblastoma is thought to be the embryonal hepatoblast, a precursor to the normal liver cell, the hepatocyte. Histologically, there are a number of subtypes that are important because they have different outcomes. Pure fetal histology (PFH) hepatoblastoma is one such variant, which has an excellent outcome if completely resected. Conversely, the presence of undifferentiated (i.e., not resembling any normal tissue) small cells in the tumor indicates an unfavorable outcome.

Hepatoblastoma patients tend to be very young, usually in the first or second year of life. Typically, they present with an abdominal mass. Other symptoms include fever, vomiting, jaundice, and lethargy. They may also be anemic and failing to thrive (i.e., they are not gaining weight as expected). Symptoms and signs of associated syndromes may also be present.

Generally, the workup is similar for both hepatoblastoma and hepatocellular carcinoma. An abdominal ultrasound scan usually will be done to determine the location and size of the tumor. Other imaging modalities include computerized tomography (CT) scan or magnetic resonance imaging (MRI) to assess the local extent of the tumor and involvement of nearby lymph nodes. CT scans are also used to detect metastases, for example, in the lung. Magnetic resonance angiography (MRA) outlines important blood vessels and helps to assess resectability. Additional scans may be done in certain situations, for example, a nuclear bone scan to detect bone metastases.

The most important diagnostic test is a liver biopsy. This is taken surgically, and a pathologist will determine the type of liver cancer and the biological aggressiveness of the tumor.
Other valuable tests include the tumor marker alpha-fetoprotein (AFP). This is usually raised; however, a low alpha-fetoprotein may be associated with the undifferentiated small cell type of hepatoblastoma, which has a poor outcome.

AFP, though not very specific, is especially useful to detect recurrence of a cancer after initial therapy.

Blood tests may also be done to check the general condition of the patient and include liver enzyme tests to determine the amount of liver damage and a complete blood count (CBC) to look for anemia as well as other routine tests.

Once diagnosed, a cancer must be staged; that is, an assessment needs to be made as to how advanced the tumor is.

Liver cancers (both hepatoblastoma and hepatocellular carcinoma) are staged according to two systems. The first is the Pre-Treatment Tumor Extension (PRETEXT) system by the International Society for Pediatric Oncology Epithelial Liver Tumor Study Group (SIOPEL). This system uses presurgical criteria based on imaging by CT or MRI. There are four stages, PRETEXT 1 through 4, depending on the size and distribution of the tumor within the liver.

The second major staging system was designed by the Children’s Oncology Group (COG). The COG system uses mostly postsurgical data to stage the tumor. Stage I tumors are those that were completely resected; stage II tumors have microscopic residual deposits that were not removed; stage III tumors are those that are either unresectable or only partially resected or where there are positive (i.e., involved) lymph nodes. Stage IV tumors are those that have distant metastasis. Both staging systems predict prognosis well.

The treatment of liver cancer in childhood is best undertaken by specialist pediatric oncology centers under the care of a multidisciplinary team.

The cornerstone of management in pediatric liver cancer is surgery. The aim, wherever possible, is to excise the tumor completely, thereby maximizing the chance of a cure. Unfortunately, only about a third of hepatoblastomas are resectable at presentation. In this group, a favorable outcome can be expected. Surgery is by either resection or orthotopic liver transplantation, a technique whereby the

---

*Very high magnification micrograph of fibrolamellar hepatocellular carcinoma, one of two main subtypes of hepatocellular carcinoma. Fibrolamellar hepatocellular carcinoma was previously thought to have a better prognosis than classic or conventional hepatocellular carcinoma, but this has not been confirmed. (Wikimedia Commons)*
The patient’s liver is completely removed and the donor liver is positioned in its place.

In Europe, preoperative chemotherapy is used routinely, whereas in the United States, there is a tendency to delay chemotherapy until after surgery, whenever possible. Commonly used chemotherapy agents are doxorubicin, cisplatin, 5-fluorouracil, and vincristine. The current standard of care is a regimen that combines cisplatin, 5-fluorouracil, and vincristine. Chemotherapy has an important role in shrinking the tumor, thus making it easier to remove. Moreover, lung metastases may be eradicated by chemotherapy alone. Chemotherapy may also be used to ease symptoms in advanced cancer.

The role of radiotherapy is limited, but it may be useful to treat microscopic disease at the resection margin or to treat lung metastases that do not respond to chemotherapy or in the palliation of bone pain.

In general, the prognosis of hepatoblastoma is better than that of hepatocellular carcinoma. Patients have an overall five-year survival rate of about 70 percent. The most important prognostic factor is the stage of the tumor at presentation as this affects the resectability of the tumor. Another important factor is the histological subtype. As mentioned previously, patients with a pure fetal histology subtype have a much better prognosis than those with undifferentiated small cell histology. Other adverse prognostic factors include older age and a low alpha-fetoprotein level at presentation.

**Hepatocellular Carcinoma**

The predominant risk factor in the development of hepatocellular carcinoma is hepatitis B and C infection, especially in Asia, sub-Saharan Africa, and Melanesia, where hepatitis B and C are endemic. In these areas, hepatocellular carcinoma is more prevalent than hepatoblastoma. Papua New Guinea is reported to have the highest prevalence of hepatocellular carcinoma in the world, where it represents 8.5 percent of all childhood cancers. Some countries that have introduced universal hepatitis B vaccination have seen a significant decline in the incidence of hepatocellular carcinoma.

Hepatitis B infection is particularly important as it can be transmitted vertically from mother to baby. Hepatitis C infection is not as important in children because it takes many years to cause cancer, so it is more relevant for adult hepatocellular carcinoma patients. Hepatocellular carcinoma often occurs on a background of liver cirrhosis, that is, liver damage due to underlying liver disease from a multitude of causes.

Boys have a higher chance of developing hepatocellular carcinoma. Other significant risk factors include genetic anomalies such as biliary atresia, Alagille syndrome, and progressive familial intrahepatic cholestasis and tyrosinemia.

Histologically, hepatocellular carcinoma displays two main subtypes: classic or conventional hepatocellular carcinoma and fibrolamellar hepatocellular carcinoma. Fibrolamellar hepatocellular carcinoma was previously thought to have a better prognosis, but this has not been confirmed.

The clinical picture of hepatocellular carcinoma is very similar to hepatoblastoma, although children with hepatocellular carcinoma are often older, usually 10 to 14 years old. The abdominal lump (due to enlargement of the liver) is often large and may be painful. As in hepatoblastoma, patients may complain of jaundice, itching, nausea, and vomiting. There may also be other nonspecific symptoms, such as a loss of appetite or a reduction in weight. In young children, a failure to thrive may be noted. Symptoms due to metastatic disease may also be present, for example, bone pain or chest symptoms. Patients with underlying chronic liver disease may notice a change in their usual symptoms.

The workup for hepatocellular carcinoma is essentially the same as in hepatoblastoma. AFP is raised in 50 percent of cases. Vitamin B12 binding protein is a useful tumor marker in the fibrolamellar variant. A viral screen to look for associated hepatitis B and C is necessary.

Staging for hepatocellular carcinoma is also the same as for hepatoblastoma. As in hepatoblastoma, surgery is the only treatment that is potentially curative. In hepatocellular carcinoma, it is particularly important to have complete resection of the primary tumor as adjuvant (i.e., postoperative) chemotherapy is not as effective. A chemotherapy regimen that is often tried is cisplatin with doxorubicin (PLADO).

Hepatocellular carcinoma patients with PRETEXT stage 1 tumors have a 44 percent five-year overall survival, whereas PRETEXT stage 4 patients have only an 8 percent five-year overall survival rate. Overall, hepatocellular carcinoma patients have a 42 percent five-year survival rate.
This compares less favorably to hepatoblastoma patients. Another important prognostic factor is the resection status of the tumor, that is, whether or not it was completely removed surgically. Complete resection is less likely in hepatocellular carcinoma compared to hepatoblastoma, possibly explaining the worse outcome in hepatocellular carcinoma patients generally. Unlike hepatoblastoma, hepatocellular carcinoma subtypes have not been shown to have different outcomes based on histology.

**Other Rare Childhood Primary Liver Cancers**

Other rarer pediatric liver cancers include uterine embryonal sarcoma of the liver (UESL) and infantile choriocarcinoma of the liver.

UESL is the third-most common liver tumor in children, comprising around 10 percent of cases. Typically, it affects children between the ages of 5 and 10. Patients tend to present with an abdominal mass, which may be painful, and vague symptoms such as fatigue.

It is usually an aggressive tumor that presents frequently with extensive local invasion and metastasis, often to the lung. Treatment is by surgery (where possible) and chemotherapy. Histopathologically, it needs to be differentiated from other tumors such as rhabdoid tumor of the liver and biliary tract rhabdomyosarcoma.

Infantile choriocarcinoma of the liver is very rare and is thought to arise from the placenta. Patients present in the first few months of life with an abdominal mass and are usually in serious condition due to a high risk of bleeding. The diagnosis can be made by a typical appearance on imaging and extremely high beta human chorionic gonadotropin levels with normal AFP. There is no need for a biopsy. Treatment is usually by chemotherapy followed by surgery. The mother may also be affected by metastases from the placenta.

Epithelioid hemangiendothelioma is a rare, low-grade malignancy of the blood vessels in the liver. Usually, symptoms include abdominal pain and weight loss. The treatment is surgical resection or transplantation, and the prognosis is generally good.

---

See Also: Childhood Cancers; Hepatitis B; Hepatocellular (Liver) Cancer, Adult (Primary); Hepatocellular (Liver) Cancer, Childhood (Primary); International Society of Paediatric Oncology; Surgery.

Further Readings


---

**Lombardi Comprehensive Cancer Center**

The Georgetown University Medical Center in 1970 authorized the establishment of a cancer center. The center was established with funds from the university, the federal government, and private sources. The founding director was John F. Potter, M.D. In 1974, in conjunction with Howard University, Lombardi became the 16th National Cancer Institute–designated comprehensive cancer center.
center. The facility has and continues to demonstrate significant growth in clinical and research faculty membership. Additionally, peer-reviewed funding for cancer research, treatment, education, and community outreach activities continues to increase.

The objective of Georgetown Lombardi was, and still is, to provide the most advanced treatments available to Lombardi patients and, ultimately, to find a cure for this devastating disease. The center maintains a commitment to the highest-quality patient care. In 2000, Georgetown University Hospital, in partnership with Lombardi, became part of MedStar Health, a nonprofit network of seven hospitals in the Washington, D.C., and Baltimore, Maryland, areas. This partnership ensures that patients have cutting-edge cancer care that is provided by dedicated cancer professionals in a supportive and caring setting. In addition, Georgetown Lombardi is a member of the Capital Breast Care Center (CBCC) to control the development of breast cancer. In addition, the center established a joint partnership with the University of the District of Columbia with the objective of establishing ways to increase cancer awareness and reduce cancer incidence among African Americans.

Georgetown Lombardi comprises more than 150 professionals in programs relating to breast cancer, cancer control, and molecular studies relating to the treatment of cancer at large. Recently, the center expanded its tissue-banking and clinical annotation capabilities to support systems biomedicine in collaboration with Indivumed GmbH. Also, the center launched the Georgetown Database of Cancer (G-DOC), a data integration platform and knowledge discovery system for the oncology and translational research communities.

To educate and train the leaders of tomorrow in cancer treatment and research are some of the core missions of the center. Toward this, the center has programs spanning from high school students to those with doctorates; the Tumor Biology Training Program is one of these programs.

Georgetown Lombardi treats almost every type of cancer but has emphasis on solid tumors and adult and pediatric hematologic cancers. According to the *U.S. News & World Report*, the center ranks among America’s 50 best hospitals in the area of cancer. Georgetown Lombardi offers the best advanced clinical technology and equipment, including Cyberknife, a system using radiation beams to manage tumors in the body that might have been deemed to be inoperable at one point in time.

A significant phase 1 clinical trials program brings potential new cancer therapies into the clinic; therefore, Lombardi physicians offer cancer patients access to the newest advances in cancer therapy.

The Jess and Mildred Fisher Center for Familial Cancer Research offers patients diagnosed or with a family history of hereditary cancers the opportunity to receive genetic counseling and testing.

Currently, Georgetown gets about $100 million every year in research grants. In addition, there are nearly 200 full-time faculty members, 220 ongoing clinical trials, and six established research programs. These programs include the Breast Cancer Research Program, which consists of faculty members working exclusively on finding a cure for breast cancer. This program is aligned with the Nina Hyde Center for Breast Cancer Research established in 1989 to concentrate on Lombardi’s breast cancer activities.

The Cancer Prevention and Control Program conducts research across the range of the cancer control process from risk factors and prevention through early detection to treatment and survivorship.

The Experimental Therapeutics Program is a comprehensive translational research program with the major mission of new drugs and target discoveries for cancer.

The center is credited with numerous achievements in the field of cancer in general. The Institute of Medicine (IOM) is one key group that should be explored in this particular case. Being a member of IOM is considered a high honor in the fields of health and medicine and includes participation of Lombardi researchers in the development of the human papillomavirus (HPV) vaccine and initiations of some of the first clinical trials to test anti-cancer vaccines, for example, the TRICOM vaccine.

To promote education and training in Georgetown, the center administers four master’s programs in tumor biology, health physics, and biostatistics. In addition, the center has a joint program with cancer genetics, epidemiology, and control in which a doctorate or a combined M.D. and Ph.D. in tumor biology is offered. Other scholarship opportunities
offered by the center are medical genetics fellowships, programs in the world of hematology, and end-of-life care plus tumor biology studies.

To enhance information dissemination, the center organizes a robust program of speakers and seminars that are presented by the best minds in the international cancer research field. In the same programs, the faculty, staff, and students of Lombardi are challenged and motivated. In addition, Georgetown Lombardi has several information dissemination methods in which research work on cancer is available to the public. These methods include publications, news, and media forums. Grants are made with different controls relating to social network approaches, disease risk reviews, and genetic testing needs. All solutions are designed to help review the general components that come with working in the field of solutions.

In addition to the center’s publications are the Lombardi Magazine and the annual report. Lombardi Magazine is produced twice a year for patients and their families, community members, and friends of Georgetown Lombardi Comprehensive Cancer Center. The annual report is an annual summary of the activities of the cancer center.

Michael Fox
Independent Scholar

See Also: Massey Cancer Center; Mayo Clinic Cancer Center; University of California, Los Angeles, Jonsson Comprehensive Cancer Center.

Further Readings


Lung Cancer, Non–Small Cell

There are three main types of non–small cell lung cancer (NSCLC): squamous cell carcinoma, adenocarcinoma, and large cell carcinoma. Approximately 85 to 90 percent of all lung cancers are NSCLC. The three main types are different in shape, chemical components, and size. However, prognosis and treatment for each of these is often similar. Squamous cell carcinomas account for 25 to 30 percent of all lung cancers. This cancer starts in the flat cells that line the inside airways of the lungs. Often linked to smoking, this cancer commonly is found near a bronchus in the middle of the lungs. Approximately 40 percent of all lung cancers are adenocarcinoma. This cancer starts in areas of the cells that secrete fluids like mucus. This type of cancer is found in nonsmokers, current smokers, and former smokers. More common in women, it is more likely to occur within the younger population than other forms of lung cancer. It is usually found in the outside parts of the lungs and grows slowly. This type of cancer is usually found before it has spread outside of the lungs. Because of this, people are more likely to have a better prognosis than with other forms of lung cancer. About 10 to 15 percent of lung cancers are large-cell carcinomas. This occurs anywhere in the lungs. It does tend to be difficult to treat as it spreads quickly.

Known risk factors associated with NSCLC include tobacco smoking, exposure to secondhand smoke, radon, asbestos, air pollution, personal or family history of lung cancer, exposure to arsenic in drinking water, and radiation therapy to the chest area. Smoking may account for 80 percent or more of lung cancer cases. Prior to the early 20th century, lung cancer was less common, before manufactured cigarettes. Cigars and pipes are nearly as likely to cause lung cancer. The more one smokes and the longer one smokes, the greater the chance of developing lung cancer. Living with a smoker (who smokes indoors) increases one’s risk for developing lung cancer by 20 to 30 percent. Radon naturally occurs in the environment. It is the second-leading cause of lung cancer in the United States. It is the leading cause of lung cancer in the nonsmoking population. Both smokers and nonsmokers have an increased risk of lung cancer when exposed to
Lung Cancer, Non–Small Cell

asbestos. Asbestos is found in multiple workplaces (i.e., mines, mills, textiles, shipyards, etc.). Air pollution, especially near heavy traffic areas, increases the risk of lung cancer. About 5 percent of lung cancer deaths may be from air pollution. People who have had radiation therapy to the chest area (i.e., breast cancer treatment, Hodgkin's disease treatment, etc.) have an increased risk for lung cancer as well. Lung cancer is more common in several parts of southeast Asia and South America, where arsenic in the drinking water is high. Genetic factors associated with lung cancer are being researched still. Preliminarly, changes in a chromosome have been linked to higher incidence of lung cancer, even in families who do not smoke or smoke very little.

Most of the time, lung cancers are not found until symptoms occur. Early diagnosis is linked to prognosis. The following are the most common symptoms: chronic cough (does not go away or worsens); chest pain (often worse when laughing, coughing, or deep breathing); hoarseness; loss of appetite; weight loss; blood in phlegm; shortness of breath; feeling tired; feeling weak; chronic infections (bronchitis and pneumonia); and wheezing. Once lung cancer has spread outside of the lungs, symptoms may include bone pain (hip and back); neurologic changes (headaches, weakness, numbness, dizziness, and seizures); jaundice; and lumps near the surface of the body.

If lung cancer is suspected, physicians typically start with a physical exam and a medical history. If risk factors are present, a number of tests may be conducted. Imaging tests consist of X-rays, magnetic fields, sound waves, or radioactive substances to create images of the body. A chest X-ray often is the first test ordered to look for masses or spots in the lungs. The computed tomography (CT) scan is more precise and can reveal size, shape, and position of any tumors present. It produces cross-sectional images instead of one dimensional, like a regular X-ray. A CT scan also can assist the physician during a biopsy procedure. Magnetic resonance imaging (MRI) scans are detailed like CT scans and produce images of soft tissue. An MRI is more likely to be used to look for cancer that has spread from the lungs to the spinal cord or brain. A positron emission tomography (PET) scan is useful if the physician suspects the cancer has spread from the lungs but the physician doesn't know where. PET scans are useful for the liver, bones, adrenal glands, and other organs. PET scans can reveal useful information about the whole body. A bone scan can be used to see if the cancer has moved into the bones. PET scans also can reveal this information, so a bone scan often is used to clarify or confirm information obtained.

If symptoms and any testing indicate NSCLC, the physician will utilize further tests for a definitive diagnosis. A sample of sputum (mucus coughed up from the lungs) is examined under a microscope to see if cancer cells are present. This test is referred to as sputum cytology, and typically, the sputum is collected in the morning three days in a row. A needle biopsy may be used to obtain tissue from a suspicious mass or area. Fine-needle aspiration biopsy uses a small, hollow needle, whereas core biopsies use a larger needle to remove one or more cores of tissue. Bronchoscopy uses a lighted, fiberoptic tube passed through the nose (or mouth) into the lungs. Small instruments are then moved through the tube to take samples of tissue that are then examined under a microscope. A bronchoscope also can be fitted with ultrasound to obtain internal pictures while inside the lung. This procedure is referred to as endobronchial ultrasound. An endoscopic esophageal ultrasound is the same procedure except that the images are obtained from the esophagus as the esophagus is close to lymph nodes. Therefore, this procedure can image and obtain biopsy samples if the physician suspects the cancer has spread to the lymph nodes.

There are four main treatments available after NSCLC has been found: surgery, radiation therapy, chemotherapy, and targeted therapy. Often, these treatments may be combined. The decisions regarding treatment involve the patient and the team of doctors, who may include a thoracic surgeon (a physician who uses surgery to treat diseases of the chest and lungs); a radiation oncologist (a physician who uses radiation therapy to treat cancer); a medical oncologist (a physician who uses medicine like chemotherapy to treat cancer); and a pulmonologist (a physician whose specialty is the medical treatment of lung diseases).

Jessica Anne Hammer
Independent Scholar

See Also: Lymphoma, Hodgkin's, Childhood; Mesothelioma, Childhood; Nasopharyngeal Cancer; Rectal Cancer; Salivary Gland Cancer.
**Lung Cancer, Small Cell**

Small cell lung cancer (SCLC) is also known as oat cell cancer, oat cell carcinoma, and small cell undifferentiated carcinoma. It begins in the cells lining the bronchi, bronchioles, or alveoli and spreads quickly to nearby lymph nodes and the areas between the lungs and other organs, including the brain, liver, and bones. It grows and spreads fast and can form large tumors. SCLC comprises approximately 15 percent of all cases of lung cancer and is usually found in older people, with an average age of 70 at diagnosis. This cancer is usually caused by smoking and is rarely found in nonsmokers. Most cases of this aggressive, deadly cancer could be prevented if people never smoke or stop smoking. This entry describes the two types of SCLC, symptoms, exams used to diagnose it, treatment, prognosis, risk factors, and prevention.

**Types and Symptoms**

Most cases of SCLC are classified as small cell carcinomas, but some are classified as combined small cell carcinomas, which contain at least 10 percent of other cell types, often neoplastic squamous or gland cells. SCLC is described as limited-stage disease if it is found only in the chest and extensive-stage disease if it has spread beyond the chest area.

Symptoms include bloody or rust-colored sputum (phlegm and spit); chest pain that is worse with coughing, laughing, or deep breaths; a chronic cough; loss of appetite; weight loss; shortness of breath; wheezing; hoarseness; fatigue; and chronic or recurring bronchitis or pneumonia. Patients might also experience facial swelling, fever, difficulty swallowing, weakness, pain in the back or hips, headache, weakness or numbness of an arm or a leg, dizziness, balance problems, seizures, jaundice, and lumps near the skin in the neck.

SCLC tumors also can cause several associated syndromes, although these syndromes can also be caused by other things. Nerve damage caused by tumors in the upper part of the lung can cause Horner syndrome, which is characterized by severe shoulder pain, drooping or weakness in one eyelid, a small pupil in that eye, and reduced sweating on that side of the face. Tumors in the upper part of the right lung may press on the vein that brings blood back from the head and arms to the heart and result in superior vena cava syndrome. Symptoms include swelling in the face, arms, neck, and upper chest, headaches, and dizziness. Tumors can also cause hormonal imbalances including the syndrome of inappropriate antidiuresis and Cushing’s syndrome.

**Exams and Tests for Diagnosis**

SCLC might be found during a general physical exam or from a chest X-ray. Listening with a stethoscope may help detect fluid around the lungs or a partially collapsed lung. A history of smoking may also suggest lung cancer. Additional tests for identifying lung cancer or looking for its spread to other tissues include computed tomography (CT) scans of the chest and upper abdomen, endobronchial ultrasound, endoscopic esophageal ultrasound, tests of cells in the sputum or fluid from around the lungs, radionuclide bone scans, brain magnetic resonance imagings (MRIs), bone marrow aspirate or biopsy, liver function tests, or positron emission tomography (PET) with radioactive sugar. Diagnosis of the type of lung cancer is based on the appearance of cells from the sputum, fluid from around the lungs, or from a biopsy. In SCLC, the cancer cells are derived from epithelial cells and are seen as many small cells with little cytoplasm, ill-defined borders, finely granular chromatin, few or absent nucleoli, and nuclear molding (nearby nuclei appear attached).

**Treatment**

Treatment of SCLC may include surgery, radiation therapy, chemotherapy, or palliative therapy.
Chemotherapy often is used because the cancer spreads quickly throughout the body. It rarely cures the cancer, but it can often extend lifetimes for at least a few months. Radiation therapy is used to help treat the cancer, but it also can be used to treat some of the symptoms because it can cause shrinking of the tumors, help relieve breathing problems and swelling, and help relieve pain from cancer that has spread to the bones. Patients with SCLC often receive prophylactic cranial irradiation (PCI, radiation treatment to the brain) because there is a high risk that this type of cancer will spread to the brain. Surgery might involve removing part or all of a lung and nearby lymph nodes, but it is most helpful only for early-stage cancers. In most cases, surgery is less helpful because the cancer usually has spread to other tissues before diagnosis. Palliative therapy to aid in breathing for SCLC patients includes endobronchial laser therapy or brachytherapy to relieve pressure caused by tumors that are blocking or compressing the bronchi. Stents (tubes) can be inserted to help keep the airway open. Catheters can be used to remove fluid that builds up in the chest cavity around the lungs.

Prognosis
SCLC is the most aggressive form of lung cancer and often spreads to the brain, liver, adrenal glands, or bones before it is diagnosed. Median survival without treatment is only two to four months after diagnosis. Treatment might prolong life by six to 12 months, but only a small percentage of patients survive beyond five years. Some cases are found before metastasis during examination for another disease in the chest (heart disease, pneumonia, etc.), and some of those cases can be treated early enough for a cure, but even then, the cancer often relapses.

Risk Factors
At least 80 percent of all lung cancer deaths are likely to be caused by smoking. SCLC is characteristically found in heavy smokers and is rarely found in people who never smoked. The risk increases with the amount of smoking, both the number of years and the number of cigarettes per day. Secondhand smoke is also a risk factor. Exposure to radon or asbestos can also increase the risk. Genetics may also play a role, but the key factor is smoking.

Prevention
Don’t smoke. Stop smoking. Avoid secondhand smoke. SCLC is an aggressive, deadly form of cancer that can be prevented in most cases by not smoking. Avoiding radon, diesel exhaust, and air pollution also can help prevent some cases. Although decreasing smoking in developing countries could prevent many cases of SCLC there in the next few decades, the increasing number of people taking up this terrible habit in developing countries will result in a large increase of people suffering and dying from preventable lung cancers in those countries.

Constance Jeffery
University of Illinois at Chicago

See Also: American Lung Association; Chemotherapy; Lung Cancer, Non–Small Cell; Radiation Therapy; Smoking and Society; Smoking Cessation.

Further Readings
immune suppression. Studies have also proved a relationship between the degree of immunosuppression and risk of developing non-Hodgkin’s lymphoma. Most acquired immunodeficiency syndrome (AIDS)-related lymphomas (ARLs) are high-grade, aggressive, B-cell tumors. In AIDS, the incidence of non-Hodgkin’s lymphoma (NHL), primary central nervous system lymphoma, and Hodgkin’s disease are all increased. Histologically, there are three common variants of lymphoma: diffuse, large B-cell non-Hodgkin’s lymphoma; B-cell immunoblastic lymphoma; and small, non-cleaved cell lymphoma, which can be either Burkitt’s or Burkitt’s-like.

ARLs can be divided into three types according to their distribution: systemic NHL; primary central nervous system lymphoma (PCNSL); and primary effusion lymphomas (body cavity lymphoma).

**Systemic Non-Hodgkin’s Lymphoma**

Systemic Non-Hodgkin’s lymphoma is the most common type of lymphoma seen in AIDS patients, and according to some studies, its incidence is in up to 80 percent of patients. NHL is present in 1 to 3 percent of HIV seropositive people as they also have immunosuppression to an extent that results in the development of lymphoma.

There has been a decline in the incidence with today’s treatment of HIV seropositive people with Highly Active Antiretroviral Therapy (HAART). Distribution of NHL around the globe follows the geographical spread of AIDS.

**Histopathology and Pathophysiology.** Looking at the histopathology, NHL is of the following two variants: small, noncleaved cell lymphoma, which can be Burkitt’s lymphoma or Burkitt’s-like lymphoma; and diffuse, large-cell lymphoma, which includes centroblastic lymphoma, immunoblastic lymphoma, and plasmablastic lymphoma of the oral cavity.

Development of NHLs involves various pathways in molecular pathogenesis, including activation of c-myc, seen in all AIDS patients with Burkitt’s lymphoma. P53 inactivation is found in 50 to 60 percent of patients and Epstein-Barr virus (EBV) infection in 30 to 50 percent. BCL-6 proto-oncogene is present in 20 percent of patients. Mutation of other protooncogenes like PAX5, RHO/TTF, and PIM1 can also be seen commonly in NHL.

**Risk Factors.** These include race (in the United States, its incidence is lower in blacks relative to whites), sex (in people with AIDS, systemic NHL seems to occur equally in both sexes), age (in children and adolescents who are infected with HIV, NHL is the most common malignant disorder), EBV infection, homosexual behavior, and intravenous (IV) drug abuse.

**Etiology.** The exact cause of NHL is not known in most patients, but presence of several factors is considered to be its cause. These are EBV infection, human herpesvirus 8 (HHV-8) infection, continuous B-cell stimulation, and immunodeficiency.

**Signs and Symptoms.** With systemic NHL, patients may have no symptoms or may present with symptoms according to the organ involved in addition to the presence of B symptoms, which include fever, weight loss of more than 10 percent, and night sweats. Other symptoms include feeling a lump in the body, pain in the right upper quadrant, jaundice, fullness in the left upper quadrant (due to an enlarged spleen), bloating, and early satiety.

**Diagnosis.** Diagnosis includes following blood tests, imaging studies, and histopathology techniques: complete blood count; complete metabolic panel; chest X-ray; computed tomography (CT) scan; positron emission tomography (PET) scan; biopsy of a lymph node; bone marrow biopsy; and immunophenotyping and flow cytometry for cell surface markers.

**Treatment.** Chemotherapy is the cornerstone for the treatment of NHL. Chemotherapeutic options commonly used include the following:

The CHOP regimen is the standard treatment regimen for NHL. The components of CHOP include cyclophosphamide, doxorubicin, vincristine, and prednisone. Studies have shown an increased rate of remission and improved survival when CHOP is used with HAART.

Second, the components of the dose-adjusted (DA)–EPOCH regimen include etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin. These chemotherapeutic agents are used in low concentrations for prolonged periods and therefore are less toxic than the CHOP regimen. This regimen has shown complete remission in
more than 70 percent of patients and overall survival of up to 53 months. With the EPOCH regimen, due to the emetogenic potential of HAART therapy, the therapy stops until the cycles of chemotherapy are complete.

Third, CNS prophylaxis, as a prophylaxis in NHL, is the only intrathecal methotrexate administered, but if CNS involvement is already present, then combined treatment of intrathecal treatment of methotrexate, cytarabine, and hydrocortisone is recommended.

Fourth, the components of a CDE regimen are cyclophosphamide, doxorubicin, and etoposide. The CDE regimen is another well-tolerated and effective regimen that can be given concomitantly with HAART. The regimen is given by continuous infusion over four days. Complete response occurs in 44 percent of patients, with an overall survival of 43 percent at two years.

Fifth, the components of the CODOX-M/IVAC regimen are cyclophosphamide, doxorubicin, high-dose methotrexate or ifosfamide, etoposide, and high-dose cytarabine. It is given with HAART and given for the treatment of aggressive lymphomas like AIDS-related Burkitt’s lymphoma when the CD4 count is less than 100. This regimen has shown a two-year disease-free survival rate in 60 percent of patients. Finally, there is treatment of lymphomatous meningitis: This involves administration of intrathecal cytarabine, methotrexate with leucovorin rescue, and whole-brain irradiation.

**Primary Central Nervous System Lymphoma**

This is defined as lymphoma limited to the cranial–spinal axis with no systemic disease. It usually remains confined to the central nervous system and eye. Also known as primary cerebral lymphoma, it is a form of NHL that is very rare in immunocompetent people, but now its incidence is increasing in immunocompetent as well as immunocompromised people, also for unknown reasons. It constitutes 20 percent of all lymphomas seen in AIDS patients.

**Epidemiology.** Primary central nervous system lymphoma (PCNSL) has been decreasing in incidence since the advent of HAART. In general, its incidence is 1,000 times more in patients with AIDS as compared to immunocompetent individuals.

**Histology and Pathophysiology.** PCNSLs usually have immunoblastic histology with tumor cells having EBV infection along with expression of LMP-1 in almost all patients. Most of the patients with PCNSL also have BCL-6 mutation as well as high levels of the BCL-2 protein. It is usually seen in patients with very low CD4 counts and severe immunosuppression.

**Signs and Symptoms.** These include headache, diplopia, blurred vision, monocular vision loss, dysphagia, confusion, vertigo, progressive dementia, facial hypoesthesia, muscular weakness, altered mental status, personality changes, apathy, seizure, and stupor.

**Diagnosis.** In a CT scan in half of patients with AIDS, PCNSL shows ring enhancement after intravenous contrast administration. Due to the rapid growth of the tumor, there is central necrosis, which leads to irregularity of enhancement. CT scans of the chest, abdomen, and pelvis also are done to exclude systemic involvement. Magnetic resonance imaging (MRI) shows meningeal enhancement and gives the better diagnostic yield, especially when done with intravenous contrast. In polymerase chain reaction (PCR), the presence of EBV DNA in cerebrospinal fluid is highly suggestive of primary cerebral lymphoma.

**Treatment.** The main treatment of PCNSL is radiotherapy in combination with steroids, but tumors recur in more than 90 percent of patients. Still, median survival in patients with AIDS is around 3.5 months. Surgical resection of the tumor is usually ineffective because of its depth. The addition of methotrexate plus folic acid along with radiation has shown improvement in survival rates from four months up to more than three years. Combined use of methotrexate and radiation increases the risk of leukoencephalopathy and dementia in patients more than 60 years old. Newer treatments, such as high-dose chemotherapy combined with a stem cell transplant, are proving to increase survival by years.

**Prognosis.** This tumor has very bad prognosis with median survival of less than three months in untreated patients. Prognosis is better in patients with CD4 counts more than 200 and with no concurrent opportunistic infections.
Adherence to HAART therapy and response to treatment with methotrexate with or without radiation are also important factors. Poor prognosis is related to many other factors, including age more than 50 years; performance status greater than one or Karnofsky performance status less than 70; increased serum level of lactate dehydrogenase; high concentrations of protein in cerebrospinal fluid; and involvement of periventricular, basal ganglia, brain stem, and cerebellum, that is, parts other than the cerebellum.

**Primary Effusion Lymphoma**
This is a rare AIDS-related NHL as compared to systemic NHL and PCNSL. It constitutes about 4 percent of ARL. HHV-8 is found in all patients with EBV coinfection in 90 to 100 percent of patients. It involves body cavities such as the pleural space, pericardium, and peritoneum and spreads along the serous membrane.

Primary effusion lymphomas (PELs) are almost always seen in males.

**Histopathology and Pathophysiology.** PEL cells are morphologically variable with a null lymphocyte immunophenotype with human herpesvirus (HHV)-8.

It involves expression of p27K1P1 and a high proliferative index. HHV-8-encoded viral cyclins are important in the pathogenesis as they induce progression of cell cycle from G1 to S phase.

**Signs and Symptoms.** Patients typically present with fever, night sweats, weight loss, and hepatosplenomegaly.

**Treatment and Prognosis.** There are no specific guidelines for PEL treatment. It is usually treated with combination CHOP and HAART. It has a very bad prognosis, with a median survival of three to six months.

**Complications Related to AIDS-Related Lymphomas**
Patients may develop complications related to ARLs or as a result of treatment. These include the following: bone marrow suppression leading to anemia, neutropenia, or thrombocytopenia; repeated infections due to neutropenia; pleural and pericardial effusions; superior vena cava syndrome; tumor lysis syndrome; and focal neurologic signs secondary to PCNSL, vertebral, or spinal masses. Additionally, tumors in the gastrointestinal tract may cause bleeding, obstruction, or perforation.

Ghulam Ishaq Khan  
*Columbia University*  
Qurratulain Muhammad Iqbal  
*Heart and Vascular Institute*

**See Also:** AIDS-Related Cancers; Kaposi's Sarcoma; Lymphoma, Burkitt's; Lymphoma, Hodgkin's, Adult; Lymphoma, Hodgkin's, Childhood; Lymphoma, Hodgkin's, During Pregnancy; Lymphoma, Non-Hodgkin's, Adult; Lymphoma, Non-Hodgkin's, Childhood; Lymphoma, Non-Hodgkin's, During Pregnancy; Lymphoma, Primary Central Nervous System; Lymphoma Research Foundation of America.

**Further Readings**

---

**Lymphoma, Burkitt’s**

Lymphomas are malignancy of lymphocytes, which are immune cells resulting in impaired immunity and increased risk of infection as lymphocytes help the body to fight against infection. There are two types of lymphomas; Hodgkin's and non-Hodgkin's lymphoma, mainly differentiated from each other by the presence of Reed–Sternberg cells. Burkitt’s lymphoma is a form of non-Hodgkin's B-cell lymphoma and was first discovered in Africa in 1958 by a British surgeon, Denis Parsons Burkitt. It is
also known as small, noncleaved cell lymphoma. It is relatively rare but one of the most destructive of all human malignancies in most of the world. It develops very rapidly and becomes fatal within a few months; therefore, prompt diagnosis and treatment are very important.

**Epidemiology**
Burkitt’s lymphoma is most common in children living in sub-Saharan Africa, where it is related to the Epstein–Barr virus (EBV) infection and chronic malaria. Burkitt’s lymphoma is also seen elsewhere, including the United States, and in these places, it is most likely to occur in people who have a compromised immune system or chromosomal defects. Increase in age also has a negative impact on prognosis. Burkitt’s lymphoma is more common in people infected with human immunodeficiency virus (HIV), and before worldwide use of highly active antiretroviral therapy (HAART), the incidence of Burkitt’s lymphoma was around 1,000 times more in HIV-positive people than in the general population. The North American form of Burkitt’s lymphoma is not linked to EBV.

**Pathophysiology**
It is characterized by the translocation and deregulation of the c-myc gene on chromosome 8, resulting in uncontrolled growth of B lymphocytes.

**Types of Burkitt’s Lymphoma**
In the World Health Organization classification, there are three types of Burkitt’s lymphoma:

- **Endemic Burkitt’s lymphoma** primarily affects African children mostly of four to seven years and is twice as common in boys as in girls. It is common in malaria-endemic regions of the world (e.g., equatorial Africa, Brazil, and Papua New Guinea). EBV infection is present in nearly all patients with Burkitt’s lymphoma. It is believed that chronic malaria decreases resistance to EBV. The disease usually involves jaw or other facial bones but can also affect the distal ileum, cecum, ovaries, kidney, or breast.

- **Sporadic Burkitt’s lymphoma** occurs worldwide and is the most common variant found in places where malaria is not very common. Sporadic lymphomas are rarely associated with EBV infection. Globally, the sporadic variant is 1 to 2 percent of adult lymphoma cases, while in the United States and western Europe, it accounts for up to 40 percent of pediatric lymphoma cases. The tumor cells have a similar appearance to the cancer cells of classical endemic Burkitt’s lymphoma. The common site involved is the ileocecal region, whereas the jaw is less commonly affected.

- **Immunodeficiency-associated variant** of Burkitt’s lymphoma is more commonly found in people with HIV/autoimmune deficiency syndrome (AIDS). It accounts for 30 to 40 percent of non-Hodgkin’s lymphoma in HIV patients and may be an AIDS-defining disease. It also can occur in people with congenital conditions that cause immune deficiency and in the setting of post-transplant patients who are taking immunosuppressive drugs.

Compared to the endemic type, the incidence of EBV infection is considerably lower in the other two types of Burkitt’s lymphoma. In the sporadic disease, EBV infection occurs in about 20 percent of the patients, while in the immunodeficiency-associated type, it occurs in about 30 to 40 percent.

**Symptoms**
The symptoms of Burkitt’s lymphoma depend on the type. The endemic (African) variant usually starts as tumors of the jaw or other facial bones.
It also can affect body organs and can spread to the central nervous system, causing nerve damage, weakness, and leg paralysis. Burkitt’s lymphoma may be noticed first as a swelling of the lymph nodes (glands) in the neck, groin, or under the arm. These swollen lymph nodes are most of the time painless but can grow very quickly.

The types more frequently seen in the United States—sporadic and immunodeficiency-associated—typically start in the bowel and form a massive tumor bulk in the abdomen, often with enormous involvement of the liver, spleen, and bone marrow. Patients with more than 25 percent bone marrow involvement are usually said to have Burkitt’s leukemia. These variants also can start in the ovaries, testes, or other organs and spread to the brain and spinal fluid. Symptoms associated with Burkitt’s lymphoma include the following:

- Loss of appetite
- Unexplained weight loss
- Fatigue
- Night sweats
- Unexplained fever
- Nausea and vomiting
- Change in bowel habits
- Abdominal pain
- Gastrointestinal bleeding
- Mass in the upper or lower jaw
- Headaches
- Vision problems due to cranial nerve involvement
- Paralysis of the legs and lower half of the body
- Painless lymph node enlargement

**Diagnosis**

As Burkitt’s lymphoma spreads rapidly, immediate diagnosis is essential in case of a patient presenting with suspicious signs and symptoms. Whole or part of an enlarged lymph node or other disease site is biopsied, which usually confirms or rules out Burkitt’s lymphoma. Additional tests for staging of the disease are done quickly to look for any life-threatening complications from the rapid tumor growth, and these tests may include the following:

- Complete blood count (CBC) with differential
- Coagulation studies
- Serum levels of electrolytes and uric acid
- Serum creatinine, lactate dehydrogenase (LDH), and beta 2 microglobulin levels
- Chest X-ray
- Computed tomographic (CT) imaging of the chest, abdomen, and pelvis
- Magnetic resonance imaging (MRI) of the head and spinal cord
- Positron emission tomography (PET) or gallium scan
- Bone marrow aspiration and biopsy
- Echocardiogram
- Examination of spinal fluid
- Kidney function test
- Liver function test
- Testing for HIV disease and hepatitis B
- Cytogenic studies
- Flow cytometry

**Complications**

Complications of the disease include metastasis (spread of the cancer) to various body organs such as the liver, spleen, bone marrow, ovaries, testes, and spinal fluid. Bone marrow and the central nervous system are considered as medical emergencies and require immediate diagnostic and therapeutic intervention.

Renal failure due to retroperitoneal disease and renal involvement are also problems, sometimes as a result of tumor lysis syndrome. Intestinal perforation is another possible complication.

Complications and side effects of radiation therapy or chemotherapy include the following:

- Anorexia
- Aplastic anemia
- Low platelet count
- Low white blood cell count
- Increased risk of infection
- Constipation and diarrhea
- Hair loss
- Mouth sores (mucositis), nausea and vomiting
- Weakness and fatigue

**Treatment**

Burkitt’s lymphoma is treated mainly with chemotherapy, which can be high dose in a short duration or long duration or in combination with other therapeutic options.
For intensive intravenous chemotherapy treatment, it is preferred if the patient stays in the hospital. As Burkitt's lymphoma can spread to the fluid surrounding the brain and spinal cord, chemotherapeutic drugs also may be injected directly into the cerebrospinal fluid, a treatment known as intrathecal chemotherapy. Examples of chemotherapeutic medicines that may be used in various combinations for Burkitt's lymphoma include cyclophosphamide (Cytoxan), cytarabine (Cytosar-U of Tarabine PFS), doxorubican (Adriamycin), etoposide (Etopophos, Toposar, and VePesid), methotrexate (Rheumatrex), and vincristine (Oncovin).

**Combination Therapies**
Intensive chemotherapy is used in combination with the monoclonal antibody rituximab (Rituxan), which sticks to proteins on cancer cells, causing the immune system to attack cancer cells; urate-oxidase enzymes (e.g., rasburicase); autologous stem cell transplantation, in which the patient’s stem cells are removed, stored, and returned to the body; radiation therapy; and steroid therapy. In some cases, surgery may be needed to remove parts of the intestine that are blocked, bleeding, or ruptured.

**Supportive Therapies**
Intravenous antibiotics are used for the treatment of neutropenic fevers. Growth factors also are given like granulocyte-macrophage colony stimulating factor to help with neutropenia. Prophylactic allopurinol and aggressive hydration with urine alkalization may prevent tumor lysis syndrome and uric acid nephropathy during chemotherapy. Other supportive therapies include platelets transfusion in case of thrombocytopenia and irradiated and leukodepleted red cell transfusion.

**Prognosis**
In children, prompt intensive chemotherapy usually cures Burkitt’s lymphoma, leading to long-term survival rates of 60 to 90 percent. In adult patients, results are more variable. Overall, prompt treatment is associated with long-term survival rates of 70 to 80 percent.

Prognosis mainly depends on the spread of lymphoma, response to treatment, and incidence of relapse. Survival may be less if it has already involved bone marrow or spinal fluid. Most of the relapses occur during the first year of treatment, but in a few patients, especially those with HIV infection, delayed relapses have also been reported. Failure to achieve complete remission is the worst prognostic sign. Most of the patients with relapse are usually treated with salvage therapy involving chemotherapeutic agents named DHAP (dexamethasone, cytarabine, cisplatin). Very few patients show response to salvage therapy and, in them, it is followed by high-dose chemotherapy treatment and bone marrow transplantation or autologous stem cell transplantation. Patients with no response to chemotherapy are managed with supportive care.

Ghulam Ishaq Khan  
*Columbia University*  
Qurratulain Muhammad Iqbal  
*Heart and Vascular Institute*

**See Also:** Chemotherapy; Lymphoma, AIDS-Related.

**Further Readings**


---

**Lymphoma, Hodgkin’s, Adult**

More than half of the cases of Hodgkin’s lymphoma in the United States involve individuals below the age of 35, making it the most common neoplasm affecting young adults, and the third leading cancer with the highest mortality. Improvements in treatment
options have significantly decreased the mortality rate of Hodgkin's lymphoma, including the five-year survival rate, which has been estimated to be at least 80 percent, and the cure rate calculated as more than 75 percent. Hodgkin's lymphoma is considered as the most favorable malignancy because of the availability of effective treatment options and higher survival rates, although these outcomes also increase the risk of recurrence as these cancer survivors live longer.

Applying state-of-the-art therapy, as well as regularly monitoring the condition of the patient after treatment could decrease the risks of recurrence of Hodgkin's lymphoma. These activities entail hospital visits, which could vary in frequency depending on the details of the patient's socioeconomic status, educational background, and income. Previous reports have shown that the outcomes of Hodgkin's lymphoma patients after treatment are generally poorer among individuals of lower socioeconomic status or those of non-white ethnicity.

According to Simone Oerlemans and colleagues, survivors of Hodgkin's lymphoma are at a higher risk of experiencing severe physical as well as psychosocial effects after cancer treatment; this in turn influences their quality of life. Social factors include the development of fatigue and mental depression; these survivors could also experience problems with their marriage or infertility. In terms of financial problems, survivors of Hodgkin's lymphoma often have to face issues with insurance and mortgages after completing cancer treatment.

Interestingly, the report of Simone Oerlemans et al. described that survivors of Hodgkin's lymphoma who underwent a combination of chemotherapy and irradiation were at higher risk of experiencing a worse quality of life. Their report showed that these survivors often develop additional conditions that render their posttreatment lives less comfortable, which include dyspnea, diarrhea, pain, and emotional instability. In addition, their study also showed that older adults and female patients with Hodgkin's lymphoma are more likely to experience worse quality of life after cancer treatment.

A research team led by Erlyn Smith conducted a study that assessed the relationship between socioeconomic characteristics and the risk for advanced stages of Hodgkin's lymphoma among adolescents and young adults. By reviewing the cases listed in the California Cancer Registry, the study identified a total of 7,343 cases of Hodgkin's lymphoma among patients from 15 to 40 years old. The results of the study showed that advanced stages of Hodgkin's lymphoma were more common among male adolescents and young adults than their female counterparts. There was also a higher incidence of Hodgkin's lymphoma among foreign-born patients compared to those who were born and raised in the United States.

The study also showed that there were more Hodgkin's lymphoma patients who were single than those who were married. In terms of financial situation, individuals of lower socioeconomic status were more likely to present with advanced stages of the malignancy upon medical consultation. There were also more Hodgkin's lymphoma patients without insurance coverage than those with insurance coverage. These findings thus indicate that insurance and other cost-related issues played critical roles in the frequency and likelihood that an individual would undergo screening for Hodgkin's lymphoma at an earlier time.

For individuals who have no insurance coverage, visiting a physician or requesting a screening test for Hodgkin's lymphoma was therefore highly unlikely because of the expenditures that these entail. Further delay in screening thus results in a later diagnosis of Hodgkin's disease at a more advanced stage. It is also important to note that when a patient is diagnosed with an advanced stage of Hodgkin's lymphoma, the treatment scheme that would be utilized for this particular patient would be more intense and aggressive than patients with early stages of the disease. In addition, more intense and aggressive treatments are much more expensive than the simpler treatment regimens for early stages of Hodgkin's lymphoma.

Socioeconomic profiling of Hodgkin's lymphoma in adults often identifies the major issues that need to be resolved in terms of providing health care to the general public. Previous reports have shown that age range of 18 to 34 years is associated with the highest number of individuals who have no health insurance. This finding supports the idea that better health plans need to be developed for this particular age-group in order to help decrease the risk of having Hodgkin's lymphoma that goes undetected.

Another possible explanation for the correlation between advanced Hodgkin's lymphoma and the age range of 18 to 34 years is that these individuals might have health insurance, yet screening tests
for this specific neoplasm or possibly any other type of cancer may not be covered by their insurance. This scenario is therefore as serious as not having health insurance because it still prevents an adult from seeking medical attention at a time when the first few symptoms appear. For example, individuals with Medicaid coverage generally experience the same financial difficulty in getting support to undergo various screening tests for Hodgkin’s lymphoma as the uninsured. These individuals therefore hesitate in consulting a physician because of their inability to pay the corresponding medical fees. There are also some analysts who wonder whether being uninsured and underinsured are the same in terms of receiving coverage for chronic diseases such as Hodgkin’s lymphoma.

An inverse correlation between socioeconomic status and the risk for receiving a diagnosis of Hodgkin’s lymphoma has been reported by several independent research studies. Individuals of low socioeconomic status are thus more likely to develop Hodgkin’s lymphoma, and by the time they have undergone testing, a more advanced stage of the malignancy is often detected. A similar correlation has also been reported between the survival of patients diagnosed with Hodgkin’s lymphoma, wherein individuals of higher socioeconomic levels have a greater chance of surviving the disease because they are well supported by their health insurance. These relationships may thus be useful in developing health care programs that would assist in conducting early diagnostic screening of patients as a preventive measure against Hodgkin’s lymphoma.

Rhea U. Vallente
PreventionGenetics, LLC

See Also: American Cancer Society; American Society of Hematology; Bone Marrow Transplants; Lymphoma, AIDS-Related; Lymphoma, Burkitt’s; Lymphoma, Non-Hodgkin’s, Adult; Lymphoma, Non-Hodgkin’s, Childhood; Lymphoma, Non-Hodgkin’s, During Pregnancy; Lymphoma, Primary Central Nervous System; Lymphoma Research Foundation of America; National Cancer Institute.

Further Readings
National Cancer Institute. “Hodgkin Lymphoma.”


Lymphoma, Hodgkin’s, Childhood

The majority of Hodgkin’s lymphoma cases are curable, often achieving remission after receiving treatment with multi-agent chemotherapy either in combination with irradiation or not. In patients with recurrent or refractory Hodgkin’s lymphoma, the use of salvage therapy results in long-term survival, ranging from 25 percent to 90 percent, depending on the influence of a number of risk factors. According to the 2009 guidelines on surveillance imaging issued by the National Comprehensive Cancer Network (NCCN), routine monitoring of Hodgkin’s lymphoma patients should be conducted during their first remission. However, the optimal approach in conducting the surveillance to detect the recurrence of Hodgkin’s lymphoma has not been established.

The general procedure in staging and in assessing the response of a patient with Hodgkin’s lymphoma to treatment is by conducting positron emission tomography (PET) using F-18-fluorodeoxyglucose (FDG), which is then often coupled with computed tomography (CT). Although this approach has been performed for several decades, its role and significance in the surveillance of patients with Hodgkin’s lymphoma during complete remission remains uncertain. In response to this dilemma, the NCCN has recently opposed the application of PET scans in patient surveillance, particularly when a number of reports have described the occurrence of false-positive radiographic findings. Although further studies validating the use of PET scans in patient surveillance are
warranted, this technique remains very useful in identifying most diseases at their earliest stages of progression. Surveillance radiography also entails additional expenditures as well as further exposure to radiation, not to mention referrals to specialists and the induction of anxiety in the patient and his or her immediate family.

A similar dilemma is also affecting pediatric patients with Hodgkin's lymphoma. Although the majority of pediatric Hodgkin's lymphoma cases are also curable, there is a growing concern regarding the risks of developing cancer due to exposure to radiation during diagnosis and treatment of the disease. There are also reports that have assessed the risk of developing secondary malignancies due to irradiation treatment. The typical surveillance schedule for a pediatric patient with Hodgkin's lymphoma involves imaging every three to five months during the first two years of remission, followed by yearly imaging for the next three to four years, depending on the patient's risk of disease recurrence.

Given the intensity of the irradiation dose that is generally used for imaging, and the expected growth and development that a child would still have to go through, it is therefore imperative to determine whether multiple exposures to posttreatment irradiation for surveillance is worthwhile. For families of pediatric cases with limited financial resources, surveillance imaging can be both a health hazard and an economic burden.

To address the dilemma regarding the safety of irradiation during surveillance imaging of Hodgkin's lymphoma cases during complete remission, estimations of the applied irradiation dose on specific organs as well as tissues could be performed. This allows the generation of a weighted sum of irradiation disease based on the sensitivity of the target organ and the rest of the neighboring organs that could be incidentally exposed during imaging. In a study conducted by S. C. Chawla and colleagues, a total of 248 pediatric patients with Hodgkin's lymphoma were retrospectively assessed in terms of the effective dose of radiation that has been applied during surveillance imaging.

The study showed that each pediatric patient received an average of 3.2 PET/CT scans for the disease, starting from the diagnosis to treatment. In addition, the average effective dose of each pediatric patient during a CT scan was 20.3 mSv, whereas for PET, the effective dose was 4.6 mSv and for PET/CT, 24.8 mSv. The total radiation dose that each pediatric patient received from the entire treatment scheme was 64.4 mSv using CT imaging, 14.5 mSv using PT imaging, and 78.9 mSv using PET/CT scans. Although these values show that CT scans utilize higher doses of irradiation, be it used as a single technique or in combination with PET, it is still possible that these estimations might reflect uncertainties because of the inter-individual variations in response to irradiation and chemotherapeutic drugs.

In order to more extensively assess the impact of surveillance imaging on pediatric patients with Hodgkin's lymphoma, a study led by Neha Rathore et al. investigated the radiation dosage employed in monitoring tests at their institution from 2000 to 2010. This prospective study identified a total of 99 pediatric patients that underwent therapy for Hodgkin’s lymphoma. Their records showed that during the first two years after therapy, pediatric patients who were determined to be in remission were subjected to an average of 11 surveillance tests, which ranged from 0 to 26.

Of the 99 pediatric patients included in the study, 13 had relapses, 11 of which occurred during the first five months after completion of treatment. Interestingly, the use of chest radiographs and CT and PET scans of the abdomen and pelvic region did not result in the identification of relapsed cases among the pediatric patients with Hodgkin's lymphoma. On the other hand, chest and neck CT scans, as well as chest and neck PET/CT scans resulted in the detection of relapsed Hodgkin's lymphoma.

Their study thus showed that only 17 scans out of a total of 1,358 resulted in the detection of a relapse. Based on this data, the proponents of the study concluded that surveillance monitoring could be ineffective in detecting relapse in Hodgkin's lymphoma, thus requiring a new method of monitoring disease recurrence in patients who have achieved complete remission. The results of the study also indicated that pediatric patients might be spending more than what is necessary, based on the findings that only approximately 1 percent of the imaging tests positively detected the recurrence of the disease. It is also possible that the low rate of detection of relapse might be due to the high cure rate of the treatment regimens, thus requiring less
imaging after multi-agent chemotherapy and radiation treatment. If the number of surveillance imaging tests were decreased, patients with Hodgkin's lymphoma would have a lower risk of developing a secondary malignancy due to the constant exposure to ionizing radiation.

Rhea U. Vallente
PreventionGenetics, LLC

See Also: Leukemia, Acute Lymphoblastic, Childhood; Lymphoma, Hodgkin’s, Adult; Lymphoma, Non-Hodgkin’s, Adult; Lymphoma, Non-Hodgkin’s, Childhood.

Further Readings

Lymphoma, Hodgkin’s, During Pregnancy

One of the most challenging scenarios involving Hodgkin’s lymphoma is defining the appropriate treatment regimen when the patient is pregnant. In past decades, Hodgkin’s lymphoma has been considered as a highly curable neoplasm that is generally treated using both chemotherapy and irradiation. Reports have shown that this treatment approach results in a high (approximately 87 percent) progression-free survival rate, even in the most unfavorable stages. The treatment also results in long-term survival, thus allowing young patients to experience and enjoy several more years of their lives, hopefully without having to deal with a relapse or recurrence of the disorder.

The optimal approach in treating a pregnant patient who has been diagnosed with Hodgkin’s lymphoma remains elusive, although some reports have been published in past decades that describe the effects of specific treatment settings on pregnancy and other pregnancy-related issues. To date, there are less than 20 reports that have specifically described the pregnancy outcomes and survival of pregnant Hodgkin’s lymphoma patients; these consist of case reports, case series, and case-controlled studies.

A review of the case reports shows that, as long as the treatment for Hodgkin’s lymphoma is conducted during the early stages of gestation, it is possible for the developing fetus to progress until full term and potentially be born without any gross morphological or anatomical abnormalities. These case reports describe pregnant patients who were diagnosed with Hodgkin’s lymphoma to have received either single-agent treatment or combination therapy. For single-agent treatment case reports, these generally involved the use of vinblastine during the first trimester, which resulted in either normal fetal development as well as a favorable response to the administered drug or the occurrence of fetal syndactyly or the fusion of two or more fingers or toes.

There are also case reports of combination therapies for pregnant women diagnosed with Hodgkin’s lymphoma. These treatments could consist of vinblastine that is administered in the second trimester (as Hodgkin’s lymphoma was diagnosed during that period) and subsequently with cyclophosphamide, which has been reported to result in a partial remission of Hodgkin’s lymphoma and the birth of a healthy full-term infant; however, the mother eventually progressed with the malignancy. Another case report has described the use of procarbazine and chlorambucil during the first trimester, which then resulted in normal fetal development. There is also another case report that utilized the combination of mechlorethamine, vincristine, procarbazine, and prednisone, which is collectively known as the MOPP treatment.

Case series reports generally present the findings of several cases that have been treated with the same medications for a specific disease. Hodgkin’s lymphoma case series reports show a spectrum of outcomes in relation to the options and outcomes of treatment for Hodgkin’s lymphoma during
pregnancy, ranging from a series showing spontaneous abortions and fetal malformations after MOPP treatment, or a combination of cyclophosphamide with irradiation, to normal, healthy infants after treatment with a combination of doxorubicin, bleomycin, vinblastine, and dacarbazine, which is also known as the ABVD treatment.

There are also case series reports that describe positive infant outcomes after treatment of pregnant Hodgkin’s lymphoma patients with COPP, MOPP, or a combination of MOPP and vinblastine during the last two trimesters. Another case series report that included newly diagnosed and relapsed pregnant patients with Hodgkin’s lymphoma of varying stages (stages I to III) showed complete remissions after irradiation during the 10th to the 30th week of gestation as well as patients that experienced a recurrence of the neoplasm after irradiation. Other pregnant patients decided on undergoing therapeutic abortion, whereas others deferred their therapy until their children were born. It is also possible for a pregnant patient with Hodgkin’s lymphoma to deliver a healthy infant while undergoing chemotherapy. Similarly, there are also case series reports that include patients who conceived while undergoing chemotherapy for Hodgkin’s lymphoma.

Unfortunately, there are very few case-controlled reports on concomitant pregnancy and Hodgkin’s lymphoma. One report consisted of a total of 21 patients that were treated with MOPP, irradiation, or both, which were then compared to 155 age-matched and stage-matched women who were not pregnant yet and were also diagnosed with Hodgkin’s lymphoma. Interestingly, the results showed that the long-term survival of patients belonging to both groups were similar. Another report that included 48 pregnant Hodgkin’s lymphoma patients and stage-matched, age-matched, and year of treatment-matched controls also showed similar long-term survival.

In a recent case-control study that investigated the fertility as well as gonadal function of female patients who underwent treatment for Hodgkin’s lymphoma, two cycles of ABVD in combination with gonadotropin-releasing hormone did not compromise the fertility of female patients of ages less than 45 years old. This finding was based on the observations gathered from measurements of hormone levels, symptoms of menopause, parameters that indicate the preservation of fertility, length and characteristics of the menstrual cycle, number of pregnancies, and number of children.

Based on this limited number of reports describing the outcomes of treatment of pregnant patients with Hodgkin’s lymphoma, it is therefore imperative that additional studies should be conducted to establish the effects of specific schemes on fetal development. Another component that also requires attention is whether a specific treatment for Hodgkin’s lymphoma remains as effective as that observed in a nonpregnant patient, be it a female or male. It is possible that other factors may also influence the success of every treatment plan, yet it is also important to determine the molecular mechanisms behind the success or failure of a specific treatment during pregnancy.

The ABVD treatment scheme seems to be safe when administered at any trimester, although the number of reports in the literature is limited, suggesting that moderate degrees of toxicity in the developing fetus might have gone undetected. It is therefore critical that additional data on patients with Hodgkin’s lymphoma who elected to proceed with their pregnancies be collected in order to generate more robust conclusions. It has been suggested that a central registry in which children who have been born to a parent with Hodgkin’s lymphoma be established to capture the details of the long-term effects of concomitant pregnancy and Hodgkin’s lymphoma.

Rhea U. Vallente
PreventionGenetics, LLC

See Also: Lymphoma, Non-Hodgkin’s, During Pregnancy.

Further Readings


Lymphoma, Non-Hodgkin’s, Adult

Non-Hodgkin's lymphomas (NHLs) are noncommunicable cancers of white blood cells (lymphocytes), affecting either B or T cells. These immune cells become abnormal, dividing uncontrollably, and fail to protect the body from disease. Eventually, these cells form tumors. Because lymphocytes are found throughout the body, NHL can start almost anywhere, especially in the lymph nodes. NHL can occur at any age and is often marked by enlarged lymph nodes, fever, and weight loss. NHLs are classified into fast-growing, aggressive types or slow-growing, indolent types. In 2014, the National Institutes of Health estimated 70,800 new cases and 18,990 deaths from NHL in the United States.

Types of NHL
NHLs are categorized by how quickly they grow. Indolent NHL grows slowly and tends to cause few symptoms. Aggressive NHL grows and spreads more quickly, and tends to cause severe symptoms. Over time, many indolent lymphomas become aggressive lymphomas. NHL starts in infection-fighting immune cells. B cell NHL includes Burkitt’s lymphoma, chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), diffuse large B cell lymphoma, follicular lymphoma, immunoblastic large cell lymphoma, mantle cell lymphoma, and precursor B lymphoblastic lymphoma. T cell NHL includes anaplastic large cell lymphoma, mycosis fungoides, and precursor T lymphoblastic lymphoma.

Risk Factors Associated With NHL
The specific causes of NHL are not completely clear and more research is needed. However, research shows that the following risk factors are associated with NHL: (1) a weakened immune system (such as an inherited immune disorder, an autoimmune disease, or use of immunosuppressive drugs following organ transplantation); (2) having certain types of infections such as human immunodeficiency virus (HIV), Epstein-Barr virus (EBV), Human T-cell leukemia/lymphoma virus type 1 (HTLV-1), hepatitis C virus (HCV), and the bacterium Helicobacter pylori; (3) celiac disease in which gluten intake results in an immune reaction; (4) age: although NHL can occur at any age, the propensity increases with age, with the majority affected being older than 60; (5) obesity; and (6) exposure to herbicides and other chemicals.

Signs and Symptoms of NHL
People affected by NHL might experience the following symptoms: coughing, trouble breathing, or chest pain; fever, pain, swelling, or abdominal feeling of fullness; soaking night sweats; swollen, painless lymph nodes in the neck, armpits, or groin; unexplained weight loss; and weakness and tiredness that do not go away. People experiencing these symptoms for longer than two weeks should see a doctor.

Diagnosis of NHL
A person with swollen lymph nodes or other symptoms associated with NHL should seek medical care immediately. A doctor can assess your personal and family medical history as well as perform the following exams and tests: (a) a physical exam for swollen lymph nodes, spleen, and/or liver; (b) blood or urine tests for presence and amounts of certain antibodies and number of white blood cells, as well as check for other cells and substances, such as lactate dehydrogenase (LDH); (c) chest X-rays or computerized tomography (CT scan) to search for signs of cancer; and (d) lymph node biopsy, performed by removing either an entire lymph node (excisional biopsy) or part of a lymph node (incisional biopsy). Since NHL usually starts in a lymph node, a lymph node biopsy is a significant conclusive way to diagnose it. From the lymph nodes, NHL can spread to other organs (such as the liver, lungs, bone, and bone marrow).

Staging of Non-Hodgkin’s Lymphoma
To establish the best treatment, a doctor determines NHL disease stage and severity. Such determinations may require a bone marrow biopsy or a spinal tap, tests that will identify potential presence of lymphoma cells in these tissues. Medical imaging technology (such as a CT scan, a magnetic resonance imaging [MRI] scan, ultrasound, or a positron-emission tomography [PET] scan) allows doctors to visualize a person's head, neck, chest, abdomen, or pelvis as well as lymph nodes, spleen, and liver for nucleus lentiformis mesencephali (nLM) cells. The prognostic group depends on which tissues contain cancer cells and how many different types of tissues are affected. If NHL is found outside the lymph nodes, the letter E (for extranodal disease)
is added. Additional notation is included if specific sites appear to be affected (such as H for liver, M for bone marrow, and others).

- **Stage I**: The NHL is in one lymph node group (Stage I), or is found only in one area of a single organ outside of the lymph system (Stage IE).
- **Stage II**: The NHL is found in two lymph node groups on the same side of the diaphragm (Stage II), or extends from a single group of lymph nodes into a nearby organ (Stage IIE).
- **Stage III**: The NHL is found in lymph nodes above and below the diaphragm (Stage III) or it may also have spread into an area or organ next to the lymph nodes (Stage IIIIE), into the spleen (Stage IIIS), or both (Stage IIISE).
- **Stage IV**: NHL is found in several parts of one or more organs or tissues, including lymph nodes, the liver, blood, or bone marrow.

The letters A or B are also added to describe disease symptoms.

- A: the patient does not have drenching night sweats, fevers, or weight loss.
- B: the patient has drenching night sweats, fevers, or weight loss.

**Prognosis and Treatment Strategies**
Immediate treatment is recommended because delay in treatment decreases prognosis. Chance of survival and treatment options mainly depends on the type of NHL, its stage, age and general health of the patient, growth, amount of LDH in the blood, or whether NHL is initially or recurrently diagnosed. Asymptomatic patients with indolent NHL may not require immediate treatment. Health is closely monitored (watchful waiting) and treatment is initiated when symptoms begin. A symptomatic patient with indolent NHL receives chemotherapy and biological therapy. Radiation therapy may be used for patients with Stage I or Stage II NHL. A patient with aggressive NHL is treated with chemotherapy and biological therapy. Radiation therapy may be used too. NHL that returns after treatment is relapse or recurrence. Relapse patients are treated with high doses of chemotherapy, radiation therapy, or both, followed by stem cell transplantation.

Marcos E. García-Ojeda
Arthur Durazo
University of California, Merced

**See Also**: American Cancer Society; American Society of Hematology; Bone Marrow Transplants; Lymphoma, AIDS-related; Lymphoma, Burkitt’s; Lymphoma, Hodgkin’s, Adult; Lymphoma, Non-Hodgkin’s, Childhood; Lymphoma, Non-Hodgkin’s, During Pregnancy; Lymphoma, Primary Central Nervous System; Lymphoma Research Foundation of America; National Cancer Institute

**Further Readings**


**Lymphoma, Non-Hodgkin’s, Childhood**

Non-Hodgkin’s lymphoma (NHL), or lymphoma in children, is a term for cancers of the lymphatic or lymphoid system. The lymphoid system is part of the immune system that protects the body from infections. B and T lymphocyte cells are found in lymph glands, the spleen, the tonsils, adenoids, and many other organs and tissues. In lymphoma it is B and T lymphocyte cells that are malignant.

There are more than a dozen types of NHL. The four most common types in children are Burkitt’s lymphoma, and diffuse large B-cell lymphoma, lymphoblastic lymphoma, and anaplastic large cell
Lymphoma, Non-Hodgkin’s, Childhood

There are other types of lymphoma that occur in children, which include lymphoproliferative disease and rare NHL. NHL accounts for about 7 percent of childhood cancer, with about 800 children and adolescents diagnosed in the United States every year. About twice as many boys as girls are diagnosed with a type of NHL.

Most causes of NHL are unknown, but it is known that B and T lymphocytes are prone to making mistakes or developing variations or mutations. Sometimes mutations can lead to new cells multiplying without older cells dying off, as is the normal process. These lymphocytes can grow locally in lymph nodes or tonsils or spread to distant sites in the body through the bloodstream or lymph vessels.

The following symptoms and signs may be caused by childhood NHL: trouble breathing; wheezing; coughing; high-pitched breathing sounds; swelling of the head, neck, upper body, or arms; trouble swallowing; painless swelling of the lymph nodes in the neck, underarms, stomach, or groin; a painless lump or swelling in the testicles; fever for no known reason; and weight loss for no known reason; and night sweats.

Clinicians use several tests to determine if a child has lymphoma. These tests include a physical and history, and biopsy. Biopsy may include an excisional biopsy for removal of an entire lymph node or lump of tissue, an incisional biopsy for removal of part of a lump, lymph node, or sample of tissue, a core biopsy with a wide needle or a fine-needle aspiration (FNA) biopsy. Also common is a bone marrow aspiration and biopsy or the removal of bone marrow, blood, and a small piece of bone by inserting a hollow needle. In children the needle is usually inserted in the hipbone rather than the breastbone.

Several factors affect prognosis and treatment options in childhood NHL. These factors include the age of the child, the type of lymphoma, the stage of the cancer, the number of places outside of the lymph nodes to which the cancer has spread, and whether the lymphoma has spread to the bone marrow or central nervous system. Other key factors include whether there are certain changes in the chromosomes, the type of initial treatment, whether the lymphoma responds to the initial treatment, and the child’s overall health.

After childhood NHL as been diagnosed, other tests are done to determine the stage of the disease. Stages I through IV, as in other cancers, are used as a determination. Childhood NHL is also described as either low-stage or high-stage. Treatment for childhood NHL is based on whether the cancer is low-stage or high-stage. Low-stage childhood NHL has not spread beyond the area in which it began. High-stage lymphoma has spread beyond the area in which it began. Stage I and stage II are usually considered low-stage and stage III and stage IV are usually considered high-stage.

Today referring pediatricians usually counsel parents to enroll their child in a clinical trial in which the standard treatment is one arm of a trial randomized with one to three arms which have different combinations or dose schedules. Most children are first enrolled in a phase III trial as part of the Children’s Oncology Group. A team of doctors and medical social staff are crucial as a team in treating a child or adolescent with childhood NHL. These team members usually include a pediatric hematologist/oncologist, a radiation oncologist, a pediatric surgeon, pediatric oncology nurses, social workers, and psychologists.

Four types of standard treatment are currently used in childhood NHL: chemotherapy, radiation therapy (in some patients), high-dose chemotherapy with stem cell transplant, and targeted therapy.

Cancer treatments for childhood NHL cause side effects months or even years after treatment has ended. These include physical problems, changes in learning, memory, thinking, and second or new types of cancers. In particular, girls who received radiation to the chest for childhood NHL are at much greater risk for breast cancer at an earlier age. For children with recurrent childhood NHL there is no standard treatment. Options usually include a different combination of chemotherapy, target therapy (kinase inhibitor or tyrosine kinase inhibitor), or high-dose chemotherapy with stem cell transplant.

The history of treatment of non-Hodgkin’s lymphoma in children has benefitted from the development of treatment of childhood acute lymphoblastic leukemia, which it is somewhat related. Some of the same chemotherapy drugs are used although surgery and radiation are usually key elements of treatment. Because it is a rare cancer among childhood cancers in general, it has been difficult to accrue many patients into clinical trials to test therapies. In the last 40 years the survival rate has increased over time for NHL in children from 45 percent to 88 percent in children younger than 15 years, and from 47 percent
Lymphoma, Non-Hodgkin’s, During Pregnancy

Hodgkin’s lymphoma is considered the most common hematologic neoplasm that occurs in pregnant women; reports show that its incidence rate ranges from 1:1,000 to 1:6,000. On the other hand, non-Hodgkin’s lymphoma rarely occurs during pregnancy, and its incidence has been estimated at 0.8 cases in every 100,000. This significantly low rate of occurrence when compared to females in the general population could be attributable to the hormone therapy conducted in the treatment of this particular disease. The exposure of a non-Hodgkin’s lymphoma patient to reproductive hormones in the course of gestation may enhance the immune system’s responses, which in turn decreases the risk of developing non-Hodgkin’s lymphoma.

Lymphoma development during pregnancy often occurs at an average of 24 weeks during gestation, and this has generally resulted in positive patient outcomes, with very small chances of experiencing maternal, as well as fetal complications. A variant of diffuse large B-cell lymphoma and accounting for approximately 2.5 percent of non-Hodgkin’s lymphomas is primary mediastinal large B-cell lymphoma. Interestingly, this condition occurs at a higher rate in young female adults, often close to the average age of 37 years. On the other hand, diffuse large B-cell lymphoma usually develops in the elderly population, more frequently in males.

Primary mediastinal large B-cell lymphoma initially occurs as a bulky tumor within the region of the mediastinum, thus resulting in signs of compression in the patient such as dyspnea and the superior vena cava syndrome. Half of the patients with primary mediastinal large B-cell lymphoma also present with pleural or pericardial effusion. In other cases of non-Hodgkin’s lymphoma occurring during pregnancy, other symptoms initially develop such as exudative pericarditis, which might have resulted from a connective tissue disorder, or possibly a metabolic disorder. It is also possible that exudative pericarditis might have been induced by myocarditis or a malignancy. Subsequent to the testing and the generation of a diagnosis of exudative pericarditis, a patient could then undergo an enlargement of lymph nodes, which also results in the compression of the neighboring organs. Previous studies have shown that rare cases involving primary cardiac lymphomas initially present as exudative pericarditis.

Based on these unique accounts of non-Hodgkin’s lymphoma during pregnancy, it is thus interesting to examine the factors that trigger its development during gestation. It has long been recognized that non-Hodgkin’s lymphoma is a complex, as well as heterogeneous group of lymphomas that are characterized by variations in etiology. Some non-Hodgkin’s lymphomas may thus develop as an indolent follicular type of lymphoma, whereas others would be characterized with aggressiveness such as that observed in diffuse large-cell lymphoma.

The overall incidence of non-Hodgkin’s lymphoma among women is approximately 30 percent lower than that observed in men. It has been suggested that estrogen, together with other reproductive hormones, might have played a role in reducing the risk of certain subtypes of non-Hodgkin’s lymphoma, including diffuse large-cell lymphoma. Aside from enhancing the immune response of
women, the production and/or exposure to reproductive hormones may increase the secretion of cytokines, triggering B cells to undergo differentiation, as well as proliferation. Exposure to reproductive hormones may include factors that are related to menstrual periods, pregnancy, and the application of exogenous hormones, including oral contraceptives and hormonal replacements for menopausal women.

A study that investigated the relationship between non-Hodgkin’s lymphoma and female reproductive factors showed that certain subtypes are more frequently observed in women as compared to men. For example, follicular lymphoma occurs at a similar frequency in both males and females, whereas diffuse large-cell lymphoma has a propensity for occurring in males. The mechanism behind this sex-related discrepancy in the incidence of diffuse large-cell lymphoma may be due to the higher levels of reproductive hormones in women as compared to men. It should also be noted that women have the capacity to undergo multiple pregnancies in their lifetimes and thus the reproductive hormones associated with gestation may have primed the cells of the body to be more resistant to changes in rates of proliferation.

The extended presence of reproductive hormones might have also induced cells to undergo cellular differentiation, thus preventing the accumulation of undifferentiated B cells, which is a hallmark feature of non-Hodgkin’s lymphomas. Research has also shown that the risk of developing non-Hodgkin’s lymphoma is influenced by the age at which the female patient reached menarche, or the actual age of the female patient at diagnosis, or the age of the female patient when she delivered her first child. The incidence of non-Hodgkin’s lymphoma is also influenced by the duration of hormone replacement...
therapy, wherein a female patient who received the synthetic hormone for a long period is less likely to develop the neoplasm, as compared to a woman that underwent hormone replacement therapy for a short period of time. The dosage of oral contraceptives utilized during therapy is, on the other hand, more strongly associated with the risk for developing non-Hodgkin's lymphoma. Unfortunately, the relationship between the incidence of follicular lymphoma and oral contraceptives has not been established; therefore, additional investigations on this correlation are warranted.

Previous studies have also looked into the effects of various reproduction-related physiological processes with the risk of developing non-Hodgkin's lymphoma. For example, one study examined if breastfeeding altered the propensity of women in developing this particular neoplasm. By conducting case-control studies, it has been established that women who had previously breastfed three or more children had a significantly lower chance of developing non-Hodgkin's lymphoma.

To better understand the inhibitory mechanism of reproductive hormones on the pathogenesis of non-Hodgkin's lymphoma, studies have assessed the immunologic status of female patients during pregnancy and compared these with non-pregnant patients, as well as their male counterparts. The results of these studies showed that an immunologic shift is essential in promoting the implantation of the developing embryo.

Furthermore, this enhanced immunologic capacity also helps in protecting the fetus from tissue rejection, as it acts as an additional allograft within the system of the female non-Hodgkin's patient. It has been postulated that this immunologic shift might have been induced by a continuous increase in the level of progesterone during pregnancy. Progesterone has the capacity of inhibiting helper T cells, which are responsible for eliciting a cell-mediated immune response that in turn activates the machinery for cell-mediated immune responses.

Rhea U. Vallente
PreventionGenetics, LLC

See Also: Lymphoma, Hodgkin's, Adult; Lymphoma, Hodgkin's, Childhood; Lymphoma, Hodgkin's, During Pregnancy; Lymphoma, Non-Hodgkin's, Adult;

Lymphoma, Non-Hodgkin's, Childhood; Lymphoma, Primary Central Nervous System.

Further Readings

Lymphoma, Primary Central Nervous System

Primary central nervous system lymphoma pertains to a subtype of non-Hodgkin's lymphoma that does not occur within the lymph nodes (extranodal) and thus develops within the components of the central nervous system, including the brain or eyes. Primary central nervous system lymphomas account for around 3 percent of reported primary tumors of the brain. In the case of immunocompetent patients, most of the primary central nervous system lymphomas are categorized as diffuse, large B-cell lymphomas, in accordance with the criteria established by the World Health Organization. The standard of care for patients diagnosed with primary central nervous system lymphoma consists of high doses of methotrexate or methotrexate-based formulations, administered either alone or in combination with whole-brain irradiation. Despite the established protocol in treating patients with this specific neoplasm, information on the molecular details of its pathogenesis is limited.

One of the major reasons for the scarcity of information on the molecular biology and genetics of primary central nervous system lymphoma is the difficulty in collecting tissue specimens that could be used in the analysis. The majority of the tissue samples from patients diagnosed with primary central nervous system lymphoma are derived from stereotactic biopsies. Another reason for the
limited knowledge on the molecular biology of primary central nervous system lymphomas is the short overall survival of patients, which, on average, ranges from two to five years. This average survival time is relatively short when compared to other subtypes of lymphomas. Clinicians have also speculated whether this characteristically short survival time is a reflection of the complexity of the molecular mechanisms involved in the development of primary central nervous system lymphomas. The detected MYD88 mutation represents the most common polymorphism in primary central nervous system lymphomas to date. The MYD88 gene encodes for a protein that acts as a signaling adaptor that is responsible for the activation of the NF-κB pathway, once the Toll-like receptor and interleukin-1 and interleukin-18 receptors have been activated. This genetic mutation results in an amino acid known as L265P, which involves the substitution of the amino acid lysine to the amino acid proline at position 265. Further analysis by independent researchers showed that this specific variant occurs at a lower frequency in other hematopoietic cancers, including chronic lymphocytic leukemia and lymphoid tissue lymphoma.

The identification of the MYD88 mutation in future cases will therefore assist in the diagnostic evaluation of patients and this will be very useful when a case presents symptoms that are highly similar to those of other lymphoid malignancies. The mutation involving the TBL1XR1 gene results in an amino acid change in the transducin-β-like 1 X-linked receptor 1, a regulatory protein that controls transcriptional activity and directly interacts with the corepressors of nuclear hormone receptors. The mutation in the TBL1XR1 gene could therefore result in the inhibition of specific pathways such as the Wnt pathway, although additional studies regarding this relationship are warranted.

A more recent study conducted by the same team reported additional mutations in primary central nervous system lymphoma specimens. These mutations were detected in a total of 37 genes, in which some played a major role in signaling pathways, in differentiation of the B cell lineage, and in the control of the cell cycle. The observation of novel mutations involving additional genes that were not reported in their previous study suggests that primary central nervous system lymphomas are a genetically heterogeneous group of neoplasms that also show similarities with other lymphoma subtypes. It appears that prior to the development of the tumor itself, the tissues involved in the pathogenesis of primary central nervous system lymphoma accrued single nucleotide mutations that altered specific cellular activities, including
cellular differentiation, proliferation, and signaling. The combination of mutations in various genes thus orchestrate a specific genomic scenario that triggers the cells to transform into the malignant type, which is then eventually detected using the clinical, histological, and biochemical diagnostic assays. The use of genetic screening, particularly using exome sequencing followed by Sanger sequencing, may thus help in the early detection of hallmark aberrations that commonly occur in primary central nervous system lymphomas and in the design and development of appropriate treatment regimens.

Rhea U. Vallente
PreventionGenetics, LLC

See Also: Lymphoma, Hodgkin's, Adult; Lymphoma, Hodgkin's, Childhood; Lymphoma, Hodgkin's, During Pregnancy; Lymphoma, Non-Hodgkin's, Adult; Lymphoma, Non-Hodgkin's, Childhood; Lymphoma, Non-Hodgkin's, During Pregnancy.

Further Readings

Lymphoma Research Foundation of America

The Lymphoma Research Foundation (LRF), currently headed by Steven J. Prince, the chair of the LRF board of directors, was formed in November 2001 after a merger between two independent organizations—the Cure for Lymphoma Foundation (CFL) in 1994 in New York to provide funding for research leading to treatments for patients suffering from various forms of lymphomas. The aim of the CFL foundation was to provide reliable support and educational materials to patients in order to access the available treatment options as electronic media was not widespread and the information resources for patients seeking support were limited. Jerry Freundlich served as the CFL president and on the LRF board of directors through 2003. He is presently an executive committee member. Barbara Freundlich served as the executive director of CFL for the first four years and is currently an active member of the board of directors.

The Lymphoma Research Foundation of America (LRFA) was founded in 1991 by Ellen Glesby Cohen, a sufferer of non-Hodgkin's lymphoma. As a patient, she was discouraged by the limited amount of information available on the disease and decided to start the LRFA to serve the needs of lymphoma patients and to create materials to educate newly diagnosed patients. The LRFA funded lymphoma-specific projects and awarded nearly $3 million to this cause. The LFRA also created a network of physicians and researchers who have made valuable contributions to this project. The Ellen Glesby Cohen Award is granted every year to an outstanding volunteer for public service in the lymphoma community.

The LRF is the largest nonprofit organization devoted exclusively to funding innovative treatments against lymphoma as well as promoting lymphoma research in the United States. The LRF also provides up-to-date information about the current research and treatment options on lymphomas to people and health care professionals. The mission of the LRF is to eradicate lymphoma and serve those touched by this disease. The LRF is dedicated to providing funds for biomedical research focusing on the origins of lymphomas, treatment methods, and identification of cures for lymphomas and to raising public awareness about the disease.

Since 1992, the LRF has awarded more than $50 million in the form of more than 300 grants, fellowships, and clinical development awards to understand, treat, and cure lymphomas. John P. Leonard, M.D., currently chairs the Scientific...
Advisory Board (SAB) of the LRF, which also includes 45 senior researchers with established leadership in the field of lymphoma research and patient care in the United States and Canada.

Research supported by the LRF, as stated in the research strategy, covers 67 forms of lymphomas. The LRF not only provides research grants but also supports young investigators undertaking important research projects. The LRF advances the development of therapeutics against lymphomas and funds translational research projects, applying knowledge gained from the basic sciences in clinical settings.

The foundation has a provision to fund a broad spectrum of grants supporting postdoctoral fellows, young investigators, and clinical career development awards, specifically targeting physician researchers. Apart from these, the LRF also supports key focused areas of lymphoma research through Disease Focus Area awards. These include senior investigator awards, correlative grants, planning grants, and experimental or developmental grants to explore novel scientific ideas targeting translational research. The LRF also provides grant funding for basic, translational, and early clinical research. Grants are selected for funding twice a year after a review by a panel of grant application reviewers made up of SAB members, who are experts in lymphoma research. The panel recommends the applications to the LRF board of directors for funding.

Another major important aspect of the LRF is to develop activities and resources to support and enhance the research focus on lymphomas. The LRF provides comprehensive service to lymphoma patients and information on disease-specific programs to more than 60,000 people each year. This information includes focused publications and Web sites dedicated to creating awareness about the disease, information on workshops, help lines, patient aid grants, podcasts, and conferences, as well as public policy and advocacy. The Clinical Trials Information Service initiated by the LRF provides up-to-date information to lymphoma patients on the investigational new treatments for lymphoma at cancer treatment centers across the United States.

The LRF also fosters collaborations and sharing of research ideas and knowledge by supporting meetings, workshops, and conferences. It extends its support via in-person meetings for physicians and health care professionals through the Lymphoma Rounds program, which provides a platform for local health care professionals to regularly meet to address issues related to the diagnosis and treatment of their lymphoma patients. Participants network, share best practices, and learn the latest information on new therapies and advances in the management of lymphoma through interactive case studies presented by lymphoma experts in their local areas. In addition, the LRF provides special in-person meetings of nurses caring for lymphoma patients to learn from the experiences of lymphoma experts.

The LRF offers a financial assistance program to help with the quality-of-life expenses for people undergoing lymphoma treatment. As an initiative to raise awareness about lymphomas and to generate funds, the LRF organizes the Lymphomathon program across the United States, which is a noncompetitive 5K walk, where survivors, family, friends, community members, and corporate teams walk to honor those who have suffered from lymphomas. The funds raised during the Lymphomathons are dedicated to the mission of the LRF.

Since 2003, the LRF has raised almost $11.7 million through Lymphomathons. The LRF also raises funds for research through donations and research rides. It encourages volunteers to communicate the voice of the lymphoma community to policy makers through its advocacy program. In July 2014, the LRF announced the launch of the Lymphoma Education and Advocacy Partners (LEAP), which is a coalition of foundations involved with funding in lymphoma research. LEAP includes the Cutaneous Lymphoma Foundation (CLF), the International Waldenstrom’s Macroglobulinemia Foundation (IWMF), the T-Cell Leukemia Lymphoma Foundation (TCLLF), and The Double Hit Lymphoma Foundation (TDHLF). LEAP will focus on public policies impacting health care and treatment options for lymphoma patients.

Poonam Balani
Independent Scholar

See Also: American Cancer Society; Leukemia & Lymphoma Society; Lymphoma, AIDS-Related; Lymphoma, Burkitt’s; Lymphoma, Hodgkin’s, Adult; Lymphoma, Hodgkin’s, Childhood; Lymphoma, Non-Hodgkin’s, Adult; Lymphoma, Non-Hodgkin’s, Childhood; Lymphoma, Non-Hodgkin’s, During Pregnancy.
Further Readings

Madagascar

Madagascar is an island nation located in the Indian Ocean off of the southeast coast of Africa. The island of Madagascar separated from the Indian subcontinent 88 million years ago, which allowed native flora and fauna to develop there in a state of relative isolation from the rest of the globe. Madagascar’s unique biodiversity makes it a popular destination for ecotourism. The island is the home of the Madagascar periwinkle, a native plant species with anticancer medicinal uses. Like many African nations, Madagascar has no cancer registry. Widespread poverty and ongoing political instability create obstacles for cancer diagnosis and treatment among the Malagasy population.

Madagascar is the fourth-largest island in the world with a population of 20 million people. It ranks among the poorest nations in the world, with two-thirds of the population living in poverty. The Madagascar economy consists largely of subsistence farming. Cash crops of vanilla, coffee, cocoa, sugarcane, and cloves are grown for export. Industries include meat and sugar processing, mining, and tourism.

People from Africa and Southeast Asia settled on the island of Madagascar between 400 B.C.E. and 1000 C.E. In the 19th century, the island was united under the Kingdom of Madagascar. Prior this monarchy, no government ruled the entire island. The monarchy ended in 1897 when Madagascar became a French colony, and the island became an independent nation in 1960.

Following independence from France, Madagascar retained the centralized French model of administration for its national health system. The new Malagasy constitution laid out a plan to decentralize the system, handing funding and decision-making power over to regional health centers. Health care in Madagascar is provided by the public and private sectors as well as traditional healers. The majority of health care facilities are publicly operated, and people choose providers based on the perception of quality, availability of medicines, the cost of care, and the proximity of health centers.

Historically, cancer rates in Madagascar have tended to be lower than those in developed countries because of the relative lack of lifestyle-related cancers. Smoking and alcohol use are less common in Madagascar than in Western countries, making alcohol-related and tobacco-related cancers less common as well. The traditional Malagasy diet is low in meat and animal fat and high in fruits and fiber, contributing to the relatively low incidence of colon and rectal cancers. However, these are on the rise as alcohol, tobacco, and processed foods become more widespread across Africa.

Prostate and lung cancers constitute the majority of cancer mortalities among men in Madagascar. Childhood hepatitis B infections are widespread
among the Malagasy population, and carriers can develop liver cancer later in life. There is also a significant incidence of urinary bladder cancer related to *Schistosoma haematobium* infections. Additional cancer mortalities among Malagasy men are attributable to esophagus, oral cavity, and colorectal cancers.

For Malagasy women, cancer mortalities are most often due to cervical cancer or breast cancer. Mortality rates for cervical cancer in Madagascar are inversely proportional to social status. Cancer mortalities are more common among lower-class women and rarer for the upper classes. The more affluent Malagasy women have better access to health care and can afford to travel to receive treatment, lowering their general risk of mortality from these cancers. Social barriers prevent access to cancer treatment among the population of Madagascar. With 50 percent of the population living below the poverty line, very few Malagasy citizens can afford access to cancer treatment. As a result, cancers tend to be both underdiagnosed and underreported in Madagascar. In 2012, GLOBOCAN estimated approximately 18,000 new cancer cases and approximately 13,000 cancer deaths. According to the indigenous form of Christianity in Madagascar, cancer and other diseases are often considered to be preordained by fate. Preventative measures can be considered both ineffectual and to go against the will of God.

The government of Madagascar considers malnutrition and human immunodeficiency virus (HIV) and acquired immune deficiency syndrome (AIDS; only 1 percent of the population is infected, a very low rate for Africa) to be the primary threats to public health on the island, and there is no comprehensive national strategy for treating cancer. The Madagascar Action Plan (MAP) set goals to improve health and nutrition in order to reduce poverty. A military coup jeopardized these plans in 2009. The international community refused to recognize the new government and has suspended aid to the country. This political crisis has contributed to sluggish economic growth, further reducing the average Malagasy citizen’s access to health care in the country.

Since 2009, the government has reduced its contribution to national health care, and the global economic crisis has lowered most family incomes. As of 2011, Madagascar had only one cancer treatment ward located in Joseph Ravoahangy Andrianavalona Hospital in the capital of Antananarivo. This cancer ward consists of 60 beds intended to serve the entire population of the island. If they can afford treatment, the largely rural agricultural Malagasy population must travel to the capital to see an oncologist.

In the 1950s, scientists discovered that the Madagascar periwinkle (*Catharanthus roseus*) produced anticancer substances. Established by the United States government, the Cancer Chemotherapy National Service Center (CCNSC) discovered the medicinal uses of the Madagascar periwinkle. This member of the dogbane family is native to Madagascar, and the medicines vinblastine and vincristine are derived from it. Vinblastine is used in the treatment of childhood leukemia, and vincristine is used to treat Hodgkin’s disease. Malagasy folk healers have used it to treat diabetes, dysentery, menstrual disorders, and toothaches.

Jessica A. Hutchins
Independent Scholar

See Also: Breast Cancer; Cervical Cancer; Colon Cancer; Disparities Within Nations (Elimination of Cancer); Esophageal Cancer; Hepatitis B; Liver Cancer, Adult (Primary); Oral Cavity Cancer, Lip and; Poverty; Prostate Cancer.

Further Readings


Malawi

The majority of cancers and deaths associated with cancer occur in developing countries. A 2030 global cancer death rate projection is estimated to reach 13.2 million as compared to 12.7 million in 2008. Many factors exist that make screening, diagnosis, treatment, surveillance, and follow-up of various cancers difficult in poor, underdeveloped countries in sub-Saharan Africa. With only two pathology laboratories in the entire country of Malawi, underreporting and misdiagnosis are major clinical barriers for adequate cancer care.

Annually, it is estimated that more than 8,000 new cases of cancer occur in Malawi. From 2007 to 2010, there were 18,946 new cancer cases registered. The majority were females and adults between the ages of 15 and 59. However, less than 18 percent of the cases had been confirmed with histology, about 33 percent were diagnosed clinically, and slightly less than 50 percent of the cases were based on minimal investigations and the clinical exam. Cervical cancer was the most common cancer among the females. Kaposi’s sarcoma comprised 50.7 percent of the cancer cases in males.

The leading risk factor for cancer deaths worldwide is tobacco use. About 25 percent of men smoke tobacco in sub-Saharan Africa. Seventy-one percent of global lung cancer deaths can be linked to smoking, yet lung cancer is less common in this region. Possible explanations for the surprising low rates of lung cancer could be the result of underreporting, misdiagnosis, or lack of affordability.

Most countries rely heavily on tobacco imports. However, Malawi’s economy is heavily supported by its tobacco exports and is one of the world’s most tobacco-dependent economies. A large percentage of Malawi’s total workforce is employed in tobacco farming or tobacco processing. Because of this reliance on tobacco, antismoking campaigns often are targeted by the large tobacco companies who effectively influence the population at large and the government about the potential loss of jobs and revenue.

As a result of the numerous studies connecting tobacco use with a multitude of diseases, tobacco advertisement and public use are more regulated in the United States than they are in Malawi. The Malawi government does not mandate that cigarette packages contain health warnings nor is tobacco use prohibited in government buildings, restaurants, and health care facilities. Furthermore, as of 2012, nicotine replacement products were not legally sold in Malawi.

In most developed nations, there are established cancer screening protocols for breast and colon cancers. Cervical cancer, however, is the only malignancy in Malawi for which a screening program exists. Approximately 1,600 women die each year from cervical cancer. In 2004, the Malawi Ministry of Health implemented recommendations for women age 30 to 50 that consisted of a screen and treat program for cervical cancer utilizing acetic acid visual inspection. Roughly 80 centers in Malawi now offer some type of treatment for cervical cancer that includes visual inspection, cryotherapy, loop electrosurgical excision, major surgery, or any combination of the above.

Even so, few women take advantage of the cervical cancer screenings, and when they do present for care, the cancer is usually too far advanced for surgical intervention. Knowledge of the perceived benefit and poor health literacy are possible explanations for this obvious disparity of cancer screening as proposed by a study done by Victoria Fort and colleagues. Per the study, women were more likely to get screened if they were seeking care for something else.

Although human papillomavirus (HPV) types 16 and 18 cause 70 percent of cervical cancers, little is known about the types affecting Malawi women. Though there are two vaccines available for cervical cancer prevention, the vaccines are not readily available in Malawi. The vaccines are indicated for girls and boys ages 9 to 26. Even though the two manufacturers that developed the HPV vaccine, Merck and Company and GlaxoSmithKline, have lowered the costs of the vaccine for developing countries, Malawi has yet to include the vaccine in its national immunization program. Malawi has only recently begun pilot programs to administer the vaccine to a small minority of girls between the ages of 9 and 13.

Per Katie Ports and her colleagues, lack of information regarding HPV vaccines and their relationship with preventing cervical cancer were barriers noted within their small study, yet the women were receptive to the idea of HPV vaccination once educated about its benefit. Women reported previous positive experiences with vaccines and expressed...
willingness and a sense of responsibility to keep their babies healthy from preventable diseases. Women were also more likely to accept recommendations if they were suggested by their doctor.

It is not known if antiretroviral therapy has helped to decrease the prevalence of acquired immune deficiency syndrome (AIDS)-linked cancers such as Kaposi's sarcoma, but this could be related to lack of access to widespread medication and treatment. In regard to esophageal cancers, it is believed that the cause arises from a mycotoxin found in maize and fumonisin along with smoking and alcohol consumption. Future studies are needed to determine how eliminating these possible contributors will affect the prevalence of cancer in Malawi.

Furthermore, lack of resources, access to care, and human immunodeficiency virus (HIV) burden are instrumental to the cancer devastation to the citizens of Malawi. Global aid, physician and community worker training, and education materials are needed to help improve outcomes. History has shown how nationwide immunization programs have affected disease outbreaks such as measles. This same public health module could be utilized in Malawi in regard to the HPV vaccine and cervical cancer prevention. The vaccine would be most beneficial if it were disseminated and advertised widely throughout the country and given at every potential opportunity.

The future health of Malawi in regard to cancer will depend upon specific improvements in screening, tissue sampling, and prevention. Infrastructure changes that include additional pathology labs and cytotechnologists are desperately needed to improve accuracy and resultant outcomes of cervical cancer, for example. Adopting other worldwide-accepted screening recommendations for disease entities such as breast and colon cancer are also logical next steps in improving cancer outcomes in Malawi.

Denise Hooks-Anderson
Saint Louis University

See Also: AIDS-Related Cancers; Cervical Cancer; Tobacco-Related Exposures.

Further Readings

Malaysia

The southeastern Asian nation officially termed Malaysia was composed in 1974 out of the federation of the three territories of Labuan, Kuala Lumpur, and Putrajaya. The modern Malaysian state is a constitutional monarchy composed of the three federal territories as well as 13 other Malaysian states. With regard to population, Malaysia is currently in the top 30 largest nations in the world with more than 30 million citizens.

Unlike many other nations who currently do not have national cancer registries, Malaysia has one of the most expansive and well-maintained cancer registry systems in the world. Whenever a cancer incidence is initially observed, Malaysian clinicians, hospitals, and laboratories quickly will send that information off to a national database where domestic trends and incidence rates can be studied by researchers. Such excellent cancer registries have proved invaluable in that nation’s battle against cancer, giving researchers the capability to track every single cancer case that is observed within any given year. For instance, researchers were able to use the data in Malaysia’s national cancer registry to deduce that there were approximately 46,048 incidences of cancer in the country in the year 2005.

Cancer is certainly a mounting problem for Malaysian society as nearly 8 million Malaysian citizens died in 2005 as a result of various cancer incidences. Cancer is currently in the top five leading causes of death for Malaysian citizens, and scientists expect this trend to increase consistently in the coming years. Public awareness in Malaysia regarding cancer, its symptoms, and risk factors is regarded as
Poor. In the small, nonurban villages that make up the nation’s countryside, Malaysian citizens know virtually nothing about the disease and what causes it. This lack of awareness extends even to urban communities in the country, however. In a recent study, undergraduate-level Malaysian university students were surveyed in an attempt to gauge their awareness and knowledge regarding cancer. The results of the study conveyed that nearly 95 percent of all students surveyed had what could be considered poor awareness regarding cancer, while 65 percent of all students surveyed had what could be considered poor knowledge concerning the disease.

Such poor public awareness leads to consistent increases in annual cancer incidences as a large portion of the Malaysian population is totally unaware of what behaviors to avoid in order to prevent the disease. If cancer risk behaviors such as smoking or heavy alcohol consumption cannot be adjusted in the Malaysian population due to lack of public awareness, then cancer incidence rates will continue to climb in the coming years.

However, there are other obstacles to cancer treatment in Malaysia besides a mere lack of public awareness, which include emotional obstacles, practical obstacles, and service obstacles. In a recent study that was conducted, researchers found that many Malaysians had emotional obstacles in the way of cancer screening and treatment, such as them being too afraid to go to the hospital or being too concerned that the doctor might find something that is seriously wrong. Other Malaysians explained they would be too shy to talk to a doctor regarding such matters. Related to practical obstacles, many Malaysians described not having enough time to go to the hospital, and with regard to service obstacles, many Malaysians avoid care facilities because they are concerned about being able to afford the costs of a medical visit.

Presently, the most prevalent forms of cancer in Malaysia are breast, bowel, cervical, liver, and prostate cancer. Bowel, lung, and prostate cancers are the most prevalent forms of cancer incidences in males in the country, while breast, cervical, and bowel
cancers are the most common incidences of cancer in females here. Current Malaysian cancer registry data reveals that, in general, cancer incidences are tangibly decreasing in the nation. For example, there were 46,048 cases of cancer diagnosed in Malaysia in 2005, while there were only 18,219 cases diagnosed only two years later in 2007. However, certain cancers are consistently gaining traction in the nation; incidences of breast and bowel cancer have been increasing steadily in the country over the past several years and are set to continue this trend.

Malaysia has several facilities in the country that can provide cancer treatment services, but the country is in need of more highly trained oncologists in order to better cope with the nation’s current incidences of cancer. It is currently estimated that there are just over 30 practicing oncologists operating in the entire nation, and this number will need to increase if the country is to adequately meet the needs of its cancer patients in the coming decades.

William M. Peaster
Independent Scholar

See Also: Breast Cancer; Cervical Cancer; Liver Cancer, Adult (Primary); Prostate Cancer.

Further Readings
Baba, A. A., B. M. Biswal, R. Ja’afar, and A. Zakaria. “Assessment of Knowledge, Attitude and Exposure to Oncology and Palliative Care in Undergraduate Medical Students: A Survey.” Medical Journal of Malaysia (March 2004).


Mali

The Republic of Mali is situated in west Africa. It is bordered on the north by Mauritania, on the north and east by Algeria, on the east by Niger, and on the south by Burkina Faso, Côte d’Ivoire, and Guinea. It is the 19th-most populous country in Africa and the 69th in the world, with an estimated population of 13.5 million. The official national language is French, and there are 66 living indigenous languages still spoken by respective ethnic groups. The most widely spoken ethnic languages include Bambara, Fula, Jula, and Senoufo. Each ethnic group has its own rich traditions of ethnomedicine. For example, a traditional healer who uses medicinal plants for treating cancers and other ailments is known as furakeland in Bambara, chafrrowo in Fula, and fi la-cha in Jula. The Department of Traditional Medicine in Mali has led research to develop improved traditional medicines that are sold in pharmacies alongside conventional medicines.

There are many traditional medicinal preparations used in Mali for treating cancers and associated conditions. Most of these incorporate the use of myriad local plant materials, many of which have shown medicinal properties in laboratory studies. For example, an aqueous extract of Ximenia americana, a medicinal plant used in Mali, demonstrated significant anticancer activity. Research also suggests that use of certain plants may actually help protect against cancers by reducing oxidative stress and stimulating enzymes and other processes that help the body fight carcinogens. For example, extracts from Malian medicinal plants such as Cussonia barteri, Glinus oppositifolius, and Lannea velutina demonstrated substantial antioxidant as well as antifungal, larvicidal, and molluscicidal
activities. Many other medicinal plants traditionally used in Mali, such as *Diospyros abyssinica*, *Crossopteryx febrifuga*, and *Parkia biglobosa*, also have demonstrated good antioxidant potential.

Medicinal plants are used traditionally in Mali to treat many health problems associated with cancers. For example, powdered *Biophytum petersianum* is used traditionally for treating different types of pain, as is *Cola cordifolia* and *Combretum molle*. *Opilia celtidifolia* is used traditionally for treating varied skin disorders.

There are serious deficiencies of modern pharmaceutical supplies, as opposed to traditional preparations, and in modern medical services for cancer and similar conditions in Mali. There is a relative shortage of doctors, with about 1,291, at a density of 0.889 per 10,000 population, and there are also about 1,067 licensed pharmacists in Mali, with a density of 0.74 per 10,000 population. Furthermore, according to the World Health Organization’s Health System Response and Capacity, as of 2010, there was no general availability of radiotherapy in the public health system in Mali, although chemotherapy was generally available.

Mali is a signatory to the Single Convention on Narcotic Drugs, Convention on Psychotropic Substances, and the United Nations Convention Against the Illicit Traffic in Narcotic Drugs and Psychotropic Substances; consequently, laws exist to control narcotic and psychotropic substances and precursors. Accordingly, the annual consumption of controlled substances is highly regulated to curtail abuse. Therefore, the annual consumption of morphine in 2010 was 0.011237 milligrams per capita (mg/capita), fentanyl was 0.021693 mg/capita, and phenobarbital was 7.044131 mg/capita. This creates a serious lack of access to basic pain relief that makes cancer experiences in Mali, particularly living with and dying from cancers, very different from elsewhere in the world.

Due, in part, to the shortage of medical services and supplies, health problems are endemic in Mali. The 10 leading causes of mortality, in rank order, are malaria, malnutrition, hypertension, trauma and accidents, human immunodeficiency virus (HIV) and acquired immune deficiency syndrome (AIDS), anemia, pneumonia, postpartum complications, pregnancy complications, and diarrhea. The average number of cancer cases annually are 120 per 100,000 of the population.

Cancers account for a substantial amount of disability and suffering among impacted populations. According to the World Health Organization’s disease and injury country estimates, according to the age-standardized, disability-adjusted life-year estimates for 2004, the ten most prevalent cancers in Mali were led by liver cancer at 395 per 100,000 of the population; stomach cancer at 318 per 100,000; cervical and uterine cancers at 200 per 100,000; breast cancer at 133 per 100,000; bladder cancer at 105 per 100,000; lymphomas at 81 per 100,000; colon and rectal cancers at 72 per 100,000; esophageal cancer at 44 per 100,000; leukemia at 40 per 100,000; and trachea, bronchial, and lung cancers at 33 per 100,000.

Modern medical supplies and services are generally, if available at all, in short supply in Mali. Both prescription and over-the-counter products are often unavailable. Consequently, health problems are endemic and limit development. For example, an estimated 140,000 people live with HIV in Mali, which ranks the country 27th highest in Africa and 40th highest in the world. In 2007, the mortality rate for HIV/AIDS was 47 per 100,000 of the population. Debate continues on the relative risks in Africa for respective cancer types for those infected with HIV. The mortality rate for tuberculosis was 81 per 100,000 population, and that for malaria was 201 per 100,000 of the population, while the mortality rate for cancers in 2009 was 166 per 100,000 of the population. Furthermore, according to the World Health Organization’s Global Health Observatory Data Repository, in 2008, the age-standardized estimates of deaths from all cancers were 106 per 100,000 of the population for males and 124 per 100,000 of the population for females. As a consequence, life expectancy is only 45.28 years, which ranks Mali as the 37th-highest country in Africa and the 208th in the world. There is a clear and urgent need for improved cancer awareness, early detection programs, and health services infrastructure in Mali.

Victor B. Stolberg
*Essex County College*

**See Also:** Burkina Faso; Côte d’Ivoire; Developing Countries; Guinea.

**Further Readings**
Diallo, D., A. Marston, C. Terreaux, Y. Toure, B. Smestad Paulsen, and K. Hostettmann. “Screening of
Malignant Fibrous Histiocytoma of Bone/Osteosarcoma

Osteosarcoma ranks as the most common malignancy involving bones and more frequently affects children and adolescents. However, osteosarcoma is generally considered as a rare cancer, accounting for less than 1 percent of all neoplasms occurring in the United States. Unfortunately, population-based information on the incidence of osteosarcoma and patient outcomes for this specific disorder is limited. Osteosarcoma in young individuals usually emerges in the metaphyses of the major bones of the lower limbs, including the femur, tibia, and humerus. Although this bone cancer most frequently affects adolescents, the elderly, particularly those within the age range of 70 to 80 years, are also often afflicted with this malignancy. Osteosarcoma of the elderly generally involves the axial bones or areas that were previously exposed to irradiation or harbored congenital bone abnormalities. Males also are more frequently affected by osteosarcoma than females.

Based on the information on the incidence of this neoplasm, it is therefore interesting to know whether there are other factors that are strongly associated with its occurrence in specific subpopulations. The first epidemiologic study on the incidence of osteosarcoma was conducted by the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute of the National Institutes of Health in Bethesda, Maryland. The program reviewed case reports of osteosarcoma from 1973 to 2004, from 17 cancer registries located around the United States. The incidence of osteosarcoma was also further classified into three age-groups, namely zero to 24, 25 to 59, and 60 years of age and greater, as well as according to sex, race or ethnicity, disease stage, pathological or histological subtype, and anatomical area involved. The races or ethnicities of the patients were classified into any of the following groups: white, black, American Indian, Alaskan Native, or Asian or Pacific Islander. In terms of pathological or histological subtype, the cases were categorized according to neoplasm occurrence in the patient (i.e., first, second, or third neoplasm) and the presence or absence of Paget’s disease.

The SEER study reviewed a total of 3,482 patients who had been diagnosed with osteosarcoma between 1973 and 2004. Interestingly, significant differences in the incidence as well as the survival rates of the osteosarcoma patients were observed. For example, the highest incidence of osteosarcoma in the youngest age interval (i.e., 0–24 years) was observed in the non-American races or ethnicities, which included the American Indians, Alaskan Natives, and Asian or Pacific Islanders. On the other hand, the highest incidence of osteosarcoma with Paget’s disease occurred in the elderly age-groups. Differences in the site of tumor occurrence also varied among the different age-groups. In addition, the survival rates of the patients diagnosed with osteosarcoma varied according to the anatomic site as well as the disease stage of the patient.

Despite the extensive information that was generated by the SEER program, additional issues emerged in the incidence, prognoses, and survival
rates in osteosarcoma. For example, despite the improvements in the treatment strategies for osteosarcoma, the survival rate of this malignancy remained at 70 percent for several years. This dilemma thus prompted analysts to further examine the details of the osteosarcoma cases, including the characteristics of the patients who developed this disorder. Saminathan Nathan and John Healey embarked on two major epidemiological studies on this rare bone malignancy by evaluating patient records on osteosarcoma from two national health registries of two countries. Furthermore, these records were also compared to those previously gathered from the SEER study.

The results of the study showed that survival rates were more reliable when gathered from a specific institution and not from a national health registry because it is possible that other critical data might have been left out during the collection of information. The investigation also showed that patients of Oriental descent (i.e., those coming from China, the Philippines, Japan, Kampuchea, Korea, and Vietnam) were strongly associated with good disease prognoses. The type of treatment applied to the osteosarcoma patient also influences the success in the therapeutic regimen as well as the survival rate. Interestingly, women are more likely to survive or show good prognoses than men. Elderly individuals within the 90-year age interval also have been associated with better treatment outcomes. Tumor characteristics such as being low grade, small sized, and intra-compartmentalized have also been strongly correlated with higher survival rates among osteosarcoma patients. Last, patients who underwent large resections were more likely to survive this bone malignancy compared to smaller-sized resections, such as forequarter or, in other cases, hindquarter amputations. Patients who developed single primary tumors were also associated with higher survival rates than patients who were observed to harbor several primary neoplasms.

In terms of socioeconomic and sociodemographic features, black patients showed a higher frequency of large neoplasms compared to the other ethnicities, although this specific subpopulation presented with similar survival rates as those of the Caucasians. The Oriental populations showed a higher propensity of developing osteosarcoma in their 90s, which then required wider resections despite the smaller size of their tumors. Interestingly, patients of Oriental background residing in the United States or in Singapore showed similar survival rates. In addition, the survival rate of patients with an Oriental background and residing in Singapore did not significantly vary from that of other ethnicities. One significant difference that was noted in the study was that the health care of the United States extensively varied among the states, whereas that of Singapore was uniform regardless of the site of medical consult within the country. Based on this observation, it is thus possible that the discrepancies in the survival rates and patient outcomes of osteosarcoma patients in the United States were due to differences in socioeconomic parameters. The prognosis of osteosarcoma patients is therefore affected by the ethnicity and the socioeconomic status of the patient. Furthermore, the observation that the patients of Oriental background showed similar survival rates in Singapore and the United States thus suggests that patients of Oriental background in the United States are more likely to show a more superior rate of survival.

Although these demographic studies have generated highly significant findings, it is also possible that genetic variations among ethnic groups also might have played a role in the discrepancies in survival rates of osteosarcoma patients. For example, the level of the enzyme alcohol dehydrogenase is significantly higher among individuals of Oriental background compared to Caucasians. This may in turn influence the metabolism of cyclophosphamide, which is the major chemotherapeutic drug administered to osteosarcoma patients, thus resulting in higher bioavailability in the tissues of the body. Additional studies relating to these discrepancies could further resolve the variations in survival rates and prognoses among osteosarcoma patients of various sociodemographic backgrounds.

Rhea U. Vallente
PreventionGenetics, LLC

See Also: Asian Diet; Bone Cancer, Osteosarcoma/Malignant Fibrous Histiocytoma; Malignant Fibrous Histiocytoma of Bone/Osteosarcoma.

Further Readings
Cancer drug marketing is becoming more common. Marketing may include anything from news releases to public service announcements to industry-sponsored health fairs, but advertisements are the mainstay of every campaign. Cancer patients are increasingly exposed to direct-to-consumer advertising (DTCA). While DTCA may educate patients about new treatments, critics argue misleading ads highlight benefits and downplay risks. This type of marketing also can negatively impact patients’ relationships with their physicians: Studies show 80 percent of physicians feel pressured to write prescriptions for advertised drugs, and 39 percent believe DTCA damages the physician–patient relationship. Physicians themselves are also targets of pharmaceutical industry-sponsored marketing and sales calls. Drug reps promote cancer treatments for off-label use; while marketing an off-label use to physicians is illegal, educating them about it is not. The practice is controversial and can harm patients. The World Health Organization has predicted a 50 percent increase in global cancer rates by 2020, and the Federal Drug Administration (FDA) has expedited the approval process for new cancer drugs. Together, growing need and increased treatment options will spawn even more advertisements as pharmaceutical companies compete for market share.

Patient-focused drug advertising is a long-contested marketing practice. DTCA, legal only in the United States and New Zealand, is any unsolicited promotional message appearing in popular media (television, print, or radio) informing audiences about prescription drugs. Direct mailings, brochures, and billboards are also considered DTCA. Drug ads have been appearing in newspapers since the 1700s, but they were largely unregulated. In 1906, Congress passed the Pure Food and Drug Act, which established truth in labeling and purity standards. The FDA was formed in 1938 and given authority over drugs, but the Federal Trade Commission regulated advertising. Oversight was transferred to the FDA in 1962, and a fair balance approach was adopted: Ads had to balance drugs’ benefits and risks. Most ads were physician directed until 1981, when a pneumonia vaccine ad ran in Reader’s Digest. Two years later, the first television commercial appeared. Following a brief moratorium to study DTCA’s potential ramifications, the FDA upheld the 1962 fair balance guidelines, requiring a full statement of risks and side effects. In 1997, the FDA relaxed the television ad rules. Now, DTCA only mentions a drug’s major side effects, while viewers are referred to other sources for additional information (Web site or toll-free number). While the FDA is supposed to review ads for accuracy and balance, it lacks the resources to do so. In 2001, the agency had only 30 people to review 34,000 ads. As a result, the pharmaceutical industry is largely self-regulating. It adheres to the rules established by its own trade group, the Pharmaceutical Research and Manufacturers of America (PhRMA). PhRMA maintains DTCA is educational, designed to stimulate conversation between patients and physicians, but a 2010 National Institute of Health report concluded DTCA is not an effective educational tool because it typically emphasizes benefit over risk.

Numerous studies have shown DTCA impacts physician prescribing behavior and physician–patient relationships, but few studies have focused exclusively on ads for cancer drugs. A survey of oncology nurse practitioners found 94 percent reported their patients had requested advertised drugs, with 40 percent experiencing up to five requests per week. A 2009 survey of cancer patients found 86 percent had seen DTCA. The majority of respondents believed ads presented information in a balanced fashion, were educational, and helped them have better discussions with their physicians, but 11 percent reported the ads made them less confident in their physicians’ clinical judgment. Perceptions were more favorable among those who had not gone to college. A 2000 study concluded cancer drug ads were the hardest to understand and had the least educational value. Similar results were reported in 2007: Researchers analyzing magazine ads for cancer drugs found them incredibly
difficult to read. The ads were also biased: Side effects were printed in a font size several millimeters smaller than benefit text. Misleading ads are common. AstraZeneca and TAP Pharmaceuticals violated the Prescription Drug Marketing Act while promoting their prostate cancer drugs (both companies pled guilty in 2005 and paid fines). In 2010, Dendreon was criticized for its Provenge marketing. The Center for Biologics Evaluation and Research argued ads overstated the efficacy of the prostate cancer drug and minimized its risk; the ads also distorted survival rates by failing to present them in context.

While DTCA has been studied extensively, direct-to-physician pharmaceutical marketing has received comparatively little attention even though it accounts for 80 percent of all drug promotion costs. Most marketing campaigns include drug ads in medical journals. A 2009 study found 21 percent of journal editors do not review ads before publication. Half of ads cite industry-sponsored research, failing to mention side effects or warnings. Researchers found journal ads were the third-most trusted source of drug information among physicians after drug reps and drug samples.

Physicians increasingly rely on drug reps for information about new treatments, drug interactions, and new uses for existing medicines. While it is illegal for drug companies to market medications for uses other than those approved by the FDA, physicians are not constrained by this law and can write prescriptions for any use they wish. Drug reps, however, need to educate physicians about off-label uses. In 2004 and 2006, Genentech was cited for inappropriate off-label promotion of Rituxan to treat cancers other than non-Hodgkin’s lymphoma, for which it had been approved. A 2007 lawsuit filed against Celgene Corporation charged the company with illegally promoting off-label use of two of its cancer drugs. A 2011 study found 75 percent of off-label recommendations lack evidence of benefit and expose patients to harm. Drug rep visits and education programs constitute the majority of physician-focused marketing costs, about $7 billion a year.

Marketing cancer drugs ensures that both patients and physicians learn about new treatments and new uses for existing drugs, but advertisements can be misleading. Many campaigns emphasize benefits but downplay risks. Sources other than industry-sponsored marketing materials should be consulted for balanced information about cancer drugs.

Barbara Cook Overton
Louisiana State University

See Also: Cancer Drugs, Costs and Benefits of; Drugs; Food and Drug Administration; Pharmaceutical Industry.

Further Readings

Marketing, Hospitals and Clinics

Cancer care marketing takes many forms. Hospitals and clinics endeavor to promote their services through a broad range of marketing activities including issuing news releases, producing public service announcements, staging health fairs, hosting educational forums, and advertising. Marketing efforts target several different audiences: patients and their families, physicians who refer patients for cancer care, and purchasing agents for managed care companies. Marketing cancer care to rural populations is particularly challenging. Partnering with local media to produce stories, while sometimes blurring the lines between news and promotion, is a common marketing tactic. Traditional advertising (television, radio, and print ads) is ubiquitous, but many campaigns have been criticized for misleading patients. Advertising is not stringently regulated, and emotional appeals often
promote unproven interventions, lack scientific evidence to support claims, misrepresent survival data, and downplay risks.

Marketing cancer care services is difficult for many reasons. The product is something no one wants: Most consumers ignore the topic of cancer unless they are personally impacted. This creates a barrier for marketers trying to reach potential customers, requiring multifaceted and multichannel campaigns. Messages must also be tailored for specific audiences: Referring physicians and patients, for example, have different information needs and evaluate messages differently. Research has shown physicians respond to messages communicating information about a hospital’s or clinic’s type and number of specialists, available nursing support, and new technologies or equipment. Physicians also value information about administration's responsiveness to requests or suggestions.

Patients, however, are attracted to hopeful messages that promote an attentive and caring medical staff, new treatments, and the possibility of a cure. Campaigns featuring cancer survivors’ testimonials are particularly effective. Patient-targeted media promotions often coincide with nationally recognized events like the Great American Smokeout and Breast Cancer Awareness Month. Other public relations activities include organizing health fairs and screenings, staging community education sessions, staffing cancer information hotlines, and hosting survivors’ celebrations. Rural populations, however, are not as responsive to mass-media campaigns. Research has shown generalized messages about cancer prevention and screening are not as effective as more personal, tailored communications. Campaigns employing local community leaders, business owners, and clergy carry more weight with this audience. This type of marketing is important because Americans living in rural communities underutilize screening services, delay seeking care, and suffer a disproportionate number of cancer deaths when compared with urban populations.

Many hospitals and clinics form partnerships with local media, ensuring important cancer stories get press coverage, but the distinction between marketing and news is often blurred. Press releases announcing new equipment or treatment options often run in local newspapers in their entirety. Critics argue press releases are positively skewed advertisements masquerading as news unless journalists balance claims with independently gathered information. Because press releases are not advertisements per se, the claims in them are not subject to regulatory oversight. Video news releases (VNRs) can also be misleading. A VNR is crafted to look like a television news story, but it promotes the services of a single hospital or clinic. Some hospitals pay for airtime, and their sponsorships guarantee a certain number of stories or VNRs will air on local newscasts each month.

While many hospital public relations departments produce VNRs in-house, some contract with news stations to provide video production services. Local reporters sometimes appear in the VNRs; while the reporters lend journalistic credibility, the marketers write and control the stories. VNRs’ sources are rarely disclosed, so viewers think they are watching real news. VNRs can increase awareness for a service or treatment that may be beneficial for cancer patients, especially in smaller media markets where television stations lack the resources to cover major events. Nonetheless, VNRs are marketing tools designed to win customers and seldom balance benefits with potential risks.

Traditional advertising is a key factor in most marketing campaigns. One of the most heavily
advertised service providers is Cancer Treatment Centers of America (CTCA). CTCA is a network of five for-profit hospitals with a strong media presence. Media kits with ready-made stories, interviews, and photos are regularly circulated to national publications like *Reader’s Digest* and *Newsweek*. Marketing also includes public radio underwriting, television commercials, and a strong Web presence. Emotionally poignant ads target audiences segmented by type of cancer, age, race, and gender. While the ads tout impressive survival rates, critics have claimed the numbers are misleading. In 1996, the Federal Trade Commission alleged CTCA made false claims in promotional materials and required disclaimers and scientific evidence to substantiate its claims in future advertisements.

A 2013 investigative report found CTCA used questionable statistics in its ads: Its better-than-average survival rates were compared with national figures; however, CTCA treats a very small subset of cancer patients and only includes survival rates for patients whose entire course of treatment was administered at CTCA. While national figures report survival at five years, most of CTCA’s statistics report survival up to four years; at five years, CTCA’s survival rates are no better than the national average. Critics have also complained ads promote therapies like acupuncture that have no scientifically proven benefit for cancer patients. Consumers expect bias in advertising, but critics decry selling hope to desperate patients with false claims and misleading statistics. One of the major challenges in marketing cancer care is maintaining sensitivity to the concept of promise: Marketers cannot promise a cure, and promotional materials should balance hope with realistic expectations.

Marketing cancer care ensures both patients and physicians learn about new treatment options and support services, but advertisements can be misleading. Campaigns often emphasize the benefits of new treatments and technologies while downplaying risks. Care should be taken to differentiate marketing tools, like press releases and VNRs, from actual news. Sources other than marketing materials should be consulted for balanced information about the range of cancer care services available at hospitals and clinics.

See Also: Association of Community Cancer Centers; Hospitals; Media.

Further Readings


Massachusetts Medical Society

The Massachusetts Medical Society (MMS) is the state of Massachusetts’s professional association for physicians and medical students. In addition to its long history of sponsoring cancer-related screenings and promoting awareness of the disease, the MMS also remains one of the state’s staunchest advocates against tobacco use, notably through the efforts of its Committee on Student Health and Sports Medicine. Membership in the MMS is available to both doctors of medicine and doctors of osteopathy practice in the state of Massachusetts and to those who are presently medical students in the state.

The MMS also is internationally renowned for the publication and evaluation of cancer-related research through its two flagship publications: the *New England Journal of Medicine* and the *Journal Watch* series of newsletters.

History

The MMS was founded in 1781 and is today headquartered in the city of Waltham, Massachusetts. The society is the oldest continuously operating organization of its kind active in the United States.
The MMS was originally founded as a state-sponsored body that could offer official licensure to doctors and surgeons. The organization’s founding also aimed to promote medical and surgical knowledge throughout the state while advocating the effects of hygiene, sanitary living and working conditions, and preventative care.

By the mid-19th century the MMS had established itself as a national model for other, similar state organizations. It was the first such organization to create a statewide system with which to collect medical statistics from its citizenry, the results and study of which were ultimately published for use by the general public and medical schools. The society’s broad findings led to changes in both medical practice and statewide public health legislation, including the establishment of the State Board of Health.

Today, the society is active in legislation surrounding health topics such as medical marijuana, health care reform, and Medicare, as well as with the monitoring of state and federal regulations affecting Massachusetts physicians.

Organizational Structure and Resources
The official policies of the MMS are created by the body’s House of Delegates, which convenes biannually to discuss recent state and national developments in health policy, public health legislation, and administration. The MMS House of Delegates is also responsible for the election of the society’s rotating panel of officers, comprised of society president and roles such as speaker and treasurer. Its board of trustees, comprised of medical professionals and students who can serve a maximum of two three-year terms, operates the society’s administrative management.

The MMS is also home to numerous committees comprised of medical professionals dedicated to particular health-related issues. Prominent MMS subcommittees include the Committee on Global Health, the Committee on Violence Intervention and Prevention, and the Committee on Nutrition and Physical Activity.

Publications
The society’s flagship medical journal, the New England Journal of Medicine (NEJM), is widely recognized as one of the most prestigious peer-reviewed medical journals in the world and has been the source of several groundbreaking articles outlining research dedicated to cancer prevention and treatment.

First published in 1914 as the Boston Medical and Surgical Journal, the publication became the New England Journal of Medicine in 1928.

In 1973, a study published in the journal illustrated the importance of the removal of colorectal polyps as a method in preventing colorectal cancer. In 2004, the NEJM was the source of a groundbreaking new study outlining molecular advances in the treatment of advanced lung cancer.

The MMS also owns and publishes Journal Watch, a medical journal review series for doctors and health professionals. Several Journal Watch newsletters offer coverage of cancer-related research, including topics such as oncology and hematology, breast cancer, and skin cancer.

The NEJM Journal Watch Oncology and Hematology newsletter offers medical scholars and doctors a monthly survey of key research developments and findings derived from several prominent, cancer-related medical journals, including the Annals of Oncology, Journal of Clinical Oncology, the Journal of Clinical Cancer Research, and the Journal of the National Cancer Institute.

Antitobacco Efforts
The MMS has been one of the most active state medical boards in the United States in combatting the use of tobacco among both adults and children. In 1992, the society joined with the American Cancer Society and Blue Cross and Blue Shield of Massachusetts to form Tobacco Free Mass, a nonprofit coalition aimed at promoting legislation to reduce and ban the use of tobacco in public spaces.

Many MMS-backed antitobacco programs are conducted in alliance with the Massachusetts Medical Society Alliance, the society’s sister organization, which is comprised of MMS members and aims at promoting good health among Massachusetts citizens.

The society’s Committee on Student Health and Sports Medicine leads and advises members on issues pertaining to the health of Massachusetts schoolchildren and sports medicine, most notably through its promotion and support of scholastic health education programs.

Student Advocacy
Another paramount function of the MMS is acting as an important resource to the 2,500 students
who study medicine in the state each year. MMS has in place a variety of scholarship, loan, and grant programs aimed at offsetting the cost of medical training.

The MMS also provides both career advancement and networking seminars that assist medical students in issues related to licensing exams, residency applications, and mentorship programs.

The society’s Waltham, Massachusetts, headquarters is also home to the Boston Medical Library, which offers a myriad of scholarly and academic resources to the state’s medical student population. In addition to expansive selections of medical journals and publications, the MMS’s Boston Medical Library also assists students in research and offers tutorials that assist students in identifying materials for both course work and thesis writing.

John Pritchard
Independent Scholar

See Also: Education; Smoking and Society; Tobacco in History.

Further Readings

Massey Cancer Center

Cancer centers exist to develop more efficacious methods to prevent, diagnose, and treat cancer patients. These programs use multidisciplinary teams to provide state-of-the-art treatments to cancer patients. The Virginia Commonwealth University Massey Cancer Center happens to be one of the world-class centers offering the latest range of treatments for all types of cancer.

The Virginia Commonwealth University (VCU) Medical Center opened the VCU Massey Cancer Center in 1974 to become one of only 68 facilities out of 1,500 cancer centers in the United States designated by the National Cancer Institute (NCI). The nonprofit VCU Medical Centers program ranks in the top 4 percent of cancer centers in the nation.

The VCU Massey Cancer Center grew in leaps and bounds from its initiation in 1974. Some of the key high points in the history of the Cancer Center include the following:

- 1974: VCU board of visitors established a cancer center on the MCV campus (health science campus of VCU), and NCI provided a planning grant to the University.
- 1975: NCI funded the first cancer center support grant (CCSG).
- 1983: Because William and Evan Massey gave a major gift to the cancer center, the name VCU Massey Cancer Center came from their involvement with the center.
- 1986: VCU Massey Cancer Center’s Dalton Oncology Clinic, BMT inpatient and outpatient clinics, and Thomas Palliative Care Unit moved into North Hospital (a renovated former E. G. Williams Hospital).
- 1987: VCU Massey Cancer Center established the Department of Radiation Oncology.
- 2006: An 80,000-square-foot, state-of-the-art cancer research facility opened at VCU Massey Cancer Center with funding from the NCI.
- 2008: The VCU Medical Center opened the Critical Care Hospital that houses the VCU Massey Cancer Center’s inpatient oncology care unit.

VCU Massey Cancer Center grew steadily over a few decades and put a solid scientific base in place, perfecting its cancer focus and shifting to concentrate on translational research. VCU Massey Cancer Center aspires to serve Virginia and the nation in a role of superior quality in cancer research, prevention and control, patient care, and education. Their overarching mission strives to uncover crucial discoveries about cancer and
to rapidly translate the findings into care for individuals with cancer.

VCU Massey Cancer Center emphasizes patient-centered care with 12 convenient clinical locations in Richmond and surrounding areas in the state of Virginia. The cancer center brings together the most comprehensive multidisciplinary team to provide highly coordinated care. Unified teams of practitioners include medical and radiation oncologists, surgeons, pathologists, genetic counselors, clinical research nurses, physical therapists, and social workers, to name a few. Each patient receives customized and personalized care. The VCU Massey Cancer Center stands out in treating not just the usual cancers of breast, colon, prostate, and lung but also complicated and atypical cancers like acute leukemia, esophageal, gastric, head and neck, liver, myelomas, pancreatic, and primary brain cancers.

The physicians at VCU Massey Cancer Center offer a variety of treatments based on multiple factors including type, location, and stage of the cancer and the patient’s age, health, and lifestyle. The patient plays an integral part in his or her treatment process and receives a great deal of information about the treatment options for the cancer. The variety of treatment options can vary from chemotherapy, radiation therapy, immunotherapy, nutrition, surgery, and biological therapy to bone marrow transplant.

The cancer patients at VCU Massey Cancer Center obtain holistic care with services other than the treatment for just their disease. These support services consist of resources in the areas of lodging, pharmacy services, wig salon, rehabilitation services, pain and symptom management, employee rights and workplace issues, alternative and complementary therapies, legal and financial issues, support groups, and survivor health. These resources go hand in hand with the principal mission to heal the person with cancer.

VCU Massey Cancer Center offers cancer patients the opportunity to participate in clinical trials as a way to uncover novel and improved methods to treat and prevent cancer. The research studies from clinical trials assess innovative medical therapies and novel devices along with expanding the scientific knowledge of a broad range of diseases. Massey proffers more than 150 clinical trials to cancer patients at any point in time.

The cancer center continuously develops novel research in both laboratory and clinical studies. Steven Grant and colleagues, using laboratory studies, uncovered a favorable treatment approach for multiple myeloma that couples two targeted agents to destroy cancer cells. The group of scientists showed the novel effect of combining the two to kill the myeloma cancer cells. In clinical research, Thomas Smith and colleagues tested a device for pain management while patients receive chemotherapy treatment. By applying electrodes to the skin of the cancer patient, the Calmare pain device effectively treated chemotherapy-generated peripheral neuropathy. Peripheral neuropathy causes pain in the nerves in the body brought on by the chemotherapy.

VCU Massey Cancer Center remains active on social media (Facebook, YouTube, and Twitter) and on major television news channels to share progress occurring in cancer treatment. The cancer statistics described on an ABC Twitter chat with Steven Grossman, MD, a deputy director at Massey, indicated that more than 1.6 million people in the United States alone will receive a diagnosis of cancer in a year, with a cost of approximately $216.6 billion. The deputy director detailed the major progress made recently in cancer immunotherapy and new knowledge about the function of cancer stem cells in resistance to treatment. Research at Massey also shows that, for cancer treatment to produce meaningful results, treatment must be directed to at least three distinct pathways to destroy the cancer cells. The cancer center does extremely well in continuously delivering the latest messages about all-around cancer care and cancer cures.

In conclusion, VCU Massey Cancer Center offers a phenomenally comprehensive program for cancer patients. Massey actively works at conquering the scourge of cancer, from education to research. Using state-of-the-art interdisciplinary teams and treatments, the cancer center helps all patients in a holistic manner to heal or to assist in the end-of-life processes. As an NCI-approved center, Massey excels at every stage of the process in cancer management.

Sharon A. Takiguchi
Independent Scholar

See Also: Kimmel Cancer Center; Lombardi Comprehensive Cancer Center; Mayo Clinic Cancer Center; National Cancer Institute.
Further Readings

Mayo Clinic Cancer Center

The Mayo Clinic Cancer Center (MCCC) is a service of the Mayo Clinic, and it is spread over three locations: Rochester, Minnesota; Scottsdale, Arizona; and Jacksonville, Florida. The clinic employs approximately 350 physicians and engages in patient care, administering radiation, chemotherapy, and surgery. The clinic serves more than 135,000 cancer patients per year. The clinic also conducts extensive research via clinical trials. In addition, the clinic provides cancer education, which benefits patients and cancer caregivers. The MCCC developed a system, now used worldwide, for grading cancer on a numerical basis. The MCCC is the only cancer treatment facility in the United States with three sites.

The MCCC has been recognized for its high level of patient care and research. It is one of 67 cancer treatment centers to earn the National Cancer Institute (NCI) cancer center designation. The NCI recognizes cancer treatment facilities that have achieved scientific excellence and diverse research approaches to dealing with cancer. The NCI designation places the clinic in the top 4 percent of approximately 1,500 cancer treatment facilities in the United States.

The clinic is also a member of the National Comprehensive Cancer Network, which inducted the MCCC into its ranks because of the clinic's expertise and potential to improve the lives of patients.

*U.S. News and World Report* ranked 900 cancer treatment centers. In this review, the Rochester campus of the Mayo Cancer Clinic ranked third in the nation. *U.S. News and World Report* based this rating in part on patient survival rate, which is much higher than expected at the Rochester MCCC. The Rochester campus also received the highest possible scores in patient safety, patient volume, and the ratio of nurses to patients. The Phoenix, Arizona, campus ranked 26 on the same report, and the Jacksonville, Florida, campus was not ranked.

The MCCC maintains 10 research programs: women's cancer, neuro-oncology, hematologic malignancies, genetic epidemiology and risk assessment, gene and virus therapy, gastrointestinal cancer, development therapeutics, cell biology, cancer prevention and control, and cancer immunology and immunotherapy.

The clinic runs approximately 900 clinical trials at a time. Trial subjects are recruited from all parts of the world, with populations that are underserved in cancer care, including Hispanics, African Americans, Alaska Natives, and American Indians. Participants in the clinic's trials do not necessarily travel to one of the three clinic locations. Instead, the MCCC has many off-campus sites, approximately one per state, where patients can be studied. Data is then collected at these sites and sent to the clinic. In these off-campus studies, the clinic follows protocols developed by the Alliance for Clinical Trials in Oncology. The Cancer Prevention Network is a clinical trial study group that is based at the clinic.

Clinical trials at the MCCC have resulted in important scientific breakthroughs in the understanding of and treatment of cancer. Among its achievements, the clinic has found ways to stimulate the body's immune system so that it can better fight cancer; identified types of breast cancer tumors and treatments; developed new drugs, gene therapies, and immunological therapies; and performed a groundbreaking genetic study of lymphoma cells.

The clinic developed and refined a computer-assisted method of performing brain surgery to remove deep-seated brain neoplasms (abnormal growths). It also developed an effective surgery for high-risk rectal cancer. And the MCCC was the first
research institute to test the use of the oncolytic measles virus in treating cancer.

In 2001, a team of researchers led by the clinic’s S. K. McDonnell conducted a study of 745 women who were treated for breast cancer at the Mayo Clinic for 30 years prior to 1993. The study found that, in the case of women diagnosed with breast cancer who also had family histories of breast cancer, survival rates were higher for women who had contralateral prophylactic mastectomies, that is, surgical removal of both breasts.

In 2006, a clinic study found that a combination of medications, paclitaxel and carboplatin, may be effective in treating malignant metastatic melanoma.

In 2013, two clinic scientists, Winston Tan and John Copland, identified a specific protein called stearoyl-CoA, which occurs more often in cancerous kidney cells than in healthy ones. This discovery led to more research aimed at developing an effective drug to suppress stearoyl-CoA. Because many cancers start in the kidneys and spread, this research has the potential to help many people. Tan and Copland have also identified 30 genes that promote growth of cancerous tumors.

In 2014, C. C. Chini, a physician at the clinic’s Rochester campus, led a team of scientists in isolating nampt, an enzyme linked to pancreatic cancer. The team found that targeting nampt with medications and gene therapy could slow the growth and limit the survival of pancreatic cancer cells. The scientists believe that their research has the potential to lead to new therapies in the treatment of pancreatic cancer.

The MCCC publishes an online magazine titled Forefront, which provides general information on cancer treatment as well as articles that distill the clinic’s research for a general audience of readers.

The clinic receives funding from many sources including the United States federal government, individual state governments, and private foundations. The clinic receives $140 million in competitive peer review grants, including the NCI’s Specialized Programs of Research Excellence (SPORE) grants. In 2014, the clinic received $28.6 million in federal funding in the form of a five-year federal cancer center support grant.

See Also: Breast Cancer; Mayo Clinic Cancer Center, Jacksonville; Mayo Clinic Cancer Center, Scottsdale.

Further Readings

Mayo Clinic Cancer Center, Jacksonville

The Mayo Clinic Cancer Center is a cancer treatment service provider that has a multisite presence in three states: Scottsdale, Arizona; Jacksonville, Florida; and Rochester, Minnesota. This multilocation gives the center access to broad geographical research for wide and diverse service to patient populations around the world.

Mayo Clinic Cancer Center campuses have some of the best and internationally recognized scientists and physicians, and they collaborate across the spectrum of cancer research, starting from basic biology to treatment of the diseases,
and seek to establish ways in which to reduce the burden of cancer.

Mayo Clinic Cancer Center Jacksonville campus is a general medical and surgical hospital. It is categorized as a not-for-profit, and it is at the level of a nationally ranked *U.S. News* best hospital in 12 adult specialties. The Jacksonville campus is ranked number eight in Florida and ranks second in the Jacksonville, Florida, metro area as per *U.S. News* best hospitals. The center has 214 beds and, as of June 2014, the Jacksonville campus alone had 12,547 admissions, backtracking for one year. During the same year, the center successfully performed 5,853 inpatient and 6,505 outpatient surgeries. Its emergency room had 27,500 visits. In addition to treatment services, the campus does offer educational and training services; hence, it is also a teaching hospital.

The center is ranked as having high performance in adult service and also as a specialist in some adult health services including cancer; heart surgery; diabetes treatment; ear, nose, and throat solutions; gastrointestinal surgery; gynecology; and orthopedics, among several other solutions and specialties for the needs that patients often have.

For hospitals operating in the United States, there is a federal program in which hospitals are required to sample recently discharged patients and get their opinions about their stays. The survey’s purpose is to essentially get a measure of patient satisfaction on the services offered by the hospital. For the last year, the survey showered encouraging responses for some of the key questions at both state and national levels; for whether patients would recommend the hospital to friends and family, 90 percent of the patients responded definitely yes, with an average of 68 percent at the state level and 71 percent at the national level. For the same questions, 2 percent of the respondents indicated probably or definitely not, with an average of 8 percent at the state level and 5 percent at the national level.

As per the statistics from the American Hospital Association (AHA), which compiles data on all U.S. hospitals through an annual survey and from other sources (some of the details that AHA shows include hospital ownership, number of doctors and nurses, volume of births and emergency room visits, and available services such as sports medicine), Mayo Clinic Cancer Center Jacksonville inpatient has a wide range of services for cancer patients. Heart catheterization is available as well as palliative care solutions, infection isolation assistance, rehabilitation, chemotherapy, breast cancer testing, geriatric support, antismoking programs, and even sleep study spaces. All sorts of solutions are offered to patients who have various critical needs with regard to the many health issues that they may have over time.

For patient or family support services, Jacksonville center has the Alzheimer center and offers services through help with government services, chaplaincy and pastoral care services, cancer services, patient support groups, patient representatives or ombudsmen, and translation services. In addition to support services, the center undertakes community outreach programs, which include health fairs and health screenings.

Mayo Clinic Cancer Center also offers imaging services of both a diagnostic and therapeutic nature. These include computed tomography (CT) scanning and radioisotope studies plus magnetic resonance imaging (MRI), multislice CT, and ultrasound exams for all patients who require assistance. The center has staff members who are under full employment terms and others under part-time employment terms. Employees under full-time terms include 390 physicians and dentists, 405 registered nurses, and a single licensed practical nurse. Under part-time employment terms, the center has 19 physicians and dentists, 182 registered nurses, and one licensed practical nurse.

According to hospital statistics, each year, thousands of patients who have any of more than 200 kinds of cancer seek treatment at Mayo Clinic in Florida. For treatment of these patients, professionals who work in the Division of Hematology/Oncology will help all cancer patients as needed. To ensure effective and optimized health care service to their patients, the Mayo Clinic in Jacksonville, Florida, works in conjunction with the entire Mayo Clinic Cancer Center. Actually, to foster this initiative, division staff in Mayo Clinic Jacksonville work within the Mayo Clinic Cancer Center.

At the center, new drugs, biological targeted therapies, and immunology and gene therapies are studied to determine their potential for preventing and treating cancers. This research opportunity means the right facilities are available at the center; therefore, it allows qualified patients to enroll in cutting-edge clinical cancer research studies and receive the most advanced treatments. For a patient
who seeks medical help at the center, they have an opportunity to participate in the clinic’s exceptional research programs; this enables patients to learn about their condition and helps them become active participants in their cancer care.

As per Mayo Clinic Jacksonville’s records, the most common cancers seen are cancer of the colon, breast, prostate, and lung. However, Mayo Clinic’s oncologists have extensive experience in the diagnosis and treatment of every kind of cancer. The center has innovative and advanced cancer care available not only in the Jacksonville center but throughout the entire Mayo Clinic Cancer Center.

Michael Fox
Independent Scholar

See Also: Mayo Clinic Cancer Center; Mayo Clinic Cancer Center, Scottsdale; National Cancer Institute.

Further Readings


Mayo Clinic Cancer Center, Scottsdale

The Mayo Clinic Cancer Center is a National Cancer Institute (NCI)-designated comprehensive cancer care and research center. In addition to the center’s Arizona site, the center has sites in Rochester, Minnesota, and Jacksonville, Florida. The three sites collaborate to improve cancer patients’ care and quality of life.

The centers also cooperate on some research projects. The focus is on better understanding cancer biology and discovering new ways to diagnose, treat, predict, and prevent cancer. All Mayo cancer centers meet NCI standards for cancer care and research, including basic laboratory research, participation in high-priority NCI clinical studies, cancer prevention and control programs, education and training of health care professionals, public information services, and community service and outreach.

As part the Mayo Clinic Cancer Center, the Arizona center is affiliated with numerous cancer programs and institutions. In addition to NCI, these include the North Central Cancer Treatment Group (NCCTG), the Cancer Prevention Network (CPN), and the Coalition of National Cancer Cooperative Groups, Inc. The center also participates in 11 major cancer research programs: cell biology, developmental therapeutics, gastrointestinal cancer, gene and virus therapy, genetic epidemiology and risk assessment, hematologic malignancies, immunology and immunotherapy, neuro-oncology, prostate cancer, women’s cancer, and cancer prevention and control.

The Arizona center conducts numerous clinical trials focusing on cancer. It has conducted or has ongoing clinical trials focusing on patients with previously treated multiple myeloma, hematologic malignancies, small cell and non–small cell lung cancers, and breast cancer. Other clinical trials include a focus on acute myeloid leukemia, esophagus cancer, acute lymphoblastic leukemia, chronic myeloid leukemia, oropharynx cancer, and melanoma.

The three Mayo Clinic Cancer Centers, including the Arizona center, received a Clinical and Translational Science Award from the National Institutes of Health (NIH) in 2006. The $72.5 million grant was for five years and focused on the translation of basic science discoveries into effective clinical care approaches. In 2011, the centers were awarded a five-year extension of the grant amounting to $64.6 million.

Oncologists at the Phoenix center treat more than 100 different types of cancer. These include acute lymphocytic leukemia, anal cancer, melanoma, mesothelioma, ovarian cancer, pancreatic cancer, stomach cancer, throat cancer, uterine cancer, and vaginal cancer, to name a few. As of 2014, the Mayo Clinic included three hospital facilities: a five-story,
240-exam room outpatient clinic in Scottsdale; the Mayo Clinic Specialty Building, an outpatient clinic located in Phoenix; and Mayo Clinic Hospital, a 268-bed facility in Phoenix, which opened in 1998.

The cancer center in Arizona treats more than 90,000 cancer patients each year. These patients are seen by disease-oriented treatment groups featuring collaboration among oncologists, hematologists, surgeons, radiation oncologists, and other specialists. Individualized treatments feature surgery, chemotherapy, radiation therapy, and supportive care. Clinical care at the center also includes a multimodal treatment approach for lung cancer and asbestos-related cancers such as mesothelioma.

The Phoenix center includes various cancer education initiatives designed to help patients learn more about their cancer and cancer treatments. These initiatives provide information on cancer prevention, diagnosis, and complementary medicines and strategies. An important part of the education initiative is to help patients and families learn about coping strategies and caregiving.

The clinic provides cancer-related classes covering chemotherapy treatments and radiation treatments. It is also part of the American Cancer Navigator Program. The program provides information on cancer resources in the community, such as how to find assistance for financial and lodging needs, wigs from the American Cancer Society, and support groups. The Arizona clinic includes a Patient and Health Education Library, where patients and families can find cancer-related resources from books to DVDs. The library also features an interactive cancer education resource and a program to help cancer patients keep in touch with family and friends.

Consolidation
The Mayo Clinic Cancer Center first opened in Scottsdale in 1987. In 2012, the Mayo Clinic announced that it was building a new cancer center in Phoenix, Arizona, scheduled to open in 2015. The center in Phoenix is designed to create a single-center site to consolidate operations of the Mayo Clinic Cancer Center in Arizona. The facility is to include a $130 million, 217,200-square-foot facility featuring clinical and office space.

The idea behind the creation of the new facility was partially to provide convenience for cancer patients and their families. As a part of this effort,

The Mayo Clinic building in Scottsdale, Arizona. In 2012 the Mayo Clinic announced plans to build a new cancer center in Phoenix to create a single-center site and consolidate the operations in Arizona; the site was scheduled to open in 2015. The Arizona cancer center treats more than 90,000 patients each year. (Flickr/Mayo Clinic)
the Hematology/Oncology Department located on the Scottsdale campus is being moved to the Phoenix location. In addition, various other cancer-related units will be transferred to the new Phoenix location, including chemotherapy, bone marrow transplant, and research efforts.

The consolidation also features relocation of 32 chemotherapy infusion stations from Scottsdale to Phoenix, with an additional 18 more infusion stations planned. Exam rooms for cancer patients at the new site feature a new design concept that allows for more integrated team care of patients. The facility also features kiosks for virtual check-in and access to information.

The Phoenix facility features a $181.5 million proton-beam therapy program that represents the only one of its kind in the American Southwest. Scheduled for completion in 2016, the proton-beam therapy pinpoints tiny tumors hidden away deep inside the body and then destroys tumor tissues with large doses of radiation. These large doses can be used because the technology spares more healthy tissue surrounding the tumor, which is especially important when the tumors are located near major organs. Traditional radiation therapy has been known to cause future cancers.

The proton-beam facility is being built on the bottom floors of Mayo's six-story facility in Phoenix and will feature four treatment rooms. The overall space includes enough room for a three-story, 190-ton mechanical apparatus needed for the proton beam as well as a 20-ton magnet to guide the beam. The cancer center in Arizona will be the only facility of its kind in the state and one of less than 20 such facilities in the United States, one of which is in the Mayo Clinic Cancer Center in Rochester, Minnesota.

David Petechuk
Independent Scholar

See Also: Breast Cancer; Clinical Trials; Mayo Clinic Cancer Center; Mayo Clinic Cancer Center, Jacksonville; National Cancer Institute.

Further Readings

Meat, Cooking

Meat, the cooking process, can be described as transforming raw animal muscles into an edible product by adding high temperature and different spices such as salt, pepper, and herbs to improve the taste. This practice emerged several thousand years ago. However, the exact date and time is not yet clearly established. According to the literature, humans cook food to increase nutritive values such as protein and other essential nutrients. Choice of cooking methods sometimes depends on cultural norms, religious beliefs, and personal preference. For example, traditional ancient Romans cooked their meat with salt, smoke, and honey. Similarly, Jewish culture prohibits their meats from being cooked with other animal products; for example, fish should be cooked separately from beef. This means that at no time can the meat or the utensils be combined.

History of Meat Cooking
Historically, farm animals were used for textile and edible products such as milk and eggs. Overused animals that were unable to fulfill these purposes were eventually slaughtered and served for domestic cooking and eating. Today, numerous animal products are sold in grocery stores and food markets. The type, quality, and size vary according to economic demands. Some of the most common ones are processed meats, which contain a significant amount of sodium and sugar preservatives. These meats include pork bacon and sausages, roasted beef ready prepared, chicken nuggets and strips, and processed fish patties and sticks.

Interestingly, other meat products are available to consumers in different packages. For example,
some meats are raw and seasoned, ready to be cooked. These packages provide ease and convenient cooking methods. In contrast, other raw meats are available to be cooked and require more labor to prepare. Meats also are available in a complete package with other food groups ready to be placed in the microwave. Whichever way meats are purchased or obtained, some form of heating must be applied before humans can actually consume them.

**Meat Cooking Methods**

There are many different methods for cooking meats, whether they are purchased already prepared, seasoned, or raw. Meat cooking decisions are based on the animal muscle type, meat cut size, and tenderness. The most frequent cooking methods include grilling, smoking, frying, stewing, and baking. Grilling and smoking are used on all types of meats, particularly on tender cuts. This involves applying direct intense heat to the meat (beef, pork, chicken, etc.) over a pit or rack.

The cooking time depends on the age of the animal. Older animals usually take a longer time to cook, while meats high in fat content cook more quickly. Frying methods refer to cooking meat in fat at very high temperature. This process contributes flavor and a crispy texture outside the meat. Tender cuts of meats (breast and thighs) are often fried. Stewing is also another way of cooking meats. This is done by adding a small amount of liquid to the meat and allowing it to simmer until cooked. Baked meats are done in the oven with a temperature above 350 degrees Fahrenheit.

The internal temperature of the meat determines how well the meat is cooked. According to the U.S. Department of Agriculture (USDA), beef, veal, and lamb should be cooked to an internal temperature of 145 degrees F or 63 degrees C in order to prevent food-borne illness. It is well documented that one out of every seven hospital cases is caused from food-borne illness. Most times, the insides of meats that are prepared rare appear pink in color. This is associated with myoglobin and hemoglobin (iron) content of the meat. Medium-rare meat has an internal cooking temperature between 140 degrees F and 150 degrees F. During this level of meat cooking, the pink color changes to a gray color. The fully cooked or well-done meat has a brown color. This change in the meat is called oxidation.

Throughout the meat cooking process, raw meat constantly changes its physical and chemical structure. Raw muscle fibers are straight and connect with other muscle tissues. Once heat is applied to the meat fiber, it begins to change shape and produces fluid. During cooking, the meat becomes dry, and fluid excretion intensifies. The well-done cooked meat cell molecules are broken apart and recombine to give the meat a distinctive aroma.

**Reasons for Cooking Meat**

There are many reasons people cook meats. Three of these reasons are for personal preferences, to destroy food-borne pathogens, and to preserve the quality of the meat. First, meats are cooked based on personal preferences. For example, an individual may prefer grilled beef when compared to stewed beef. Studies have documented that raw meats are very tasty, but cooking increases flavor. Secondly, meats are cooked to prevent food-borne illness. Recently, the Centers for Disease Control and Prevention (CDC) reported between 1998 and 2008 approximately 9.6 million cases of food-borne illness, with more than 46 percent of the cases linked to animal products. The most frequent pathogens identified were *Escherichia coli* O157:H7, *Campylobacter jejuni*, salmonella, and *Listeria monocytogenes*. Third, meats are cooked to preserve shelf life and denature the long chain protein found in meats. Extending meat shelf life helps manufacturers to maintain the meat market. The protein denaturation promotes easy digestion in the human gastrointestinal tract.

**The Link Between Meat Cooking and Cancer**

Recently, many researchers have linked meat cooking to several types of cancers such as breast, pancreatic, colon, and prostate. The science illustrated that, during meat cooking, some meats produce carcinogens that interfere with human cell division.
When meats are cooked on high heat (above 350 degrees Fahrenheit), the animal muscle produces by-products called heterocyclic amines and polycyclic aromatic hydrocarbons (PAHs). These two chemicals are known to be carcinogenic in the human body and can cause change in the human DNA structure. Heterocyclic amine is a special protein that is combined with sugar and reacts at extremely high temperatures. On the other hand, PAH is produced when the juice of the meat escapes into the fire and fat from the meat begins to blaze. This example is quite obvious during grilled or barbeque cooking methods. The cancer prevalence is high in both males and females who consume a large amount of well-cooked meats and meats cooked with direct smoke.

**Meat Cooking Recommendations and Cancer**

Presently, there is no policy that governs meat cooking. However, in 2007, the World Cancer Research Institute and other collaborating cancer agencies recommended that red meat processed with high temperature should be consumed in moderation, especially if a person is diagnosed with cancer. Meats like bacon, salami, sausage, hotdogs, and ham should be avoided because of the high exposure to cancer-causing substances and excessive preservatives. The Delaney Clause prohibits the use of cyclamates and saccharin on human food.

In addition, the American Academy for Nutrition and Dietetics encourages patients who are diagnosed with any form of cancer and undergoing chemotherapy to eliminate raw and rare-cooked meats from their diets. Raw and rare-cooked meats not only contribute cancer-causing agents but promote possible stress on the immune system. Cancer patients have a very weak immune system, and animal products should be consumed with caution. The body has low white blood cells called neutrophils. The association recommends a neutropenic diet for cancer patients. The word *neutropenic* refers to a weak immune system. Most times, the diet is free from bacteria and harmful organisms. Foods in this diet include animal products like cheese, milk, and yogurt.

**The Importance of Meat in the Diet**

Animal protein is very crucial to human growth and development. When meat is digested, it is broken down into amino acids. These amino acids play a role with wound healing, growth, biological processes, and muscle structure. Poor meat intake can cause protein deficiencies and death if the body is deprived for a very long time. Individuals with cancer can prevent protein deficiencies by consuming meats that are well cooked, thus preparation should be done in a sterile environment. This is to ensure the meat is bacteria free.

According to the CDC, cancer is the second-leading causes of death in the United States. More than 575,743 people died from cancer in 2011. Because cooked meat consumption is linked highly to the growing cancer prevalence, it is pertinent that individuals control the amount and type of meat consumed. For example, many epidemiologists suggest that red meats are associated with certain breast, colorectal, and prostate cancers, and limiting the amount of this product can help reduce cancer rates. In addition, meat that is burned or gets a dark color during cooking should be avoided. Most times, these foods are high in heterocyclic amine and PAH, which can be detrimental to the human body.

One recommendation is to eat less cooked meats and increase plant-based proteins that are high in antioxidants and phytochemicals. These foods include legumes, fruits, and vegetables. This will help fight and reduce cancer-causing cells.

Andrea McDonald
Lenna Dawkins-Moultin
Texas A&M University

**See Also:** Alternative Therapy: Diet and Nutrition; American Association for Cancer Research; American Cancer Society; Chemotherapy; Colon Cancer; Food Additives; Food and Drug Administration.

**Further Readings**


---

**Meat Processing**

Processed meat includes meat that is treated in some way for long-term preservation other than simply freezing. This includes prepared meat-heavy foods that may be canned, like stews or chili, as well as cured meats (which are treated with salt for a period of time to transform their proteins), smoked meats (usually salted or cured, as with bacon), dried meats (not just jerky but the more finely textured dried meats of Asian cuisines, jarred dried beef, and freeze-dried meats), and pickled meats (nearly always cured first). Cooking itself originated as a form of short-term preservation—it may not seem like it to us in the age of refrigeration, but the difference in shelf life between raw meat and cooked meat is profound and life changing to a premodern civilization, particularly as cooking was discovered before salt curing or smoking—but meat processing is a longer-term preservation method, especially with the use of salt.

Specifically, sodium nitrite and potassium nitrate are salts commonly used to preserve meat. Potassium nitrate or saltpeter has been produced from cave deposits, bat guano, and urine since the Middle Ages and was used in gunpowder both in early Chinese fireworks and in 19th-century firearms. In west Africa, it is used to thicken soups and soften beans and tough meat, while in the West, it has long been used to cure meat. Less used as a preservative today, it is still often used for specific, traditional cured meats, such as corned beef and French sausages.

When it is used to cure meat rather than simply to help preserve canned, jarred, smoked, or dried meat, salt has four functions. It partially dehydrates meat by pulling excess water out of the protein, which inhibits bacterial growth by providing a less-suitable environment for it. (Salt’s inhospitability to bacteria is key in its ancient use as a preservative.) It halts the fermentation process, which would otherwise result in the meat breaking down. (Though in southeast Asia, pork is salted and fermented in a wet environment with the addition of rice rather than being brined in a strong salted solution or cured in a dry preparation; this ferments the meat via lactobacillus bacteria, much as kimchi and sauerkraut are made, allowing friendly bacteria to grow, while harmful bacteria are killed off. The final product is often eaten raw.) It induces cellular osmosis, in which water is drawn outside the cellular membrane before being absorbed back in, bringing the salt with it. And it denatures the proteins, tenderizing them and changing the texture and flavor of the meat. These changes are seen both before and after cooking: Even without additional seasonings, the flavor and texture of corned beef brisket are distinct from those of untreated brisket. And dry salami starts out the same as fresh sausage but over time develops a much different flavor due to the salt, the behavior of the seasonings interacting with fat and salt over a long period of time, and the growth of healthy bacteria during the dry aging process, resulting in a tanginess similar to sourdough bread (and derived from the same bacteria).

The late 19th century brought new scientific sensibility to meat processing and curing, and potassium nitrate was mostly phased out in favor of sodium nitrite and sodium nitrate, usually in combination with sodium chloride (table salt). During the curing process, some of the nitrates are converted into nitrites by healthy bacteria. They are generally used in meats that are cured or stored for long periods of time, including prosciutto (which, like the Southeast Asia fermented pork, is eaten uncooked), country ham, dry salami, and some bacons. Meats that will be cured for a shorter period of time and...
cooked before eating, like most mass-produced bacons and cold cuts, city ham, and hot dogs, favor the use of nitrates.

Nitrates, nitrites, and the nitrosamines formed by interactions between the meat and the nitrites are all implicated in increased risk of chronic obstructive pulmonary disease and gastric cancer. Nitrosamines are believed to be the primary factor here, though the role of nitrates and nitrites on their own is not fully understood yet. Nitrosamines are formed from nitrites interacting with amines in the meat’s protein but can only form in specific conditions like high temperatures (the frying of bacon) or highly acidic environments, like the human stomach. Ascorbic acid and other compounds can minimize their formation.

There are a number of different nitrosamines, some of which are probable carcinogens, some of which are possible carcinogens, and some of which have no known carcinogenicity. The mechanism by which they are carcinogenic has not been shown. Gastric cancer is the strongest correlation, but there is also evidence of an esophageal cancer risk. Nitrosamines also are present in preserved fish and some cheeses as well as tobacco smoke, smokeless tobacco, and e-cigarette vapor.

Bill Kte’pi
Independent Scholar

See Also: Diet and Nutrition; Food Additives; Meat, Cooking.

Further Readings

Media

Media content is paramount to our personal and societal understanding and conceptualization of cancer. Most individuals in developed countries have ample general media exposure and media use. Individuals often cite news media as important sources of health information, including cancer information.

Media campaigns are at the forefront of many public health efforts to educate about, portray, and fight against cancer. Indeed, media messages may influence health-related behaviors, including those associated with cancer prevention, detection, treatment, and recovery.

Media also contribute to individuals’ narratives, myths, images, and beliefs about cancer. It is possible that media coverage of cancer has unintended effects as well as intended effects that should be taken into consideration when examining media’s impact on cancer in society. Media content, characters, and stories also feature images, behaviors, and messages that intensify the cancer epidemic.

Exposure and Attention
As information moves online (and mobile), certain groups may be marginalized due to occupation (e.g., a construction worker who cannot check his or her news feed during the day), geography (e.g., an individual in a rural location without access to broadband Internet), or income. Issues like the digital divide and the knowledge gap must be recognized at the intersection of media and cancer. If news organizations and public health campaigns focus primarily on multimedia and online information dissemination, there may be deleterious health consequences for those without access to important cancer information.

Individual-level factors also contribute to different types of media experiences. Factors such as personality, individual motivation, and personal values as well as whether the user is engaged in multitasking can potentially influence message effectiveness at the time of processing.

Conflicting messages in the news about cancer prevention and screening may lead to greater individual uncertainty about the effectiveness of cancer prevention efforts (e.g., proper nutrition) and cancer screening guidelines (e.g., age for mammography screening). For example, consumers may read
an article about how increased consumption of tofu and soy products increases risk of breast cancer but read another article about incorporating a reduced-meat diet for overall health and weight loss (which is also encouraged to reduce risk of cancer).

Exposure and attention to media content may also not accurately reflect epidemiologic trends for specific types of cancer. There are many types of cancer, and media sometimes disproportionately portray their incidence, prevalence, and severity. Breast cancer images, references, organizations, and news often outweigh other types of cancer with higher mortality rates (e.g., lung).

Additionally, media content that may seem desirable (e.g., prominence of tan skin in models or popular movie stars smoking) may serve to perpetuate some of the risky habits that contribute to greater risk of cancer. In this way, media content sends a different message from public health efforts to alert the public of the lifestyle changes society can make to prevent cancer.

**Information Seeking**

A prominent question about cancer in the media is what catalyzes individuals to seek out cancer information. Individuals may have discomfort or notice visible changes in their bodies and, subsequently, turn to media resources in an effort to understand a symptom and diagnose. On the other hand, individuals without particular symptoms may actively seek out additional cancer information after hearing a particular news story on cancer. Research indicates that individuals who pay close attention to health news and those with a family history of cancer are more likely to seek out cancer information.

Regardless of the exact rationale for paying particular attention to cancer in the media, the action of information seeking often makes the information obtained more effective and memorable. These media messages may prompt individuals to take action, encouraging them to engage with cancer communication sources: primary care providers, support groups, families, and social networks. Cancer prevention researchers point to active information seeking as a major precursor to reducing risky behaviors known to be associated with cancer diagnoses.

In order to increase the likelihood of high-risk individuals seeking out cancer information in the media, cancer messages must be appropriately tailored for channel effectiveness and the content tailored and made salient for the specific audience segments.

**Community and Social Media**

Media also allow society to join the cancer conversation by accessing support groups, asking questions, sharing cancer-related media links, posting personal content on social networking sites, and making online contributions and donations to cancer-related causes and organizations. This user-generated content is therefore part of cancer’s landscape in the media. It has both enriched the amount and diversity of cancer information available in the media and contributed to disproportionate coverage of cancer information noted previously.

Humorous or lighthearted cancer content may dominate media attention. For example, Facebook status updates about bra color status have dominated news feeds around the world in an effort to raise breast cancer awareness. In another example, “hashtag mamming,” which was introduced in the fall of 2013 for breast cancer awareness month,
encouraged women to post a picture on Instagram showing their cleavage in order to show solidarity with women getting mammograms. In another example, Movember is a new global charity that encourages men to grow a moustache in November and post pictures of their mustaches online in order to raise awareness about prostate and testicular cancer. These examples demonstrate the integration of user-generated content into the media environment. It is clear that these social media efforts create a larger sense of a cancer community, especially highlighting the ability for social media to intermingle support from cancer-free and cancer-affected voices.

Social media also has contributed to a more serious cancer community and greater understanding of the realities of cancer diagnosis. For example, Twitter has been utilized by individuals undergoing cancer treatment to detail their experiences or, as noted by journalist Bill Keller of the New York Times, to “live cancer onstage.” Lisa Boncheck Adams made national news as she live Tweeted and blogged about her experience living with stage 4 breast cancer. Although Adams’s decision to make public a very personal experience caused a large debate about what was appropriate for social media, she has approximately 14,000 followers at the time of this writing, demonstrating a larger community interested in her well-being through the cancer process.

The community aspect of cancer also can be understood by looking at philanthropic content. The social understanding and production of cancer is bound to symbols and events like the pink ribbon and Race for the Cure. Media coverage contributes to the culture and experience of cancer and allows community to be a part of the cancer experience, even if it is not firsthand.

Studies and Impact
Direct effects of media are varied, but the preponderance of evidence supports an association between exposure to risky health habits in the media and initiation of those same habits (e.g., smoking). Media advertisements, sponsorship, and promotional events play a health advocate role as well as showcase companies and behaviors that may contribute to greater cancer incidence. Media studies on the influence of media on cancer-related knowledge and behaviors have recently emphasized the processes by which media influences individuals’ health behaviors. This type of influence is called an indirect influence and asserts that media affects individuals’ beliefs and cognitions. Thus, strategies at improving health outcomes focus on how media affect these internal processing factors.

Conclusion
Media messages related to cancer, risky behaviors associated with cancer, and cancer information may be positive or negative and may have intended and unintended consequences. Individuals often seek out or encounter cancer information in the media, although it is likely that they will encounter ambiguous or conflicting information that may cause uncertainty or further information avoidance. Widespread media consumption and daily routines filled with mobile devices accessing information and sharing information via social media necessarily affects our societies’ understanding, knowledge, and decision making surrounding cancer, which may be vital to public health efforts to ease individual and societal cancer burdens.

Jennette Lovejoy
University of Portland

See Also: Diet and Nutrition; Electronics; National Cancer Institute; Smoking and Society; World Health Organization.

Further Readings

Medicare and Medicaid
Medicare and Medicaid are public insurance programs in the United States. Medicare provides insurance for Americans based on being elderly or having
Medicare and Medicaid

Medicare

Medicare recipients mainly have disabilities or are elderly. Medicare recipients must be 65 years old or older, disabled, or with permanent kidney failure that necessitates transplant or dialysis. Medicare is a federal insurance program that has four parts: A, B, C, and D. Parts A and B are for hospital and medical insurance. Parts C and D are for flexibility and prescription drugs. A variety of hospital and outpatient services are covered, at least partially, by Medicare Part A, or hospital insurance: semiprivate room, meals, testing, and supplies. Home health care is also covered under Part A, which includes various forms of therapy, such as occupational and physical therapies. Payroll taxes fund Medicare's expenditures; the recipient does not have to pay premiums. Payroll taxes are gained through the Federal Insurance Contributions Act (FICA) and Self-Employment Contributions Act. For every $100 a worker earns, $2.90 is paid to the FICA account. For workers who are not self-employed, they pay $1.45 to FICA for $100 earned, and their bosses pay the same amount. Money earned through self-employments is taxed the same amount, but the workers themselves have to pay the full amount of $2.90 per $100 earned.

Medicare Part B, also called Supplementary Medical Insurance, is completely voluntarily. In 2014, monthly premiums were nearly $104 with a $147 deductible. Medicare Part B pays for outpatient physician treatment and home health care services. Part B covers a variety of services such as eyeglasses, blood transfusions, vaccinations, physician and nursing services, and diagnostic tests. Medicare Part C is an attempt to allow users to more specifically design their treatment services to the recipient’s needs. Medicare Part D offers prescription drug coverage and is voluntary, but enrolling at any time after the Initial Enrollment Period may carry a late enrollment penalty. Medicare Part D is offered by private companies, and the premium and coverage offered varies by plan, within boundaries set by the federal government.

Medicaid

Each state must set the specific conditions that recipients must meet to be eligible for Medicaid benefits. In general, young children (those under 6 years old) and pregnant women whose families earn less than 133 percent of the federal poverty level qualify. Those who receive supplemental security income also qualify. Certain adopted children and foster children and Medicare beneficiaries qualify also. States may also extend coverage to those who are low-income, institutionalized people, those with tuberculosis, those who are medically needy, and those who qualify at a higher percentage level of the federal poverty level (at 250 percent instead of 133 percent). Fees are paid directly to the health care provider on a fee-for-service basis. States may have a nominal deductible for services but may not create deductibles for pregnant women or children under 18. In addition, deductibles may not be charged for family planning or emergency services. States receive a varying amount of finances from the federal government depending on the financial resources that that state currently has. The range of federal funding for state Medicaid services ranges from 50 to 83 percent.

Medicaid is administered by the states. Each state establishes specific Medicaid eligibility. States determine the nature and scope of the services and how much each of the services will be reimbursed. Medicaid pays for inpatient and outpatient services, prenatal care, vaccines for kids, nursing home care, physician services, and rural health care. In addition, states may provide funds for diagnostic tests, transportation, pharmaceuticals, and rehabilitation services.

Medicaid and Medicare Fraud

Given that nearly $900 billion annually is spent on Medicaid and Medicare, it is easy to believe that white-collar criminals would be attracted to Medicaid and Medicare as a way to make money. In fact, a great deal of money could be made through Medicaid and Medicare fraud without the government even knowing about it. Medicaid and Medicare fraud comes in several different forms. One estimate of Medicaid and Medicare fraud is 8 to 10 percent. The first is phantom billing, which bills the federal government for unnecessary procedures and tests that were never performed. The fraud may also include equipment that is billed as new but is actually used. Patient billing fraud happens when a health care provider gets the necessary billing information from a client, who is a
confederate who receives a kickback, and then bills for a series of procedures that have not been provided. Upcoding is an additional fraudulent scheme by which the federal government is billed for more procedures or more serious procedures than what was necessary. This causes the bill to be larger than what it should be, thereby causing fraud and waste for taxpayers, not to mention depleting resources needed by those on Medicare and Medicaid.

There have been large Medicare arrests across the United States. In 2012, 91 doctors, nurses, and other health care providers were arrested nationwide and found to be responsible for about $430 million of fraudulent expenditures. Other raids have shown that foreign mobsters have become involved with Medicare fraud schemes because of the amount of money to be made. To combat this fraud, a Medicare Fraud Strike Force was developed. This task force has made large, nationwide arrests for fraud and regularly makes spot checks of health care organizations to make sure that fraudulent charges are not being made.

Cancer

Medicaid is operated jointly between the federal government and state governments. Medicaid benefits, therefore, will vary by state. In this section on cancer, Medicare benefits only will be examined. Medicare will cover certain things when it comes to different types of cancers. For breast cancer, one screening mammogram every 12 months is fully covered for all women with Medicare age 40 and older. One baseline mammogram between ages 35 and 39 is also covered. Medicare also covers newer digital mammograms. Medicare pays for a clinical breast cancer exam once every 24 months for women at average risk of breast cancer. A clinical breast exam (CBE) is covered once every 12 months for women at high risk and those of childbearing age who have had an exam that showed cancer or other changes in the past three years. Medicare’s cancer screening coverage information does not include magnetic resonance imaging (MRI) along with a mammogram as a screening method for women who are at high risk for breast cancer. And if a mammogram shows a change that requires more pictures, the patient might have to pay the deductible and co-pay for a diagnostic mammogram.

Medicare covers one Pap test and pelvic exam every 24 months if the patient is at average risk for cervical cancer. If a patient is at high risk for cervical or vaginal cancer or is of childbearing age and has had an abnormal Pap test in the last three years, the tests are covered every 12 months. The patient pays nothing for the Pap test or for collecting the Pap test and the pelvic exam. As part of the pelvic exam, Medicare covers a clinical breast exam to check for breast cancer. As of 2014, Medicare’s cancer screening coverage information does not list human papillomavirus (HPV) testing as a covered screening test for cervical cancer.

Medicare covers colorectal screening tests in people 50 and over to help find colorectal cancer or precancerous polyps, so they can be removed before they turn into cancer. Coverage for these tests depends on the person’s risk for colorectal cancer, when he or she had the last test, and whether something is found that needs to be removed during the test.

For men over age 50 with Medicare, one digital rectal exam (DRE) and one prostate-specific antigen (PSA) blood test are covered every 12 months. This coverage starts the day after the 50th birthday. The patient pays nothing for the PSA test, but the patient must pay 20 percent of the Medicare-approved amount for the DRE, and the yearly Part B deductible applies for the DRE. Medicare does not cover lung cancer screening tests at this time, even in people with a high risk of lung cancer.

Daniel Webster Phillips
Chryslee Sherrill
Lindsey Wilson College

See Also: Age; Government; Insurance; United States.

Further Readings

Kern, R. “Panel Recommends Against Low-Dose CT for Lung Cancer in Medicare Patients.” Oncology Practice Digital Network (May 1, 2014).
MedImmune (United States)

MedImmune, with headquarters in Gaithersburg, Maryland, creates, produces, and sells preparations of biologicals and live-virus vaccines. This company began as Molecular Vaccines, Inc., an establishment started by Wayne T. Hockmeyer in 1988, and the name changed to MedImmune, Inc., in 1990. MedImmune spent the next two decades developing innovative biological and viral therapies.

The University of Rochester cultivated the human papilloma virus (HPV) technology. In October 1995, MedImmune gained sole rights to the HPV technology for further growth in the HPV methodology. The company’s interest lies with developing this type of virus technology. By June 1996, MedImmune acquired the license of the HPV intellectual property from the German Cancer Research Center.

The company then obtained approval from the U.S. Food and Drug Administration (FDA) in January 1996 to sell RespiGam, an immune globulin given by intravenous injections, for children at high risk of contracting serious lower respiratory tract infections precipitated by Respiratory Syncytial Virus (RSV). RSV remains the most common germ to trigger lung and airway infections in infants and young children. RespiGam went off the market in 2004.

After approval by the FDA, MedImmune sent Synagis (palivizumab) to market for the prevention of serious lower pulmonary tract infections in June 1998. Synagis is a human monoclonal antibody used to prevent RSV in children. In July 2004, MedImmune placed a liquid version of Synagis on the market.

MedImmune acquired U.S. Bioscience in November 1999. The attainment of U.S. Bioscience gave the company three oncology and infectious disease products. The merger increased expansion capabilities for the promotion of oncology products. Next, MedImmune secured the rights to the drug amifostine from ALZA Corporation. Ethyol (amifostine), an oncology drug, with an action of a cytoprotective adjuvant mediator, is used in cancer patients receiving radiotherapy or chemotherapy involving DNA-binding chemotherapeutic agents. Amifostine reduces neutropenia-related fever and infection triggered by DNA-binding chemotherapy agents (e.g., alkylating agents and platinum-containing agents like cisplatin). The drug also decreases xerostomia in patients receiving radiation to the head and neck for cancer.

In January 2002, MedImmune acquired Aviron, a company with research compiled in the area of infectious diseases. The Aviron Company completed research trials on the product FluMist (Influenza Vaccine Live, Intranasal), and the FDA continued to review it at that time. The product entailed a novel method of flu vaccine delivery by nasal mist administration. It took another year and a half (June 2003) before the FDA approved FluMist. FluMist became the first nasally administered vaccine for healthy people age five to 49 years in the United States. In 2007, the FDA expanded the age range from age two to 49 years.

MedImmune announced its collaboration with the National Institute of Health to develop pandemic flu vaccines in July 2005. The plans for a flu vaccine helped MedImmune to receive $170 million for a five-year contract under the Department of U.S. Health and Human Services for a cell-based vaccine. MedImmune initiated the building of a biologics manufacturing facility in Frederick, Maryland, in September 2006 to move forward with a cell-culture-based industry.

AstraZeneca purchased MedImmune in June 2007 and merged MedImmune with Cambridge Antibody Technology by December 2007 but maintained the MedImmune name. The MedImmune name remained because AstraZeneca envisioned a worldwide biologics business.

MedImmune forged a relationship with Inserm and Inserm Transfert in February 2011 in an effort to expand research across a variety of therapeutic venues. Research moved more into the areas of oncology, respiratory, inflammation, and autoimmunity. The year 2011 also saw MedImmune’s Frederick Manufacturing Center receiving the International Society for Pharmaceutical Engineering’s 2011 Facility of the Year Award.

In April 2012, MedImmune established an affiliation with Amgen to collaborate on creating and commercializing a respiratory, inflammation, and autoimmunity (RIA) portfolio. The current work focuses on systemic lupus erythematosus (SLE), asthma, idiopathic pulmonary fibrosis (IPF), psoriasis, chronic obstructive pulmonary disease, multiple sclerosis, and rheumatoid arthritis (RA).
Oncology represents just one of the five areas of main concentration for the MedImmune Company. The oncology research aims to study solid tumors (e.g., breast or lung cancers) and hematologic cancers (e.g., lymphoma or leukemia). This research probes novel technology designed to destroy cancer cells in more efficacious and directed ways (e.g., effector-enhanced, polyspecific, and toxin-carrying antibodies). The scientists study strategic biologic capacities crucial to the initiation and progression of cancer. The areas of biologics include immune-mediated cancer therapy, tumor-associated antigens, cancer stem cells, growth factor signaling, and survival and oncolytic viruses.

MedImmune’s work on immune-mediated therapies represents a thriving field of cancer research. These therapies strive to restore and strengthen a patient’s immune system so it is able to intensify the recognition of cancer and then be able to attack the cancer. With the enhanced ability of the immune system, the body is able to respond to treatment and to prolong survival. One of the immune-mediated therapies happens to be Tremelimumab, a CTLA-4 blocking immunotherapy that remains under study in melanoma and other solid tumors. R. W. Georgantas and colleagues published results demonstrating tumor suppression in melanoma.

Immunotoxins represent a second example of promising research in oncology at MedImmune. Referred to as the Trojan horse of cancer therapies, scientists cleverly linked a toxin to an antibody. The goal is to deliver a toxin directly into a tumor cell without injury to the normal cells near it. Research by D. Bannister and colleagues demonstrates early research on monoclonal antibodies linking to toxic payloads and resulting in clinical efficacy in cancer treatment.

In conclusion, MedImmune, Inc., represents an extraordinarily innovative drug company working in the field of biologics and vaccines for treatment of diseases like cancer. Biologics and vaccines embody new areas in the last two decades to be added to the treatment regimens in cancer. The company focuses on these areas of oncology: infectious disease and vaccines, cardiovascular and metabolic diseases, neuroscience, and respiratory, inflammation, and autoimmunity (RIA). MedImmune presently conducts more than 120 research projects with the hope of coming up with breakthroughs and improvements for treatment in many diseases.

Sharon A. Takiguchi
Independent Scholar

See Also: Chemotherapy; HPV Vaccination; Vaccines.

Further Readings

Melanoma

Melanoma, also known as malignant melanoma and cutaneous melanoma, is a skin cancer originating from melanocytes, the melanin pigment-producing cells in the basal layer of the epidermis. Melanoma is the most lethal form of skin cancer because it has a higher potential for metastasis (i.e., spreading to other tissues). The primary cause of melanomas is overexposure to ultraviolet (UV) light either from direct exposure to sunlight (UVA and UVB) or from tanning beds (UVA), which is absorbed by the skin and results in DNA damage. This DNA damage causes aberrant gene expression in multiple genes and can lead to malignant tumor formation. Minimizing one’s exposure to these harmful UV rays by avoiding tanning beds and applying sunblock cream to any potentially exposed skin prior to outdoor activity as well as wearing protective clothing (such as wide-brimmed hats and long-sleeved shirts and pants) can greatly reduce susceptibility to melanoma.

Melanomas usually develop from existing moles (nevi). The first signs of melanoma are changes in the color, size, shape, or surface texture of an area of skin or existing mole. The majority of melanomas are usually either black or brown; however, other colors have been observed such as red, blue,
Melanoma may develop anywhere on the body, but are more likely to be found on the torso, head, or neck in men and on the arms or legs of women. Less-common melanomas have been found under nails and on the palms of hands, soles of feet, eyes, mouth, genitals, and the anal area.

Due to the fact that melanomas occur on the skin, the changes in shape and coloration of existing moles as well as abnormal growth of melanomas usually can be readily seen by the patient. In fact, patients are frequently the first to notice early-stage melanomas. If diagnosed early enough, most melanomas can be cured and excised with minor surgery. Early detection and treatment are key because, once the cancer has metastasized to other parts of the body, no reliably effective therapy is available and the chances of the patient succumbing to the disease are therefore high.

Melanoma progression can be characterized by five stages (stages 0–IV) where stage 0 indicates the melanoma to be in situ, meaning that abnormal melanocytes are located only in the epidermis, while stage IV is the most advanced, where the melanoma has metastasized to other parts of the body. Surgery is the first treatment of all stages of melanoma. After stage 0, other therapies besides surgery may be necessary to cure or remove the skin cancer.

Types of Melanoma

There are four main types of melanoma. Three of these—superficial spreading melanoma, lentigo maligna melanoma, and nodular melanoma—comprise 90 percent of malignant melanoma, while acral lentiginous melanoma and some other rare types make up the remaining 10 percent.

Superficial spreading melanoma is the most common type of melanoma, accounting for approximately 70 percent of all diagnosed melanomas. True to its name, this melanoma spreads along the surface layer of the skin for an extended period of time before penetrating more deeply. This type of melanoma can form from preexisting, benign moles. The first signs are darkened, flat, barely-raised lesions with irregular borders and color variations (black, brown, red, tan, or white). This melanoma can be found anywhere on the body. It is found most commonly on the backs of men, the legs of women, and the upper backs of both sexes.

Lentigo maligna melanoma arises from lentigos, which are flat, brown spots that are associated with aging or sun-damaged skin rather than moles. For this reason, this type of melanoma is found commonly among the elderly in chronically sun-exposed areas, such as the face, ears, arms, and upper torso. Because this melanoma arises from lentigos, it closely resembles lentigos but may contain different shades of brown and other color variations of black, blue, red, gray, or white.

Nodular melanoma is the most aggressive of the four main melanoma types because it grows more deeply and more quickly compared to the other three types. The melanoma appears as a blue-black, dome-shaped nodule, but as with most melanomas, color variations of blue, gray, white, brown, tan, red, or even flesh tones can be possible. This type of melanoma is invasive when it is first diagnosed, and malignancy is recognized when the damaged area becomes a bump or a highly raised area on the skin. This type of melanoma may not necessarily form from an existing mole and often occurs in areas of the body that only receive intermittent sun exposure (e.g., the chest).

Acral lentiginous melanoma is the most common melanoma among African Americans and Asians and the least common among light-skinned individuals. This melanoma appears as tan, black, or brown discoloration with irregular borders on the palms of hands, soles of the feet, or under nails, particularly the big toenail. The specific causes for this type of melanoma are unknown and unrelated to sun exposure, so the cancer cannot be attributed to UV radiation.

Treatment

Treatment strategies for malignant melanoma depend on several parameters, including histological classification and stage of the disease. Standard treatment for primary melanoma is wide excision of the primary tumor through surgery. Excision margins are based on the thickness of primary melanoma; wider excision margins are needed for the removal of a melanoma as its thickness increases. Due to the potential of metastases of melanomas to the lymph nodes, excision of the draining lymph node (or sentinel lymph nodes) is considered critical because this is most likely to be the first lymph node to which a melanoma will metastasize. Currently, sentinel lymph node biopsies (SLNB) are sensitive
enough to evaluate metastasis to the first draining lymph node. If lymph node metastasis is detected in the sentinel lymph node, then other lymph nodes in the area of the primary melanoma may also be removed surgically. When surgery of the tumor or metastatic lymph nodes is impossible or unreasonable, radiation therapy of the primary tumor or the regional lymph nodes is a viable option. Both types of therapy are appropriate for solitary or localized lesions but are not sufficient for patients diagnosed with metastatic disease. Adjuvant therapy (i.e., additional treatment provided after surgery or radiation) is recommended to patients with potential for recurrence (stages II and III) and may include immunotherapy, radiotherapy, or even the testing of a new treatment in a clinical trial. However, adjuvant therapies may reduce the quality of life for the patient without extending survival. Because there is no effective treatment for the most advanced form of melanoma (stage IV), many treatment options may be offered to the patient, which include participation in a clinical trial, chemotherapy, or immunotherapy.

**Follow-Up**
People who have been treated for, or with a family history of, melanoma should be monitored frequently to ensure an early diagnosis. For patients with melanoma thickness of less than one millimeter, less-intensive follow-ups are necessary. However, patients with high melanoma thickness (greater than one millimeter) will need more intensive checkups, that is, every three months for the first five years followed by every six months for a 10-year period.

Anh-Vu Do
Behnoush Khorsand
*University of Iowa*
Sean Geary
Aliasger K. Salem
*College of Pharmacy, University of Iowa*

**See Also:** Skin Cancer, Childhood; Skin Cancer, Melanoma; Skin Cancer, Non-Melanoma; Skin Carcinoma, Merkel Cell.

**Further Readings**

---

**Melanoma, Intraocular (Eye)**

Intraocular melanoma is a disease in which cancer cells arise from melanin-producing cells of the eye (melanocytes). The most common type of intraocular melanoma is uveal melanoma, where the cancerous cells arise from the uvea. The uvea is the middle layer of the wall of the human eye and is composed of three main parts—iris, ciliary body, and choroid. Depending on the primary site of development, the tumor may be called an iris melanoma, ciliary body melanoma, or choroidal melanoma. Eye melanoma can occur on the conjunctiva or in the eye socket, but these types of eye melanoma are very uncommon. Although the incidence of intraocular melanoma is rare—only six per million—this cancer is noteworthy as it is the most common malignant tumor arising in the eye, and the second-most common type of melanoma after cutaneous. Unlike most cancers, the survival rate of intraocular melanoma has not improved despite the newer treatment options, and currently, there is no effective systemic therapy available once the cancer spreads to the other organs. Nearly half of all patients diagnosed with uveal melanoma will develop metastases, and the estimated five- and 10-year survival rates from the diagnosis of uveal melanoma are 75 and 60 percent, respectively. Hence, prevention and early identification are critical for individuals at risk of developing intraocular melanoma metastasis.

**Symptoms**
Symptoms of intraocular melanoma can include decreased peripheral vision, blurred vision, changes in the shape of the pupil, irritation, redness, the sensation of flashing lights, and specks of dust...
or floaters in vision. However, up to one-third of patients are completely asymptomatic at the time of diagnosis. Additionally, these symptoms are not unique to intraocular melanoma. Individuals experiencing any of these symptoms should be evaluated by an ophthalmologist for an appropriate examination and workup.

Complications
Growing tumors can impinge on adjacent structures within the eye and can lead to increasing pressure within the eye, causing glaucoma. It can also lead to vision loss or spread to adjacent organs—such as the liver, lungs, and bones.

Causes
There are no known causes for the development of intraocular melanoma. Exposure to ultraviolet (UV) radiation has been studied as a possible cause of intraocular melanoma. Although excess UV radiation is known to cause skin melanoma, it has not conclusively been shown to cause intraocular melanoma and is likely noncausal. Genetic risk factors, such as mutation of the BAP1 gene, are currently being studied as a cause of uveal melanoma.

Risk Factors
Known risk factors for intraocular melanoma include light eye color, white ethnicity, older age, and certain inherited skin disorders, such as dysplastic nevus syndrome. Studies have shown that intraocular melanoma rates are eight to 10 times higher in whites compared to blacks, and that the peak incidence is the seventh and eighth decades of life.

Diagnosis
Multiple methods exist for diagnosis; however, in 99 percent of cases, noninvasive indirect procedures such as ophthalmoscopy, slit lamp biomicroscopy, and ultrasonography are used. Invasive procedures, such as an angiogram or biopsy (removing a sample), are sometimes required to examine the suspicious tissue.

Prognosis and Prevention
Currently, there are no treatments for intraocular melanoma post metastasis. Although cutaneous melanoma (skin cancer) is related to intraocular melanoma, medications used to treat cutaneous melanoma, such as decarbazine and temozolomide, are not effective for treating intraocular melanoma. Naturally, this has put the emphasis on prevention and identification of individuals at risk of intraocular melanoma metastasis.

One way patients with intraocular melanoma may be monitored for metastasis is through liver function tests as uveal melanoma has a high propensity for metastasis to the liver. Liver metastasis makes up 93 percent of uveal metastasis, followed by 24 percent for lung and 16 percent for bones. It can also spread to the brain, skin, or any other organ of the body, so imaging tests, such as X-ray, computed tomography (CT), and magnetic resonance imaging (MRI), are also used to monitor whether the melanoma has metastasized systemically.

Tumor location, size, histology, or mitotic index (growth potential) all can be used to predict metastasis. These features are helpful in counseling the patient; however, they are not absolutely predictive for the progression of intraocular melanoma. Recently, chromosome analysis and gene expression profiles have been used to predict metastasis. Monosomy 3 and duplication of chromosome 8 are two examples of chromosomal anomalies associated with increased risk of metastasis.

In gene expression profiling, a patient’s gene expression profile is compared to the gene expression patterns from more than 40,000 cancer-related genes of other intraocular melanoma patients who
had either survived or died from the disease. The closer the genetic expression is to those who died from their disease, the worse the prognosis; the closer the genetic expression is to those who survived the disease, the better the prognosis. The genetic profile can be used to classify intraocular melanoma as either class 1 (unlikely to metastasize) or class 2 (very likely to metastasize).

**Treatment**

It is important to consider the size of the tumor when looking at treatment options. A small intraocular melanoma may not require immediate treatment, whereas a large melanoma may require a more aggressive treatment. Treatment options include surgery, radiation therapy, laser therapy, and cold treatments. Surgery can be done to remove a part of the eye that has the melanoma, or the entire eye can be removed if the tumor is large. Radiation therapy uses high-power protons or gamma rays to kill the cancer cells. Laser treatment involves the use of infrared laser, and cold treatment uses extreme cold (cryotherapy) to kill the melanoma cells.

**Drugs in Clinical Trial**

In June 2013, Carvajal and colleagues presented a study on the experimental drug selumetinib. Treatment of metastatic uveal melanoma with selumetinib was shown to shrink the tumor size, making selumetinib the first systemic therapy ever to treat patients with systemic ocular melanoma effectively. With selumetinib, 50 percent of patients experienced tumor shrinkage, with 15 percent achieving major shrinkage.

Krishna Subhash Vyas
Kristine Song

*University of Kentucky College of Medicine*

**See Also:** Experimental Cancer Drugs; Intraocular Melanoma; Retinoblastoma.

**Further Readings**


---

**Memorial Sloan Kettering Cancer Center**

The Memorial Sloan Kettering Cancer Center (MSKCC) in New York City is the oldest and largest private cancer center and hospital in the United States. MSKCC was founded in 1884 as the New York Cancer Hospital by a group of people that included John Jacob Astor and his wife Charlotte. The name of the hospital was changed in 1899 to General Memorial Hospital for the Treatment of Cancer and Allied Diseases. In 1936, the hospital was relocated on land donated by John D. Rockefeller Jr. and the new Memorial Hospital opened in 1939.

The Sloan Kettering Institute was established in the 1940s by Alfred P. Sloan and Charles F. Kettering, former executives of General Motors. Today, the institute is one of the leading biomedical research centers in the United States. The Memorial Sloan Kettering Cancer Center was established in 1960 to coordinate and oversee the policies of the Memorial Hospital and the Sloan Kettering Institute. In 1980, the two combined to form a single institution headed by a president and chief executive officer.

MSKCC is one of 41 institutes designated by the National Cancer Institute as a comprehensive cancer center because of their excellence in basic research, clinical science, and cancer treatment. MSKCC has 471 inpatient beds and a surgical area covering 72,000 square feet. MSKCC physicians work in close collaboration with research scientists to make the highest-quality care available to cancer patients and to develop effective strategies for cancer prevention, control, and cure. MSKCC also offers specialized training for physicians and scientists. The center...
provides care to patients with all types of cancer and allied diseases through professional counselling, patient information, and education.

The research programs at MSKCC are divided into eight categories, including cancer biology and genetics, cell biology, computational biology, developmental biology, immunology, molecular biology, molecular pharmacology, and chemistry. In 2014, MSKCC's research division was under the leadership of Joan Massagué and comprised more than 100 laboratory investigators, 400 research fellows, and about 200 doctoral students. Many members of both the National Academy of Sciences and the Howard Hughes Medical Institute are affiliated with the Sloan Kettering Institute. The research activities at MSKCC are spread across three buildings—the Rockefeller Research Laboratories, Schwartz Research Building, and Zuckerman Research Center.

The Sloan Kettering Institute offers a range of training programs, including a tri-institutional M.D.-Ph.D. program, doctoral programs, and summer internships. In 2004, the Louis V. Gerstner Jr. Graduate School of Biomedical Sciences was established at MSKCC and offers a doctoral program for laboratory scientists in the field of cancer biology. The primary aim of this program is to train the next generation of researchers, clinicians, scientists, physicians, and other allied health care professionals to assume leadership roles in the life sciences and medicine, with a special emphasis on cancer treatment, prevention, and care.

The education and training programs at MSKCC form a vital and integral part of the center's mission. These programs include graduate training, post-doctoral training, and continuing education to prepare the next generation of physicians, scientists, nurses, and technicians.

MSKCC awards the Paul Marks Prize for Cancer Research, named after Paul A. Marks, the center's president emeritus, to recognize young leaders making significant contributions to the understanding and development of new cancer treatments. The prize encourages researchers to create novel cancer therapies and to better understand the mechanisms of cancer development and progression. The prize is awarded to a maximum of three investigators every alternate year, and nominees for the award have to be 45 years old or younger. Prize winners are selected by a panel of cancer research investigators from leading research institutions, and the winners share a cash award of $150,000 and present their work at a scientific symposium at MSKCC.

Fred's Team is the athletic fund-raising program at MSKCC, named in honor of running legend and New York City (NYC) marathon cofounder Fred Lebow. Fred's Team participates in the TCS NYC Marathon, the Boston Marathon, and other events, raising money to support more than 50 areas of cancer research. Fred's Team has raised more than $59 million since its founding in 1995. The Society of Memorial Sloan Kettering Cancer Center, a volunteer organization, also plays an important role at the center. Founded in 1946, the society develops and funds programs to enhance patient care and provides public education materials on cancer prevention, early detection, and treatment.

See Also: Comprehensive Cancer Center of Wake Forest University; Dana-Farber Cancer Institute; Holden Comprehensive Cancer Center at the University of Iowa; Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins; University of Chicago Medicine Comprehensive Cancer Center; University of California, Los Angeles, Jonsson Comprehensive Cancer Center; University of California, San Francisco, Helen Diller Family Comprehensive Cancer Center; University of Michigan Comprehensive Cancer Center; University of Southern California Norris Comprehensive Cancer Center.

Further Readings
Menarche is a woman's first menstrual cycle; the age at which it begins can vary considerably. Of both social and medical significance, menarche is the principal event of female puberty, signaling the entrance into adolescence as the result of becoming potentially fertile. The age of 13 is a traditional estimate given as an average or typical start time, but the average age in the United States is closer to 12, while in general, Asian women experience menarche later than Western women do.

Menarche requires a certain set of biological events as prerequisites: the release of estrogen by the ovaries in response to signaling from pituitary hormones; the growth of the uterus, widening of the pelvis, increase of fatty tissue, development of the breasts, and height growth, all in response to estrogen; the estrogen-driven growth of the uterine lining, the endometrium; and the accumulation of sufficient body mass (which results in delayed menarche among the malnourished). There is no one specific signal in the body that causes menarche to occur; rather, these many physiological changes lead up to it. Menarche often differs from later menstruation: While also accompanied by abdominal cramps (typically less severe than in a postadolescent woman), the flow is usually scantier, sometimes limited to brief spotting, and is visually brighter. Menarche does not always indicate that ovulation has occurred; studies indicate that most women's cycles remain anovulatory (without ovulation) as much as three years after menarche and six years for about 10 percent of women. Thus, although menarche is commonly taken as a sign of fertility, this is true for only a minority of women, for whom there is no clear external sign indicating their first ovulation. A small number of women ovulate before their first menarche, and can conceivably become pregnant from a conception that precedes menarche, which further demonstrates the error of the commonly assumed conflation of menarche and the ability to conceive and carry a child.

While the amount of time, if any, between menarche and first ovulation varies from woman to woman, studies have established that early menarche correlates with early onset of ovulatory cycles. D. A. N. Apter and Reijo Vihko, for instance, established that not only does early menarche lead to early onset of ovulatory cycles but that earlier menarche also correlates with a shorter span of time between menarche and ovulatory cycles. For instance, in their study, the time from menarche until half of the woman's cycles were ovulatory was only one year among girls whose menarche came before age 12, but 4.5 years for girls whose menarche came at or after age 13. This is of particular concern for girls whose menarche is unusually early.

Environmental factors are known to impact the timing of menarche. Malnutrition was already mentioned as a delaying factor. Studies have identified the following as factors associated with early menarche: childhood obesity (due to its impact on estrogen), low birth weight, being a single child, experiencing preeclampsia in the womb, not having been breast-fed, insufficient exercise as a child, high-conflict family relationships, and nonwhiteness. In light of the fact that menarche is later in Asia than in the West, nonwhiteness is an especially complex factor and is attested in a study of early menarche in the United Kingdom; here, it should be assumed that the relevance of nonwhiteness to early menarche in the UK is due not to genetic factors, or at least not to genetic factors alone, but to some social or environmental factor that is demographically correlated with being a nonwhite citizen or resident of the UK.

Childhood stress in general has an impact on the onset of puberty, which seems to be more pronounced in girls. Stress that threatens physical survival or introduces sufficient uncertainty—such as being a war refugee—is more likely to delay menarche than bring it about early. While the reasoning, such as it is, behind this delay makes sense—if the individual's own survival is uncertain, the survival of potential children is more likely if their conception can be delayed—the mechanism by which social effects impact the timing of menarche is not understood. In animal research, pheromones have been implicated as influencing hormonal release. As with nonwhiteness in the previous paragraph, it is likely that many social factors are correlations rather than causes; many young women whose physical survival is in chronic jeopardy also face malnutrition, for instance, and so many social factors simply indicate a greater chance of the presence of a specific physical factor, the mechanism of which is much better understood.

Malnutrition may also explain why the average age of menarche in the West declined significantly.
Menarche, Early

in the 20th century. As late as 1850, average age of menarche in Europe was 17, and 110 years later, it had declined to 13. (The fact that menarche used to come later in the West is likely reflected in the fact that American girls celebrate their sweet sixteen as a sort of coming of age ritual, as Latin American girls celebrate their quinceanera on their 15th birthdays.) It remains significantly close to that number more than 50 years later. The late 19th and early 20th centuries included many developments that impacted famine and nutrition, from the development of modern fertilizers and agricultural science to improved crop yields to the science of nutrition and a better understanding of what nutrients children and pregnant women require, to the introduction of modern canning and preservation, rapid transportation, and refrigeration—all of which made it comparatively easy to have fresh food year round, a challenge that northern climates had struggled with for all of human history. It is not too much of an exaggeration to say that, until the 19th or 20th centuries, in much of the world, some level of malnutrition was the norm for a large percentage of children a large percentage of the time.

Menarche is important not only for its cultural significance but because early menarche is correlated with a higher risk of breast cancer. Breast cancer risk is higher in three relevant groups: women whose breast development began at a younger age; women who experience early menarche (with risk increasing by 5 percent for each year, according to one analysis); and women with the BRCA1 gene who experience early menarche—who face an increased risk relative to the general population that is greater than the cumulative risks of BRCA1 carriers and women with early menarche. (BRCA2 carriers, on the other hand, face only that cumulative risk.) This risk is largely faced in the form of an increased risk of estrogen-receptor-positive tumors. The source of the risk is believed to be the exposure to ovarian hormones; thus, while menarche is taken as the indicator, the risk actually refers to the woman's lifetime number of ovulatory cycles. (Late menopause is similarly tied to breast cancer risk, though not as strongly as early menarche.)

However, for many women, the risk of early menarche is significant in another sense as well. Age at first birth is a risk factor, with higher ages carrying higher risk. While that risk is usually expressed in terms of absolute age—with a woman bringing her first child to term at 30 facing a higher risk than a first-time mother at 25—at least one study suggests that the relevant figure to consider is not absolute age but the interval between menarche and first full-term birth. Assuming, then, that a given population of women has their first children at the same age, the greater risk of breast cancer is faced by those of them with the earliest menarche.

In the last 30 years, precocious puberty—a term encompassing both early menarche in girls and early development in boys—has been on the rise in the United States, disproportionately affecting African American and Hispanic girls, though the most rapid increase was seen in white girls. (Precocious puberty is 10 times more common in girls than boys.) Environmental chemicals, whether in the atmosphere, drinking water, beauty products (including body soap, toothpaste, sunscreen, and children's shampoo), or food, are sometimes suspected as being culprits; the industrial petrochemical bisphenol A, used in many plastics and food can linings, is known to mimic estrogen, and chemicals like polyvinyl chloride act as endocrine disrupters.

Bill Kte’pi
Independent Scholar

See Also: Breast Cancer; Chemical Industry; Diet and Nutrition.

Further Readings
Jean, Rosenie Thelus, et al. “Psychosocial Risk and Correlates of Early Menarche in Mexican-American...

Merck (Germany)

Merck Germany, or Merck KGaA, was founded in Darmstadt, Germany, in 1668 by pharmacist Friedrich Jacob Merck and is the oldest pharmaceutical and chemical company in the world. The establishment of Merck and company as a subsidiary in the United States took place in 1887 in New York. Merck & Co. was expropriated in 1917 after World War I and has since been an independent company based in the United States. Since its inception as a pharmaceutical company, Merck Germany has expanded into a world leader for innovative and high-tech products in the pharmaceutical and chemical industry. In 2013, Merck Germany had total revenues to the tune of €11,095 million. Merck of Darmstadt, Germany, holds the global rights to the name and the trademark MERCK, with headquarters in Darmstadt, and is presently headed by Karl Ludwig Kley, who holds the position of chair of the executive board.

Merck Germany operates the key businesses of the Merck Group. Darmstadt houses the research and development (R&D) units, production plants for pharmaceuticals and chemicals, and the departments of human resources, patents and scientific information, procurement, sales, and accounting. The headquarters at Darmstadt are expected to expand over the next years to convert the site into a global headquarters with a new innovation center promoting innovative interdisciplinary projects. Merck Germany group has an approximate head count of 38,000 employees in 66 countries. Merck Germany introduced a strategic change in management in 2007 and refocused on the product portfolio. This change was followed by a number of acquisitions and portfolio realignments for a sustainable business development model.

Although a leading global corporation, Merck Germany remains a family owned company. Shareholders own 30 percent of the total capital of Merck Germany, and the rest is held by the Merck family. Merck Germany is a corporation with general partners (Kommanditgesellschaft auf Aktien [KGaA]), where at least one partner has unlimited liability for the company’s creditors (general partner). The shareholders hold an interest in the share capital without any personal liability for debts. It is a combination of a German stock corporation (Aktiengesellschaft) and a limited partnership business (Kommanditgesellschaft). The company has no management board, and the business is carried on by the personally liable partners with limited rights and obligations of the supervisory board.

Merck Germany operates in Europe, Africa, Asia, Oceania, and Latin America. The pharmaceutical and chemical businesses of Merck are divided into four major divisions:

Merck Serono—Biopharmaceuticals, which is the largest division of Merck focusing on specialized therapeutics for neurodegenerative diseases, oncology, immune-oncology, fertility, cardiovascular diseases, endocrinology, and biosimilar business. Merck Serono was founded in 2007 when Merck acquired the Swiss biotechnology leader Serono, merging the two companies. Merck Serono has a present head count of 14,600 employees and a presence in 150 countries. Merck Serono has four R&D hubs, one each in Boston (United States), Darmstadt (Germany), Beijing (China), and Tokyo (Japan), representing the strategic business regions for Merck Serono. Merck Serono invests heavily in R&D activities, amounting to approximately 20 percent of total sales. Merck Serono also has smaller R&D laboratories in Italy and Israel. Merck Serono also has strategic research partnerships.
with biotech companies, clinical research groups, and academic institutions and universities. In September 2014, Merck Germany announced that the biopharmaceutical division Merck Serono was on track for the expected transformation and growth program, reflected by the successful execution of growth initiatives as well as progress of pipeline drugs, most importantly in the immuno-oncology and biosimilars arena. Merck Serono plans to invest 130 million to 50 million euros, in addition to the already committed 100 million euros, in biosimilars by 2015, depending on the outcome of phase I studies.

The consumer health division of Merck Germany offers over-the-counter pharmaceuticals and products and has a presence in 100 countries with approximately 1,600 employees. The division includes multivitamin supplements, cold remedies, and women’s and children’s health supplements. As of 2013, Europe accounted for 65 percent of the total sales in the consumer health care division, and emerging markets accounting for 32 percent of total sales. The consumer health division business was worth 477 million euros in 2013. The consumer health division has the strongest presence in Europe, but it is rapidly expanding into emerging markets in Asia and South America.

The performance materials division focuses on advanced-technology chemicals and covers six areas that include display materials and lighting materials needed for liquid crystal display and organic light emitting diodes (OLEDs); the solar and energy division develops novel photovoltaic materials that are supplemented with process chemicals for printing technologies. The division also works on the chemical coating processes used for solar cell manufacturing. The cosmetics division concentrates on the development of active ingredients for light protection, insect repellents, and skin perfection. The performance materials division also produces specialized fillers and active ingredients for the foods and cosmetic industry. The coatings division produces specialized paints and coatings for architecture, the automobile industry, and electronics. The printing and plastics division manufactures pigments for screen printing, offset printing, and offset coating as well as pigments for soft-touch plastic drinking bottles, food-grade plastics, and various automotive components.

Merck Millipore is the division for chemicals and tools for life science research. Millipore Corporation of the United States was acquired by Merck Germany in 2010 and became part of the company’s life science tools division. Merck Millipore is headquartered in Billerica, Massachusetts, and offers more than 60,000 products with a global presence in 66 countries. Merck Millipore offers a broad range of products and services for the high-growth, high-margin market segments, such as bioresearch and bio-production.

In September 2014, Merck Germany signed a definitive agreement for the acquisition of U.S. Company Sigma Aldrich for 13.1 billion euros, establishing it as one of the leading players in the life science industry. The transaction has been unanimously approved by the board of directors of Sigma Aldrich. The acquisition of Sigma Aldrich expands the global reach of Merck and increases its presence in North America as well as the fast-developing Asian markets. The acquisition of Sigma Aldrich will support the delivery of more than 300,000 products and will offer a complementary range of products to research laboratories and academia business. Sigma Aldrich would also complement the products of Merck Millipore in pharmaceutical and biopharmaceutical production.

The Merck group focuses on innovation and spent 1.5 billion euros for research and development in the year 2013 and plans to continue the trend in coming years.

Poonam Balani
Independent Scholar

See Also: Merck & Co. (United States); Pharmaceutical Industry.

Further Readings
Merck and Co., known as Merck Sharp and Dohme outside the United States, is an American pharmaceutical company based in New Jersey. Originally established as the American subsidiary of the Germany pharmaceutical company Merck, it was seized by the federal government during World War I and established as an independent American company.

Today, it is the seventh-largest pharmaceutical company in the world and the publisher of the Merck Manuals, a best-selling series of medical reference books that includes the best-selling medical textbook in the world, the Merck Manual of Diagnosis and Therapy. It operates in 120 countries with about 76,000 employees, though between 2011 and 2015, it cut its workforce by about 20 percent in an effort to cut costs.

In the past, Merck developed the first vaccines for mumps and rubella, Vioxx for the treatment of arthritis, and Mevacor, the first statin. It has also developed a number of treatments for cancer and cancer-related side effects. Fosamax, for instance, is the trade name for alendronate, developed to treat postmenopausal osteoporosis and later applied as a preventative of bone problems as a result of certain cancers.

Fosamax is a bosphophonate, which is absorbed by the bone with a terminal elimination half-life of 10 years. The absorbed drug binds to exposed bone surfaces and inhibits osteoclast-mediated bone resorption. This results in a reduction of fractures as a result of osteoporosis and helps prevent osteoporosis induced by corticosteroid usage. However, side effects include osteonecrosis of the jaw in a
small number of patients, especially cancer patients given intravenous Fosamax. In 2013, Merck agreed to a $27.7 million settlement in a class action lawsuit over the side effect.

Merck produces Gardasil, a vaccine that prevents many strains of human papillomavirus (HPV). HPV causes 70 percent of cervical cancers and many anal, vulvar, vaginal, and penile cancers, making Gardasil a cancer vaccine of considerable efficacy against those cancers. HPV infections also contribute to about a third of head and neck squamous cell carcinomas, so although it has not been clinically proven for this purpose, in theory, Gardasil reduces the incidence of those cancers. Gardasil was approved by the Food and Drug Administration (FDA) in 2006 and by 41 states by 2008 and is approved for use in 120 other countries. The FDA specifically recommends the vaccination before adolescence or sexual activity. In men, Gardasil is expected to protect against penile and anal cancer and should also help curtail the spread of HPV in order to reduce cervical cancers in women.

Gardasil became politicized when it was revealed that Merck was lobbying state legislatures to make vaccination compulsory as a requirement for public school attendance for young girls. Despite the medical sense of the requirement, even before the issue of vaccination as a personal choice became politicized by the anti-vaccination movement, the HPV vaccine specifically was controversial because of its association with a sexually transmitted disease (STD) rather than a disease spread through casual contact, like measles and mumps. Surprisingly perhaps, Texas governor Rick Perry, a Republican who later ran for president, made Gardasil a mandatory school vaccination in the state; his order was overturned by the legislature, which in Texas wields more power than the governor. Conservative groups opposing compulsory vaccination suggested that being vaccinated against an STD would lead to girls being more promiscuous.

Merck manufactures Keytruda, the trade name for pembrolizumab, which was approved by the FDA in 2014 as a breakthrough therapy for metastatic melanoma. Keytruda targets programmed cell death (PD-1) receptors and is used following treatment with the monoclonal antibody ipilimumab. The drug is an early example of what promises to be a vibrant class of cancer drugs that boost the immune system's ability to fight cancer and has shown potential to treat stomach cancer in initial studies. Merck beat out Bristol-Myers Squibb, Roche, and AstraZeneca in the race to develop the first PD-1 receptor blocker. A Bloomberg report extrapolated likely sales of $1.5 billion for Keytruda alone in 2017.

Emend is the trade name of aprepitant, Merck's antiemetic approved by the FDA in 2003 to prevent nausea and vomiting induced by surgery or chemotherapy. It is also available as an intravenous drug. Merck's Intron A is an antiviral drug used to treat chronic hepatitis C and B, hairy cell leukemia, chronic myelogenous leukemia, multiple myeloma, follicular lymphoma, carcinoid tumor, and malignant melanoma.

Sylatron is Merck's trade name for pegylated interferon alfa-2b, a hepatitis C treatment that has been approved to treat melanoma with nodal involvement after surgical resection. It is on the list of the World Health Organization's essential medicines.

Temodar is Merck's brand name for an oral chemotherapy drug, temozolomide, an alkylating agent used to treat the aggressive brain tumor glioblastoma multiforme, as well as melanoma, relapsed anaplastic astrocytoma, and as an off-label use, oligodendroglioma brain tumors.

Zolinza is Merck's trade name for vorinostat, an inhibitor of histone deacetylases, used to treat cutaneous T-cell lymphoma.

Like many pharmaceutical companies, Merck's ethical record is not spotless. In 2009, it was revealed that it had sponsored the Australasian Journal of Bone and Joint Medicine, a medical journal that reprinted from other journals articles that portrayed Merck's products favorably. The relationship was not disclosed, and the journal was published by Elsevier under the guides of a normal independent peer-reviewed scholarly publication. Merck has also been investigated for routine overbilling to Medicaid and other health care programs and for compensating health care professionals in return for prescribing Merck products.

Bill Kte'pi
Independent Scholar

See Also: Anticancer Drugs; Merck (Germany); Pharmaceutical Industry.
Merkel Cell Carcinoma

Merkel cell carcinoma pertains to a rapidly progressing neuroendocrine skin cancer that is thought to have arisen from the Merkel cells that line the basal layer of the epidermis. The concept of its origin is based on the presence of neuroendocrine granules in the cytoplasm as well as keratin filaments, which are also observed in skin cells. It also has been suggested that Merkel cells might have emerged from pluripotent stem cells that are programmed to differentiate into dermal cells. Since its first historical description in 1972, information on Merkel cell carcinoma has significantly increased with the development of immunohistochemical detection techniques and improvements in electron microscopy. Interestingly, the incidence of Merkel cell carcinoma has also increased markedly in the past few decades, possibly due to improvements in detection methods. It is thus timely that biologic updates on this malignancy be presented in this entry.

In 2008, a novel human polyomavirus known as Merkel cell polyomavirus was described in the literature and was identified as a contributing factor in the etiology of Merkel cell carcinoma. The Merkel cell polyomavirus is a tiny, circular virus that harbors double-stranded DNA and belongs to the family Polyomaviridae. The genome of the Merkel cell polyomavirus is 5.3 kilobases in length and encodes for the major components of polyomaviruses, such as the large tumor antigen (LT-Ag) and the small T antigen (ST-Ag). These components are encoded in the early region and induce cells to enter the cell cycle and initiate viral DNA replication. The late region is a distinct region from the T antigens and encodes for the structural VP capsid proteins through the action of a noncoding region. This particular noncoding sequence acts as the promoter or origin for viral replication.

Genomic studies have shown that mutations alter the function of the LT-Ag of the Merkel cell polyomavirus, which inhibits viral DNA replication and eventually results in cell death. On the other hand, studies have indicated that ST-Ag is a distinct oncoprotein that imparts its effects in downstream activities, including that of the mammalian target of rapamycin (mTOR) pathway. Recent studies have shown that 80 percent of Merkel cell carcinoma samples harbored Merkel cell polyomavirus sequences, whereas normal skin samples presented only a 16 percent detection rate for the same viral sequences. A mouse-derived monoclonal antibody has also been described to possess a high level of sensitivity in detecting a segment of the LT-Ag of the Merkel cell polyomavirus. Knowledge on the DNA sequence of the LT as well as ST-Ag regions also has facilitated the design of primers for polymerase chain reaction (PCR) analysis of Merkel cell carcinoma tissue samples.

In terms of clinical management of Merkel cell carcinoma, a four-level staging system was proposed in 2010, which was based on the results of assessments of a total of 5,823 cases of Merkel cell carcinoma submitted to the National Cancer Database registry. The National Cancer Database later adopted this staging system for Merkel cell carcinoma. The

Further Readings
current staging system consists of two groups of stages; one group comprises stages I and II, whereas the other groups comprise stages III and IV. These are further classified according to the nodal features, including histological findings after biopsy and the clinical stage based on analysis of images.

Several factors have been identified as predictors of Merkel cell carcinoma, which include invasion into the lymphovascular regions of the primary tumor, advanced stages of the disease, and the occurrence of immunosuppression. The overexpression of specific proteins such as survivin and VEGFR2 also has been associated with a highly aggressive form of Merkel cell carcinoma. These recent findings on molecular markers may be used eventually as tools in predicting treatment outcomes of patients diagnosed with Merkel cell carcinoma.

Unfortunately, the relevance of imaging in analyzing and staging Merkel cell carcinoma has not been fully established. However, recent studies have suggested that positron emission tomography and computed tomography (PET and CT) be used as the first-line methods of imaging instead of CT alone or magnetic resonance imaging (MRI). The use of PET and CT is most appreciated in cases of Merkel cell carcinoma that do not present with palpable adenopathy; thus regional screening of nodes using PET and CT may further assist in the diagnosis of Merkel cell carcinoma. Several studies also have reported that the chances of patient survival are lower when only clinical exams to detect nodes were performed, without the application of PET and CT.

Recent studies also have shown that a multidisciplinary approach is the best treatment of Merkel cell carcinoma. Primary Merkel cell carcinoma generally is treated by surgical resection, which may or may not be coupled with irradiation. Resection should include approximately two-centimeter margins beyond the affected area, which in turn decreases the need to expose the patient to irradiation. When an adjuvant setting is required in a particular Merkel cell carcinoma case, then irradiation is recommended as the next treatment. Some reports have shown that irradiation of the surgical bed does not confer any direct benefits to the patient with Merkel cell carcinoma, thus indicating a need to conduct more extensive studies. A clinical trial was earlier launched, with a primary goal of determining the benefits of irradiation on the early stages of Merkel cell carcinoma. However, this clinical trial was prematurely terminated due to a sudden decrease in the number of recruited study participants when other novel treatment options were presented to potential treatment patients.

Rhea U. Vallente
PreventionGenetics, LLC

See Also: Radiation; Radiation, Ionizing; Radiation Therapy; Skin Carcinoma, Merkel Cell.

Further Readings

Malignant mesothelioma is a relatively rare and difficult-to-treat form of cancer that arises in the mesothelium, the thin layer of tissue covering the majority of organs inside the human body.

Mesothelioma is classified into types based on where in the mesothelium the cancer first emerges. Pleural mesothelioma is the most common type and affects the tissue known as pleura that surrounds the lungs. Less-common forms are peritoneal and pericardial mesothelioma, which arise in the lining of the abdomen (peritoneum) and the lining of the heart (pericardium), respectively. The signs and symptoms vary depending on the specific type of mesothelioma, but the underlying cause is almost always due to long-term exposure to asbestos.

Treatments are available to help improve quality and longevity of life for individuals with mesothelioma, but for most patients, a complete cure is not achievable.
Prevalence and Risk Factors
According to the American Cancer Society, approximately 3,000 new cases of mesothelioma are diagnosed annually in the United States, with the prevalence being among men aged 65 or older. Exposure to asbestos is considered to be the primary risk factor for developing mesothelioma.

Asbestos is a strong, heat-resistant mineral that is naturally present in the environment. Traditionally, it has been used as a component in a vast array of consumer products, from adhesives to oven mitts, and in all types of building materials, such as roofing shingles, insulation, and flooring. While asbestos is still used in some products, its widespread application ceased in the late 1980s in the United States after the link between the substance and the deadly cancer became known.

When asbestos fibers become disturbed during construction, installation, or removal of asbestos-containing products, a thick dust is created that can be harmful to health if inhaled or swallowed. The tiny asbestos fibers can get lodged in the mucus of the throat, windpipe, or airways and eventually settle in the lining of the lungs, chest wall, or abdomen, causing irritation that may injure the cells of the mesothelium and lead to mesothelioma. The time from asbestos intake to mesothelioma outbreak may span as much as three or four decades, although the disease can develop more rapidly in some individuals and not at all in others.

There are several factors that may increase the risk of developing mesothelioma. Individuals who were exposed to asbestos at an early age, for an extended period of time, and at higher levels are more likely to develop the cancer. In addition to anyone who has been directly exposed to asbestos fibers, there is a higher risk among individuals who live with someone who has been directly exposed, usually through work. Asbestos-exposed workers may inadvertently bring harmful asbestos dust into the home on their clothing and skin, putting everyone who lives in the home at higher risk for mesothelioma.

Another risk factor for mesothelioma may be linked to the polio vaccine given to millions of individuals between 1955 and 1963. The vaccine contained a virus known as SV40 that was derived from monkeys and is believed by some to have a link with mesothelioma. There also may be a link between mesothelioma and injections of a radioactive agent known as Thorotrast used in some X-ray tests until the 1950s.

Signs and Symptoms
The specific signs and symptoms of mesothelioma depend on where in the body the cancer originates. In pleural mesothelioma, which affects the lungs, early symptoms mimic minor common ailments, such as fatigue, cough, hoarseness, and fever. As a result, many individuals with mesothelioma ignore their symptoms until they progress to include other signs and symptoms, such as chest pain under the rib cage or in the lower back, shortness of breath, unusual lumps of tissue under the skin on the chest, swelling of the face and arms, excessive sweating, and unexplained weight loss. The majority of individuals with pleural mesothelioma have active symptoms for several months before being diagnosed with the cancer.

Some early indicators of peritoneal mesothelioma, which affects the abdomen, also can be confused with symptoms of less-serious conditions. For example, nausea, vomiting, and stomach pain can signal a host of illnesses and are not exclusive to mesothelioma. More-telling symptoms of peritoneal mesothelioma include the additional ailments of swelling or fluid buildup in the abdomen, lumps of tissue in the abdomen, and unexplained weight loss.

Diagnosis and Treatment
If symptoms and patient history—such as known exposure to asbestos—suggest a possibility of mesothelioma, a complete physician's exam would be performed to check for lumps, fluid, or other markers. Blood tests and imaging tests of the lungs or abdomen also might be ordered to help identify or rule out a potential diagnosis of likely mesothelioma. However, the only way to make a definitive diagnosis of mesothelioma is through a biopsy procedure in which a small portion of tissue is extracted from the affected area to be examined in a laboratory. The tissue sample is analyzed under a microscope to determine if the abnormal tissue is mesothelioma and, if so, what types of cells are involved. The cellular identification and involvement determines the definitive diagnosis, disease staging, and treatment options for the patient.

Once a diagnosis of mesothelioma is made, the cancer is staged into one of four categories based on its level of infiltration within the body. Using
peritoneal mesothelioma as an example, stage I is limited to a single portion of the mesothelium in the chest and is considered to be localized cancer. Stage II involves spread beyond the lining of the chest into the diaphragm or lungs. Stage III includes spread to other structures within the chest and possibly nearby lymph nodes. Stage IV mesothelioma is considered advanced cancer and typically has spread more extensively within the chest and potentially to distant sites within the body, such as the brain and liver.

The staging system helps determine an appropriate treatment plan. Generally, stage I, II, and III mesothelioma cancers have some potential to be surgically removed. However, the decision to remove the cancer is determined more by a combination of the patient’s overall health, the tumor’s location and infiltration pattern, and the cellular subtype of the tumor. Even when surgical resection is performed, in a majority of cases, damaging and aggressive mesothelioma cancer cells are left behind after surgery. As a result, chemotherapy and radiation often are used in conjunction with surgery in mesothelioma patients.

The survival outlook for individuals with mesothelioma is generally one to two years, depending on stage at diagnosis and other prognostic factors, such as age, blood cell count, and weight maintenance. Usually, mesothelioma is diagnosed at an advanced stage, and the only treatment option is palliative care, which focuses on making the patient as comfortable as possible while the cancer follows its course.

Shari Parsons Miller
Independent Scholar

See Also: American Lung Association; Asbestos; Chemistry; Mesothelioma, Childhood; Surgery.

Further Readings

Mesothelioma, Childhood

Mesothelioma is a rare cancer that originates in the mesothelium, a membrane that lines many body cavities (including the thoracic cavity, abdominal cavity, and heart). Most mesothelioma originates in the thoracic or abdominal cavities (the pleura and the peritoneum). Nearly all mesothelioma is caused by exposure to asbestos. While this is commonly associated with workplace exposure, that obviously does not apply to childhood mesothelioma, which more often originates as a result of asbestos being present in the home, school, or child-care facility. It also can develop in children of workers who are exposed to asbestos dust in the workplace and bring it home on their clothes. In a small number of cases—less than 10 percent—the environmental factor may be something other than asbestos, such as radiation or inhalation of fibrous silicates.

Symptoms of mesothelioma usually begin with pain in the chest wall or respiratory problems, including shortness of breath, a feeling of tightness that may be caused by pleural effusion (fluid surrounding and constricting the lung), wheezing, coughing, hoarse voice, persistent irritation in the throat or chest, or coughing up blood. Mesothelioma in the abdominal cavity can cause a buildup of fluid in the cavity, weight loss, bowel obstruction, and abdominal swelling. Often, abdominal mesothelioma is discovered later than thoracic cavity mesothelioma. Either mesothelioma can result in anemia or fever, and if the cancer has spread beyond the mesothelium, pain, swelling in the neck and face, and difficulty swallowing are common. Advanced cases can result in blood clots, jaundice, low blood sugar, and severe bleeding in the organs, a condition called disseminated vascular coagulation.

Asbestos was used widely in the industrial ramp-up during and following World War II, when its toxicity was not well understood (though concerns had been raised in the previous decades due to health
Mesothelioma, Childhood

problems with miners and shipyard workers). It was used commonly as both building insulation and electrical insulation in construction not only of residences but of workplaces, warehouses, and factories, which introduced a secondary problem once its dangers were understood: the danger of being exposed to, and aerating, the asbestos while removing it in order to replace it with a safer insulation. Indeed, this is the very manner by which many children were exposed to asbestos. Mesothelioma also can develop as a result of exposure to naturally occurring asbestos in the environment. This led to a widely studied epidemic of mesothelioma in several Turkish villages, for instance, where asbestos was present in both the air and the water supply. Mesothelioma can be caused by asbestos exposure of as little as one month, and it can take as long as 40 years to manifest in adults.

Despite efforts in 1989 by the Environmental Protection Agency (EPA), asbestos is not banned in the United States, one of the few developed countries to permit its use. Asbestos content is regulated in most products, and consumer products can contain only trace elements (resulting from airborne asbestos in the factories where they are made, usually). The Occupational Safety and Health Administration (OSHA) has limited the density of asbestos presence in workplaces. Asbestos continues to be used in vinyl floor tiles and sheet flooring, cement board, window putty, stucco, furnace tape, cement pipes and flues, the stipple used to texture walls and ceilings, and drywall joint filler compound and in fireproofing, acoustic, and roofing materials.

Asbestos seems to lead to mesothelioma as a result of mechanical damage, not chemical reactions. The small fibers of asbestos may interfere with chromosomes and disrupt mitosis, leading to the development of cancer. Smaller particles, which can be absorbed deep into the lung tissue, are believed to be more harmful and carcinogenic than larger particles. The incidence of World Trade Center syndrome, in which severe respiratory ailments have developed among workers who had exposure of only a day or two to the airborne particulates of the collapsed World Trade Center buildings after 9/11, has shed some insight on the mechanisms by which asbestos and other small particles can cause cancer.

Mesothelioma is difficult to diagnose. Chest X-rays often offer the first hints, especially in children, who do not have jobs exposing them to asbestos, in order to suggest that diagnosis to the physician. Pleural thickening may be visible on the X-ray, and if there is fluid buildup, it may appear on a computed axial tomography (CAT) scan or magnetic resonance imaging (MRI). Cytopathology can investigate the fluid—a syringe is inserted through various means depending on the location, and fluid is extracted for analysis. Even this method makes malignancy difficult to determine. A biopsy is almost always necessary, the method for which depends on where the mesothelioma has manifested. It may be necessary to open the chest to obtain a tissue sample, or a thoracoscopy may be performed, in which a small cut through the chest is made, and a thin, lighted tube is inserted between two ribs. In abdominal mesothelioma, the biopsy often may be performed laparoscopically.

The prognosis for mesothelioma is poor. Surgery does not offer good, long-term survival rates. Radiation can be used to relieve symptoms caused by tumor growth or as adjuvant therapy with surgery, but chemotherapy is the only mesothelioma treatment modality that has been proven to increase survival rates in controlled randomized trials.

Bill Kte’pi
Independent Scholar

See Also: Asbestos; Mesothelioma, Adult Malignant; Radiation Therapy.

Further Readings
The United Mexican States is a democratic republic encompassing 31 states and a Federal District. Mexico is the world’s fifth-largest country by area and the third largest in the Americas. The Mexican Consejo Nacional de Población (National Census Bureau of Mexico) estimates Mexico’s population at 119,713,203 people, ranking the country as the 11th-most populous in the world. The International Union Against Cancer reports that cancer is the third-leading cause of death in the country. Because Mexico is known for its traditional and nontraditional approaches to cancer prevention and treatment, the country is of relevance to the oncological community worldwide.

History
In the Mexican culture, the treatment of conditions consistent with the symptomatology of cancer (e.g., abscesses, hard swellings, polyps, tumors, and warts) dates back to the Mayan period, but historic records from the Mexican Society of Oncology trace the contemporary treatment of cancer to the first decade of the 20th century. This is when the Federal District of Mexico acquired the country’s first order of radium. The records report that, in the 1920s, Mexico’s General Hospital was the first medical institution to acquire equipment for the administration of deep radiotherapy treatments. By the 1930s, both radiotherapy and Wertheim-style hysterectomies were used for the routine treatments of uterine carcinomas. Wertheim surgeries required the removal of cervical cancer through abdominal incisions. During the same period, Mexican physicians began to treat malign neoplastic diseases—masses of tissues that experience abnormal growth. In 1940, Mexico’s General Hospital acquired the first radon plant in Latin America. This technological addition, together with the appointments of several Mexican physicians and surgeons trained abroad, marked Mexico’s General Hospital as the birthplace of Mexican oncology. An institute for cancer studies was soon established in 1946 to serve oncology patients, most of whom were affected by gynecologic tumors. Soon, the institute was overrun with patients and struggled to meet patient demand. Due to this rapid growth and the need for specialized medical care, the government established the Instituto Nacional de Cancerología. The institute later housed the first cobalt therapy unit in Mexico and the third in Latin America. Cobalt-60 allowed Mexican oncologists to use gamma rays for cancer treatment. Today, Mexico is recognized as a Latin American leader in cancer prevention and treatment, and the country collaborates with various international research institutions, including the United States–Latin American Research Network (US-LA CRN) and the Union for International Cancer Control (UICC).

Cancer Incidence and Mortality
Mexico has experienced demographic transitions accompanied by changes in its epidemiological profile. The country’s health concerns, for example, have shifted from communicable to noncommunicable diseases. Cardiovascular disease, diabetes, and cancer currently are the three leading causes of death in the nation. The World Health Organization reports that approximately 57,000 people die of cancer every year, accounting for 13 percent of all deaths due to noncommunicable diseases in the country. Furthermore, statistics by Mexico’s Sistema Nacional de Información de Salud (The National System of Health Information) show that prostate; lung, bronchial, and larynx; and stomach and gastric cancers cause the highest mortality rates for males; while breast, cervical, and liver cancer comprise the highest mortality rates for Mexican females; and leukemia, lymphoma, and sarcoma are the most common forms of cancer in children and adolescents.

Prostate cancer incidence in Mexico is largely attributed to age, with the majority of males affected by the disease being 50 years of age or older. The Instituto Nacional de Estadísticas y Geografía/INEG (The National Institute of Statistics and Geography) reports that prostate cancer mortality rates vary greatly by federal districts, with Quintana Roo having a death rate of 9.4 percent and Nayarit a death rate of 33.2 percent.

The high prevalence of lung cancer in Mexico has been linked to various factors, including second-hand smoke, the exposure of mine workers to radon, and the increase in teenage smokers. INECT statistics indicate that 12.3 percent (i.e., 1.7 million) of adolescents in Mexico are active smokers. These statistics place adolescents at higher risk of developing lung cancer, given that many begin smoking at 14 years of age.
The third-most frequent cancer in Mexican men, stomach and gastric cancer, has been associated with dietary patterns. Research studies have linked stomach cancer in Mexico with a diet high in salted, dried meats, such as chorizo and other sausages, as well as a high intake of fresh meats, dairy products, and fresh fish. In addition, studies have associated the disease with the consumption of chili peppers and chili powder.

Research studies associate the incidence of breast cancer in Mexico with an underutilization of early detection techniques, such as self-exam and mammography. Underutilization has been attributed in part to cultural beliefs about the causes and treatments of the disease. In addition, the breast cancer rate has been associated with an increase in alcohol intake and a folate and vitamin B12 deficiency.

Although cervical cancer is responsible for 3,900 deaths a year in Mexico, the incidence and mortality have decreased during the past decade. Scientists attribute the improved incidence and mortality rates to Pap smear screenings and lower birthrates. Nonetheless, Mexican women are still at risk, especially those living in the central and southern parts of Mexico.

Statistics from a Mexico Cancer Profile issued by the Pan American Health Organization indicate that liver cancer killed approximately 2,500 Mexican males and approximately 2,700 Mexican females per year during the past decade. Hepatocellular carcinoma is the most common form of liver cancer, with higher mortality rates found in individuals 60 years of age or older. Alcohol consumption and hepatitis C virus (HCV) infections are linked to the incidence of the disease in the country.

Cancer Institute and Research
The Secretaría de Salud de México (Mexico's Health Ministry) is the government institution in charge of social assistance programs, medical services, and public health issues. The ministry supports initiatives for cancer prevention, treatment, and care, and most of them are coordinated through the National Center of Cancerology. The center is dedicated to provide specialized medical care to cancer patients and oversees 25 cancer centers around the nation. The administration works on developing common national programs and strategic plans that focus on cancer prevention, detection, and treatment.
The national programs center on five main topics: early detection and prevention, development of health education materials concerning the 10 most-common forms of cancer in the country, palliative care, medical infrastructure, and tobacco control. To disseminate information about the disease, the institute launched InfoCancer, a resource available online and on the phone to cancer patients and their families, friends, and caretakers.

In addition to providing information and services to cancer patients, Mexico also works with the scientific community to support cancer research. The Consejo Nacional de Ciencia y Tecnología (National Council of Sciences and Technology), for example, oversees the promotion of scientific and technological agency. The organization also works with other institutes and academic institutions and offers a wide range of grants to support scientific research. In addition, the National Council offers a wide range of opportunities for postgraduate studies at home and abroad.

**Nontraditional Treatment**

In addition to the traditional medical approach, Mexico is known for its alternative approaches to cancer treatment. Cancer patients from around the world visit the country, seeking to ingress in its many facilities centering on holistic methods. Alternative cancer treatment facilities are more common along the U.S.–Mexico border, where dozens of clinics have opened to serve patients from the United States. Alternative methods offered at the border clinics can be divided into two main groups: metabolic therapy and antitumor treatments. Metabolic therapy focuses on improving body function rather than on specific ways to treat the disease. The metabolic approach includes chelation, colon therapy, nutritional therapy, and immune system support. Antitumor treatments are designed to specifically target the cancer. Some of these treatments offered at the Mexican clinics include oxygen therapy, electromagnetic therapy, hydrotherapy, hyperthermia, antineoplaston therapy, and cell therapy. The use of these alternative methods is not regulated, but the Mexican government investigates and closes clinics operating illegally in the country.

The scientific community in Mexico is actively engaged in national and international efforts to prevent, detect, diagnose, and treat cancer in the country and abroad. Their efforts and initiatives provide the oncological community with material for further inquiry into the disease and its impact around the globe.

Johanne I. Laboy  
North Carolina State University

**See Also:** Alternative Therapy: Diet and Nutrition; Breast Cancer; Cervical Cancer; Drugs; Exercise; Liver Cancer, Adult (Primary); Lung Cancer, Non–Small Cell; Prostate Cancer; Stomach (Gastric) Cancer.

**Further Readings**


---

**MIT Center for Cancer Research**

The David H. Koch Institute for Integrative Cancer Research (Koch Institute), which upon its opening in 2010 replaced the Massachusetts Institute of Technology (MIT) Center for Cancer Research, is one of eight National Cancer Institute
(NCI)-selected basic research centers. Founded in 1969, the Koch Institute conducts research on cancer, with a special emphasis upon the genetic and molecular bases of cancer, how changes in cellular processes affect cell growth and behavior, and how the immune system develops and recognizes antigens. In addition to its research efforts, the Koch Institute serves as an organizational body for researchers across the MIT community with an interest in cancer research.

Founded in 1861 in response to the increasing industrialization of the United States, MIT is a private research university located in Cambridge, Massachusetts, with a stellar international reputation for excellence. Unlike many other colleges and universities of the time, which had the classics as the central focus of their undergraduate educational experience, MIT concentrated on technology and collaboration with industry. With an $11 billion endowment and traditional strengths in engineering, the physical sciences, economics, biology, and other areas, MIT is one of the most highly regarded universities in the world and has been affiliated with more than 80 Nobel Prize winners, 50 National Medal of Science recipients, and two field medalists. As medical research has grown as a field, MIT has sought to increase its involvement in this area of study.

In 1974, Nobel laureate Salvador Luria, known for his work with the replication mechanism and the genetic structure of viruses, founded what was then known as the MIT Center for Cancer Research. Under Luria’s leadership, the MIT Center for Cancer Research was organized to study basic biological processes as these related to cancer. MIT viewed the Center for Cancer Research as having a twofold purpose. First, the MIT Center for Cancer Research served as a much-needed physical research center where studies regarding cancer could be undertaken. Second, it also served as an organizational mechanism for the larger MIT cancer research community, one that could foster the exchange of information and collaboration. Initially funded with a National Cancer Institute Center Core grant, the MIT Center for Cancer Research relied upon funding from a variety of sources, including the Howard Hughes Medical Institute and the National Institutes of Health. The MIT Center for Cancer Research quickly gained a reputation for excellence, producing four Nobel laureates, including David Baltimore, Susumu Tonegawa, Phillip Sharp, and H. Robert Horvitz.

In 2006, then-MIT president Susan Hockfield announced plans for a new building for the MIT Center for Cancer Research in an effort to build upon the prior accomplishments of the group and to provide state-of-the-art facilities for the scientists and researchers who worked there. In 2007, the Ludwig Fund announced a $20 million gift that would allow the founding of a Center for Molecular Oncology at the new facility. This grant was joined by a $100 million gift from industrialist David H. Koch. Part of Koch’s gift was devoted to the new building, which was estimated to cost approximately $250 million, and half was dedicated to research endeavors. In response to Koch’s gift, the MIT Center for Cancer Research was renamed in his honor.

Cancer Research

One of eight NCI-designated basic research centers, the Koch Institute differs from the other such centers insofar as it does not provide medical care to patients or conduct clinical research. Instead, the Koch Institute has partnered with a variety of oncology centers that do this work. The new facility permitted the MIT Center for Cancer Research’s existing faculty to be joined with an equivalent number of engineering faculty. This was seen as crucial in promoting interdisciplinary approaches to diagnosing, monitoring, and treating cancer. The Koch Institute is comprised of faculty members from various MIT departments, including biology, biological engineering, chemistry, and mechanical engineering. In all, the Koch Institute is comprised of more than 40 laboratories and 500 researchers spread across the MIT campus.

The Koch Institute has identified five discrete areas that it has chosen to focus upon in an effort to control cancer. These five areas include developing nanotechnology-based therapies; creating devices that will permit better cancer detection and monitoring; exploring the molecular and cellular bases of metastasis; advancing personalized medicine through analysis of cancer pathways and drug resistance; and engineering patients’ immune systems to combat cancer. To this end, the Koch Institute remains funded by an NCI center grant and is also the home to more than 100 fully funded studies.
Researchers at the Koch Institute are engaged in an ongoing series of studies to address the five areas of research it has focused upon. Darrell J. Irvine, for example, has worked to help patients' immune systems to recognize cells that have undergone changes as a result of cancer and then to destroy them. Matthew Vander Heiden and his team of researchers have worked to better understand cancer cell metabolism and how small molecules might be used to activate enzymes that might help to restore the normal state of cells with cancer. Jacqueline A. Lees, who also serves as associate director of the Koch Institute, has investigated how proteins and pathways are mutated in cancer as well. It is hoped that further knowledge regarding these mutations will allow advances in detecting and hopefully treating osteosarcoma.

Michael J. Cima and his laboratory are working to create tiny nanosensors that are chemically sensitive to different molecules. It is hoped that these sensors will be able to be used to help determine proper dosage for chemotherapy. Sangeeta N. Bhatia and her team are working to engineer new therapeutic agents that can home in on cancer cells and selectively destroy them, while leaving surrounding healthy cells alone. This type of therapy will permit stronger pharmaceuticals to be used to fight cancer and increase patient well-being. Together, these and other efforts are revolutionizing research that addresses cancer as it focuses on using approaches that are tailored to a specific patient's condition and health. Over time, the Koch Institute will undoubtedly continue to produce further research that will affect how cancer patients are treated.

Stephen T. Schroth
Towson University

See Also: American Association for Cancer Research; Genetics; Massachusetts Medical Society; National Cancer Institute; North American Association of Central Cancer Registries.

Further Readings

Moldova

Moldova is a country located in eastern Europe between Romania to the west and Ukraine to the north, south, and east. Historically known as Moldavia, it is officially known as the Republic of Moldova, with its capital city being Chisinau. The republic declared its independence in 1991 but had the same boundaries as the Moldavian Soviet Socialist Republic as part of the dissolutions of the Soviet Union. A new constitution for the country was adopted on July 29, 1994.

Health care in Moldova has known dynamic development in the past years. The development has seen the country's hospitals being equipped with ultramodern equipment, especially the new surgical blocks and general medical departments being built in Chisinau, the capital city. The country's number of physicians is about 264 per 100,000 people. In 2004, health expenditure was $138 per capita, and as per statistics from the World Bank, the health expenditures per capita was at about $223.

The health sector in Moldova is under the health ministry. According to the health ministry, for the period before 2011, the number of people living with cancer in the country was 42,000. Per year, cancer caused about 5,600 deaths in the country. Given these statistics, cancer was the second-most dreaded disease in the country based on the number of deaths, the first cause of deaths being cardiovascular diseases. Narrowing down to cancer, the type of cancer that has the most number of deaths is lung cancer. The second is stomach cancer, the fourth liver, and the fifth colorectal cancer. The number of cancer-related deaths is higher than in most other European countries. Of the persons who are diagnosed with cancer, less than half survive. Based on the five-year survival record, the survival rates for persons with cancer are well below that of the countries in the European Union. According to the Moldovan health ministry, these damning results are as a result of late diagnosis of the disease.
The Moldovan government has, for the first time, allocated 80 million lei ($5,400,000) to acquire medication for cancer patients. It is the first time that the executive arm of the country is spending such an amount of money for cancer treatment. A donation by the Norwegian charity organization under the initiative Help Moldova saw the Oncology Institute from Chisinau receive 25 medical beds, special clothes, and other much-needed products. This donation was made during the World Cancer Day that is marked on February 4. After the completion and the opening of the cancer facility in Chisinau, data from the ministry of health indicates that, in 2012, the number of patients with cancer was 8,204, and these patients were taken on primary evidence in Moldova. The data shows that 5,734 people with cancer died in 2012, which is a slight increase compared to a year before.

The only specialized center for cancer diagnosis and treatment in the country is the Oncology Institute of Moldova, where help will come to patients who need help. It was founded in 1964 and has long since been upgraded to include a series of surgery, radiotherapy, and chemotherapy departments. The breast cancer unit in the institution has two branches and offers surgical treatments for many forms of cancer, with breast cancer being the most critical aspect. According to data from the institution, every year, more than 1,000 breast cancer patients are treated and surgery performed for about 2,500 patients. Of these patients, 600 have breast cancer and the others have benign diseases of the breast.

Just like every other country, Moldova has almost all types of cancer diagnosis among its citizens. However, some are more prevalent than others and consequently cause more deaths than others. The top type of cancer as per deaths is lung cancer, with a rate of 21.24, breast cancer is second with a rate of 20.93, colon—rectum cancers are third with a rate of 17.97, stomach cancer is fourth with a rate of 12.53, liver cancer is fifth with a rate of 9.83, oral cancer is sixth with a rate of 6.95, pancreas cancer is seventh with a rate of 6.31, lymphomas are eighth with a rate of 4.44, cervical cancer is ninth with a rate of 4.13, and at the tenth place is prostate cancer with a rate of 3.22. Other types of cancer that have high rates in the country are ovary cancer, bladder cancer, skin cancer, leukemia, and uterine cancer, among others.

As earlier stated, coronary heart disease and cancer predominate as the main causes of death in the Republic of Moldova for both men and women, according to research by nongovernment organizations in the country; this fact can be attributed to very heavy alcohol and tobacco consumption among both men and women. According to statistics from the research, in 2010, most mortality issues can be attributed to smoking-related actions, while about 18 percent for men and 14 percent for women were related to alcohol use.

In 2007, the government of Moldova approved the Unified Program, which was modified in January 2009 (Government Decision No. 44). The program includes the cervical smear test as part of the family planning services provided within the specialized ambulatory care and a series of other prophylactic checkups for cervical and breast cancer. However, even though this might qualify as a worthy cause against cancer deaths through early diagnosis, the program could not be treated as screening as it is not based on clear criteria for enrollment of target groups presenting no clinical signs.

Policy recommendations for the development of national screening programs for cervical and breast cancer were made in 2007 based on international experience and cost–benefit analyses within a project supported by the Department for International Development of the United Kingdom. However, they have not yet been put into practice. In 2011 and 2012, the 90 health systems in transition in the Republic of Moldova National Health Insurance Company provided financial support for pilot screening programs for cervical and breast cancer in some territories, but this is still far from nationwide coverage.

Michael Fox
Independent Scholar

See Also: Breast Cancer; Cervical Cancer; Lung Cancer, Non–Small Cell.

Further Readings


Morocco

Cancer in the north African nation of Morocco is one of the country’s leading causes of mortality and morbidity, with roughly 35,000 new cases of cancer reported annually. The International Agency for Research on Cancer and the World Health Organization (WHO) GLOBOCAN 2012 project reported 16,829 cases of cancer in men and 18,189 cases of cancer in women annually. The overall world age-standardized rate (ASR) for all sites combined was 136.6 per 100,000 for men and 114.5 per 100,000 for women. The most frequently diagnosed cancers in the nation for men are lung (19.0 percent, ASR 24.8/10[5], 3,497 cases), prostate (15.5 percent, ASR 22.9/10[5], 2,332 cases), colorectum (8.8 percent, ASR 12.0/10[5], 1,358 cases), bladder (6.9 percent, ASR 9.7/10[5], 1,429 cases), and non-Hodgkin’s lymphoma (6.0 percent, ASR 8.2/10[5], 1,089 cases). The most common cancers for women in Morocco are breast (39.9 percent, ASR 43.4/10[5], 6,650 cases), cervix uteri (11.4 percent, ASR 13.0/10[5], 2,258 cases), colorectum (7.5 percent, ASR 9.0/10[5], 1,126 cases), thyroid (3.4 percent, ASR 3.9/10[5], 929 cases), and ovarian (735 cases). Of all cancers, 2 percent are observed in childhood (0–14 years), and approximately 43 percent of them are malignant hemopathies. The incidence of cancer is increasing due to growth of the population in the country, population aging, and the pervasiveness of tobacco smoking.

Health Care Infrastructural Challenges

At the time of independence following French colonial rule (1877–1956), there were only 33 qualified doctors in Morocco. In the decades since independence, the government embarked upon a long series of health care reforms and implemented plans to build new hospitals and update and undertake repairs on existing health care facilities built during the French protectorate.

Much remains to be done to expand both health care infrastructure and practitioners, particularly in the public sector, although there does exist growing nonprofit and for-profit private sectors. In 2006, the World Health Report indicated Morocco was one of 57 countries with a severe lack of health personnel to serve the nation’s population of 32.52 million through its network of 2,626 health care bodies, 1,731 of which are located in rural areas. Further, Morocco is vulnerable to an exodus of medical practitioners to other nations. The WHO in 2008 reported that the global expenditure for the Moroccan health care system totaled $4.3 billion, or 5.6 percent of the gross domestic product (GDP). Compared to other nations at Morocco’s level of development, these figures are low given the needs of modernizing health care infrastructure and given that the epidemiological profile of Morocco is changing with increases in noncommunicable diseases such as cardiovascular diseases, diabetes, and cancer.

National Cancer Control Plan

The Ministère de la Santé of Morocco established its Plan National de Prévention et de Contrôle du Cancer 2010–2019. The plan has supported more than 80 cancer research projects by 135 cancer researchers from 20 institutions across 32 research teams. It also established regional cancer registries. However, there remains a need for further research, better primary prevention activities, increased programs for early detection, specialized infrastructures and human resources, enhanced management of available oncological resources, establishment of standards for diagnosis and
treatment management, policies regulating generic drugs in addition to a cancer communication strategy, and increased palliative care and psychosocial support. Further, increased funding is needed for the thousands of Moroccans for whom cost of treatment exceeds financial capabilities; fewer than one-third of the Moroccan population has adequate medical insurance.

Additional development needs include the epidemiology of cancer through the establishment of more cancer registries in Morocco. The National Center for Biotechnology Information recently reported that there has been no population-based data of cancer incidence in Morocco. At present, the only sources of epidemiological information currently deemed valid on the epidemiology of cancer in Morocco are, first, the Rabat Cancer Registry, which registered 2,473 new cancer diagnoses in the nation’s capital city in 2008 and, second, the Grand-Casablanca-Region Cancer Register (GCRCR), which is based on a population sample accounting for 10 percent of the overall Moroccan population. The GCRCR has recorded 3,336 cases of cancer, including 1,833 in women and 1,503 in men. The standardized incidence was slightly higher in females (104.2 for 100,000 females per year versus 100.3 for 100,000 males per year).

Noteworthy research centers in oncology and radiotherapy include la Laboratoire d’Onco-virologie, Institut Pasteur du Maroc in Casablanca, Morocco, Service de Radiothérapie, Institut National d’Oncologie in Rabat, the Al Azhar Oncology Center in Rabat, and the Laboratory of Genetics and Biometry, Faculty of Science, Ibn Tofail University, in Kenitra, Morocco. HRH Princess Lalla Salma, president of the Lalla Salma Foundation for Cancer Prevention and Treatment, has led an effort to establish resources to support cancer diagnosis, treatment, education, and prevention throughout Morocco. The Lalla Salma Foundation funded the construction of a regional oncology center situated in the Moulay Ismail hospital in the Moroccan city of Meknes, which is aligned with the Plan National de Prévention et de Contrôle du Cancer 2010–2019. Another newly developed regional oncology center and host facility for cancer patients, located in the northeastern city of Al Hoceima, allows for providing care and treatment to cancer patients living below the poverty level. Such patients often experience additional challenges of extensive travel and lack of family support if they are forced to relocate to a distant location for cancer treatment.

Health Partnerships
The Moroccan government established collaborative partnerships with a number of Jordanian and Gulf nations, the United States, and European organizations for health care generally and cancer research and care specifically. The Cancer Prevention & Control Research Training Program of Morocco (CPCRT) is a five-year (2010–2015) public health research and training program supported by the U.S. National Institutes of Health that has established a partnership among the University of Rabat Medical and Pharmacy School, the Moffitt Cancer Center in Tampa, Florida, and the CoEmpower organization in Bethesda, Maryland, to train Moroccan mid-career professionals and support existing Moroccan public health research infrastructures in cancer prevention and control.

Other research collaborations include Cancer Research Morocco (CRM), a group that links Moroccan clinical and basic research cancer groups to collectively develop strategies for prevention, diagnosis, treatments, and cures. Cancer specialists are members of international organizations such as the Middle-Eastern Association for Cancer Research, the Arab Medical Association of Cancer, l’Association Internationale des Registres du Cancer, la Société Internationale de Chirurgie Hépatopancréato-Biliaire, la Fédération Pan-Arabe de Chirurgie, la Fondation Française de Carcinologie Digestive, and la Société Française de Cancérologie.

Specific Contexts
Domestic cooking fumes intake in Morocco by using a compact charcoal oven known as a kanoun, particularly during childhood, has increased the risk of nasopharyngeal carcinoma (NPC). Among adults across north Africa, NPC rates are at the level of 5.4 in men and 1.9 in women, 10 times higher than that in Europe.

One unique cancer risk in Fez, Morocco, is found in the Leather Souq, the oldest leather tannery in the world, which dates back at least nine centuries. While ancient practices in the tanneries used natural dyes, more current practices may be using synthetic dyes. Environmental impact assessments have been made to evaluate the potentially carcinogenic metabolites of dyes. In addition, Moroccan
environmental activists contest that the contemporary textile and leather industries use chemicals such as chromium 3, widely known to be lethal.

Tobacco use continues to be an important risk factor for lung cancer in Morocco and its north African neighbors. A World Health Organization study reported that 29 percent of adult men and 0.2 percent of women in Morocco use tobacco. Ministères de la Santé et de l'Éducation Nationale have partnered with Lalla Salma Foundation for a nationwide antismoking campaign in a range of public places, including hospitals, schools, and universities.

Lara Lengel
Catherine Cassara
Bowling Green State University

See Also: Age; Algeria; Breast Cancer; Cancer Communication; Developing Countries; Disparities Within Nations (Elimination of Cancer); Egypt; France; Global Health Issues and Cancer; International Agency for Research on Cancer; Libya; Lung Cancer, Non–Small Cell; Lung Cancer, Small Cell; Mali; Passive Smoking; Poverty; Smoking and Society; Textile Dyes; Tobacco Smoking; Tobacco-Related Exposures; Tunisia; Women's Cancers; World Health Organization.

Further Readings


Mozambique

The Republic of Mozambique is a southeastern African country, whose coastline directly faces Madagascar island. Originally inhabited by the Swahili, Arabs, and Persians, Mozambique was colonized and conquered in the 1500s by the Portuguese, who ruled the country for more than 400 years. The Portuguese held their grasp over Mozambique’s rich natural resources (such as aluminum, gold, gemstones, and petroleum) up until the end of the 19th century, when other European powers (mostly British and French) started to siphon its economic power through various private companies’ administrations. Similar to the apartheid system in neighboring South Africa, in Mozambique, a small white Portuguese minority concentrated much of the overall country’s wealth in their hands, possessing far better education and skill than the black indigenous majority. This situation evolved into significant social tensions, giving birth to a guerrilla movement called the Front for the Liberation of Mozambique (FRELIMO), which in 1964, initiated a military campaign against the Portuguese army. In 1974, the FRELIMO took control of the territory, forcing the expulsion of the entire Portuguese population and establishing a one-party communist regime. After only three years of peace, in 1977, the Mozambican Civil War erupted, when the Anti-Communist Mozambican National Resistance (RENAMO) militia started an armed opposition to the new government. This civil war plagued the country with violence and the destruction of its infrastructures, causing the nation’s economy...
to collapse until the declaration of peace in 1992, when a new democratic constitution was enacted, bringing back to Mozambique more than 1.5 million refugees who had left the country in the last 15 years.

During the 1970s, the primary health care system in Mozambique was quite developed, and the government invested significant resources in vast vaccination programs that covered more than 90 percent of the population. During the civil war, though, severe budget cuts were made to public health care expenditures, and many mass human rights violations, including terror strategies such as isolation or deliberate destruction of medical facilities, caused a large setback to this country’s health services. Corruption is also a significant issue in Mozambique, and the public health sector is rife with it: Many doctors or nurses ask for bribes, further reducing the opportunity for patient equality, especially as the country is plagued by poverty. Today, Mozambique is facing many severe challenges, such as high infant mortality and child malnutrition rates (up to 53 percent), a significant human immunodeficiency virus (HIV) and acquired immune deficiency syndrome (AIDS) prevalence in both adult and child populations (11.5 percent), malaria still being largely endemic in many territories, and natural disaster emergencies such as flooding and cyclones. HIV constitutes a risk factor for cancer (mostly for Kaposi’s sarcoma), while malaria is a risk factor for children’s Burkitt’s lymphoma. Like many other underdeveloped, developing countries, many nongovernmental organizations (NGOs), such as the United Nations Children’s Fund (UNICEF) and Save the Children, operate in the territory, supporting primary health care by funding hygiene awareness campaigns, building modern clinical facilities, and employing the expertise of expatriate medical personnel.

The largest hospital in Mozambique is the Hospital Central de Maputo, which was built in 1976, has a total of six departments, 1,500 beds for inpatients, and serves an average of 700 outpatients every day. Nonetheless, no radiation therapy (RT) centers are available in Mozambique, and very few patients can afford to receive proper RT in overseas clinics. Many of the most common cancer types in this country (cervix, breast, and prostate) would greatly benefit from this treatment modality, with a potential reduction of mortality for up to two-thirds of

*Image: The skyline of Maputo, capital of Mozambique and home of the country’s largest hospital. The Hospital Central de Maputo has six departments, 1,500 beds for inpatients, and serves an average of 700 outpatients every day. Nonetheless, no radiation therapy (RT) centers are available in Mozambique, and very few patients can afford to receive proper RT in overseas clinics. (Flickr/Andrew Moir)*
the patients affected. In Mozambique, there is only one national cancer registry, the Registro de Cancro de Beira, within the pathology department of the Hospital Central in Beira. It was established in 2005 to collect and provide data on all cancer cases in the Beira region, but it has very limited resources: There is only one staff member paid by the International Agency for Research on Cancer (IARC) and just a single computer. Although due to the lack of data still available, the overall picture is probably incomplete, some early assessment on the actual cancer burden in Mozambique was made. The most common sites for cancer are cervical cancer, with an age-standardized incidence rate (ASIR) of 50.6 and the highest age-standardized mortality rate (ASMR) of 34.5, prostate cancer (ASIR: 16.1, ASMR: 12.9), followed by Kaposi’s sarcoma (ASIR: 15.5, ASMR: 13.2), breast cancer (ASIR: 13.1, ASMR: 7.5), and esophagus cancer (ASIR: 12.8, ASMR: 12.4).

Due to the high HIV prevalence in the Mozambique population, the risk of persistent human papillomavirus (HPV) infections is significantly increased. HPV constitutes by itself an important risk factor for cervical cancer, especially when both viruses are combined, a situation further aggravated by the overall lack of screening tests (Pap tests) for early detection and proper prevention. For these reasons, Mozambique has the second-highest incidence (42–60 per 100,000 women each year) and mortality rate for cervical cancer in all Africa, after Malawi. In order to address this major health issue, the Mozambique Ministry of Health, together with the GAVI Vaccine Alliance, decided in 2013 to start a massive vaccination campaign against HPV and a parallel PapVac study project to assess a proper strategy of implementation of vaccination programs for about 8,300 preadolescent girls throughout the country.

Other risk factors for cancers include tobacco use, which in turn may explain the higher rate of esophageal cancer in South African men. To address this problem, Mozambique authorities implemented moderate public smoking bans, although they are not very strongly enforced, and thus cancer prevention is still lagging behind.

Claudio Butticè
Independent Scholar

**See Also:** AIDS-Related Cancers; Breast Cancer; Cervical Cancer; Poverty; Prostate Cancer.

**Further Readings**


---

**Multiple Endocrine Neoplasia Syndrome, Childhood**

Multiple endocrine neoplasia type 2b (MEN2B), also known as multiple endocrine neoplasia type 3, Williams-Pollock syndrome, Gorlin–Vickers Syndrome.
syndrome, and multiple endocrine neoplasia syndrome, is a genetic disease that causes the development of multiple tumors, nearly always including one or more cancers in childhood. MEN2B is caused by variations in the RET proto-oncogene, with the M918T variation accounting for 95 percent of cases. About half of MEN2B patients inherited the variant gene from a parent, but the other half are spontaneous mutations. Older fathers are more likely to conceive children with MEN2B, and boys are twice as likely as girls to have it.

Signs of MEN2B may occur in infancy and are nearly always present before age 10. Children with MEN2B are tall with long limbs, an elongated face, and protruding lips—sometimes called a Marfanoid build because of its similarity to the features of Marfan syndrome—and benign tumors develop in the submucosa of most or all organs as well as in the mouth and eyes. Most patients develop medullary thyroid cancer; at least half develop pheochromocytoma, a cancer of the adrenal glands. Other symptoms include a lack of tears when crying and uncomfortably dry eyes—often an early sign detected in infants—as well as low muscle mass, gastrointestinal problems, delayed puberty, and craniosynostosis, a fusion of sutures in the skull that results in changes to the skull's growth pattern and a swelled-seeming head as the child gets older. Though MEN2B children often look the same as children with Marfan syndrome, they lack the cardiovascular complaints of that disease.

Depending on the child's age at onset, any number of the above symptoms may suggest the MEN2B diagnosis, which can be confirmed with a nearly 100 percent accurate DNA test. Older tests relied on serum calcitonin levels. Medullary thyroid carcinoma and pheochromocytoma are rare enough cancers that the question of MEN2B is always raised when they are diagnosed.

The thyroid is one of the largest endocrine glands and is located in the neck below the Adam's apple. The thyroid makes proteins, produces hormones, and influences how the body reacts to other hormones. Most thyroid cancers have a high survival rate. Medullary thyroid carcinoma originates in the parafollicular cells, neuroendocrine cells in the thyroid that secrete calcitonin, a hormone that reduces blood calcium. The importance of calcitonin in the human body is not well understood as it does not appear to be a significant part of the body's regulation of calcium homeostasis. Medullary thyroid carcinoma accounts for only about 3 percent of thyroid cancers, and 25 percent of medullary thyroid tumors are found in MEN2B patients. The most common symptom is diarrhea, but the tumor may also cause periodic flushing of the face, sometimes accompanied by hot, itchy skin. When medullary thyroid carcinoma symptoms are the first presented, they may be mistaken for carcinoid syndrome, which causes the same symptoms because of elevated serotonin; in this case, the symptoms result from elevated calcitonin.

If detected early enough, medullary thyroid cancer can be surgically removed with little complication, though there is always a chance of recurrence. In MEN2B patients, early detection is highly dependent on age; the older the child when they develop medullary thyroid cancer, the more likely they have already presented some other MEN2B symptoms. In the non-MEN2B population, on the other hand, half of medullary thyroid cancer cases have metastasized (spread to other parts of the body, usually the lymph nodes) before diagnosis. When there is a high risk of recurrence, radiation therapy is recommended. Though Caprelsa has been approved for metastatic medullary thyroid cancer in adults, it has not been trialed for children or MEN2B patients.

Pheochromocytoma is a neuroendocrine cancer of the adrenal glands, developing in the chromaffin cells. It develops in about half of MEN2B children. Early symptoms are those of sympathetic nervous system hyperactivity, including elevated blood pressure and heart rate, palpitations, panic attacks, excessive perspiration, headaches, flank pain, unexplained weight loss, and elevated blood glucose levels. The most common symptom is an attack lasting up to an hour and consisting of elevated heart rate, sweating, headache, and sometimes panic or anxiety. In non-MEN2B patients, pheochromocytoma usually goes undiagnosed and is easy to mistake for anxiety disorder; often, the real cause is not discovered until an autopsy. In MEN2B patients, however, the link with pheochromocytoma is well-known, and the patient's pediatric oncologist will know to look for it. Blood tests give a reasonable indication of pheochromocytoma's presence. The preferred treatment is surgical resection by laparotomy or laparoscopy, a complicated procedure undertaken...
only at surgical and cancer centers with appropriately specialized surgical staff. Sometimes a complete removal of the adrenal gland is necessary to prevent recurrence.

Without intervention, children with MEN2B will not likely survive their 30s, though a few cases of untreated individuals have been diagnosed in their 50s—likely with late-onset MEN2B, however. Because thyroid cancer is nearly universal in MEN2B patients, even children who have not yet developed medullary thyroid carcinoma may be given a prophylactic thyroidectomy, ideally before age four. Benign mucosal tumors need not be removed but can be if they are the source of pain or for cosmetic reasons.

Abraham Lincoln has been proposed as a possible late-survivor of MEN2B, due to his Marfan-like syndromes, history of constipation, bumpy lips, and family history of a similar disorder. However, Lincoln lived, apparently fairly healthily, much longer than a MEN2B patient is expected to live without surgery.

Bill Kte’pi
Independent Scholar

See Also: Genetics; Radiation Therapy; Thyroid Cancer, Childhood.

Further Readings


Mastroianno, Sandra, et al. “Coexistence of Multiple Endocrine Neoplasia Type 1 and Type 2 in a Large Italian Family.” Endocrine, v.40/3 (2011).


Multiple Myeloma/Plasma Cell Neoplasm

The application of novel therapeutic agents in the treatment of multiple myeloma has changed the notion that this malignancy is incurable and, instead, has suggested that it is a chronic disease that someday would have a cure. The backbone of the new therapies for multiple myeloma consist of proteasome inhibitors as well as immunomodulatory agents that play an important role in reducing the occurrence of relapses. Most of the patients diagnosed with multiple myeloma undergo a relapse during the course of the entire disease. The recent findings of clinical trials using proteasome inhibitors as well as immunomodulatory agents could help clinicians in designing and developing new treatment strategies for multiple myeloma. Information generated from studies using these novel agents may also improve the clinical effectiveness and safety of treatment schemes for multiple myeloma patients.

Multiple myeloma comprises 1 percent of all hematologic malignancies and is recognized as the second most frequent cancer involving the hematopoietic system. Almost 22,000 new cases are diagnosed each year, and more than 10,000 deaths due to multiple myeloma were reported in the United States for 2013 alone. The average age of patients at diagnosis is 69 years. The average duration of overall survival of multiple myeloma patients has markedly increased in the past several years due to the identification of novel drugs and their subsequent inclusion in clinical trials for the treatment of various stages of multiple myeloma. Clinical trials using novel agents against multiple myeloma have improved the basic knowledge on its pathogenesis, as well as facilitated in distinguishing malignant clones, thus serving as potential therapeutic strategies. The aim of clinical trials is to identify a novel agent that would result in the sustained toxicity of tumor cells, thus resulting in the control of multiple myeloma and an improvement in the overall long-term survival of patients.

Proteasome inhibitors are protein complexes located within the cell and are responsible for the destruction of regulatory proteins, including those that control the cell cycle, cell death or apoptosis, and DNA repair. Proteolytic breakdown of ubiquitinated proteins inside a proteasome core can occur
Multiple Myeloma/Plasma Cell Neoplasm

in at least one of its subunits, including a1 that has a caspase-like activity, a2 that presents a trypsin-like activity, and a5 that provides a chymotrypsin-like activity. Inhibition of the activity of proteasomes results in cell cycle arrest and cell death, two activities that do not occur in cancer cells because these inherently possess elevated levels of proteasome activity that effectively detect any impending inhibitory effects in their immediate microenvironment.

One of the most recognized proteasome inhibitors is bortezomib, a novel drug that received accelerated assessment and review by the U.S. Food and Drug Administration due to the results of Phase II clinical trials that established its safety and efficacy compared to dexamethasone in the treatment of patients with relapsed multiple myeloma who have earlier received at least one treatment regimen. The initial findings of the clinical trial showed that the administration of bortezomib resulted in a significant improvement in the survival of the patient, as well as in generating a response from the drug. The subsequent trials resulted in a six-month improvement in rates of patient survival and in generating a response to the drug. The depth of response to the drug also improved from 1 percent to 9 percent, and a 2.7-month improvement in the time for disease progression.

Another proteasome inhibitor is carfilzomib, which has been recently approved as a treatment drug for multiple myeloma. The ideal candidates for carfilzomib are patients who have undergone at least two therapies that used bortezomib as well as an immunomodulatory drug and have shown relapse. The term relapse, which is used interchangeably with refractory disease, pertains to the progression of the disease within 60 days after the administration of the last therapy.

A Phase II clinical trial involving carfilzomib showed that the proteasome inhibitor also caused thrombocytopenia as a side effect, which was also observed with bortezomib. The clinical trial also showed that carfilzomib did not cause severe renal impairment, and that only 1.5 percent of the patients had to be discontinued from the study because of the development of renal dysfunction. More clinical studies are currently being conducted on carfilzomib. These trials include the identification of the optimal dose for the treatment of multiple myeloma that results in an improvement of the disease yet shows the lowest incidence of severe adverse reactions or side effects to the drug.

In addition to bortezomib and carfilzomib, other novel proteasome inhibitors are in the pipeline for the treatment of multiple myeloma. These new batches of inhibitors will have to undergo screening for safety and efficacy using a study population of patients of varying stages and responses to previous therapies. Marizomib is an intravenous, irreversible proteasome inhibitor that has been assessed for its safety and overall response rate. Toxicities caused by marizomib include transient hallucinations, changes in cognition, and physical imbalance. As of 2014 the drug was being evaluated based on a dose frequency of twice a week, using a dose of 0.5 mg/m² IV for a total of 120 minutes. Thus, the treatment schedule would include the administration of the drug on days 1, 4, 8, and 11, with the entire cycle lasting for a total of 21 days. Marizomib is administered as a single agent or in combination with a low dose of dexamethasone, which is orally administered at a dose of 20 mg one day before and one day after receiving marizomib.

Another novel proteasome inhibitor in the pipeline is ixazomib, an oral drug that was being assessed in a 2014 Phase I clinical study using a dosing schedule of weekly and biweekly and involving relapsed multiple myeloma patients. Initial results have shown that ixazomib causes various adverse events in 91 percent of the patients; these include thrombocytopenia, diarrhea, fatigue, rashes, and nausea. Approximately 10 percent of the study population developed mild peripheral neuropathy. Based on the promising results of proteasome inhibitors in the treatment of multiple myeloma, these novel drugs may assist in improving the conditions of patients. It is thus essential that additional clinical trials be performed to determine the extent of efficacy and safety of these novel drugs.

Rhea U. Vallente
PreventionGenetics, LLC

See Also: Cancer Drugs, Cost and Benefits of; Drugs.

Further Readings
Mycosis Fungoides

Though the name means mushroom fungus disease, mycosis fungoides, granuloma fungoides, or Alibert–Bazin syndrome is a type of cutaneous T-cell lymphoma, a non-Hodgkin’s lymphoma. Lymphomas are cancers of the immune system, originating in white blood cells called lymphocytes. Traditionally, they are divided into Hodgkin’s lymphoma, which is more responsive to radiation therapy, and all others. However, in the last decade, this distinction has fallen out of favor, given the extreme variation among different non-Hodgkin’s lymphomas, some of which are caused by infectious agents, while others result from genetic diseases, autoimmune diseases, or chemical exposure. Some are associated with haemophilus influenzae type B (HIB), some are not, and their aggressiveness varies considerably.

Cutaneous T-cell lymphomas begin with a mutation of T cells, a lymphocyte that matures in the thymus or tonsils and is key in cell-mediated immunity.

Mycosis fungoides does not seem to be hereditary or genetic in origin, and it is much more common in men than women. The rate of incidence is highest over age 50 and very low under age 20. It is related to Sézary syndrome, a leukemic form of the disease.

The first symptom of mycosis fungoides is the skin condition that gives it its name, a patchy rash of plaque that may have reddened lesions or bumpy tumors surrounded by patches of rough skin. Itching is not uncommon but present in only about a quarter of cases. Otherwise, it often resembles psoriasis, eczema, and other less-serious skin conditions. Usually, it is not identified as a cancer until a skin biopsy is performed. Usually, several biopsies are performed in different spots as not all of the rash tissue is malignant.

Mycosis fungoides has three stages: premycotic, which looks like other skin conditions; mycotic, in which infiltrative plaques begin to appear and atypical lymphoid cells can be found microscopically; and tumorous, which is malignant, with medium-sized lymphocytes infiltrating. Premycotic fungoides may last for decades before progressing. Untreated mycosis fungoides may metastasize to lymph nodes or blood and internal organs or develop into a higher-grade lymphoma.

Treatment varies. Naloxone, an opioid antagonist used since the 1960s to counteract opioid overdose, was approved in 2010 to treat pruritus resulting from all cutaneous T-cell lymphomas. Although mycosis fungoides is considered incurable like other cutaneous T-cell lymphomas, it may go into indefinite remission. Treatments include local radiation therapy and either topical chemotherapy (applied like an ointment) or conventional systemic chemotherapy and photopheresis, a photodynamic therapy in which the patient’s blood is treated with a photosensitizing agent and irradiated with ultraviolet light (UVA) before being returned to the patient. Other photodynamic therapies are possible as well, including the use of topical photosensitizers before exposing the skin to sunlight or ultraviolet light. Other treatments like topical steroids help to treat the rash and itching and may be sufficient in premycotic or mycotic cases.

Mycosis fungoides can also be treated with Ontak, an antineoplastic agent that binds to interleukin-2 receptors and kills the cells, which can cause remission if other treatments have been ineffective; Tar-gretin, an anticancer treatment approved in 1999; Zolinza, a compound that inhibits histone deacetylases, is used to treat persistent cutaneous T-cell lymphomas that do not respond to or recur after other medications, and which is often used to treat Sézary syndrome; and Istodax, which was approved for cutaneous T-cell lymphomas in 2009. Clinical trials are exploring the use of Panobinostat, an experimental drug developed by Novartis as an on-selective histone deacetylase inhibitor, and Resimmune, an anti-T-cell immunotoxin developed by the National Institutes of Health and trialed by Angimmune.

Bill Kte’pi
Independent Scholar
See Also: Anticancer Drugs; Lymphoma, Non-Hodgkin’s, Adult; Sézary Syndrome.

Further Readings

Myelodysplastic Syndromes

Myelodysplastic syndromes (MDS) are a heterogeneous group of blood cancers arising from the early death of hematologic cells derived from bone marrow (BM). The death of these cells can lead to severe fatigue, infections, bleeding, and more, causing significant impairment in daily functioning or even death. Though the incidence is low relative to many other cancers, the burden is large on patients and families due to extended periods of suffering and financial hardship, with many having no hope for a cure at this time. However, many advancements in research and therapy are being made to improve life for people with MDS.

Epidemiology and Prognosis

Myelodysplastic syndromes generally affect elderly men and women, with more than 85 percent of cases occurring after age 60. There are up to 75 cases diagnosed per 100,000 people over age 65. Up to 15,000 people are diagnosed with MDS each year in the United States alone, and it is estimated that more than 60,000 people are living with MDS in the United States. Worldwide, MDS is grossly underdiagnosed, and thus the global disease burden is unknown at this time. Studies have shown that MDS seems to occur at a younger age in Asia, independent of race, but strong evidence is lacking.

MDS is sporadic with no identifiable causative factor in almost all cases. However, some cases may be initiated by chemotherapy or radiation from prior cancer therapy or an environmental radiation exposure. Additionally, high levels of benzene exposure can cause MDS. This is generally seen in chemical plant workers that manufacture benzene, often in China, and is also thought to occur from tobacco use or high levels of industrial emissions or hazardous waste, though significant data for the latter three is poor at this time.

Approximately one-third of MDS cases progress to acute myeloid leukemia (AML), most often those considered high risk due to certain clinical and genetic abnormalities. Patients who develop this secondary AML generally have a poorer prognosis than those with primary AML (no prior predisposing disease) and often do not respond as well to chemotherapy. In the two-thirds who do not develop AML, prognosis is still generally poor, and predicted survival (based on the median survival data of a large cohort) can range from less than a year to more than seven years, though the prognosis is impossible to determine exactly for any given individual. Predicted survival for a particular patient is based on disease subtype and risk category as defined by French-American-British (FAB) classification and the
Myelodysplastic Syndromes

Revised International Prognostic Scoring (IPSS-R) scoring system, respectively.

Disease Mechanisms and Clinical Characteristics
MDS is caused by the early death of cells in the BM that become red and white blood cells and platelets. The combination of cells affected, severity of the illness, and response to treatment is variable and gives each patient a distinctive disease presentation, determined by their unique signature of abnormal processes in cancer cells compared to normal cells.

The three cell types affected lead to characteristic symptoms with decreased levels of the corresponding cells, and patients may have only one or any combination of deficiencies in these cells. Low red blood cells (anemia) are the most commonly decreased cell type in MDS, leading to chronic fatigue and low tolerance to exertion, so patients have extremely limited daily functioning compared to baseline. This fatigue can be emotional or mental as well as physical, affecting a patient’s mood and ability to perform routine tasks. This anemia often leads to blood transfusion dependence when untreated. Chronic transfusion therapy has many potential side effects, such as an immune attack of transfused cells (the likelihood increases proportionally with higher numbers of transfusions), liver and heart disease, arthritis, infections, and more.

The frequency of transfusions required by a patient is a commonly used marker for worsening disease and increased resistance to treatment.

Low white blood cells (leukopenia) can lead to severe, life-threatening infections due to inability of the immune system to respond to certain pathogens. Minor infections occur frequently in patients with leukopenia, including mucosal yeast infections (commonly in the mouth), skin infections, and pneumonias. However if levels decline significantly, more severe infections may occur and can lead to death.

A low platelet level (thrombocytopenia) leads to poor blood clotting, which causes easy bruising and can lead to spontaneous bleeding if levels drop too low. These bleeds can lead to worsening anemia, stroke, or a multitude of other effects depending on the location of the bleed within the body.

Treatment
MDS is incurable with medical therapy alone, and the only curative treatment is with a BM transplant. However, this treatment is not ideal for all patients; only some are eligible, fewer find a matched donor, and the risks of transplant are high. There are supportive and medical therapies available that slow the progression of the disease and can significantly alleviate symptoms. Because the vast majority of MDS patients are anemic, red blood cell (RBC) transfusions and erythropoiesis-stimulating agents (ESAs, which increase RBCs by BM stimulation) are often a mainstay of therapy.

The three Food and Drug Administration (FDA)-approved drugs at this time that have proven to be effective for prolonged medical therapy are lenalidomide, azacytidine, and decitibine. All have certain indications depending on the subtype of the patient's disease. While not curative, response to these therapies can lead to significant improvement in quality of life by increasing blood cell counts and corresponding improvement of symptoms. This can lead to higher energy and return to daily functioning as well as decreased risk of infections and bleeding. If the anemia improves (the patient achieves transfusion independence), this is a sign that the drug will give him or her clinical resolution for some time. However, not all patients respond to the recommended therapies, and even if they do, the dysplastic cells often become resistant to these therapies over time, and symptoms again worsen. In this case, other approved therapies may be tried, or the patients can be put on clinical trials for treatments under study. Patients receiving frequent transfusions are also usually started on an iron-chelating agent, like deferasirox, to reduce the risk of iron overload.

Other treatments are not currently FDA approved but are frequently used due to high rates of resistance to approved drugs. One such drug is rigosertib, which has been shown to give significant clinical improvement in patients with high-risk disease in clinical trials. Clinical trials for rigosertib are currently under way in low-risk patients, with promising results so far. High-dose all-trans retinoic acid (ATRA, a vitamin A derivative) therapy also has been shown to have a significant positive effect in some patients. The subset of patients these drugs work best on has yet to be completely identified, though genetic and epigenetic studies are currently under way to better understand their mechanisms at a biochemical level. Other medications currently being studied are DNA deacetylase and methyltransferase (HDAC and DNMT) inhibitors, isocitrate dehydrogenase 2 (IDH2) inhibitors,
and transforming growth factor-β (TGF-β) pathway inhibitors, as well as many others in early stages with only preliminary data.

BM or umbilical cord blood transplant is ideal for younger patients who are otherwise healthy and have high-risk disease or are progressing to AML. BM transplants can significantly improve life expectancy by eliminating all MDS and return a patient’s quality of life to a healthy state. However, many risks come with BM transplant, including a high risk of infection and death, ranging from 20 to 40 percent survival in most studies, though some have reported a higher survival rate. The patient’s oncologist and BM transplant physician must be consulted to decide if this procedure is right for him or her if significant quality of life and life expectancy improvement may be achieved in persons with a poor prognosis.

Looking to the Future

Advancements in drug design, clinical genetic and epigenetic testing, and research on the driving mechanisms of MDS are rapidly progressing. Many experimental therapies are entering clinical trials, though they are still in the early phases. Our understanding of the underlying drivers of MDS is leading to personalization of therapy, something that exists for many other cancers but thus far has not existed in MDS therapy. Curative therapy for all MDS patients is far from ready for clinical practice, but improvement of therapy targeting symptoms and improved life expectancy is imminent, and huge advances will be seen in the next five to 10 years, leading to improved quality of life in all people who develop this disease. MDS patients and their families should be hopeful for significant advances in the coming years.

Ghulam Ishaq Khan
Columbia University
Nicholas Reed Iverson
Albert Einstein College of Medicine

See Also: Anticancer Drugs; Bone Marrow Transplants; Myelodysplastic/Myeloproliferative Diseases.

Further Readings

Myelodysplastic/Myeloproliferative Diseases

Myelodysplastic and myeloproliferative neoplasms (MDS/MPNs) are a group of disorders that do not have the characteristic unique features to be classified as an MDS or an MPN alone but instead have features of both. These disorders are characterized by simultaneous low levels of some types of blood cells and elevated levels of other types, with abnormal growth patterns seen on bone marrow biopsy.

MDSs are a heterogeneous group of blood cancers characterized by early death of more mature blood cells exiting the bone marrow. The three types of blood cells that can be affected are red blood cells (RBCs), white blood cells (WBCs), or platelets and are collectively called myeloid cells. Any one of these or a combination may be affected in a particular patient. The cell types affected, severity of disease, age of the patient, and genetic changes observed are just a few of the factors that contribute to an individual’s prognosis and clinical presentation. Low RBCs lead to anemia, causing debilitating fatigue that can be emotional, mental, or physical, as well as dependency on blood transfusions (which has its own complications). Anemia is present in the vast majority of patients with MDS. Low WBCs, termed leukopenia, lead to infections. These infections may be minor, such as mucosal yeast infections or skin infections.
However, when WBCs are severely low, the infections can be systemic and life threatening. Low platelets cause thrombocytopenia, a disorder that leads to poor blood clotting. This can cause a range of complications depending on severity, from easy bruising if mildly decreased to spontaneous internal bleeding if severely decreased, leading to hemorrhagic stroke, gastrointestinal bleeding, or even death.

On the other hand, MPNs are a group of blood cancers characterized by uncontrolled cell replication of myeloid cells in the bone marrow, leading to elevated levels of RBCs, WBCs, or platelets. These patients are often asymptomatic. If symptoms are present, they can lead to a large range of minor, nonspecific symptoms or symptoms as severe as blood clots, stroke, ulcers, heart attack, and gout, among others.

The combined MDS/MPNs are a collection of four categories of poorly understood disorders, all having a cancerous stem cell expansion in the bone marrow and some abnormal combination of low and high levels of various mature blood cells in circulation. These disorders are chronic myelomonocytic leukemia (CMML), atypical chronic myeloid leukemia (aCML), and myelodysplastic and myeloproliferative neoplasms—unclassifiable (MDS/MPN-U). The frequency of these disorders is very rare independently, combining for an incidence of up to six new cases per million people per year in one study, much less than that of MDS or MPNs. These diseases present many challenges for the people who are afflicted and for their physicians due to lack of understanding of the disease processes and poor treatment options. However, research is ongoing, and clinical drug trials continue to improve care. Here the current standing of the knowledge of these four disorders and future directions for research and therapy are presented.

**Chronic Myelomonocytic Leukemia**
CMML is a disease of the elderly and occurs more often in males (up to 3:1), with a median age of onset of approximately 70 years old. It is characterized by persistent elevation of a type of WBC called monocytes in the bloodstream. To make the diagnosis, chronic myeloid leukemia (CML) and acute myeloid leukemia (AML) must be ruled out, and another bone marrow abnormality must be detected. These patients usually present with bone marrow failure and corresponding symptoms, which mirror the symptoms seen in MDS with low blood cell levels. Nonspecific symptoms that frequently occur include fever, night sweats, enlargement of the liver or spleen, and weight loss. Approximately 15 to 20 percent of patients progress to secondary AML. Median survival in patients with CMML is between one and two years, with various clinical and genetic factors affecting an individual’s prognosis. The International Prognostic Scoring System (IPSS) can be used for calculating prognosis in a subset of CMML patients, and the subtypes CMML-1 and CMML-2 further categorizes a patient’s risk based on the extent of abnormal immature cell expansion in the blood and bone marrow.

**Atypical Chronic Myeloid Leukemia**
ACML presents very similarly to CMML, with bone marrow failure symptoms, nonspecific systemic symptoms like fever and weight loss, and an enlarged spleen. The diagnosis of this disease involves ruling out a few others, including primary myelofibrosis and chronic neutrophilic leukemia, and the criteria that differentiate this disease from...
others are defined but shaky as this disease has such close resemblance to others. It can be differentiated mainly by the high proportion of WBCs called neutrophils in the blood and by ruling out the classic CML mutation BCR-ABL1 fusion in addition to other genetic and blood cell-level studies. Median survival is less than two years, and this disease also puts patients at risk for progression to AML.

**Myelodysplastic and Myeloproliferative Neoplasms—Unclassifiable**

MDS/MPN-U is a group of disorders that do not meet the criteria for MDS or MPN and also do not fit into one of the other MDS/MPN overlap syndromes. The best-characterized disorder in this group is termed *refractory anemia*, with ringed sideroblasts and thrombocytosis (RARS-T), also generally found in the elderly population. RARS is an MDS that leads to anemia with abnormal blood cell maturation, and thrombocytosis is an elevated platelet count that often is asymptomatic but can lead to increased risk of blood clots forming in the patient’s blood vessels. This also can be accompanied by nonspecific symptoms. The median overall survival is good compared to other MDS/MPNs, at nearly six years, and is similar to RARS. Though RARS-T is clinically similar to RARS in that the bone marrow findings and prognosis are similar and symptoms of anemia are the most common features, it is important to distinguish this disorder from RARS because they respond to different types of medical therapy. Other MDS/MPN-Us (non-RARS-T) are associated with a poorer prognosis, with median overall survival just longer than one year. These unclassifiable disorders may have no defining diagnostic features other than not meeting the requirements for another category and have very limited treatment options compared to RARS-T. MDS/MPN-U also may lead to secondary AML, though the rate of conversion is not well documented.

**Juvenile Myelomonocytic Leukemia**

In contrast to the other overlap syndromes, JMML is a disease of the young. It is a rare disorder, causing only 2 percent of childhood leukemias, and occurs in individuals (more often males) at a median age of just one year. Though risk factors are not well established for the other overlap syndromes, JMML is known to occur with much higher frequency in patients who have neurofibromatosis type 1 (NF1). Diagnosis requires increased monocytes in the blood, as in CMML. Additionally, CML and AML must be ruled out, and two other characteristic findings must be documented, as denoted by the World Health Organization (WHO) diagnostic criteria. Affected individuals usually have nonspecific symptoms (as in the other disorders) and commonly have a bronchitis or tonsillitis-like illness. It often leads to a predisposition to easy bleeding, rash, enlarged lymph nodes, and enlargement of the liver and spleen. The easy bruising and bleeding are due to a low platelet level, which is very common in these patients. Unfortunately, the prognosis for JMML is poor, with median overall survival between 10 months and four years, depending on age at diagnosis (younger patients tend to have a better prognosis) and features of the blood, such as platelet level (lower platelets are associated with worse prognosis). Between 10 and 20 percent of patients progress to AML.

**Diagnostics and Treatment**

Diagnosis of these disorders involves drawing a blood sample to assess levels of RBCs, WBCs, and platelets as well as taking a bone marrow biopsy and aspiration to assess for abnormal-looking, immature, or cancerous cells and for genetic abnormalities. All of these disorders are diagnoses of exclusion, and other blood cancers must be ruled out before a diagnosis can be made. All can be treated partially with supportive therapy (i.e., without chemotherapeutic drugs) depending on the type of low blood cell count the patient has. This includes blood transfusions and bone marrow-stimulating agents (termed ESAs) to increase production of RBCs for anemia and antibiotics to treat infections when they occur due to low WBCs. Bone marrow transplant is also an option for some people, and each disorder has a corresponding therapy plan that generally works best for the individual.

Once a diagnosis is established, treatment options for these disorders are unfortunately very limited. For CMML, medical therapies include azacitidine and decitabine, which are more effective in higher-risk patients (an overall response rate of about 25 percent is seen), as well as hydroxyurea, especially in patients with elevated WBCs. Resistance to these therapies is common and may develop later on in patients who initially saw improvement. The only curative therapy is bone marrow stem cell transplant. This is by far the best option for some patients, especially those who are younger than these patients. Unfortunately, the prognosis for JMML is poor, with median overall survival between 10 months and four years, depending on age at diagnosis (younger patients tend to have a better prognosis) and features of the blood, such as platelet level (lower platelets are associated with worse prognosis). Between 10 and 20 percent of patients progress to AML.

**Diagnostics and Treatment**

Diagnosis of these disorders involves drawing a blood sample to assess levels of RBCs, WBCs, and platelets as well as taking a bone marrow biopsy and aspiration to assess for abnormal-looking, immature, or cancerous cells and for genetic abnormalities. All of these disorders are diagnoses of exclusion, and other blood cancers must be ruled out before a diagnosis can be made. All can be treated partially with supportive therapy (i.e., without chemotherapeutic drugs) depending on the type of low blood cell count the patient has. This includes blood transfusions and bone marrow-stimulating agents (termed ESAs) to increase production of RBCs for anemia and antibiotics to treat infections when they occur due to low WBCs. Bone marrow transplant is also an option for some people, and each disorder has a corresponding therapy plan that generally works best for the individual.

Once a diagnosis is established, treatment options for these disorders are unfortunately very limited. For CMML, medical therapies include azacitidine and decitabine, which are more effective in higher-risk patients (an overall response rate of about 25 percent is seen), as well as hydroxyurea, especially in patients with elevated WBCs. Resistance to these therapies is common and may develop later on in patients who initially saw improvement. The only curative therapy is bone marrow stem cell transplant. This is by far the best option for some patients, especially those who are younger than these patients. Unfortunately, the prognosis for JMML is poor, with median overall survival between 10 months and four years, depending on age at diagnosis (younger patients tend to have a better prognosis) and features of the blood, such as platelet level (lower platelets are associated with worse prognosis). Between 10 and 20 percent of patients progress to AML.

**Diagnostics and Treatment**

Diagnosis of these disorders involves drawing a blood sample to assess levels of RBCs, WBCs, and platelets as well as taking a bone marrow biopsy and aspiration to assess for abnormal-looking, immature, or cancerous cells and for genetic abnormalities. All of these disorders are diagnoses of exclusion, and other blood cancers must be ruled out before a diagnosis can be made. All can be treated partially with supportive therapy (i.e., without chemotherapeutic drugs) depending on the type of low blood cell count the patient has. This includes blood transfusions and bone marrow-stimulating agents (termed ESAs) to increase production of RBCs for anemia and antibiotics to treat infections when they occur due to low WBCs. Bone marrow transplant is also an option for some people, and each disorder has a corresponding therapy plan that generally works best for the individual.

Once a diagnosis is established, treatment options for these disorders are unfortunately very limited. For CMML, medical therapies include azacitidine and decitabine, which are more effective in higher-risk patients (an overall response rate of about 25 percent is seen), as well as hydroxyurea, especially in patients with elevated WBCs. Resistance to these therapies is common and may develop later on in patients who initially saw improvement. The only curative therapy is bone marrow stem cell transplant. This is by far the best option for some patients, especially those who are younger than these patients. Unfortunately, the prognosis for JMML is poor, with median overall survival between 10 months and four years, depending on age at diagnosis (younger patients tend to have a better prognosis) and features of the blood, such as platelet level (lower platelets are associated with worse prognosis). Between 10 and 20 percent of patients progress to AML.

**Diagnostics and Treatment**

Diagnosis of these disorders involves drawing a blood sample to assess levels of RBCs, WBCs, and platelets as well as taking a bone marrow biopsy and aspiration to assess for abnormal-looking, immature, or cancerous cells and for genetic abnormalities. All of these disorders are diagnoses of exclusion, and other blood cancers must be ruled out before a diagnosis can be made. All can be treated partially with supportive therapy (i.e., without chemotherapeutic drugs) depending on the type of low blood cell count the patient has. This includes blood transfusions and bone marrow-stimulating agents (termed ESAs) to increase production of RBCs for anemia and antibiotics to treat infections when they occur due to low WBCs. Bone marrow transplant is also an option for some people, and each disorder has a corresponding therapy plan that generally works best for the individual.

Once a diagnosis is established, treatment options for these disorders are unfortunately very limited. For CMML, medical therapies include azacitidine and decitabine, which are more effective in higher-risk patients (an overall response rate of about 25 percent is seen), as well as hydroxyurea, especially in patients with elevated WBCs. Resistance to these therapies is common and may develop later on in patients who initially saw improvement. The only curative therapy is bone marrow stem cell transplant. This is by far the best option for some patients, especially those who are younger than these patients. Unfortunately, the prognosis for JMML is poor, with median overall survival between 10 months and four years, depending on age at diagnosis (younger patients tend to have a better prognosis) and features of the blood, such as platelet level (lower platelets are associated with worse prognosis). Between 10 and 20 percent of patients progress to AML.
(generally up to age 70), high risk, resistant to available medications, and in whom the treatment will significantly prolong the life span. However, bone marrow transplant is a dangerous procedure with a high risk of infection and death, in up to 60 to 80 percent of patients in some studies. However, when the transplant goes well, the treatment can completely restore daily functioning, totally alleviate symptoms, and significantly prolong life. Affected individuals and their families should talk to an oncologist and bone marrow transplant physician to decide if this procedure is right for them.

For aCML, there has been no effective medical treatment so far, and diagnosis is associated with a poor prognosis. Hydroxyurea is effective in some patients for symptom alleviation, but the only real therapy is bone marrow stem cell transplant. Though transplant is a high-risk procedure, because of the lethal nature of this disorder, patients who are eligible and have a matched donor should be considered strongly for transplant.

In RARS-T, though the prognosis is better than that of other MDS/MPN overlap syndromes, the treatment options remain limited. Because of the similarity to RARS, therapies used for MDS have been tried in small studies with some success. Lenalidomide is one such drug, which led to transfusion independence in two patients, one of whom also went into remission. Because RARS-T is associated with a better prognosis in elderly patients, bone marrow transplant is not recommended for most patients but is at the discretion of the patient’s physician as to whether an individual is a good candidate. Some patients also have responded to an MPN therapy called ruxolitinib, which inhibits a protein called Jak2. Other MDS/MPN-Us are treated with similar methods, but none have proven to be very effective at this time, and prognosis is poor. Additionally, patients with a platelet-derived growth factor receptor (PDGFR) gene abnormality are candidates for imatinib therapy, a drug that was initially designed for CML treatment.

JMML therapy is not well established and even with chemotherapy has had less than a 10 percent survival rate. Patients rarely have long-term survival, but it can occur more frequently in patients who have undergone bone marrow transplant. There was greater than 50 percent survival after four years in one study of patients with bone marrow transplant. Additionally, experimental therapies such as vitamin A derivatives (13-cis retinoic acid) have shown some success as well.

Looking to the Future
As these disorders are so rare, studies to find appropriate therapies for each one have been small and often anecdotal. Some therapies have proven effective in a limited number of patients, and multicenter efforts to create larger-scale studies are under way, integrating knowledge of MDS, MPN, and clinical and basic science research of the overlap syndromes to develop new therapies. One such target is the Ras gene, which is known to be involved in many cancer types and has been shown to be involved in all of these disease categories. Additionally, combination therapies are being tried to see if they improve outcomes over a single chemotherapeutic agent alone. For example, a phase II trial is under way for combination therapy with ruxolitinib (as described previously as commonly used in MPNs) and azacitidine (a drug commonly used in MDS). Further research is required to discover the causal genetic mutations that lead to development of these syndromes. Once more candidate targets have been identified, therapies can be applied or developed to target those mutations in each patient, leading to personalized therapy in MDS/MPNs with increased efficacy. Bone marrow transplant remains a good option for many patients, and studies are ongoing to increase the efficiency of transplant and survival.

As it stands now, prognosis and treatment options for these disorders remain poor. However, the rapid expansion of our knowledge about the molecular mechanisms of these disorders will certainly lead to improved therapy and survival for patients affected with these devastating disorders in the next few years.

Ghulam Ishaq Khan
Columbia University
Nicholas Reed Iverson
Albert Einstein College of Medicine

See Also: Myelodysplastic Syndromes; Myeloma, Multiple; Myeloproliferative Disorders, Chronic.

Further Readings
Multiple myeloma (MM) is a hematologic cancer, or cancer of the blood, that develops in plasma cells of bone marrow. Plasma cells, also known as B cells, are normally responsible for producing antibodies that provide long-term protection against foreign antigens. MM develops when a single mutated, or cancerous, plasma cell proliferates uncontrollably, known as monoclonal proliferation. Collections of these cancerous plasma cells form tumors within the bone that interfere with normal blood cell production. Plasma cell tumors crowd out the production of other blood cells, leading to bone lesions and abnormally low numbers of red blood cells, white blood cells, and platelets. Additionally, cancerous plasma cells produce abnormal antibodies that damage the body and, in particular, the kidneys. MM is considered incurable but treatable, and the introduction of stem cell transplantation and the development of more effective therapies have improved management of the disease and extended patient survival.

Risk Factors
MM is noncontagious, and although most people who develop the disease have no clearly identifiable risk factors, there are several factors that may increase a person's risk for the disease:

- **Age**: The risk for MM increases with age. Less than 1 percent of cases are diagnosed in people younger than 35, and the majority of people who develop MM are older than 50, with the median age of diagnosis at 69.
- **Gender**: Men are at a slightly greater risk for developing MM than women.
- **Race**: African Americans are twice as likely to develop MM as are white Americans. The disease shows the lowest prevalence in Asians.
- **Family History**: MM appears to run in families. According to the National Cancer Society, someone who has a sibling or parent with the disease is four times more likely to develop the disease than would be expected otherwise.
- **Radiation**: People who have been exposed to radiation are at an increased risk for MM.
- **Workplace Exposure**: Although no clear link has been identified, the prevalence of MM is higher among agricultural and petroleum workers.
- **Obesity**: Risk for MM increases slightly if an individual is obese, although the mechanism is not well understood.

Prevalence
After non-Hodgkin’s lymphoma, MM is the second-most common blood cancer and represents 1 percent of all cancers in white individuals and 2 percent of all cancers in black individuals. According to the National Cancer Association, in the United States in 2014, 24,050 new cases will be diagnosed (13,500 men and 10,550 women), and 11,090 deaths are expected to occur (6,110 men and 4,980 women) as a result of MM. This translates into a lifetime risk of one in 143 for the disease.

Disease Presentation and Symptoms
Many organs can be affected by MM, but most individuals (70 percent) present with bone pain. The source of this pain is usually lesions, or tumors, within the spine or ribs, but persistent, intense pain can reveal a pathological bone fracture. In addition to forming tumors within the bone, cancerous plasma cells release factors that lead to bone breakdown and elevated blood calcium levels. The crowding out of normal red blood cell production by overproliferative plasma cells can cause anemia, wherein decreased red blood cell production impairs oxygen delivery to the body's tissues.

Anemia can be asymptomatic or cause feelings of fatigue, weakness, and shortness of breath on exertion. Additionally, the cancerous plasma cells
produce paraprotein, an abnormal, nonfunctional antibody fragment that impairs the body’s defenses and damages the kidneys. The weakened immune system, lacking the ability to produce functional antibodies, puts patients at risk for infection. Kidney damage can lead to a decrease in urine production, blood in the urine, and eventual complete kidney failure.

**Diagnosis and Staging**

It is important to note that, in all patients, MM is preceded by a monoclonal gammopathy of undetermined significance (MGUS). MGUS is a benign condition in which paraprotein is found in the blood but in lower levels than with MM. MGUS can then progress into a range of blood diseases, with MM developing at a rate of 1 to 2 percent per year. MM is diagnosed based on the finding of bone marrow that is at least 10 percent monoclonal plasma cells and monoclonal protein in the blood or urine. In patients with less-common, nonsecretory MM, the diagnosis is based on the presence of at least 30 percent monoclonal plasma cells in the bone marrow.

The recommended tests if MM is suspected include a detailed medical history and physical examination, laboratory testing of blood and urine to characterize and quantify abnormal blood cell counts and protein production, and bone marrow examination. To identify bone lesions, X-ray and magnetic resonance imaging (MRI) of the spine, skull, chest, pelvis, and legs is recommended.

According to the International Staging System (ISS), staging the progression of the disease places the individual into one of three escalating risk groups that are defined by the levels of $\beta_2$-microglobulin and albumin in the blood. Further staging is determined by genetic analysis of the plasma cells to detect the presence of specific genetic or chromosomal abnormalities that are associated with a worse outcome.

**Treatment and Prognosis**

Treatment of MM is dependent on the stage of the disease and the health of the individual. Asymptomatic (smoldering) MM requires only close monitoring. Symptomatic (active) MM is treated immediately with high-dose chemotherapy and with stem cell transplantation depending on the age of the patient. The standard chemotherapy regimens—thalidomide-dexamethasone, bortezomib-based regimens, and lenalidomide-dexamethasone—are employed to eliminate rapidly dividing, cancerous cells. Following the elimination of the individual’s bone marrow cells with chemotherapy (and radiation if necessary), in patients under 65 years of age, transplantation of healthy, blood-forming stem cells gives the individual an opportunity to reestablish their blood system free of cancer. Unfortunately, the MM tends to relapse, and the cancerous cells can become treatment resistant.

While there is no cure for MM, effective management of the disease can significantly extend survival. ISS stage I patients have a median survival of 62 months. ISS stage II patients have a median survival of 44 months. ISS stage III patients have a median survival of 29 months. These survival times are measured from the point that treatment is started, and many patients, especially those with smoldering MM, begin treatment months or years following diagnosis. Of patients diagnosed with MM, 44.9 percent survive for longer than five years.

Eamon Duffy
Andrew Robert Branagan
Yale School of Medicine

**See Also:** Bone Marrow Transplants; Chemotherapy; International Myeloma Foundation.

**Further Readings**

A group of oncologists have recently expressed their concern regarding the price of cancer drugs, particularly those for the treatment of chronic myelogenous leukemia.

First, they point out the doctrine of just price, in which a fair value should be given to any kind of commodity, based on the price and the worth of the product. Thus, the higher-priced drugs should reflect higher levels of efficacy and safety. However, these clinicians are also aware of the doctrine of free market economy, wherein the prices of the cancer drugs are representative of what the customer is willing to pay in order to receive the product. These clinicians therefore want to identify which doctrine is better and which offers a morally and medically acceptable concept of marketing cancer drugs.

One argument for this dilemma could be based on the impact of the cancer drug on the lives of the patients, particularly in curing them and improving their medical conditions. In this scenario, the just price should prevail based on the moral implications of the treatment outcome. Prime examples of this scenario include the cost of bread in situations afflicted by famine, the price of polio vaccines, and the drugs employed for the treatment of various chronic conditions such as diabetes, hypertension, and multiple sclerosis. When an item does not save lives or is not critical in alleviating the suffering of an individual, then the market inherently controls the price of the product because it is highly likely that the item is not restrained by matters involving ethics. For example, buying an original painting by Picasso, embarking on a luxury cruise, and spending a two-week vacation in New York are all very expensive activities yet are not products that are essential to life.

In the case of chronic myelogenous leukemia, three drugs have been approved by the U.S. Food and Drug Administration (FDA) a couple of years ago, namely, bosutinib, ponatinib, and oxacetaxine. These most recent drugs were then included in the list of drugs that are commonly used for the treatment of chronic myelogenous leukemia, which include imatinib, nilotinib, and dasatinib. The latest three drugs may be as effective or more effective than the older drugs, yet their prices have been described to be astronomically high. The price of using ponatinib for the treatment of chronic myelogenous leukemia for one year is estimated to be at $138,000. On the other hand, oxacetaxine, which is recommended for induction, could cost approximately $28,000; ponatinib also could be employed in the maintenance course of the treatment, and this may cost $14,000. The cost of bosutinib has been estimated to be at around $118,000 each year.

Financial analysts, together with clinicians, have assessed and discussed the prices of the recently released drugs for cancer treatment. This collaborative effect unanimously expressed that the current market prices of drugs for the treatment of chronic myelogenous leukemia are way too high, and that these prices are unsustainable. Based on this consensus, the group of analysts feels that this situation can compromise the patients’ need for highly effective and safe therapies for their health conditions. The group also expressed their concern that, if the prices of these cancer drugs are not controlled very soon, the health care system of the United States might also be compromised, particularly losing its capacity in sustaining itself using the revenue that it receives from drug sales.

An extensive assessment of the prices of cancer drugs resulted in serious discoveries—11 of the 12 most commonly used FDA-approved drugs cost at least $100,000 each. Furthermore, the prices of these drugs have increased by at least 200 percent in the past decade; the average cost of cancer drugs each month used to be $5,000, whereas this currently costs more than $10,000 every month. Both financial analysts and clinicians recognize the fact that innovative methods and new discoveries in any field of practice should be appropriately rewarded. The efforts of pharmaceutical companies in conducting research and developing new drugs are therefore very tedious, time-consuming, and challenging, with the aim of developing better and safer drugs that the public could use in the treatment of specific medical disorders. The average cost of developing a new drug has been estimated at $1 billion; this price thus somehow dictates that the market value of the new drug should be high enough to compensate for the investment that the pharmaceutical company made.

Analysts should understand that the cost of developing a new drug does not only entail expenses in buying reagents and equipment in the
laboratory as well as paying highly trained scientists to conduct these investigations in drug development. There are also ancillary expenses that go with the cost of developing a new drug, including the amount required to conduct a clinical trial, which is a requirement for all drugs prior to their approval for sales in the market. Advertising the new drug on television and other forms of mass media also requires a considerable amount of money. Thus, for a pharmaceutical company to generate a new drug, it has to be ready to spend close to $1 billion, and more importantly, it has to generate sales revenue greater than $1 billion in order to compensate for the initial costs that they spent in its development, testing, and marketing. Analysts from various fields are currently assessing the value of each new drug that has been released in the market. Are these drugs being sold at the right price based on their value? The answer to this question may be released in the near future and may cause further dismay, particularly when drug development is now considered as another marketing arena.

Rhea U. Vallente
PreventionGenetics, LLC

See Also: Anticancer Drugs; Drugs; Food and Drug Administration; Marketing, Drug.

Further Readings
Nasopharyngeal Cancer

The global impact of nasopharyngeal cancer has not been established due to the scarcity in the number of studies that investigate the epidemiology of this disease. Nasopharyngeal cancer is considered as a malignancy that is strongly influenced by ethnicity as well as geographic distribution. Based on the limiting feature of this malignancy, the details of its etiology have remained uncertain. The incidence of nasopharyngeal cancer around the world is generally very low; also certain parts of the world present relatively high rates of incidence. For example, in certain populations in southern China, north Africa, southeast Asia, and the Arctic region, nasopharyngeal cancer is recognized as the most common type of malignancy. The unique distribution of nasopharyngeal cancer in specific geographical areas around the world indicates that its development, occurrence, and transmission could be influenced by environmental and genetic factors.

To determine the impact of environmental and genetic factors on the incidence of nasopharyngeal cancer, it is essential to initially establish the global incidence rate of this malignancy. However, previous reports have shown that nasopharyngeal cancer is associated with variations in rates of incidence because of a lack of integration in conducting epidemiological studies. Furthermore, the mortality data of nasopharyngeal cancer has not been established as most of the areas afflicted by this malignancy do not have a disease database that registers every case that develops in the country. The only organization that might probably have the most comprehensive information on the incidence of nasopharyngeal cancer at the global scale or at a country-by-country level is the International Agency for Research on Cancer (IARC).

The IARC was established by the World Health Organization (WHO) as an agency that would collect information on various cancers at the global scale. The section of Cancer Information maintains a large database that holds specific information on various aspects of different cancers. Aside from the incidence of each type and subtype of cancer, the IARC also collects information on the mortality rate of various cancers and lists international and national cancer registries. Unfortunately, information on mortality rates of specific cancers only represents those of selected countries. It is thus possible that certain countries have not been assessed in terms of the incidence and mortality of rare malignancies, including that of nasopharyngeal cancer.

In order to generate a useful database that documents various types of information on nasopharyngeal cancer, scientists have embarked on integrating the data from various countries and reviewing these in terms of accuracy. Through this approach, misinterpretations of the data could be avoided, and further research studies could be
developed based on the information provided by this database. One of the major contributions of the IARC is GLOBOCAN, which is a database on the incidence of cancer in five continents. For example, the GLOBOCAN2008 report contains the latest data as of the year 2008. Data on the incidence of various cancers are then compiled in this report, which is printed in several volumes and contains information collected from 300 registries located in a total of 61 countries around the world.

Epidemiologists utilize data from incidence and mortality rates in the design and development of preventive programs against a specific disease. In the case of cancer, these same sets of data are collected from each country and region around the world. Analysis of this data would then identify the top 20 countries that show the highest mortality for a specific cancer as well as determine the trends of each cancer in every country and on the global scale. For example, the incidence of one particular cancer is increasing in country X, whereas this has been observed as decreasing in country Y. Yet, on a global scale, the incidence of this specific cancer has remained the same in the past five years.

Assessment of the data on nasopharyngeal cancer showed that there were significant variations in the incidence of this specific malignancy around the world. Furthermore, the incidence of nasopharyngeal cancer between males and females varied per country. For example, the incidence of nasopharyngeal cancer in central America was estimated as 0.2 per 100,000 person-years, whereas that in southeast Asia was 6.5 per 100,000 person-years. On the other hand, the incidence rates for nasopharyngeal cancer were lowest in central America, as well as in South America and western Europe. At the national level, the incidence rates of nasopharyngeal cancer were highest among males from southeast Asian countries such as Malaysia, Indonesia, Singapore, Cambodia, and Brunei, as well as in Myanmar.

The incidence rates of nasopharyngeal cancer in females also varied per country. For example, the incidence rate of this malignancy in women in central America was 0.1, whereas that in southeast Asia was 2.8, reflecting at least a twofold increase in occurrence. The highest incidences of nasopharyngeal cancer at the national level were observed in the registries of southeast Asian countries such as Singapore, Myanmar, Indonesia, Bhutan, and Thailand. All these data indicate that nasopharyngeal cancer occurs at a higher rate among males than in females, reaching a 200 percent increase. On the other hand, the low incidence rate of nasopharyngeal cancer in both males and females in China were uniquely low, possibly reflecting a dilution in this specific population. However, in order to fully establish and validate this claim, additional investigations are warranted.

Another approach in studying the epidemiology of nasopharyngeal cancer is through mortality rates. By comparing mortality rates between that of the WHO and that collected by GLOBOCAN, it is possible to generate a more accurate estimate of this parameter within a five-year period. The mortality rates of nasopharyngeal cancer varied across the globe, ranging from 0.1 among males in central America to 4.2 among males in southeast Asia. Most of the registries showing the highest mortality rates involved males from counties in Asia, South Africa, and Micronesia. On the other hand, the lowest mortality rates were observed in countries of western and northern Europe, South Africa, central America, and Melanesia. The mortality rates of nasopharyngeal cancer in females ranged from 0.1 to 1.8 in central America and southeast Asia, respectively. The highest mortality rates in females were observed in countries from Asia, South Africa, and Micronesia. These variations in incidence and mortality rates thus make it more difficult to assess the severity of this particular malignancy at a global scale. Additional studies could possibly improve the statistics on this specific cancer.

Rhea U. Vallente
PreventionGenetics, LLC

See Also: International Agency for Research on Cancer; Nasopharyngeal Cancer, Childhood; World Health Organization.

Further Readings
Nasopharyngeal Cancer, Childhood

Nasopharyngeal cancer is a unique form of head and neck malignancy because it has a distinct epidemiological pattern by being prevalent in countries situated in southeast Asia. Nasopharyngeal tumors also have been reported to be radio sensitive, which brings hope to most clinicians as well as their patients. However, this therapeutic approach also has been associated with a higher risk for its recurrence, particularly in patients who are at the advanced stages of the disease. The five-year rate of cancer control among patients diagnosed with stages III and IV nasopharyngeal cancer ranges from 70 to 80 percent. Based on this trend, it is therefore also important to determine whether the same pattern occurs among pediatric patients who developed nasopharyngeal cancer.

Previous studies have shown that local control of nasopharyngeal cancer is strongly associated with the total dose and the duration of radiation that is directly delivered to the tumor. In the advent of two-dimensional radiotherapy, various strategies have been employed to improve the control of advanced stages of nasopharyngeal cancer. One approach would be to use higher amounts of radiation, which is the main principle behind stereotactic radiosurgery, whereas the other approach involves the application of an external beam of radiation, a technique employed in brachytherapy. The introduction of a higher radiation dose through accelerated fractionation has been utilized in the treatment of advanced cases of nasopharyngeal cancer. In this technique, several fractions of radiation are applied each day, whereas in other patients, around six smaller doses are administered within a span of one week. Unfortunately, these methodologies also can result in severe toxicity effects on the patient as well as a higher risk of developing late complications that are often fatal. Various other organs that are critical to the life of the patient also occupy the head and neck region, which includes the spinal cord, the brain stem, the parotid glands, and the orbits. Thus, administering higher doses of radiation may result in better control of the tumor yet would also result in the rapid deterioration of the quality of life of the patient due to the toxic and fatal effects of higher radiation doses on neighboring organs of the head and neck.

Intensity-modulated radiotherapy (IMRT) is a recent advancement that allows the delivery of higher dosages of irradiation to the target tissue or organ, thus sparing the adjacent and unaffected regions from the damaging effects of radiotherapy. The principle of IMRT is that the application of higher doses facilitates the local control of radiation, thus resulting in a higher survival rate for patients with nasopharyngeal cancer. Previous studies have shown that the effective IMRT dose for adult patients with nasopharyngeal cancer is 85 Gy. Furthermore, the application of IMRT is associated with a 95 percent local control rate. The five-year disease-free rate of nasopharyngeal cancer treated with IMRT was roughly 77 percent, whereas the overall survival rate was 75 percent. On the other hand, late toxicity effects due to IMRT were observed in 84 percent of the patients at a four-year follow-up, which included deafness, skin dystrophy, and subcutaneous fibrosis. Only 5 percent of the patients showed recurrence at the fifth year of follow-up.

Despite the extensive information on the effectiveness and side effects of IMRT on nasopharyngeal cancer, its actual effects on pediatric patients have not been fully assessed. Chang-Juan Tao and colleagues thus recently conducted a research study on the long-term toxicity effects of IMRT combined with chemotherapy on 34 pediatric and adolescent patients with nasopharyngeal cancer. The study population consisted of patients of ages ranging from eight to 20 years old who were histologically diagnosed with nasopharyngeal cancer. Patients who showed metastatic nasopharyngeal cancer were excluded from the study.

The effective IMRT dose for the pediatric and adolescent patients with nasopharyngeal cancer was 66 Gy, which was significantly lower than that applied to adult patients. The local control rate in this young population that received IMRT combined with chemotherapy was 97 percent, which was relatively similar to that reported in adult nasopharyngeal patients. The five-year disease-free
survival of the pediatric and adolescent patients was 85 percent, whereas the overall survival was 88 percent, which was significantly higher than that observed among adult patients with nasopharyngeal cancer. Among the 34 patients enrolled in the study, only 24 survived for at least two years; however, these patients showed side effects due to the treatment regimen that they received. Approximately 67 percent of the patients presented xerostomia of grades 1 and 2, whereas 63 percent of the same cohort developed deafness. The findings of the study thus showed that the combination of IMRT with chemotherapy resulted in a longer control of nasopharyngeal cancer in pediatric and adolescent patients. Furthermore, the application of IMRT in combination with chemotherapy resulted in a low number of cases of late toxicities, wherein an 84 percent incidence rate was observed in adult patients, whereas only 67 percent of the pediatric and adolescent patients showed the same response to the treatment.

A recent study led by Martina Buehrlen used another therapeutic regimen consisting of a combination of irradiation and chemotherapy using cisplatin, folinic acid, 5-fluorouracil, and finally, interferon beta. The study population included a total of 45 pediatric patients with ages ranging from eight to 20 years and positively diagnosed with nasopharyngeal cancer. The treatment design was based mainly on the cancer stage of each patient. For example, patients with stage II nasopharyngeal cancer underwent radiotherapy at a dose of 59.4 Gy, whereas those with stages III and IV underwent three courses of the three chemotherapeutic drugs. All patients were administered interferon beta for a period of six months. Patient outcome was determined by magnetic resonance imaging of the tumor to determine treatment response. The results showed that 43 of the 45 pediatric patients achieved complete remission using the combination therapy. In addition, only three patients developed metastases after treatment. The progression-free survival rate using the combination therapy was determined to be 92.4 percent, whereas the overall survival rate was 97.1 percent. Late toxicities among patients included deafness and hypothyroidism. These findings thus indicate that a combination therapy using irradiation, chemotherapy, and interferon beta was effective, well tolerated, and superior to earlier therapeutic regimens for nasopharyngeal cancer in pediatric patients.

Rhea U. Vallente
PreventionGenetics, LLC

See Also: Head and Neck Cancer; Nasopharyngeal Cancer; Paranasal Sinus and Nasal Cavity Cancer.

Further Readings

National Alliance of Breast Cancer Organizations

The National Alliance of Breast Cancer Organizations (NABCO) was a leader in the field of health care advocacy from its founding as a nonprofit in 1986 until it closed its doors in 2004. It was cofounded by Nancy Brinker, Ruth Spear, Diane Blum, and Rose Kushner. During their tenure, NABCO’s mission was to advance knowledge by providing information and be the leading educational resource center available on breast cancer. It established a network of nearly 400 member organizations and agencies in the United States that provided education to the public as well as information, resources, and referrals to medical professionals and their organizations. All NABCO services were offered free of charge. NABCO also worked on the community, state, and federal levels for regulatory change and legislation to benefit those with breast cancer, breast cancer survivors, and those at risk of developing breast cancer.
Resources and Information
NABCO’s legacy included the NABCO Breast Cancer Resource list. This reference guide contained more than 3,000 breast cancer resources, including fact-based books, brochures, booklets, other breast cancer organizations, hotlines, and Web sites. This guide was made available to women and health care providers free of charge and covered a broad range of topics and useful information on treatment choices, insurance and financial issues, adjusting to the diagnosis, family support and care giver resources, hospice, and planning for the end of life. This comprehensive compilation of information was also made available online.

As a pioneer in providing breast cancer information, NABCO was the first organization to launch an extensive, disease-specific cancer site on the World Wide Web in 1995. This was instrumental in expanding their outreach in their ongoing efforts to educate both patients and health care providers about good breast health and to provide the latest breast cancer information and garner community support for the treatment and prevention of breast cancer. The Web site also featured an e-mail reminder system and an online calendar. The reminder system encouraged women to schedule breast exams and mammograms, and the calendar tracked breast cancer conferences, medical meetings, public policy and advocacy-related activities, outreach and fund-raising events, business or work-related health promotion activities, and locations for free and low-cost mammograms. NABCO was a one-stop shop for information and resources.

Research and Pharmaceutical Companies
NABCO was skilled in establishing working relationships and collaborations with government agencies, other nonprofit organizations, and corporations, particularly drug companies. Although some critics found the relationship with drug companies troublesome, these relationships funded the work and mission of NABCO. Examples of their collaborative efforts include projects with the National Cancer Institute (NCI) Board of Scientific Advisers (BSA), Breast Cancer Intergroup of North America (BCINA), Novartis, and Avon Products Foundation. The NCI collaboration worked to create plain-English summaries of clinical trials, which made it easier for breast cancer patients to find out about experimental treatments. This work was also undergirded by work with BCINA.

Another noteworthy project was the NABCO Recurrence Project, of which Novartis was a major sponsor. The NABCO Recurrence Project sought to fill in the gaps related to the lack of information regarding recurrent or advanced-stage breast cancer or metastasis. Current trends in research and public information are still lacking in this area. In addition, NABCO was the recipient of a $1 million unrestricted grant from the AVON Foundation to develop and provide continued breast health education.

It should be noted that NABCO was also aware of the needs of underrepresented populations of medically underserved women with breast cancer and launched the Within Our Reach program in 2001. This collaboration was funded by individuals, corporations, and foundations to provide focus and support to specific demographics of breast cancer patients, survivors, or those at higher risk. Special attention went to women of African American, Haitian, Native American, Latina, and Pacific Islander ethnicities; women located in rural areas; and disabled, homeless, lesbian, and bisexual women.

Coming to an End
As the landscape for funding changed, NABCO strategically closed its doors in 2004 with $2 million in the bank and a host of intellectual property. Part of its plan to close was to distribute its funds and intellectual property to other nonprofit organizations. The following 12 nonprofit cancer and health organizations received nonexclusive rights free of charge to NABCO’s educational materials, including its well-known Breast Cancer Resource List:

- American Cancer Society
- Breastcancer.org
- Cancer Care Inc.
- CDC Foundation
- Foundation for the National Institutes of Health
- National Coalition for Cancer Survivorship
- National Medical Association
- Oncology Nursing Foundation
- SistersNetworkInc.
- Susan G. Komen Breast Cancer Foundation
- Y-ME National Breast Cancer Organization (now defunct)
- Young Survival Coalition
It also should be noted that, in addition to using these resources to support their respective missions, the recipients agreed to make the educational materials available to other appropriate organizations to further benefit women with breast cancer and in essence continue what NABCO started.

The following eight nonprofit breast cancer education and service programs received NABCO cash grants:

- Northeast Medical Center in Concord, North Carolina
- Planned Parenthood of Cameron and Willacy Counties in Harlington, Texas
- The Rose in Houston, Texas
- Scripps Health in San Diego, California
- Southeast Mississippi Rural Health Initiative in Hattiesburg, Mississippi
- I. M. Sulzbacher Center for the Homeless in Jacksonville, Florida
- YWCA of Seattle, Washington
- YWCA of White Plains and central Westchester, New York

According to statements taken from an interview with Amy Langer, longtime executive director of NABCO, in the Harvard Business School online alumni magazine in 2013, “NABCO was instrumental in changing the course of breast cancer screening, treatment, and care. Our physician and corporate partnerships to educate women replaced fear with facts. We helped craft and implement laws and regulations, improving mammography’s quality and accuracy and making screening more accessible to poor and underserved groups. Our efforts started a movement that vastly escalated breast cancer research funding, and gave patients and survivors a permanent voice in medical decision making.”

Annette D. Madlock Gatison  
Southern Connecticut State University

See Also: Breast Cancer; Breast Cancer, Male; Europa Donna, the European Breast Cancer Coalition.

Further Readings
Disorders (NIDCD); the National Institute on Drug Abuse (NIDA); and the National Institute of Diabetes on Digestive and Kidney Diseases (NIDDK).

The NCI was established as the principal agency within the NIH for conducting cancer-related research in the United States. This includes conducting clinical research on cancer diagnosis, detection, and innovative and promising new cancer therapies; examining the basic structures, mechanisms, biology, and chemistry of cancers to increase scientific understanding of this pervasive health threat; examining the best strategies for cancer prevention and control; and conducting research to develop best practices for the dissemination of relevant cancer information to key audiences. The development of the NCI was mandated and funded by the U.S. government through passage of the landmark National Cancer Acts of 1937 and 1971. These National Cancer Acts have spurred a major national investment in cancer research, treatment, and survivorship and have initiated a concerted program of research and intervention to reduce the nation's cancer burden. Publically, these cancer control efforts have become known popularly in the United States as the war against cancer.

The NCI is charged formally with coordinating the U.S. National Cancer Program action plan for eliminating cancer in the United States by confronting the threat of cancer, disseminating relevant information about cancer research, cancer prevention, and cancer treatment, and evaluating the use of state-of-the-art cancer treatments. The NCI receives funding to accomplish these goals through an NIH budget as well as through an additional direct bypass budget that comes straight to the NCI from the U.S. Congress. These federal government funds support research at NCI's headquarters in Bethesda, Maryland, and in laboratories and medical centers throughout the United States, as well as in many other countries around the globe. The NCI is the only NIH institute to receive a direct bypass budget from Congress, and it is also the only institute whose director is appointed directly by the president of the United States. These unique factors indicate the high priority for addressing cancer issues in the United States and the importance of the NCI. In 2014, the director of the NCI was Harold Varmus, MD, a prominent scientist, Nobel laureate, and former director of both the NIH and the prestigious Memorial Sloan Kettering Cancer Center in New York City.

The NCI's 2014 operating budget was $5.126 billion. This is the largest operating budget of any NIH unit, and it accounted for more than 17 percent of the total 2014 NIH operating budget of $29.925 billion. The NCI uses these federal funds to coordinate the National Cancer Program, including conducting its own research, training, infrastructure development, and health information dissemination programs (intramural activities) as well as supporting research, training, and health information dissemination about the causes, diagnoses, prevention, and treatment of cancer at many sites across the United States and internationally (extramural activities). The NCI supports a number of important cancer rehabilitation and treatment programs that provide care for cancer patients and their families. The intramural research supported by the NCI is generally conducted by NCI-employed scientists, and the extramural research supported by the NCI is generally conducted by outside scientists who are typically employed at major research universities and medical centers, including at NCI-designated cancer centers. However, there are some projects that involve collaborations between intramural and extramural scientists. The NCI also supports the Cancer Prevention Fellowship Program, a four-year postdoctoral training program that provides research and educational opportunities for scholars who have already received doctoral degrees (such as the MD, PhD, ScD, and DPH degrees) across different areas of the health sciences to enhance these postdoctoral fellows’ abilities to conduct important new research concerning cancer prevention and control and train the next generation of leading cancer prevention and control scientists.

Funding from the NCI supports the following important cancer research and control activities:

The NCI funds relevant cancer-related research projects conducted by universities, hospitals, foundations, and businesses throughout the United States and abroad that are funded through competitively selected research grants, contracts, and cooperative agreements. Research grants support investigator-initiated and NCI-designated research projects. The NCI-designated grant topics are introduced with targeted calls for applications such as requests for applications (RFAs) and program announcements (PAs) that are developed
by NCI scientific program staff. These calls for applications are designed to encourage intramural and extramural researchers to submit research grant applications that address critically important research topics that can advance cancer knowledge and applications. Grant applications submitted to the NCI are competitively evaluated for funding by standing NIH review groups (referred to as study sections) composed of leading cancer scientists or by specially established NCI review groups (referred to as special emphasis panels) also composed of leading cancer scientists to review grant applications for targeted calls that may fall outside of the scientific purview of the established NIH study sections. These standing grant review panels are rigorously administered to maintain high scientific integrity by the NIH Center for Scientific Review (CSR), and in the case of the special emphasis panels, they are supervised by the NCI Grants Administration Branch.

There are several different grant mechanisms that are supported by the NCI. Several of the major research grant mechanisms employed by the NCI include the R-01 Research Project grant (sometimes referred to as a program project grant), which is designed to support major, sophisticated, multiyear cancer research and intervention efforts conducted by leading cancer researchers; the R-21 Exploratory/Developmental grant, which is designed to support innovative new cancer research activities over a few years on a smaller scale than the R-01 research project grants but that might lead to larger R-01 investigations; the R-03 Small Research grant, which is designed to encourage less-experienced cancer researchers to test new techniques and pilot studies over just a few years that are likely to lead to successful applications for larger R-01 and R-21 grants; the P-50 Specialized Center grant, which is designed to support large-scale, multi-project research programs over a number of years conducted by the most experienced and sophisticated transdisciplinary research teams (composed of leading scholars from multiple disciplinary perspectives who coordinate efforts and expertise) to
significantly advance cancer science, lead to new cancer research programs and applications, spur new exploratory cancer research projects, and train the next generation of cancer scientists in targeted high priority areas; and the R-13 Conference grant, which is designed to support important scientific meetings and workshops that hold the promise to advance cancer science and applications.

Contracts funded by the NCI also support targeted research and application projects initiated by the NCI. Calls for contract proposals are designed by NCI program staff to address important cancer research topics and to provide work to enhance NCI programs and activities. Cooperative agreements are funded by the NCI to support collaborative research projects conducted jointly by NCI scientists and extramural investigators concerning NCI-initiated research topics. Cooperative agreements are developed by NCI program staff to address important cancer research topics and also are designed to enhance the research capabilities of NCI staff.

Research projects conducted in NCI's own intramural research laboratories and clinics are awarded funds through a competitive internal application and selection process. These intramural research projects generally are conducted at the NCI's extensive and state-of-the-art research laboratories in Bethesda, Maryland, the NCI Frederick National Laboratories for Cancer Research (located in Frederick, Maryland), and at the NIH Clinical Center (located on the NIH campus in Bethesda, Maryland).

Education and training programs in basic and clinical science disciplines are supported by career award grants (these are referred to as K grants, which are designed to support the career development of cancer researchers at different levels in their careers and in different areas of cancer research (some of the major K awards that are most relevant to cancer and society include the K-01 Mentored Research Scientist Development grant to support career development in the biomedical, behavioral, or clinical cancer sciences, leading to research independence in one of these targeted areas; the K-05 Established Investigator grant in Cancer Prevention, Control, Behavioral, and Population Research, which is designed to support career development for research scientists who are already qualified to pursue independent research and will help to extend their relevant cancer research programs; and the K-07 Cancer Prevention, Control, Behavioral, and Population Sciences Career Development grant, which is designed to support junior candidates in developing their academic and research expertise or to support senior candidates with acknowledged scientific expertise to improve curricula and enhance the research capacity within an academic institution). The NCI also supports training grants and fellowships that are awarded through a competitive selection process. These training programs typically are conducted at major research universities and medical centers around the United States and internationally as well as on site at NCI offices and laboratories.

The NCI is the only institute or center within the NIH that supports a national network of major clinical and applied medical centers (referred to as NCI-designated cancer centers) that conduct cutting-edge cancer research, provide state-of-the-art cancer care, and collaborate with the NCI on important cancer research and outreach projects. Medical centers must meet stringent requirements and pass a competitive review to earn approval to become a designated NCI cancer center. There are two types of NCI-designated cancer centers: (1) an NCI-designated cancer center that must demonstrate scientific leadership, resources, and capabilities in laboratory, clinical, or population science or some combination of these three components. It must also demonstrate reasonable depth and breadth of research in the scientific areas it chooses and transdisciplinary (combining multiple scientific perspectives and expertise) research across these areas; and (2) an NCI-designated comprehensive cancer center that must demonstrate reasonable depth and breadth of research in each of three major areas: laboratory, clinical, and population-based research, as well as substantial transdisciplinary research that bridges these scientific areas. In addition, a comprehensive NCI-designated cancer center also must demonstrate professional and public education and outreach capabilities, including the dissemination of clinical and public health advances in the communities it serves. Of the 68 NCI-designated cancer centers, 41 have been designated as NCI comprehensive cancer centers. The comprehensive cancer centers receive higher levels of funding and are eligible to participate in a broader range of NCI-supported activities than the other designated cancer centers.

The NCI funds collaborations with voluntary organizations and other national and foreign institutions engaged in cancer research and training.
Because the NCI is widely recognized as the leading center for cancer science, it provides guidance and support to many other cancer research organizations around the globe.

Cancer research by industrial concerns, including collaborations with pharmaceutical and biotechnology organizations to develop new cancer treatments and equipment, are supported by the NCI. Many of the most successful NCI-funded cancer drug and biotechnology development clinical trials are eventually commercialized and brought to market by major pharmaceutical and biotechnology organizations. These collaborations with corporations enable the NCI to work with industrial partners to actively translate new research findings into health care practice.

The NCI funds collection and dissemination of relevant information on cancer through publications (scientific journals, monographs, and cancer information pamphlets); the cancer.gov Web site, which provides the latest information about cancer research and treatment; the Cancer Information Service (CIS), which operates a toll-free telephone hotline, 1-800-4-CANCER, and provides information via the Internet; and collaborations with media and news representatives about cancer research and treatment. The CIS also informs consumers about where they can seek cancer treatments and where they can apply to participate in cancer clinical research trials. One of the major mandates established in the National Cancer Act of 1971 was for the NCI not only to conduct cutting-edge cancer research but also to disseminate widely the latest information from this research about cancer prevention, treatment, and control to relevant public audiences.

The NCI also supports construction of laboratories, clinics, and related facilities for cancer research with construction grants. The NCI has an active program of expanding the national and international cancer research capabilities by expanding cancer research infrastructure and technologies.

The NCI is composed of the Office of the Director and seven major research units—two of these research units are intramural units, and the remaining five are extramural units. The intramural units are the Center for Research (CCR) and the Division of Cancer Epidemiology and Genetics (DCEG). CCR manages NCI’s basic and clinical intramural research program; DCEG conducts population and multidisciplinary research to examine genetic and environmental determinants of cancer and the best means for cancer prevention. The five extramural units are the (1) Division of Cancer Biology (DCB), supporting basic research in all areas of cancer biology; (2) Division of Cancer Control and Population Services (DCCPS), supporting genetic, epidemiologic, behavioral, social, and surveillance cancer research; (3) Division of Cancer Prevention (DCP), supporting research to determine and reduce a person’s risk of developing cancer as well as research to develop and evaluate cancer screening procedures; (4) Division of Cancer Treatment and Diagnosis (DCTD), supporting the translation of promising research into improved diagnostic and therapeutic cancer treatments; and (5) Division of Extramural Activities (DEA), coordinating scientific review of extramural research before funding and providing systematic surveillance of that research after awards are made. There are also a number of units coordinated by the Office of the Director, including the Office of Communication and Education that oversees NCI’s communication with key publics.

The DCCPS is the NCI division that conducts research and applications programs that are most relevant to cancer and society issues, including promoting cancer prevention activities, screening and early detection of cancers, adoption of the best cancer diagnosis and treatment strategies, successful cancer survivorship, and competent end-of-life care. The DCCPS hosts the innovative and active Behavioral Research Program (BRP), which includes major research branches concerning important cancer and society issues: the Basic Biobehavioral and Psychological Sciences Branch (BBPSB), the Health Behaviors Research Branch (HBRB), the Health Communication and Informatics Research Branch (HCIRB), the Process of Care Research Branch (PCRB), the Science of Research & Technology Branch (SRTB), and the Tobacco Control Research Branch (TCRB).

HCIRB advances research on the processes and effects of communication and informatics in modern society across the cancer control continuum, including the development of a communication and technology infrastructure that increases access to and use of cancer information, improves public understanding of cancer information, enhances consumer–provider interaction, and translates research discoveries into clinical and public health practices. The HCIRB’s two major research priorities are (1) communication science research,
improving the interactions between science, media, journalism, and clinical care; raising cancer control awareness and knowledge by improving access to and understanding of relevant cancer information; investigating influences of the changing media environment on knowledge and attitudes toward cancer prevention and control; and evaluating communication processes for effective patient-centered cancer care; and (2) technology-mediated communication research, supporting development and adoption of innovative, evidence-based, multilevel information technology interventions, including Web, mobile, and social media technologies; improving communication and care coordination for patients and caregivers; and encouraging evidence-based, translational health communication technology intervention research for cancer control.

HCIRB conducts the important biennial representative Health Information National Trends Survey (HINTS) about public access, use, and preferences for health information, providing important data about national health information needs and opportunities for guiding health communication interventions. The HCIRB also coordinates the extramural Centers of Excellence in Cancer Communication Research at five major research centers across the United States to conduct innovative and far-reaching health communication research as well as training the next generation of cancer communication researchers. The NCI has been and continues to be a major facilitator of advanced health communication research and practices.

The DCCPS also supports the important Office of Cancer Survivorship (OCS) that promotes research and applications concerning helping the growing number of cancer survivors in society to adjust effectively to living with cancer. The OCS works to enhance the quality and length of survival of all persons diagnosed with cancer and to minimize or stabilize adverse effects experienced during cancer survivorship. The office supports research that both examines and addresses the long- and short-term physical, psychological, social, and economic effects of cancer and its treatment among pediatric and adult survivors of cancer and their families.

Gary L. Kreps  
George Mason University  
Lisa L. Sparks  
Chapman University

See Also: Cancer Communication; Clinical Trials; Survivors of Cancer.

Further Readings

National Cancer Policy Board

In March of 1997, the Institute of Medicine (IOM) and National Research Council (NRC) established the National Cancer Policy Board (NCPB). The NCPB tackled major U.S. cancer policy issues by drawing together leading cancer experts to research, workshop, and disseminate information with the goal of cancer prevention, treatment, and awareness. Under the IOM, the NCPB conducted studies and created advisory reports on several aspects of cancer policy relating to prevention, treatment (physical, psychological, and social), survivorship, and palliation. Recommendations made in the studies and reports of the NCPB have been addressed and implemented by organizations, the government, and health care providers. The NCPB lasted for eight years. In May 2005, the IOM created the National Cancer Policy Forum (NCPF) to replace the NCPB.

Funded primarily by the National Cancer Institute (NCI) and Centers for Disease Control and Prevention (CDC), the IOM created the NCPB to focus
on U.S. cancer policy concerns. Consumers’ declining confidence in the U.S. cancer care system led the NCPB to study the effectiveness of cancer services, quality assurance mechanisms used in cancer care, and barriers that block access to cancer care. Their report Ensuring Quality Cancer Care responds to five questions: What is the state of the cancer care system? What is quality cancer care, and how is it measured? What cancer care quality problems are evident, and what steps can be taken to improve care? How can we improve what we know about the quality of cancer care? What steps can be taken to overcome barriers to access to quality cancer care? The report provided 10 recommendations to improve cancer care quality, increase understanding of quality cancer care, and reduce or eliminate barriers to quality care. The report outlined a hoped-for ideal model for cancer care guided by standards with special attention to innovation and equal access. The report however did raise concerns about the safety and quality of U.S. cancer care at that time.

The NCPB had a 20-member board with wide representation including consumers, health care providers, and investigators across disciplines for a total of three chairs and 52 members over the board’s lifetime. This scope of membership is reflected in the diversity of cancer policy study produced in the board’s eight years of operation. The NCPB produced 28 peer-reviewed reports along with 21 additional studies of cancer care, science, and research, including two reports on palliative care, a nationally distributed report on survivors of childhood cancers, a report on the psychosocial needs of women with breast cancer, and an oncology report with 10 recommended changes to the U.S. response to the long-term effects of cancer and cancer treatment. Congress has worked to address many cancer issues raised by the NCPB, including survivorship (and children), data systems, health care costs, insurance coverage, and palliative care as have outside organizations, health care professionals, and scientists and researchers.

Through its published reports, workshops, and communications the NCPB helped draw vital attention to overlooked issues relating to U.S. cancer care. In the late 1990s, it drew public attention to questions relating to the quality of U.S. cancer care. In the early 2000s, the board raised the issue of palliative care and advocated for supports for palliative patients (e.g., providing sufficient insurance compensation for end-of-life care). Additionally, the NCPB highlighted the long-term effects of childhood cancer (e.g., impairments in learning, growth, and maturation) that at that time had not been documented sufficiently. Other important policy issues that the NCPB addressed included preventative medicine, health care coverage for the poor and underinsured, regional health care quality (e.g., Georgia), evaluating treatment approaches (e.g., colorectal screenings, magnetic resonance imaging (MRI) versus mammography), and state and federal legislation and support in reaching these goals and answering these questions.

On May 1, 2005, the IOM created the NCPF to replace the NCPB. Different reasons are suggested in the discourse for this change (i.e., narrower work focus, changes in funding, and seeking partnerships with representatives of governmental agencies).

Sponsors first promised two years of funding for the forum. Funding for the NCPB initially came from the NCI (75–80 percent) and the CDC (20–25 percent). In contrast, initial funding of the NCPF came from the NCI (38 percent), CDC (26 percent), other agencies (6 percent), and the private sector (30 percent). Both the NCPB and the NCPF raised additional monies to fund their work, but total annual funding for the forum provided for fewer staff and narrower work focus than the board had previously.

Participants in the forum include clinicians, patients, researchers, professional and advocacy organizations, pharmaceutical manufacturers, and policy makers. The forum identifies high-priority cancer policy issues and examines them via discussion-promoting activities. All forum members can identify and debate cancer care and research policy issues and study ways to improve these areas. Like the NCPB, the NCPF produces publicly available reports and sponsors of the forum work to implement its recommendations.

Gordon Alley-Young
Kingsborough Community College

See Also: Childhood Cancers; National Cancer Institute; Survivors of Cancer.

Further Readings


The National Cancer Registrars Association (NCRA) represents thousands of figures in the cancer registry field and has been in operation since 1974. The mission of the organization is to serve as the key group for educating and certifying cancer treatment professionals. The organization played a vital part in the professional development of cancer registrars. For effective and efficient registration, it could be done best by professionals; therefore, NCRA developed and maintained a variety of programs for training cancer registrars. Toward this end, in 1983, the first series of exams, a group known as the CTR, for registrars began. In 2003, NCRA began administering exams for prospective professionals. In addition to the ongoing training program for cancer registry staff, NCRA provides mechanisms for communication between registry staff and other standard-setting organizations through its workshops, annual conferences, publications, and continuing education credit program. Recently, the organization has expanded its scope to include development of registries of diseases other than cancer.

The organization was founded in 1974 in Dallas, Texas, after years of attempts to get it started. This was created off of a strong committee to review the feasibility of a national organization devoted to the subject. Through the help of the American College of Surgeons, the committee conducted a mail survey of cancer registrars in all facilities with approved cancer programs and with the CEOs of these facilities to determine if an organization was needed and, if established, whether it would be supported. The results of the survey indicated that there was a need for a national organization and the required support to maintain the organization was available.

The formation of NCRA began with the ad-hoc committee drafting bylaws and other required documents. For effective planning, the committee was expanded to include additional members to help plan a formal organizational meeting. The first meeting was scheduled for May 13 and 14, 1974, in Dallas. Invitations were extended to cancer registrars across the United States, and those who attended reviewed and edited the committee's drafts of the bylaws and other formal documents. The final versions were voted on by those in attendance, and the National Tumor Registrars Association (NTRA) was formed.

The elected officers of the NTRA featured Tim Richardson of Ohio as the president; Barbara Lord from California as the president elect; Vida Peterson from Pennsylvania as the vice president; Frances Wedge from Washington, D.C., as the secretary; Jeanne Ratti from New Jersey as the corresponding secretary; and Marie Maxfield from Texas as the treasurer. President Richardson contacted Barbara Wade from California to be the organizational parliamentarian.

According to the bylaws of the final accepted version, the aims of NTRA were to promote tumor studies and reporting functions so registrars could help cancer patients, create educational standards, establish a regulated system for tumor registration functions, and enhance the knowledge of tumor functions as needed while also administering information on more functions within the organization as they came about. The purpose was to ensure that...
all members would be fully educated and understand the needs they may have at any given moment. In 1993, the organization rebranded to the NCRA. The organization is governed by the elected board of directors. In running the affairs of the organization, the board of directors follows the procedure prescribed in the adopted bylaws, code of ethics, policy and procedure manuals, and strategic management plan (SMP) and ensures legal and ethical integrity while maintaining the accountability of the committees, liaisons, and task forces. To ensure quality services and up-to-date procedures, these documents are reviewed periodically to ensure they continue to meet the needs of the association and the profession.

The current leadership of NCRA is made up of Terri M. Richardson as the president, Leah Kiesow as the president elect and secretary, Shirley Jordan as the immediate past president, Janet Reynolds as the senior treasurer, Kathleen Hess as the junior treasurer, Paulette Zinkanna as the educational director, Sharmen Dye as the professional development director, Kyle L. Ziegler as the public relations director, Linda Corrigan as the recruitment and retention director, Pamela Moats as the advocacy technical and practice board director–east, Mindy Young as the advocacy technical and practice board director–midwest, and Kendra Hayes as the advocacy technical and practice board director–west.

After training of the registrars, the organization offers accreditations. The NCRA Council on Certification promotes standardization in the collection and use of cancer data through examination and certification of cancer registrars and other cancer data specialists. The organization examination CTR credential system marks achievement, fosters professional pride, and is nationally recognized in recruitment and retention of registry personnel.

NCRA provides awards to support the efforts that its members undertake. These awards relate to educational achievements and the literary developments that members in the organization have worked for over the years.

Michael Fox
Independent Scholar

See Also: International Association of Cancer Registries; National Cancer Registrars Association; North American Association of Central Cancer Registries.

Further Readings

National Childhood Cancer Foundation

Childhood cancer remains the leading cause of death by disease among children in the United States. Childhood cancers include many common and uncommon cancers including brain tumors, hepatoblastoma, and Hodgkin’s disease. Every day, 42 children are diagnosed with cancer. Cancer affects everyone regardless of socioeconomic status. Unfortunately, more than 40,000 children undergo treatment for cancer each year.

Headquartered in Bethesda, Maryland, since 1987, CureSearch has facilitated research to help find a cure for childhood cancers. CureSearch National Childhood Cancer Foundation (NCCF) is the education, advocacy, and fund-raising arm of the Children’s Oncology Group (COG), the world’s foremost pediatric cancer research collaborative. COG includes more than 8,000 experts at more than 200 leading children’s hospitals, universities, and cancer treatment centers around the world. Together they treat more than 90 percent of all children diagnosed with cancer.

CureSearch NCCF is a nonprofit, public charity, 501(c)(3) organization that accepts tax-deductible donations. CureSearch’s mission is to secure needed resources that will enable the COG to conduct research and clinical trials in pediatric cancer and
to find a cure. CureSearch NCCF supports these efforts by raising public awareness, bringing in donations and funds from government agencies, and serving as the grantee organization to COG. They raise awareness of childhood cancer and the funding needs of those affected and their families through community events and fund-raisers, publications, and educational resources. They provide information to patients, families, and professionals on all aspects of childhood cancers including the various types of cancer, treatments, tests, and procedures and supports available to patients and families. This information is provided face-to-face through webinars and printed materials. They support research by serving as the grantee organization to COG’s funded clinical research trials.

CureSearch provides opportunities for researchers to shake up the status quo by supporting work to solve the most challenging problems in childhood cancer research. This is done through promotion of collaboration by researchers and through clinical trials at hospitals throughout the nation. CureSearch sponsors the Clinical Trial Advancement Awards. These monies and in-kind support help with the delivery of new treatment to children with cancer. Another initiative, titled the Young Investigator program, identifies individuals with the potential to make advancements in childhood cancer research while building another generation of high-quality researchers. Early-stage researchers are located throughout the United States. CureSearch funds early-stage investigators for two years in areas of study that represent the highest risk with the poorest outcomes for children with cancer. The board of directors provides executive leadership, experience, and expertise from business, economics, and medicine. Many directors have personal experience with childhood cancer, and they understand the challenges facing patients, families, and professionals. The scientific advisory council plans, develops, and implements the organization’s scientific strategy agenda and grants program. With the assistance of the scientific advisory council, CureSearch funds laboratory research. The annual symposium focuses on emerging themes in laboratory science with the potential for early implementation and offers special networking opportunities for young investigators seeking careers in clinical and translational investigation.

Lisa Hines
Wichita State University

See Also: Candlelighters Childhood Cancer Foundation; Childhood Brain Tumor Foundation; Childhood Cancers; National Childhood Cancer Foundation; St. Jude Children’s Research Hospital.

Further Readings

National Marrow Donor Program

A cord blood or bone marrow transplant may be the only hope for patients diagnosed with lymphoma,
leukemia, and other diseases. Up to 70 percent of patients who need cord blood or bone marrow do not have a matching family member who can donate. The National Marrow Donor Program (NMDP) sponsors the Be the Match registry for just such a need. Matches are made from the registry approximately 76 to 97 percent of the time, depending upon race and ethnicity. The NMDP also provides continuing medical education, resources, and guidelines, sponsors research, and offers support to patients and their families.

The NMDP registry has greater than 11 million volunteers who are on standby to provide bone marrow. Included in the registry are 193,000 umbilical cord blood units that have been donated by parents. One person is diagnosed with a blood cancer every four minutes. Someone dies from a blood cancer every 10 minutes. The NMDP registry is the largest in the world. Partnerships with other registries, including internationally, increases potential matches to 22.5 million donors and 601,000 cord blood units. The NMDP encourages joining the registry as there are still situations when an appropriate match cannot be identified. From the time physicians contact and search the registry to the delivery of the donation, the NMDP is there to support with technology, logistics, and expertise.

Patient support is of primary importance to the NMDP. Service coordinators assist patients and their families with answering questions regarding disease, transplants, the donor process, insurance, financial options, and life following a transplant. These services are free and confidential and are offered nationally and internationally by phone and by e-mail. There are multiple costs associated with treatment, including the search for a donor, travel and lodging, uninsured transplant costs, post-transplant needs, and prescriptions. The NMDP offers financial aid programs to help with these costs. More than 1,800 families received $3.2 million in 2013. Fund-raising eliminated barriers and provided financial relief so that the patients and their families could focus on recovery.

Research conducted by the NMDP has had a significant impact on cancer survival rates and has improved the quality of thousands of lives. They continue to search for answers regarding timely transplants, treatment, and better donor matching. Their research program, Center for International Blood and Marrow Transplant Program (CIBMTR), has published more than 700 research articles. They collaborate both nationally and internationally. Funds raised by the NMDP not only support research but contribute to reaching new donors and family assistance to ease the high costs associated with medical care.

Commitment to research by the NMDP has had a significant impact on the quality of life for patients and blood cancer survival. Leukemia, lymphoma, and other blood cancers are being cured by transplant science. Bone marrow transplants have moved from a new procedure 30 years ago to the current standard of care for multiple life-threatening diseases. Survival rates are increasing, complications are being reduced, and new science is exploring blood transplantation as treatment for other diseases. In the past five years, unrelated donor survival rates at one year are comparable to that of related donors, up from 42 to 60 percent. Survival outcomes also have improved with increased timeliness from diagnosis to transplantation.

The discovery and application of best treatment is a main goal of CIBMTR. More than 500 transplant centers nationally and internationally contribute to data collected by the CIBMTR, representing more than 330,000 transplant recipients. The research sample repository is a world-class leading resource for researchers. The repository inspects, processes, and stores 8 million DNA samples from donors, recipients, and research participants. A critical discovery from research identified a higher survival rate when transplant occurs earlier rather than later, even if there is not a close match. In other words, a close match transplant that occurs later in the disease stage does not increase survival rates. Bioinformatics scientists help develop the science of matching recipient and donor. They continue to develop strategies and models for selecting the best possible and timely match and less-toxic chemotherapy regimens. The Amy Strelzer Manasevit Research Program (and other programs) supports efforts to reduce serious complications that may arise after a transplant. The White House Office of Management and Budget’s Program Assessment Rating Tool rates NMDP above average.
The NMDP has met or exceeded the following goals: decreasing the cost of per-unit donor typing; increasing the number of cord blood units; increasing the number of transplants; improving patient outcomes post one year; and adding more than 2 million minority donor registrants. Fundraising remains an important part of these efforts. Be the Match Walk+Run events, for example, are now held in 17 cities.

To register with NMDP, donors submit a sample of cells usually collected from the inside of the cheek. The sample is then compared to specific markers for patients who need a transplant. Physicians access the registry every day. When a match is found, the donor is screened and approved for donation. Once approved, the patient’s doctor requests either peripheral blood stem cells or a bone marrow donation, whichever better suits the patient's needs. During the transplant, the donor's healthy cells are placed in the patient’s bloodstream, where they then settle in the bones. It is within the bones that the cells will produce new cells. Umbilical cord blood is increasingly available as parents have become more aware and want to donate. Blood is collected from the umbilical cord after birth, not from the baby. The blood is tested, frozen, and stored as a unit for future use. Donation and registry, in any of the above ways, is always free and anonymous.

Jessica Anne Hammer
Independent Scholar

See Also: California Blood Bank Society; Malignant Fibrous Histiocytoma of Bone/Osteosarcoma; Plasma Cell Neoplasm/Multiple Myeloma; Technology, New Therapies.

Further Readings

Natural Causes of Cancer
There are approximately 200 types of cancer caused by multifactorial reasons. Cancer belongs to a disease classification that is characterized by out-of-control cell growth, and various cancer types are further classified based on the type of cell that has been affected by the disease. The cells damaged by cancer grow uncontrollably to form lumps or masses of tissues called tumors, except in leukemia, where cancer prohibits normal blood function by abnormal cell division in the bloodstream. The tumors grow and interfere with digestive, nervous, and circulatory systems, and they can release hormones that further alter body functions. The tumors that are restricted to one spot and have restricted growth are usually considered as benign. The malignant tumors are usually the cancerous cells that manage to move through the body using the blood or lymph systems. They usually destroy the healthy tissues. This process is called invasion, and these cells further divide and grow and make new blood vessels to feed themselves in a process called angiogenesis. Subsequently, the tumor spreads to other healthy cells in the body; the process is called metastasis, and it is most difficult to treat.

Nature Versus Environment
An estimated 5 to 10 percent of the cancer cases are caused by genes, and the remaining 90 percent are attributed to lifestyles and environmental factors. The etiological factors related to lifestyle include cigarette smoking, diet comprising fried foods and red meat or food additives, alcohol, excessive exposure to sun, pollutants in the environment, infections, stress, obesity, and physical inactivity. Existing evidence suggests that almost 25 to 30 percent of cancer deaths are due to tobacco, 30 to 35 percent are due to diet, 15 to 20 percent are due to infections, and the remaining deaths are due to radiation, stress, physical activity, environmental pollutants, and so on. Owing to these causal factors, several developed countries have shifted their focus to preventing cancer deaths through effective public health messages promoting smoking and tobacco control, increased ingestion of fruits and vegetables, limited use of alcohol, control of calorie
intake, increased physical exercise, avoiding direct sun exposure, minimal meat consumption, use of whole grains, and use of vaccinations and preventive checkups for cancer. In spite of these developments, cancer continues to be one of the chronic illnesses that are causing deaths in developed countries; in the United States, cancer accounts for 23 percent of deaths followed by heart disease, which has seen a steady decline in the last decade.

If exogenous risk factors such as smoking, chronic inflammation, and unbalanced diet are eliminated, then cancer is more likely to occur at a later age, and the influence of endogenous processes will start. Usually, age is one of the natural causes of cancer as cells take a long time to develop and several changes take place in the genes before they actually turn cancerous. These are caused while the cells are dividing or due to carcinogens. Some people are born with genetic mutations, and such individuals are more likely to develop cancer at later stages of life. For example, BRCA1 and BRCA2 are examples of breast cancer genes that genetically predispose some women to breast cancer. Research also has indicated that 3 percent of women suffering from breast cancer have these genes. Similarly, some people have a genetic predisposition to colon (large bowel) cancer. Cells experience uncontrolled growth when there are damages or mutations to deoxyribonucleic acid (DNA).

The genes that are responsible for cell division are first, oncogenes, which are altered forms of genes that are known as proto-oncogenes and are responsible for cell growth. When they are altered or mutated, they lead to tumor formation. Second, tumor suppressor genes are present in our cells and control cell growth and death, which is called apoptosis. They also suppress cell growth, and therefore are recessive in nature. When these cells are mutated, they cause cancer that is due to aging or environmental exposure, or it can be inherited. In mutations, due to inheritance, one copy of the tumor suppressor gene pair is inherited from a parent and is present in all cells in the body; the second copy is acquired and occurs in one cell or a handful of cells. Most genes associated with hereditary cancer are tumor suppressor genes, but most mutations in these cells are not inherited. Third, DNA repair genes are the ones that can be described as the mismatch-repair genes that correct the naturally occurring errors in the DNA. Mutations and alterations in these genes cause cancer. One of the major causal factors that affect DNA includes the carcinogens that are present in tobacco, asbestos, arsenic, radiation such as gamma and X-rays, the sun, and compounds in car exhaust fumes. Continued exposure to these carcinogens steals the electrons from the body, which leaves it vulnerable to cancer. Usually, several mutations take place before a person acquires cancer. In cancers that are inherited, one such mutation is passed on by the parent, and other mutations are acquired. Cancers that are inherited are classified into sporadic cancer, familial cancer, and inherited cancer. Sporadic cancer occurs by chance—one of the family members is affected by cancer at an older age; familial cancer is when several members of the family are affected by cancer. There is a cluster of cancer cases in the family but no clear inheritance trend, and it occurs at an average age of onset. It could be related to the lifestyle of the family or could occur due to single gene mutation that has reduced penetrance, a mutation associated with lower cancer risks. Inherited cancer refers to families having multiple members with the same or related cancers, and it impacts the younger than average ages. Often, families with inherited cancer have it for two or more generations, with cancer displaying an autosomal dominant pattern of inheritance. A child born to a parent with an inherited predisposition to cancer will have a 50 percent chance of inheriting cancer.

A weak immune system is also seen as a risk factor for certain types of cancer vulnerability. This has been linked specifically to people who have had organ transplants and take drugs to suppress their immune systems to avert organ rejection. People suffering from human immunodeficiency syndrome or acquired immunodeficiency syndrome are likely to suffer from Kaposi’s sarcoma, which causes lesions in one area of the body including skin. People born with rare medical conditions are more vulnerable to cancer as well. Cancer caused by viruses such as cervical cancer and other cancers in genital or anal areas and certain chronic illnesses can further stimulate cells to grow abnormally.

Epidemiological studies estimate that almost 15 percent of worldwide cancer incidences are associated with microbial infection. Viruses cause some forms of cancer by causing genetic changes in cells that could potentially make it cancerous. Through existing epidemiological and biological studies, the International Agency for Research on Cancer
has classified six viruses as Group 1 carcinogens, each associated with the origin of certain types of human cancers: Epstein–Barr virus (EBV), Kaposi’s sarcoma–associated herpes virus and human herpes virus B (KSHV/HHV8), human papilloma virus (HPV), hepatitis B virus (HBV), hepatitis C virus (HCV), and human T-lymphotropic virus type 1 (HTLV-1) as well as the bacterium Helicobacter pylori (H. pylori). The HPV types cause cervical cancer as well as a subset of ano-genital and head and neck cancers, which cause 5 percent of all virus-induced cancer. Recently, a new human polyomavirus, MCV, has been discovered, which causes a rare tumor, Merkel cell sarcoma, in people with weak immune systems. The development of cancers induced by infectious agents is intimately linked to their persistence in the host. In fact, pathological abnormalities are not usually observed when infections are rapidly cleared by the immune system, while cancer development risk dramatically increases after the establishment of a chronic infection. Cancer of the cervix, liver, oral cavity, and stomach have an infectious etiology.

Prevention Versus Treatment

Human genome solutions to diagnosis, prevention, and treatment of cancer are emphasized through several observational studies and point to contrary evidence. Studies on identical twins indicate that genes are not a source of chronic illnesses, and it is lifestyle and environment that account for most of the chronic illnesses.

The last decade has witnessed a shift away from treatment to more preventive aspects of cancer. A growing shift toward prevention is also related to costs as it is estimated that prevention is assumed to be 7 percent of the cost of treatment. The global treatment estimate is $163 billion; the cost of prevention of cancer is at $11.4 billion. Preventive aspects of cancer include promotion of increased intake of fresh fruits, vegetables, and cereal grains that might impact the development of cancer of the oral cavity, larynx, esophagus, stomach, colon, lung, prostate, and rectum. One of the examples is the five-a-day campaign by the National Health Service, United Kingdom. Even though research is still ongoing on various dimensions of cancer, some research indicates that a diet rich in phytochemicals, antioxidants, and omega-3 fatty acids prevents cancer. Phytochemicals are chemicals found in plants that protect plants against bacteria, viruses, and fungi, and consuming large amounts of brightly colored fruits and vegetables and cereals can decrease the probability of certain cancers from occurring. They usually prevent carcinogens from forming in the body by acting as antioxidants or nutrient protectors. Antioxidants include vitamin C (ascorbic acid), which can prevent the occurrence of rectum, pancreas, and cervix cancer. Beta-carotene is known as provitamin A and is known to prevent cancer by enhancing white blood cells in the immune system to block cell damage from cancerous cells. Rich portions of beta-carotene are present in dark green, leafy, and yellow-orange fruits and vegetables and are known to prevent stomach, lung, prostate, breast, and head and neck cancer. Vitamin E is known to prevent prostate and colorectal cancer. Omega 3 fatty acids inhibit tumor development in breast and prostate cancer. Fish such as salmon, mackerel, sardines, herring, halibut, striped bass, tuna, and lake trout, flax seed oil, and beans contain good proportions of omega 3.

Keerty Nakray
Jindal Global Law School

See Also: AIDS-Related Cancers; Anticancer Drugs; Diet and Nutrition; Obesity; Stomach (Gastric) Cancer.

Further Readings


Nepal

The Federal Democratic Republic of Nepal is a mountainous Asian country located in the Himalayan region. Nepal has been a monarchy up until very recent times and has always been a somewhat isolated Hindu country, partially because of its geographic features: Himalaya includes some of the highest mountains on Earth, such as Mount Everest, and most of its peaks are over 20,000 feet (6,000 meters) high. Various dynasties held their power through Nepal’s history, most notably the Malla kings, who ruled from the 12th to the later 15th century, and the Gorkhali, who unified the country in 1768 under the rule of King Prithvi Narayan Shah, who founded the Kingdom of Nepal. A brief war between the Kingdom of Nepal and the British East India Company was fought in 1815 and 1816, but a century later, in 1923, the English and Nepalese crowns signed an agreement of friendship that lasted through both world wars. During the Great Wars, Nepal helped the British army, fighting their enemies with the assistance of several units of Gurkha soldiers, and also supported the military effort with raw materials, guns, food, and equipment. In 1996, the Maoist Communist Party of Nepal tried to seize power by violent revolution, leading to the long and bloody Nepal Civil War that ended in 2008, with the abolition of the monarchy and the establishment of the federal republic. Today, political tensions do still exist, and many power-sharing struggles caused various governments to be toppled one after the other, negatively affecting the country’s economic growth, which still suffers from widespread poverty and illiteracy rates.

Health care services and public health care facilities in Nepal are of very poor quality compared to international standards. Lack of hygiene and health education, inadequate sanitation and transportation systems, geographical constraints, widespread poverty, low availability of medical facilities, minimal government expenditures on health care, and considerable inequality in wealth distribution are all contributing factors. Also, social marginalization and traditional beliefs further aggravate the situation, especially in rural and isolated areas. Some important awareness campaigns to sensitize public opinion on cancer prevention and encourage proper hygiene practices and healthy behavior were made in the last few years, mostly with the help of the many nongovernmental organizations (NGOs) that operate in the territory.

The major cancer treatment facility is the National Cancer Center, BP Koirala Memorial Cancer Hospital in Bharatpur. The hospital was built in...
1992 and got its name in memory of the first democratically elected prime minister of Nepal in 1959 and 1960, Bishweshwar Prasad Koirala, who died of throat cancer in 1982. Much of the funding and medical staff of this hospital come from China and provide the local population with modern technologies to treat cancer, with many specialized oncology and surgery departments, such as advanced reconstructive urologic surgery, neurosurgery, radiation oncology, and palliative care. The other comprehensive cancer treatment facility is Bhaktapur Cancer Hospital, located in the Kathmandu valley. The oldest and most famous cancer treatment facility in Nepal, though, is the Bir Hospital in Kathmandu, built in 1889 by the government and still administered by the National Academy of Medical Sciences.

In Nepal, the cancer registry system is very poorly implemented: A central agency that coordinates all national cancer data from public and private hospitals does not exist, and there is no national population-based cancer registry. In 2005, a hospital-based registry system was established with the support of the World Health Organization (WHO), pooling data from the seven largest cancer treatment facilities, but only one analysis study was published with the data coming from this database. An evaluation of the present data coming from Nepal's major hospitals tells us that approximately 10,000 new patients seek treatment for cancer every year.

In Nepal, the most common site for cancer in males was the lung, followed by the oral cavity and stomach, while the most common in females were cervix (middle-aged women), uterus (older women), breast (young women), and lung. Leukemias and lymphomas were the most common cancer forms in children and young people. Lung cancer is the most common cancer in both male and female individuals and is also the leading cause of cancer death for both genders. Tobacco smoking and chewing are among the most important risk factors for lung, oral cavity, and larynx cancer in the Nepalese population, together with occupational hazards and worker exposure to carcinogenic substances in middle- and large-scale manufacturing industries. Other common risk factors are poor awareness and education on unhealthy lifestyle habits, lack of prevention and screening programs for early detection and treatment, alcohol consumption, and infections such as human immunodeficiency virus (HIV), human papillomavirus (HPV), and malaria.

Precocious interruption of treatment regimen is also an issue in Nepal because of sudden drops in socioeconomic conditions, political instability leading to transport blockades and strikes, and fear from treatment toxicity related to lack of proper education on health topics.

Similar to Sri Lanka, in Nepal, many hospitals and clinics also offer Ayurvedic and traditional, herbal immune therapies as complementary cancer treatment. While Ayurvedic principles mostly focus on a spiritual and philosophical approach to heal mind and body together, some of the herbal remedies and detoxification methods proposed may possess some therapeutic value for oncologic patients. However, while Ayurveda therapy may improve immune response among cancer patients and reduce the side effects of chemotherapy, it still poses a risk for heavy metal poisoning due to the high concentration of the elements often used in Ayurvedic medicines.

Claudio Butticè
Independent Scholar

See Also: Cervical Cancer; Lung Cancer, Non–Small Cell; Poverty; Smoking and Society; Sri Lanka.

Further Readings
in the Netherlands because of lung cancer. In the context of the Netherlands, lung cancer has a direct link to smoking and practically no connection to occupational or environmental agents. Nevertheless, according to statistical data from 2014, prostate cancer has climbed now to the top of the list in the case of men, and breast cancer became the main cancer in women.

Unlike other European countries, in the Netherlands, the second-most important cancer in the context of incidence is skin cancer in both men and women. But the second cancer causing more deaths among the female population is breast cancer (around 3,000 deaths in 2010; actually it is in the fourth position worldwide in terms of registration), and among the male population, it is intestinal cancer (also around 3,000 deaths in 2010). The five-year survival rate mainly depends on the kind of cancer, but in a general way, it increased to 60 percent in recent years.

It is estimated that one person in three suffers from cancer in the Netherlands. Two-thirds of the totality of new cases are people older than 60.

Risk Factors
One of the biggest problems in Western countries as a risk factor in the incidence of cancer is lifestyle and the habits it implies in terms of activity or nutrition. As an illustrative example, in the Netherlands, almost 50 percent of its population suffers from being overweight or obesity. In fact, its concerns in the field of health do not differ very much from the concerns of other Western countries. In such a way, a lot of cancer prevention campaigns try to make the population conscious of the danger of smoking, inactivity, sun exposure, alcohol, and the need of being attentive to any symptoms. National prevention programs emphasize that one-third of the cases of cancer can be reduced by a proper lifestyle and a balanced diet.

Because the incidence of breast cancer is one of the highest in Europe, special attention is paid to it. Although not all the risk factors for cancer are known, the Ministry of Public Health has considered it important to publish a complete list of risk factors (which include genetic factors, not having given birth or to give birth at an older age, early menstruation, late menopause, being overweight after menopause, hormonal treatment, and use of alcohol, among others).
Cancer Registries and Other Institutions
The Netherlands Cancer Registry intends to collect data on incidence, prevalence, survival, mortality, and risks in the country. It belongs to the International Association of Cancer Registries, and since 1989, it has offered data with reliable and objective information that contributes to epidemiological research, clinical studies, and determination of the quality of care. Simultaneously, it gives orientation in terms of trends and variations. It works, like similar institutions in the rest of Europe, through a regional network, collecting data from each patient who goes to a hospital for diagnosis or treatment. They also receive data from other sources, such as blood laboratories, pathological laboratories, or medical registries from clinics and hospitals. At the end of 2013, they implemented a new system that allowed specialists direct access to patients’ data and links to other databases, facilitating the possibility of controlling the quality of care.

The Netherlands Cancer Institute was created in 1913 by a group of pathologists with the main goal of offering the best treatments to patients suffering from malignant tumors. It had rooms for about 17 patients and a laboratory for its own scientists. Nowadays, it has places for 650 patients, and it is an important center of clinical and scientific expertise. In addition, the Dutch Cancer Society was founded in 1949, and its main goal is to collect donations to help people suffering from cancer. Actually, it has a regular base of 1 million donors, and it plays a fundamental role in cancer control policies and legislation to reduce the incidence of cancer and improve the quality of life of patients. In its programs of prevention experts from that society give priority to avoiding sun exposure as the Netherlands has an alarming increase in the number of skin cancer cases (particularly melanoma).

Natalia Fernández Díaz-Cabal
Free University of Barcelona

See Also: Disparities Within Nations (Elimination of Cancer); Future of Cancer; Global Health Issues and Cancer; Organisation of European Cancer Institutes; Solar Radiation.

Further Readings


Netherlands Cancer Institute

Spanning more than a century, the history of the Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital (NKI/AvL, Nederlands Kanker Instituut/Antoni van Leeuwenhoek Ziekenhuis) in Amsterdam reflects groundbreaking developments in laboratory research, patient care, and the public’s perception of cancer as a disease. The often ambivalent—sometimes even openly strained—relations between laboratory and clinic, between doctor and patient, between specialist cancer treatment center and the relevant disciplines in university hospitals, and between incurable patients and hopeful relatives and citizens become evident from an analysis of the history of NKI/AvL. This history qualifies the idea of the war on cancer as a process of continuous progress and shows that scientific progress is inherently intertwined with prevailing ideas about diseases and their treatment.

In 1913, the publisher J. H. de Bussy approached a few Amsterdam professors and business acquaintances with the proposal to found a specialist cancer institute. A building that had formerly housed a bank was fitted out for the treatment of patients and for scientific research. International experts were contacted, and an association, the Van Leeuwenhoek Vereeniging, was established, which in 1933 developed into the International Association to Combat Cancer, or the Union Internationale Contre le Cancer (UICC). By the end of the 1920s, NKI moved to a building that had previously been the central depot for military uniforms on Sarphatistraat in Amsterdam. This new site provided enough space to house the large numbers of mice required as standardized
test animals, which were bred in collaboration with Clarence C. Little of the Jackson Memorial Laboratory (Bar Harbor, Maine). At the same time, it housed the gradually expanding specialist library on cancer research and treatment, which was to become world renowned. The institute also was able to specialize in radiation treatment as the Dutch electronics company Philips provided it with state-of-the-art equipment, including a machine known as the millionaire, with a theoretical maximum electrical potential of 1 million volts.

Shortly after World War II, Queen Wilhelmina celebrated her golden jubilee, and the Dutch people wanted to present her with a gift. This gift was the Koningin Wilhelmina Fonds (KWF) ter bevordering van de kankerbestrijding (Queen Wilhelmina Foundation to promote the fight against cancer), which was formally founded on March 14, 1949, with the aim of ensuring ongoing fund-raising efforts. Because NKI also had been engaged in fund-raising, it was decided that it would end these activities and would henceforth get an annual grant from KWF.

In its Sarphatistraat building, NKI was an independent institute, which by 1955 had nearly 200 employees, including 13 physicians and trainee physicians and 34 nurses. By this time, a new radiotherapy department had been established, again fitted out with the latest radiation equipment provided by Philips, including a machine that could produce beams of radiation with continuous motion.

One subject that was debated for many years was whether NKI/AvL should become part of the Amsterdam University Hospital. The hospital did not have enough space on its grounds, however, so it was decided to build a new facility in the Slotervaart district in the western part of Amsterdam. This also was where the central laboratory of the Dutch blood transfusion service was to be housed (and later the new municipal Slotervaart hospital).

By the mid-1960s, when NKI had been in existence for nearly half a century, its laboratory staff had made internationally respected discoveries. Three decades of research at the mouse laboratory had elucidated the nature of the mammary tumor virus (MTV), which caused breast cancer in mice. It turned out to be an RNA virus, which was converted to a DNA copy in mice, after which it was incorporated into the host animal’s DNA. This mechanism enabled oncogenic viruses to be transmitted to the progeny without infection. Such findings put Amsterdam at the forefront of international cancer research. The spectacular progress had been made possible by the decision to abandon the tradition of the lone wolf researcher and move toward more multidisciplinary research efforts. In fact, this fit in with a prevailing trend in life sciences in the 1960s, in response to the development of new branches of science such as biochemistry, biophysics, molecular biology, and so on. However, it sometimes proved difficult to tear down the barriers between the various disciplines at universities, whereas it proved easier to create a melting pot from departments such as biology, virology, immunology, and electron microscopy in a small and dedicated institute like NKI. As a result, scientific research at NKI developed into teamwork by specialists.

By contrast, the clinic, the AvL, was going through a more difficult time. Although its equipment included devices like an ultramodern cobalt irradiator, its therapeutic efficacy was limited by the fact that patients often were referred to this specialist clinic at a late stage of their disease. Van Lier’s book on the NKI concluded that this resulted in an image among the general public that radiation therapy was only for the hopeless cases, creating a kind of taboo on this form of treatment.

At its Sarphatistraat site, the NKI/AvL was a typical small-scale institute where everybody knew each other personally and where there was a high level of cross-fertilization between the laboratory and the clinic. This was to change when the clinic moved to the brand-new complex at Slotervaart in 1973. It took another five years before the laboratory also moved to its new building at the Slotervaart complex.

The specialist cancer hospital AvL would distinguish itself from the university hospitals in the Netherlands by integrating the various oncological subdisciplines. Another unusual characteristic was that all medical specialists at the new AvL were fully employed by the institute, a unique arrangement in the medical world. Another major break with past practices was to involve patients more closely in their treatment. For instance, library staff previously had been forbidden to provide patients with specialist literature on cancer as it was thought they would not be able to interpret it correctly. In the mid-1970s, the Radiotherapy Department became the first to start handing out patient information leaflets.

By this time, the laboratory had also moved to Slotervaart, but its reputation had deteriorated
considerably. This improved when the biochemist Piet Borst was appointed director of NKI/AvL in 1982, the first time a nonclinician was appointed head of the institute. Borst managed to breathe new life into the experimental work, based on the old mouse laboratory, for instance, by concentrating the research effort on genetically modified mouse models. As a result, the laboratory fully regained its former status as a state-of-the-art cancer laboratory.

Just as elsewhere in the world, however, the process of translating laboratory findings into clinical treatment remains difficult at NKI/AvL. Nevertheless, the AvL acquired a powerful position within the European Organization for Research and Treatment of Cancer (EORTC) by participating in clinical trials. Other landmarks in the institute’s history were the establishment of the Centrum voor Kwaliteit van Leven Studies (Center of Expertise on Quality of Life) of the World Health Organization and, in 1995, an outpatient clinic for familial tumors in cooperation with both of the Amsterdam university hospitals.

In the course of the 21st century, NKI/AvL has developed into a world-renowned comprehensive cancer care center characterized by the close interaction between the laboratory and the clinic, thanks to the short lines of communication between them. This means that the ideal that its founders had in mind in 1913 has been realized.

Ton van Helvoort
Independent Scholar

See Also: American Cancer Society; History of Cancer; Netherlands; Radiation Therapy.

Further Readings
Both physicians and patients wanted to know more about the way patients and their relatives experienced hemophilia. In 1972, a joint research project was set up, titled Hemophilia in the Netherlands (the HIN study), to survey aspects like the occurrence of the disease, its treatment, school absenteeism, unemployment, stigmatization, and dependence on physicians.

The situation of hemophilia patients was greatly ameliorated in the 1970s. Boys with hemophilia were now able to go to summer camps and play sports (though not soccer) with a doctor in attendance. School absenteeism and hospitalizations were greatly reduced. Doctors also encouraged young patients to switch to treatment at home, with parents treating hemorrhages and providing prophylaxis with the missing coagulation factor. The use of self-treatment was also stimulated as many patients had developed a morbid fear of injections, which turned out to disappear when they started injecting themselves. At first, the implementation of this program was hampered by certain legal obstacles, but these eventually were solved jointly by the hemophilia experts and the NVHP.

Preparing the factor concentrates involved pooling the blood from many donors, which inevitably led to contaminated concentrates, even if just one of the donors had an infection like hepatitis. Naturally, there were international research efforts to try and solve this problem. One of the approaches was to heat the concentrates in order to inactivate the virus, but this had very limited success.

The close and institutionalized collaboration between hemophilia patients and the doctors treating them became greatly strained on the emergence of the acquired immune deficiency syndrome (AIDS) epidemic. Around 1980, a mysterious disease broke out in the United States, which was later proven to be caused by a virus, human immunodeficiency virus (HIV). On Sunday, January 30, 1983 (later referred to by those involved as Bloody Sunday), a meeting was held that was attended by all parties involved—patients, physicians, producers of blood products, and the authorities—to discuss what measures had to be taken to ensure the safety of donor blood and blood products. The relations between hemophilia patients and their doctors were severely shaken: Hemophilia once more became stigmatized, this time mostly through fear of HIV infection. The NVHP became a contributor to the process of restoring confidence and defending the interests of people infected with AIDS toward the authorities and insurance companies. Fortunately, the heat treatment of plasma products, which had proved insufficiently effective for hepatitis, was found to work well with the AIDS virus. Nevertheless, there was initially some reluctance in the Netherlands about introducing this heat treatment as doctors feared that the treated coagulation factors might induce antibodies. This problem was soon cleared and solved, however. In the 1980s and 1990s, the NVHP was very active in educating patients with hemophilia about the factor concentrates that were available internationally and the costs involved.

The HIV problem for patients needing treatment with coagulation factors was solved definitively in the 1990s as Factor VIII and Factor IX now could be produced using recombinant-DNA methods, making them completely free of viral contamination (whether HIV or hepatitis). However, the recombinant-DNA technology also created new problems. Although female relatives of patients had been able to voluntarily undergo genetic assessment since the 1960s, focusing on the identification of carriers of the hereditary trait for hemophilia, the new DNA technology also enabled doctors to diagnose children before birth (prenatal diagnostics) to assess whether they had the congenital predisposition for hemophilia. Once more, the NVHP became an important party in communications and discussions about the possibilities and limitations of this new technology.

The developments in hemophilia research over the last 50 years have been truly spectacular, despite the very serious setback caused by AIDS. As a result, there is now a large group of people in the Netherlands with severe hemophilia who have nevertheless survived beyond the age of 40, an age that they would not have attained half a century ago. As an organization, the NVHP has greatly influenced the development of a specialist branch of medical research into hemophilia, and it has contributed especially to the acceptance of new treatment approaches resulting from such research.

Ton van Helvoort
Independent Scholar

See Also: Haemophilia Society (United Kingdom); Hepatitis B; Hepatitis C; Netherlands.
Neuroblastoma

Neuroblastoma is an embryonic cancer that occurs as a result of the improper development of immature nerve cells. These cells, named neuroblasts, experience the abnormal persistence of a developmental state, which then accumulates to build tumors in sites of the sympathetic nervous system tissues. About 50 percent of these masses originate in or around the adrenal glands. Other developmental sites include the abdomen, neck, chest, and pelvis.

This disease is most commonly experienced between one and two years of age, with 90 percent of cases being diagnosed before age five. With more than 600 cases diagnosed every year, neuroblastoma is the most common extracranial solid cancer experienced in children. It is responsible for 8 to 10 percent of childhood cancers and accounts for more than 15 percent of their cancer mortality. Neuroblastoma contributes to 33 percent of cancers experienced before age one, making it the highest malignancy expressed in infancy, according to Peter Zage and Joann Ater.

Experience of the disease varies widely. Neuroblastic tumors can be completely benign and even, in some cases, spontaneously regress. However, about 60 percent of diagnosed tumors already show signs of spreading. And, in many other cases, these tumors are malignant and demonstrate aggressive metastasis. This cancer's heterogeneous nature and tendency to spread create a diversity of symptomatic expressions as well as difficulties in etiologic research, diagnosis, and treatments.

Further Readings

Symptoms
General symptoms such as headache, fever, irritability, and fatigue all can be experienced in cases of neuroblastoma. However, a variety of specific symptoms may be expressed depending on the primary tumor location, metastasis, and hormone secretion, describes the American Cancer Society.

Concerning localized tumors, many complications arise from pressure against body structures. For instance, tumors localized in the abdomen often will show a large, painless lump of tissue under the surface of the skin, which could lead to stomach pain and diminished appetite. In some cases, these lumps grow against the child’s blood or lymph vessels, preventing fluids from getting back to the heart and causing abdominal swelling. Additional complications such as difficulty during bowel movements and urination can also occur if the mass presses against the child’s bladder. In other cases a tumor that develops in the chest or neck can put pressure on areas of the body such as the throat, windpipe, and important blood vessels. Some other manifestations of these include swelling in the face, neck, arms, and upper chest.

Symptoms also can be expressed differently depending on areas affected by metastatic spread. Areas that typically are affected include lymph nodes, skin, bones, and bone marrow. Lymph node tumors can produce swelling. Spread to the bones can cause bone pain and, in cases of paraspinal neuroblastoma, spinal cord and nerve root compression. When the disease is present in bone marrow, a shortage of blood cells can be experienced. Possible effects of this include tiredness, irritability, frequent infections, and excess bleeding from small cuts.

Paraneoplastic syndromes occur when tumors release hormones that create complications in tissues and organs. One rare example of this is opsoclonus-myoclonus-ataxia syndrome, which is exhibited by irregular and rapid eye movements, muscle spasms, and uncoordinated walking and standing. Other symptoms of paraneoplastic syndromes can include constant diarrhea, fever, and flushing of the skin.

Pathogenesis
Neuroblastoma is the result of genetic mutations in critical genes that lead to abnormal cell proliferation and differentiation of immature nerve cells named neuroblasts. Little is known about what actually causes the genetic mutations in these cells. In the
less-common cases of familial neuroblastoma, the cell mutations have been shown to be inherited in an autosomal dominant manner. Those with this disease typically are diagnosed at an earlier age and have multiple primary tumors. Mutations in the anaplastic lymphoma kinase (ALK) and Phox2b genes currently are noted as the major predictors of hereditary neuroblastomas, according to Y. P. Mossé and colleagues. However, familial neuroblastoma accounts for a small 1 to 2 percent of neuroblastic tumors. In the remaining sporadic cases, cell mutations are somatic, and in most cases, causes remain unknown. The influence of these genes is not limited to inherited cases of the disease. They are also shown to be a factor that predisposes an individual to having neuroblastoma, but additional somatic mutations are necessary to actually cause the disease.

Another gene that is highly associated but not considered a cause of neuroblastoma is the MYCN oncogene. Amplification of this gene is strongly associated with aggressive tumor stage and poor outcomes, Ravikanth Balaji reports.

**Diagnosis**

Initial discovery of neuroblastic tumors often arises from the discovery of a mass or masses on plain radiography, computed tomography (CT), or magnetic resonance imaging (MRI). Calcification and hemorrhage often are observed by radiography and CT scan. Accurate tumor information such as localization, size, and extent can be determined from MRI. A diagnosis of neuroblastoma can only be made if it fulfills at least one of the following requirements, according to G. M. Brodeur and colleagues: (1) unequivocal pathologic diagnosis supported by light microscopy and (2) bone marrow biopsy containing unequivocal tumor cells and increased levels of serum catecholamines or urinary catecholamine metabolites.

Tumor tissue obtained by biopsy provides much of the biological data needed for diagnosis. In the majority of tumors, particularly when neuronal differentiation is present, histological diagnoses can be made using a light microscope. In other cases, the tumor cells are densely packed, small, blue cells with little differentiation. Here, other immunologic methods such as electron microscopy are used. Similarly, identification of neuroblastic tumor clumps is also possible in bone marrow analysis. Catecholamine metabolites such as homovanillic acid (HVA), vanillylmandelic acid (VMA), and dopamine (DA) provide biochemical support for neuroblastic tumor diagnoses. Significantly elevated levels of these tumor markers can be found in 95 percent of cases.

**Classification**

The most commonly used classification of neuroblastoma cases is the International Neuroblastoma Staging System (INSS). The INSS is a postoperative system that relies on the extent of surgical resection, in addition to lymph node involvement and extent of metastatic disease, to stage patients. Because the INSS was designed around the extent of surgical resection, it is not fully compatible with the International Neuroblastoma Risk Group (INRG) pretreatment risk classification system.

For this reason, a new method is being adopted to classify the expression of this disease. The INGR Staging System (INGRSS) classifies tumors into L1, L2, M, or MS based on image-defined risk factors and metastatic disease, explains T. Monclair and colleagues. Built around tumor imaging rather than surgical resection, it has an enhanced pretreatment utility. The primary function of the INGRSS is as a component of the INGR, and it is intended as a system to be used in coordination with the INSS in order to improve the combination of disease-staging and risk stratification.
The International Neuroblastoma Pathology Classification (INPC) is a molecular classification of neuroblastic cells. Based on neuroblast pathology, age, and the mitosis-karyorrhexis index, this system classifies tumors as either favorable or unfavorable and has significant prognostic value, as described by H. Shimada and colleagues.

Treatment and Prognosis
Current treatments of neuroblastoma cancers are used in accordance with the Children’s Oncology Group (COG) risk-group assignment. Based on the INSS, INPC, tumor biology, and patient age, this system places patients into either low-risk, intermediate-risk, or high-risk groups, according to W. B. London and colleagues. Therapy generally is chosen based on the group in which a patient is placed. Options for low-risk patients include resection or observation and, in some cases, chemotherapy. Treatments for intermediate-risk patients involve chemotherapy, surgery, and radiation therapy. High-risk tumors require aggressive multimodal therapies, which may include chemotherapy, stem cell transplantation, radiation therapy, surgery, immunotherapy, and differentiation therapy.

Outcomes of children in the low- and intermediate-risk groups have improved significantly over the past few decades, with current survival rates being higher than 90 percent in both groups. Most research for these groups is now focused on reducing therapy and decreasing long-term treatments. However, even with intensified therapeutic techniques, prognosis for patients with high-risk tumors remains poor. Survival rates for these children are between 40 and 50 percent. Also, high-risk patients are very susceptible to recurrent neuroblastoma after initial treatment, which has a survival rate only slightly higher than 50 percent. Increased studies of the biologic influences of neuroblastoma eventually will lead to new molecular and genetics-based treatments.

Further Readings

Neutrons

Neutrons are vital in the diagnosis and treatment of cancer. They can be used to form radioisotopes or be applied in external neutron therapies. The two external neutron therapies are fast neutron therapy and boron neutron capture therapy. Fast neutron therapy is still considered by many scientists as mainly experimental and remains a highly controversial topic. The new, experimental form

Christopher Edwards
Duke University Medical Center

George Dion Daniel
University of North Carolina at Wilmington

See Also: Brain Tumor, Supratentorial Primitive Neuroectodermal, Childhood; Pineoblastoma and Supratentorial Primitive Neuroectodermal, Childhood.
of neutron therapy, called boron neutron capture therapy, is showing some promising preliminary results, especially in difficult-to-treat cancers like glioblastoma multiforme. American James Chadwick discovered the neutron in 1932. A neutron beam is generated using either a nuclear reactor or a particle accelerator.

**Nuclear Reactors**
The first nuclear reactor was built in 1942 during World War II as part of the Manhattan Project. After the war, these reactors were used to generate electricity. During the late 1950s, research reactors started producing radioisotopes for medical use. According to the World Nuclear Association, there were approximately 240 research reactors in operation in 56 countries in March 2014. This number changes regularly due to important upgrades or maintenance requirements. Nuclear reactors operate on the basis of nuclear fission. Uranium-235 or Plutonium-239 is used as fuel in these reactors.

**Particle Accelerators**
Most of the accelerators used today are either cyclotrons or synchrotrons. An accelerator can have a diameter of up to 18 meters. This enormous size is necessary to accelerate particles to the required speed. A radio frequency is used to accelerate protons from the center of the cyclotron in an outward spiral. It is possible to have one accelerator simultaneously delivering multiple proton beams to several treatment rooms. When the protons strike a beryllium target, a neutron beam is generated.

Gantries are used to direct the neutron beam toward the patient. These gantries can rotate 360 degrees around the patient. Patients are positioned on mobile couches, which can also turn 180 degrees. This allows the treatment beam to enter the patient at almost any angle, which helps spare normal, non-cancerous tissue. The emitted neutron beam can be shaped using different types of collimators to create a precise treatment field.

**Fast Neutron Therapy**
Scientists have tested fast neutrons on a variety of different cancers with mixed results. Due to the risk of serious normal tissue damage, only malignant conditions are considered for treatment. Tumors that respond to neutron therapy include the following:

- Salivary gland tumors
- Paranasal sinus tumors
- Head and neck tumors
- Soft tissue sarcomas
- Uterine sarcomas
- Melanomas
- Bone tumors
- Inoperable lesions
- Recurrent cancers
- Slow-growing tumors

**Advantages of Fast Neutron Therapy**
Cells that are actively dividing are more sensitive to radiation compared to cells in a resting phase. Fast-growing tumors are very sensitive to conventional radiation like X-ray or gamma radiation. Slow-growing tumors are more resistant to these types of radiation.

Radiation damages cells through either single or double stranded DNA breaks. Neutrons deliver high linear energy transfer (LET) radiation. The lack of electric charge also means that the neutrons can travel past the electrons on the outside of the atom to collide directly with the nucleus. When the neutrons are stopped by the nucleus, they emit protons with high-ionizing capabilities. The large amount of energy produced by the emitted protons causes a great amount of single-hit double-stranded DNA breaks. This type of DNA damage is irreparable, and the cell dies.

A very controversial topic in the fast neutron therapy debate is the oxygen enhancement ratio (OER). Oxygen acts as a radio sensitizer, making cells more sensitive to radiation-induced damage. Tumor cells tend to be hypoxic, especially at their centers. Some scientists believe that neutrons are less dependent on the OER than X-ray photons.

**Disadvantages of Fast Neutron Therapy**
Normal tissue damage is an important disadvantage of fast neutron therapy. Most tumors are situated behind or around normal healthy tissue. Because of its cell killing abilities, fast neutron therapy can cause serious damage to these healthy cells. This can lead to unpleasant, long-term side effects.

**Boron Neutron Capture Therapy**
Neutron radiation has recently received more attention in the form of boron neutron capture therapy
(BNCT), especially in the treatment of glioblastoma multiforme. Glioblastoma multiforme has a very poor prognosis with mean survival of nine to 12 months after the first diagnosis. Even though boron neutron capture therapy is still in the early stages of research, some studies are delivering promising results. Other cancers that are also treated with BNCT include recurrent head and neck cancers and primary and metastatic melanoma.

With this type of neutron treatment, a patient is administered a boron containing drug. The drug delivers boron to the tumor cells. Boron-10 is non-radioactive in itself. The tumor is then irradiated with a thermal neutron beam, which causes a fission reaction with the boron. Alpha particles with a high LET as well as multiple lithium nuclei are created. This causes significant damage to the tumor cells. Alpha particles do not travel long distances inside of tissue. The rationale behind this type of treatment is that it is possible to deliver a high tumor dose with a high LET, while at the same time sparing the surrounding normal tissue.

Fast Neutron Therapy and Society
There are only two neutron therapy centers operational in the United States and one in South Africa. A third neutron facility in America, Fermi Lab, stopped its neutron therapy due to a lack of funding. The facility has been in negotiations with a medical provider in the hope that it may continue its neutron treatment program.

The cost of setting up and running neutron therapy facilities is much higher compared to X-ray treatment facilities. Neutrons still are an experimental treatment option. Therefore, the centers offering this type of treatment are highly dependent on funding from nongovernment sources. People who do not have one of these treatment facilities in their own country would have to pay large amounts of money to travel abroad for treatment.

Many scientists question the relevance of fast neutron therapy as only a very small percentage of cancers justify this type of treatment. Because it is a very expensive treatment option, many feel that the same advantages can somehow be achieved at a lesser cost and with less-severe long-term side effects.

Radioisotopes
Isotopes are different atoms with an identical atomic number (determined by the number of protons inside the nucleus), same placement on the periodic table, and similar chemical attributes. The atomic mass and physical characteristics of isotopes are, however, different. There is at least one isotope for every chemical element. The atomic mass is determined by the amount of neutrons in an atom.

A radioisotope is an artificially altered isotope with an excess of either neutrons or protons inside of the nucleus. Neutrons are added to the nucleus in a process called neutron activation. This is done in a nuclear reactor. The chosen atom is bombarded with a neutron beam. The nucleus of the atom captures some of the neutrons in the beam, resulting in a neutron-enriched radioisotope, which is unstable. A radioisotope will return to a stable condition through radioactive decay. This type of decay is characterized by the emission of alpha or beta particles. Sometimes gamma rays are also emitted during radioactive decay. The time it takes for a radioisotope to become stable again is called the half-life of the isotope.

Neutron-Rich Radioisotopes for Cancer Therapy
Neutron-enriched radioisotopes tend to decay with a negatively charged beta particle emission. The radioisotope becomes more stable by changing a neutron into a proton. For this to happen, the neutrally charged neutron needs to become a positively charged proton. It releases its negative charge through a negatively charged beta particle. Beta particles can travel very far in air, but they are stopped over only a few millimeters inside of human tissue. Their negative charge causes large amounts of ionizing reactions to occur over a short distance in tissue. This characteristic makes them ideal for use in a therapy setting.

Iodide-131 is used in the treatment of thyroid cancers or hyperthyroidism. Strontium-89, samarium-153, phosphorus-32, phenium-186, rhenium-188, and radium-223 are effective in the treatment of painful bone metastasis.

Targeted alpha therapy (TAT) is a new type of treatment utilizing the body’s own antibodies to escort an alpha-emitting radioisotope directly to tumor cells. Actinium-225 is used in this type of treatment. The first radioisotope necessary for the production of actinium is uranium-233, which is formed by enriching thorium-232 with neutrons in a nuclear reactor.
Neutron-Rich Radioisotopes for the Diagnosis of Cancer

Technetium-99 is the daughter product of molybdenum-99. It is also the most widely used radioisotope in diagnostic nuclear medicine. Molybdenum-99 is created through the fission of uranium-235. Technetium-99 is very useful in detecting cancer in the brain, skeleton, and organs.

Radioisotopes and Society

Approximately 40 million technetium-99 diagnostic procedures are performed globally every year. According to the World Nuclear Organization, diagnostic radiopharmaceutical use increases by more than 10 percent per year.

There are five research reactors that produce most of the world’s molybdenum-99. These five reactors are all more than 40 years old and frequently need to be maintained. From 2007 to 2010, multiple maintenance issues created a significant shortage of molybdenum-99. Many patients had to cancel their diagnostic procedures, while others had no choice but to pay for more expensive diagnostic procedures like positron emission tomography (PET) scans. With the continuous, rapid increase in nuclear diagnostic imaging, a serious shortage of radioisotopes may exist in the future.

Neutron-enriched uranium plates are shipped from America to the different countries responsible for manufacturing molybdenum-99. Many governments are concerned about nuclear safety, especially with the rise in terrorist activities. Recently, there has been a call for research reactor facilities to change from using high-energy uranium (HEU) to low-energy uranium (LEU).

Whether they are used either in the production of diagnostically essential radioisotopes or for the treatment of cancer, neutrons and oncology are set to remain inseparable.

René Julyan
Independent Scholar

See Also: International Cancer Alliance for Research and Education; Radiation, Gamma; X-Rays.

Further Readings


New Zealand

New Zealand is a country composed of two islands (North and South Island) situated in the southwestern Pacific Ocean. Originally inhabited by the Māori tribes, New Zealand was colonized by the British empire in 1840, two centuries after it was first discovered by a Dutch explorer in 1642. The vast majority of New Zealand’s 4.5 million population is of European descent, and it is for the most part concentrated in the urban areas of Auckland and Wellington, its capital. Due to its considerable autonomy and ability to self-govern, the British Crown gradually lost control over New Zealand’s parliament, up until 1947, when the country
New Zealand adopted the Statute of Westminster, effectively declaring its independent authority, even though it is still formally a monarchy with Elizabeth II of England as its Queen.

New Zealand fought alongside the British empire in World Wars I and II, playing key roles in various naval battles in the Pacific theater, and today, it is a very developed country with a solid economy, focused on foreign policies that benefit poorer nations among the Pacific islands, and is considered the second-most peaceful country in the world.

The health care system of New Zealand is a mixed public–private system, with a high-quality system of public hospitals and emergency services for its citizens, with a series of health insurance plans and co-payment methods to help cover the expenses, such as subsidies for paying for medications and primary care. Long waits to receive treatments are often an issue, often exceeding a year for nonurgent surgery, encouraging a significant market in private medical insurance that is mostly covered (up to 50 percent of the whole market) by the Southern Cross Health Insurance, which has its own hospital chain.

Cancer treatment in New Zealand is delivered from a network of six district health boards (DHBs) with the supervision of the Ministry of Health, which coordinates the approach to cancer control through a series of different programs that ensure patients the best treatment and support services. The six DHBs that provide cancer treatment in New Zealand are Auckland, Canterbury, Capital and Coast, MidCentral, Southern, and Waikato. Most cancer centers operate as departments integrated into major hospital complexes and are often linked to palliative care teams and facilities.

The public Regional Cancer Service at Auckland City Hospital is the largest cancer center in New Zealand, treating more than 3,000 patients per year with a very modern radiation oncology department, a hematology ward to treat hematological malignancies such as leukemia and lymphoma, and a palliative care service. Other centers like the Regional Cancer Centre located at Waikato Hospital, Hamilton, instead, offer extensive training programs in all oncology specialties: radiation, medical, hematology, and palliative care.

Many nongovernmental organizations (NGOs) operate to help increase public awareness of cancer prevention and screening, offer patient care and psychological support, and sponsor research projects and fund-raising campaigns. Among these, one of the oldest is the New Zealand Cancer Society, which was founded in 1929 by launching the New Zealand Branch of the British Empire Cancer Campaign.

In 1948, a national population-based register of all primary malignancies diagnosed, called New Zealand Cancer Registry (NZCR), was set up primarily using information sent by public hospitals to collect and store cancer incidence and mortality data. In 1993, the Cancer Registry Act made it compulsory for pathology laboratories to report every cancer diagnosed inside the register, and in 2011, plans to expand it were announced by the Ministry of Health. Also, a New Zealand Children's Cancer Registry (NZCCR) was set up in 2000, under the governance of the National Child Cancer Network.

Cancer is the leading cause of death in New Zealand, accounting for nearly a third of all deaths every year (29.4 percent), followed by ischemic heart disease (18.3 percent of deaths). Lung cancer reported the highest number of cancer deaths in 2011 (18.9 percent of total cases), followed by breast, prostate, and pancreatic cancer, and it is consistent with previous data from the last 10 years. Data from the New Zealand Cancer Registry accounts for 21,050 new cancer diagnoses and 8,891 cancer deaths in 2011.

Colorectal and prostate were the most common cancer registration sites in 2011, accounting for 28.8 percent of all registrations. The most common cancer sites for females are breast, colorectal, and melanoma (skin cancer). For males, the most common cancer sites are prostate, colorectal, and melanoma (skin cancer). The most common malignancies for children are leukemia and testis cancer. The highest incidence of new cancer diagnosis by age was for people age 65 and over (57.1 percent), followed by people between 45 and 64 years (34.7 percent).

Risk factors for cancer in New Zealand are those commonly found in other well-developed Western societies: high-fat diets, low vegetable consumptions, sedentary lifestyle, obesity, smoking, and high alcohol intake.

Inequalities in cancer survival between ethnic and socioeconomic groups are known to exist in New Zealand. Of the 21 cancer sites examined, 17 had an excess mortality rate that was higher for Māori compared to non-Māori by 10 percent or
more, from 1991 to 2004. However, more recent findings reveal that the Māori cancer mortality rate dropped by 10.3 percent between 2001 and 2011, showing a positive trend. The causes of these inequalities are still elusive and not well understood but may include disparities in health care access and the higher prevalence of comorbidities, such as diabetes or heart disease, that may restrict the ability of patients to tolerate radiotherapy or chemotherapy.

Claudio Butticè
Independent Scholar

See Also: Breast Cancer; Cervical Cancer; Leukemia, Acute Myeloid, Adult; Lung Cancer, Non–Small Cell; Prostate Cancer; Radiation.

Further Readings

Nicaragua

Nicaragua is the largest country in the central American isthmus. Officially known as the Republic of Nicaragua, the country borders Honduras to the north and Costa Rica to the south, and the Pacific lies to the west and the Caribbean Sea to the east. The total population of Nicaragua as per 2012 estimates is 5.67 million, with 2.81 million of these being men and 2.86 million women. The average annual deaths related to cancer stand at approximately 27,500. The gross national income per capita is $1,000. The health situation in the country is divergent between the urban areas and the rural areas. While the urban areas have considerably better and advanced healthy facilities and services, the poverty-stricken rural areas lag behind.

It is estimated that the number of new cancer cases in Nicaragua for the year 2008, based on GLOBOCAN data for Nicaragua as a whole, was 5,591. This was as per the 2012 estimates, and of this total number, 2,351 of these cases were men and 3,240 women. The five most-common cancers in Nicaragua are gynecological issues relating to women, urological issues relating to the bowels and other problems, hematological cancers including lymphoma in many of its forms as well as multiple myeloma, stomach, and breast cancer. Statistically, the types of cancer are gynecological cancers with 1,062 recorded cases, urological-related cancer with 813 recorded cases, hematological malignancies with 567 recorded cases, stomach cancer with 527 recorded cases, breast cancer with 468 registered cases, liver cancer with 335 recorded cases, and colorectal cancer with 299 recorded cases.

For persons who have been diagnosed with cancer, they need pathology, surgery, and chemotherapy or radiation therapy; in Nicaragua, the total number of oncologists needed may be based on the number of people who need assistance in some way. Based on estimates in relation to the number of cancer incidences recorded, in Managua, new cancer cases per year based on 2012 estimates were 1,429 and, in Matagalpa, 536. Based on annual new cancer cases, the number of hematologist oncologists required in the two cities includes radiation clinical oncologists, two; urologic oncologists, eight in Managua and three in Matagalpa; gynecologic oncologists, two in both cities; and last, pathologists, three in Managua and two in Matagalpa.

These numbers for the professionals required to handle new cancer cases are based on the number of estimated annual cancer cases. For developing countries like Nicaragua, the International Atomic
Energy Agency (IAEA), of which Nicaragua is a member, supports oncology training for managing chemotherapy and radiation together instead of having to rely on two separate people for both solutions. All cities must have a minimum of two surgical oncologists, two radiation or clinical oncologists, and two hematologist oncologists.

In addition to the professionals listed above, support staff is necessary to aid in the delivery of services. Support staff required in the treatment of cancer in Nicaragua includes oncology-pharmacists plus nurses, technicians, and those who work with end-of-life procedures. Nicaragua cancer treatment and oncology nursing staff for each 24-bed oncology unit comprises one head nurse and a nurse specialist as well as 13 nurses working eight-hour shifts, five days per week (these oncology units are operating 24 hours a day, seven days a week). Because most of the Nicaragua cancer patients require special treatment options, many facilities have to be equipped with the best possible staff members. Professionals working in the radiation oncology units include many technicians, physicists, and engineers who can work with many radiation-based procedures as necessary.

To control management and treatment of cancer in Nicaragua, both government and nongovernmental organizations are involved. These include pilot projects that are used to determine the overall efficiency of many treatment options and to see if different treatment solutions may be utilized as a means of facilitating the basic health needs of all those who are asking for solutions and getting different treatment functions to meet demand. Based on the finding, the IAEA has brought in international partners, notably the World Health Organization (WHO) and the International Agency for Research on Cancer (IARC), to develop sustainable cancer control projects and donors to fund them in Nicaragua. In addition to Nicaragua, a similar initiative by IAEA is being conducted in Tanzania, Mongolia, Ghana, Yemen, Vietnam, Albania, and Sri Lanka.

Michael Fox
Independent Scholar

Further Readings

Nickel Compounds

Nickel is a very abundant, naturally occurring chemical element, which is usually found combined in various forms with iron, sulfur, or arsenic on the Earth's surface and inside large meteorites. Earth's molten core is composed of a nickel–iron alloy known as NiFe. Some natural ores containing nickel include garnierite, pentlandite, limonite, nickeline, kamacite, and taenite.

From a chemical point of view, nickel is a metal in the group VIIIB of the periodic table that exists in the oxidation states of +2, +3, and +4. It is a silvery-white, hard, but ductile metal used in combination with other metals (especially iron, copper, and zinc) to form alloys and plating used in industrial manufacturing for electrical and magnetic properties, high resistance to corrosion, and production of magnets, rechargeable batteries, coins, ceramics, and jewelry. Nickel is an essential
element for many plants and bacteria, necessary for various biosynthetic processes, and is a constituent part of all organs of vertebrates. However, the nickel requirements for human beings and animals are so small that they are included among trace elements, and given its wide availability in the environment, there are actually no known cases of nickel deficiency.

Pure or metallic nickel is used in the chemical industry as a catalyst and for industrial purposes in the production of nickel steels and alloys, electroplating, electrical and sintered components, plumbing equipment, and batteries. Nickel alloys are appreciated for their ferromagnetic properties, high temperature resistance, and oxidation resistance against salts and are used for the production of heating elements, rocket engines, surgical implant prostheses, and storage of liquefied gases. A 75 percent nickel and 25 percent copper alloy called Monel is used for the production of naval parts, propeller shafts in boats, and desalination plants because of its great resistance to seawater corrosion.

Nickel oxides and hydroxides are finely divided powders used in the manufacture of nickel salts, specialty ceramics, alloy steels, and nickel catalysts such as those found in automobile exhaust control. Green nickel oxide is a component in the Edison battery and fuel cells, and it is often used as a porcelain, glass, and ceramics colorant.

Nickel sulfide and subsulfide are used as catalysts in the petrochemical industry, in the production of lithium batteries, as intermediates in the primary nickel industry, and in the hydrometallurgical processing of nickel ores. Together with nickel carbonyl, they are also by-products of mineral refining and metals processing.

Nickel salts are all used as intermediates in the manufacture of nickel catalysts and other nickel compounds, and many of them are also used as electrolytes in nickel electroplating. Nickel acetate, nickel ammonium sulfate, nickel titanate, and nickel carbonate also are used as dye mordant and pigments in the preparation of colored glass and ceramics. Nickel chloride is used in industrial gas masks to absorb ammonia, while nickel nitrate hexahydrate is used for the production of Ni–Cd batteries.

Nickel carbonyl is a yellow organonickel liquid compound and is one of the most toxic substances produced in industrial manufacturing, with a lethal concentration for humans as low as 30 parts per million (ppm; or three ppm for 30 minutes of exposure). It also poses additional safety risks as it is highly volatile, and its vapors can autoignite. It is used as an intermediate in the Mond process for the purification of nickel, vapor plating, and deposition of nickel in semiconductor manufacturing. Nickelocene is a paramagnetic solid metallocene, used as a catalyst and complexing agent.

Being a natural element of the Earth’s crust, small amounts of nickel are found in everyday food, water, soil, and air at very low levels. Natural emissions include volcanoes, windblown dust, forest fires, and dissolution of nickel-containing rocks in soil and water. Anthropogenic sources of nickel include oil and coal-burning power plants, steel-refining complexes, and trash incinerators’ finely pulverized emissions. Nickel usually requires a long time to be removed from air, either by solubilizing in raindrops or by slowly settling to the ground, where it ends up in soil or sediment, forming iron or manganese complexes.
The major source of nickel exposure is oral consumption as nickel is found in both food and water and may include human pollution, for example, nickel-plated faucets contaminating water and soil, mining or smelting waste-water production, cooking with nickel–steel alloy housewares, and eating in nickel-pigmented dishes. Other forms of exposure include breathing (polluted air from nickel metal refining, fossil fuel combustion, and tobacco smoking) and skin contact (through direct contact with jewelry, shampoos, detergents, and coins). A less-common form of chronic exposure is through hemodialysis as traces of nickel ions may be absorbed into the plasma because of the chelating action of albumin. The daily average amount of nickel to which most people are usually exposed does not pose a threat to human health. Most of the nickel absorbed every day by humans is removed by the kidneys and passed out of the body through urine or is eliminated through the gastrointestinal tract without getting absorbed. Nickel is not a cumulative toxicant; however, larger doses or chronic exposure may be dangerous for human health and may represent an occupational hazard due to their acute toxicity and carcinogenicity.

Acute toxicity to nickel may range from less-threatening effects such as allergic reactions, dermatitis, dizziness, and gastrointestinal discomfort to more severe effects such as potentially fatal lung and kidney damage, pulmonary fibrosis, heart failure, and renal edema, especially after exposure to nickel compounds. Workers exposed to airborne fumes, dusts, and mists containing finely pulverized nickel and nickel compounds, such as those working in nickel refineries, nickel processing plants, alloy and stainless steel manufacture, and other nickel-using processes (such as electroplating, smelting, and welding), are all considered at risk for developing cancer.

Many national and international organizations such as the United States Department of Health and Human Services (DHHS), the International Agency for Research on Cancer (IARC), and the U.S. Environmental Protection Agency (EPA) determined that nickel metal and nickel compounds range from those that could reasonably be anticipated to be a carcinogen up to known human carcinogens, and thus, exposure to these substances poses a risk for human health by causing lung cancer and cancer of the nasal cavity (sinus cancer). These claims were confirmed in recent years by numerous epidemiologic studies, cohort studies, and nested case-control studies in different industrial sites in Canada, Italy (Florence), Norway (Kristiansand), Finland, and the United Kingdom (Clydach).

Workers in smelters and refineries were exposed to metallic nickel, nickel oxides, nickel subsulfide, soluble nickel compounds, and nickel carbonyl in concentrations 100,000 to 1 million times greater than typical background levels found in the air and water. Nickel accumulated during daily work was also retained by the mucous membrane for years after retirement.

Other workers who may be exposed to nickel are spray painters, welders, battery makers, jewelers, painters, and varnish makers. Workers exposed to nickel and nickel compounds through inhalation or skin contact showed significantly increased risk (up to three times higher) for lung cancer and cancer of the nasal cavity (sinus cancer), but many recent studies showed a statistically elevated risk of developing other site-specific cancers, such as cancer of the buccal cavity and pharynx, laryngeal cancer, stomach cancer, and pancreatic cancer. Specifically, nickel may significantly increase risk for lung cancer in workers who smoke tobacco (up to five times higher) due to a multiplicative, synergistic effect, suggesting that the effects of nickel exposure and smoking may be additive.

Various forms of nickel and compound types show different potency in their carcinogenicity partly depending on their solubility and ability to reach high concentrations in target tissues. In particular, evidence demonstrated elevated risk of lung cancer and nasal sinus cancer in humans specifically for nickel chloride, nickel sulfate, insoluble and water-soluble nickel salts, nickel oxides, nickel sulfide, and nickel subsulfide.

Water-soluble nickel compounds and metallic nickel were also deemed as contributing to risk of carcinogenesis in humans. Many other nickel compounds such as nickel arsenide, nickel antimonide, nickelocene, and nickel carbonyl demonstrated carcinogenic activity in in-vivo and in-vitro animal studies.

Many studies on both human- and animal-cultured cells demonstrated that soluble nickel salts can be complete carcinogens or initiators of carcinogenesis at tissue sites distant from the site of administration. Nickel mechanisms of carcinogenesis
can be attributed to the production of 8-hydroxy-2'-deoxyguanosine in target sites (mostly lung and sinus cavity) and direct DNA attack by reactive oxygen species produced by nickel ion’s oxidoreductive activity (Fenton’s reaction). Those reactive species and nickel itself may cause chromosomal damage, inhibition of DNA repair activities, and genetic aberrations such as gene silencing that, in turn, may cause cancer. Nickel compounds also act as co-mutagens with a variety of other DNA-damaging agents and may cause oxidative stress and inflammation to tissues, indirectly contributing to carcinogenesis.

To address the human health and environmental hazards posed by nickel dust and nickel compounds, many significant improvements in the refining processes have been made in order to reduce exposure and dust emissions with complex filtration systems. Enclosed operational industrial water circulation systems, for example, greatly decreased the volume of wastewaters getting to water bodies. To protect workers, many governments published occupational safety guidelines and have set limits for metallic nickel and nickel compound concentrations in workplace air during working hours. Engineering controls reduced the environmental concentrations of toxic substances, and factory personnel are required to use personal protective equipment and follow strict sanitation procedures to reduce exposure.

Claudio Butticè
Independent Scholar

See Also: Chemical Industry; Lung Cancer, Non–Small Cell; Nasopharyngeal Cancer; Paranasal Sinus and Nasal Cavity Cancer; Smoking and Society.

Further Readings

Niger

The Republic of Niger (not to be confused with Nigeria) is an inland country in central-western Africa, named after the Niger River. Most of Niger’s population is composed of subsistence farmers who live off their land. Many of them are clustered along the more fertile river banks as around 80 percent of this country is covered by the Sahara desert. Through its history, many empires saw their rise and decline in Niger, such as the Songhai empire (600–1591), the Hausa kingdoms (mid-1350–1808), the Mali empire, and the Kanem–Bornu empire, and the first contacts with Western societies happened only much later at the beginning of the 19th century due to the landlocked nature of this country. After almost 40 years of war and bloodshed, in 1922, Niger was declared a French colony up until 1956, when it became an autonomous state within the French community. From 1958 to 2010, a series
Niger of seven republics alternated themselves with four different military regimes, following an interminable series of military coups that ended in 2010 with the election of the Seventh Republic.

Niger’s rural economy is very poor and underdeveloped, with soils degraded by over-extensive cultivation and often plagued by numerous droughts and locust infestations, although the country itself is rich in mineral deposits of uranium, gold, and coal, which comprise most of the national exports. The vast oil deposits in Niger always have been exploited by foreign countries (mainly the United States and China), and only in 2011 was its own petroleum industry born. Foreign and multinational oil corporations in the Niger delta often founded various repressive military dictatorships in Niger that showed no concern for environmental pollution or local populations’ human rights in order to better exploit the country’s oil basins. Thus, most of the Nigerien population lives in poverty conditions, with one of the lowest literacy rates in the world (especially for females), a life expectancy of just 54 years, and exceptionally high child mortality (124 per 1,000), according to the organization Save the Children.

Health care in general is very scarce in Niger, with a distinct lack of proper medical facilities and very limited resources such as medical equipment, staff, or supplies (especially drugs). The largest Nigerien medical facilities are the National Hospital in Niamey (with just 244 beds) and the Lamordé University Hospital, which is also a teaching hospital and a training center for new doctors. Many nongovernmental organizations (NGOs) such as the Red Cross and Save the Children operate in the territory, trying to guarantee some form of basic health care to the population and to promote awareness, sensitization, and cancer screening programs. Today, with the help of foreign international funds, the Nigerien Ministry of Health is trying to strengthen the quality of services provided.

The first national cancer registry, called Niger Cancer Registry, was established only in recent times (1992), and it is located in the Faculty of Health Sciences at the Abdou Moumouni University in Niamey to collect and analyze data on all cancer cases diagnosed among the population of the capital city. Despite the limitations of the available data, a total of 1,577 cancer cases were reported between 2006 and 2009. The most common cancer sites in Niger are breast, ovary, and cervical cancer in females and liver and colorectal cancer in males, followed by bone and non-Hodgkin’s lymphoma. Burkitt’s lymphoma is the most common childhood cancer because malaria is still endemic in many regions among the farming population. In Nigerien studies, the most frequent histology of breast cancers were carcinomas (46.17 percent). Thanks to the fiber-rich dietary habits of most rural Nigeriens, colorectal cancer incidence is significantly lower than in developed countries, but it is still increasing because of the recent urbanization process that has caused many Nigeriens to shift toward a high-fat and refined carbohydrates-rich diet. Liver cancer is the most common cause of cancer death in Niger with a lethality of 36.45 percent and often comes in association with liver cirrhosis, chronic hepatitis B and C virus infections, and histories of alcohol abuse or aflatoxin exposure, like in neighboring western African countries.

Ecological issues in the Niger delta related to petroleum spills and over-extensive environmental exploitation also may constitute additional risk factors for cancerous malignancies. Roughly 240,000 barrels of crude oil are spilled in the Niger delta every year, causing a vast contamination of soil, ground, air, and water, exposing the population to high levels of many known carcinogens such as benzene, dioxins, polycyclic aromatic hydrocarbons (PAHs), and benzo(a)pyrene. Benzene, for example, was found at levels more than 900 times above United Nations World Health Organization (WHO) guidelines. Gas flares often cause acid rain, which further pollutes the environment and forces rural populations to find shelter under asbestos roofing that protects their homes from corrosion but increases risk for lung cancer, asbestosis, and peritoneal mesothelioma. Oil spills reduced the ascorbic acid content of vegetables from crops by as much as 36 percent, thus reducing the daily intake of one of the most well-known natural antioxidants that help in dietary cancer prevention. Consumption of meat from oil-contaminated livestock also may increase the incidence of cancer of the digestive tract.

Claudio Butticè
Independent Scholar

See Also: Breast Cancer; Cervical Cancer; Liver Cancer, Adult (Primary); Poverty; Solvents.
Further Readings

Nigeria

The territory that makes up the western African nation officially termed the Federal Republic of Nigeria has in times past been the location of countless cultures, civilizations, and peoples. The British protectorates of South Nigeria and North Nigeria were merged in 1960 after the Nigerian peoples gained independence from the British, and in the years that followed, several civil wars ensued. The modern Federal Republic of Nigeria was created in 1999 and has been in place since. The nation currently has one of the top 10 largest populations in the entire world with more than 170 million citizens comprise more than 500 different ethnic groups.

As the Nigerian population is quickly aging according to domestic statistics, incidences of cancer are set to surge in the coming years. As Nigeria is a developing nation that is currently struggling with several other health emergences like the spread of acquired immune deficiency syndrome (AIDS) and malaria, the increased incidence of cancers within the country will only further strain an already strained health care system. Nigeria does not have the screening, treatment, or registry capabilities that other more-developed countries have. The nation currently does not have a national cancer registry or a national treatment plan, which would prove invaluable in the nation’s fight against cancer. The nation’s 11 regional cancer registries are not well maintained due to lack of resources. Also, as in any emerging country, Nigeria currently lacks the funds, oncologists, and physical resources to institute a sustained effort to prevent and remedy its domestic cancer incidences.

Researchers estimate that Nigeria experiences more than 500,000 new cancer incidences and nearly 100,000 cancer fatalities per year. In the past few years, cancer mortalities have appeared to account for more than 5 percent of all mortalities within the country. Even in spite of these estimates, the presence of cancer in Nigeria is not well understood as a result of the general lack of data on the disease in the country. Cancer literature regarding Africa accounts for just 1 percent of the world’s literature on the subject, and the amount of literature regarding cancer in Nigeria is furthermore a fraction of that 1 percent. Many cancer patients in the Nigerian population will never experience or participate in cancer care, and so countless cases go unreported. Even the current population statistics for Nigerians are not considered to be accurate, so making effective inferences regarding trends in cancer cases in Nigeria is exceedingly difficult. When these notions are combined with the fact that Nigeria has only around 100 oncologists operating out of five cancer treatment centers, then it
can be understood how cancer is emerging as one of Nigeria's most pertinent health emergencies.

Childhood cancers are currently posing a large problem to the Nigerian medical community. The most prevalent forms of childhood cancer in Nigeria are incidences of Burkitt's lymphoma, retinoblastoma, nephroblastoma, sarcomas, and leukemia. Various data compiled from some of the nation's 11 regional cancer registries suggests that there are an unusually high amount of brain tumors and leukemias occurring in Nigeria's youth, though researchers are uncertain of the reasons for this. One of the most prevalent cancer incidences in Nigeria's youth, Burkitt's lymphoma, is correlated largely with malarial infections and emaciation, though incidences of Burkitt's lymphoma have been decreasing over the past several years as the nation's malaria problem is better contained. However, childhood cancer patients in Nigeria are faced with the same obstacles that adult cancer patients are faced with there, which is namely the near total lack of access to cancer care due to financial and geographical reasons. In spite of the fact that almost four-fifths of all childhood cancer cases can be remedied with contemporary treatment practices, most Nigerian children will never be able to afford even the most basic medical care.

Currently, the most prevalent forms of cancer incidences in Nigeria are breast cancer, cervical cancer, liver cancer, lymphomas, and prostate cancer. Prostate cancer accounts for the most common incidences in the male Nigerian population, followed by cases of liver cancer and incidences of lymphomas. With regard to Nigerian women, the leading form of cancer incidence of females in the nation is by and large breast cancer, followed by cases of cervical cancer and lymphomas. In the female Nigerian population, incidences of cervical cancer are quickly growing as a result of a consistently increasing amount of infections from the human papillomavirus within the country. In comparison to other nations, lung cancer prevalence is currently fairly low in Nigeria, but researchers believe that incidences may increase in the coming years as tobacco corporations have begun to expand their advertising campaigns in the country. Females account for well over half of all cancer incidences in the nation.

Sadly, many citizens of the Federal Republic of Nigeria have had cancer throughout its history. The critically acclaimed Nigerian academic, pharmacist, and politician Dora Akunyili passed away as a result of ovary cancer in June 2014. Furthermore, Maryam Babangida, who was the wife of Nigeria's infamous former head of state General Ibrahim Babangida, also lost her battle with ovary cancer in 2009. Sam Ojebode, who was once a player for the Nigerian national soccer team, lost his bout with lung cancer in 2012 at the age of 67.

As mentioned earlier, it is difficult if not impossible for the vast majority of Nigerians to receive or have access to basic cancer treatment facilities. As there are only five medical facilities in the entire country that are equipped with any kind of radiation treatment machinery, up to 40 million Nigerians are served by a single one of these facilities. In the coming years, more facilities will need to be created in Nigeria to lessen this statistic, and cancer treatment services will need to be provided in more-affordable ways in order to more adequately serve Nigeria's undertreated cancer patients.

William M. Peaster
Independent Scholar

See Also: Breast Cancer; Cervical Cancer; Liver Cancer, Adult (Primary); Lymphoma, Burkitt's; Prostate Cancer.

Further Readings
Nixon, Richard (War on Cancer)

In 1971, President Richard Nixon declared war on cancer in his State of the Union address. Devoting a relatively small portion of his address, Nixon called for $100 million in additional funds. The State of the Union Address, building on existing support from activists and the U.S. Senate, helped result in the 1971 signing of the National Cancer Act. Since then, more than $100 billion has been spent on cancer research. While the cancer death rate has declined only marginally since 1950, there have been substantial gains in research funding, the development of treatment options, and changes in attitudes toward the disease.

Origins of the War on Cancer
At the time of the declaring of war on cancer in 1971, it was the second-leading cause of death. Cancer had a social stigma that prevented many from disclosing their illness. A philanthropist named Mary Lasker worked to change attitudes. The American Cancer Society also lobbied for increased funds and attention. Lasker conducted lobbying and advocacy efforts to bring cancer to the attention of lawmakers. She hoped to gain funding for increased research for cancer, helping to eventually find a cure for the disease.

Richard Nixon's 1971 State of the Union Address was partially directed toward declaring war on cancer. He stated, "I will also ask for an appropriation of an extra $100 million to launch an intensive campaign to find a cure for cancer, and I will ask later for whatever additional funds can effectively be used. The time has come in America when the same kind of concentrated effort that split the atom and took man to the moon should be turned toward conquering this dread disease. Let us make a total national commitment to achieve this goal."

The signing of the National Cancer Act in 1971 was a tangible result of Nixon's commitment. The act was signed on December 23, 1971. During the signing ceremony, Nixon declared, "I hope in the years ahead we will look back on this action today as the most significant action taken during my administration." Nixon's motivations for the war on cancer were mixed. The use of the war analogy also was applied to actions taken in the war on drugs. Nixon presided over unpopular actions in southeast Asia and looked for opportunities to shift attention. In 1971, wage and price controls were implemented, actions fairly surprising from a Republican president. Nixon's support for a war on cancer helped him to gain popular support as he prepared for his 1972 reelection campaign.

Cancer research was a priority of Massachusetts Senator Edward Kennedy, and the U.S. Senate had passed a resolution in 1970 that led to a study on cancer research. That research was conducted by

---


Ikawo, O. E. “A Literature Review on Cancer in Nigeria.” College of Medicine at the University of Lagos (May 2014).

what came to be known as the Yarborough Commission, which took its name from Senator Ralph Yarborough, who was defeated for reelection in 1970. Yarborough was targeted for defeat by Nixon, and Kennedy was seen as one of his key rivals. Nixon and the relatively liberal Democratic Senate each became champions of the war on cancer.

Implementation, Results, and Criticism of the War on Cancer

The war on cancer helped to result in substantially increased funding for research. Among the initial steps taken in 1971 was the conversion of the former biological warfare facility, Fort Frederick, into a cancer research center. The Frederick Cancer Research and Development Center became a major center to conduct research. The act also provided for collaborations with other federal agencies, state agencies, and the private sector. Educational campaigns such as antismoking campaigns were also promoted. The act was designed to foster research and to allow a focus on areas where there was the greatest potential for improvement.

The four decades after Nixon declared war on cancer and signed the National Cancer Act saw more than $100 billion being spent on cancer research. There were also the creation of cancer treatment centers and public health efforts throughout the nation. Some cancers such as leukemia have seen significant improvements in treatment. Other cancers such as lung cancer and breast cancer have seen changes from greater awareness as people quit smoking and obtained mammograms, which can prevent cancer from developing or allow for early detection. Another consequence of raised awareness is the banning of cigarette smoking from many public places.

Individual types of cancer also gained attention. In 1974, then First Lady Betty Ford underwent a mastectomy and helped to raise attention regarding breast cancer. That helped to gain attention for breast cancer, which impacts a huge number of women, and to encourage early screening.

There has been some criticism of the war on cancer, in terms of both the current state of the battle against cancer and the lack of initial improvement in mortality rates. There is much greater understanding of the wide variety of diseases that constitute what is commonly understood as cancer. Some note that the National Institute of Health’s (NIH’s) stringent requirements for funding have stymied further research. Strict constraints on the federal budget also may result in fewer resources available for future research as well. Research and medical and pharmaceutical treatment may be more difficult to conduct in the future.

Conclusion

More than four decades after the war on cancer, research and treatment efforts against cancer continue. Nixon called for greatly increased research, and that has certainly occurred, with more than $100 billion being spent. In addition, cancer no longer has a strong social stigma, and public health campaigns have helped to identify and reduce risks, particularly in areas such as tobacco smoking. The war on cancer has helped to create the impetus for other diseases and has provided a model for diseases such as human immunodeficiency virus (HIV) and acquired immune deficiency syndrome (AIDS) and for recent calls for increased research for Alzheimer’s disease. While progress has been made, new public health dangers such as the increase in obesity.
and lingering high mortality rates represent contemporary challenges to the war on cancer.

Matthew J. Gritter  
Angelo State University

See Also: American Cancer Society; Breast Cancer; Smoking and Society.

Further Readings

North American Association of Central Cancer Registries

Established in 1987, the North American Association of Central Cancer Registries, Inc. (NAACCR) is a professional organization that develops and promotes uniform data standards for cancer registration, provides education and training, certifies population-based registries, aggregates and publishes data from central cancer registries, and promotes the use of cancer surveillance data and systems for cancer control and epidemiologic research, public health programs, and patient care to reduce the burden of cancer in North America.

NAACCR members consist primarily of population-based central cancer registries, and all such registries in the United States and Canada are members. In addition, major cancer surveillance organizations across North America are sponsoring members of NAACCR. The members work together to provide consensus standards for coding, editing, and data exchange and promote best practices for the collection and use of cancer information. NAACCR coordinates the implementation of standards to promote continuity in data collection, data exchange, and analysis. NAACCR offers a variety of high-quality educational opportunities throughout the year, covering fundamentals of cancer registry operations, data processing, and electronic data management tools.

Central cancer registries collect data on defined populations in a defined time period and strive to collect information on every cancer case in the catchment area so that accurate incidence, mortality, prevalence, and survival statistics can be calculated. Collecting complete, timely, high-quality cancer data is essential for central cancer registries. Additionally, it is imperative that central cancer registries follow the same data collection standards and rules so that valid comparisons can be made between different geographic areas. NAACCR provides the only independent, objective certification program to assess the quality of population-based cancer registry data. Registries must meet quantifiable data quality standards to be NAACCR certified. The criteria include measures of completeness of reporting, timeliness, and accuracy (less than 3 percent of cases may have missing values for age, sex, or state or province of residence; less than 5 percent may be missing race codes; all records must pass edit checks; and less than 5 percent of cases may have information derived solely from death certificates). NAACCR certification has demonstrated marked and measurable improvement in the quality of cancer surveillance data since the inception of the program 25 years ago. In the most recent certification year (2014), 45 U.S. state and regional registries along with eight Canadian provincial and territorial registries were certified at the Gold (highest) level, while nine additional U.S. and two additional Canadian registries were certified at the silver level.

Another priority of NAACCR is the evaluation and publication of data from member registries. In order to assure comparability of the aggregated data from population-based registries in different geopolitical areas, procedures and standards are in place to assure that the data are collected using a universal case definition (reportability standard); collected using uniform rules and standards; coded using a common set of rules and definitions; assessed for completeness within a geographic area; and are from the same time period, of similar quality, and adjusted to a common standard.
NAACCR produces an annual series of publications, “Cancer in North America” (www.naaccr.org/DataandPublications/CINAPubs.aspx), consisting of three separate volumes of data (Volume I: Combined Cancer Incidence for the United States, Canada, and North America; Volume II: Registry-Specific Cancer Incidence in the United States and Canada; and Volume III: Registry-Specific Cancer Mortality in the United States). Data on more than 7.7 million cancer cases in North America covering 98 percent of the population are included and represent the most comprehensive statistical data on cancer in North America. Data are presented for all cancer site groups by gender and, for the United States, by race and ethnicity. Rates of several cancers are presented by stage at diagnosis. NAACCR data contribute to the “Annual Report to the Nation on the Status of Cancer” prepared annually by a collaborative effort of NAACCR, the American Cancer Society, the Centers for Disease Control and Prevention, and the National Cancer Institute.

NAACCR has developed a series of standards for cancer registries to ensure the comparability and quality of cancer surveillance data in North America. NAACCR Standards Volume I details a standard data transmission file layout that is used by all cancer registries in North America and many registries around the world. The NAACCR data exchange record layouts were designed to facilitate electronic transmission of cancer registry data among registries for multiple purposes. The layouts can be used to provide standardized data from reporting sources to central registries; to share tumor reports on residents of other states or provinces from one central registry to another; or to report data from diverse facilities or states or provinces contributing to a combined study. Standards Volume II serves as a data dictionary and provides a comprehensive reference to ensure uniform data collection, reduce the need for redundant coding and data recording between agencies, facilitate the collection of comparable data among groups, and provide a resource document to help registries that are establishing or revising their databases. The document is used by new and existing facility-based and central cancer registries to ensure that their programs’ standard definitions and codes are consistent with those used by regional and national databases. NAACCR Standards Volume III provides standards for completeness, quality, analysis, management, security, and confidentiality of data, and Volume IV provides standardized electronic data edits that can be run on a standard NAACCR file. The final standards volume contains standards for reporting of data using electronic pathology reports.

Since 1987, NAACCR has provided valuable services and resources to central cancer registries and the entire cancer surveillance community. Relying on outstanding volunteers from this community who are willing to work collaboratively on areas of mutual interest, NAACCR has been able to make much progress on achieving its mission. Cancer surveillance personnel from across North America contribute knowledge and expertise for the benefit of all population-based registries, which strengthens the infrastructure and improves the quality of data. NAACCR will continue to focus on five major areas, including standardization and registry development, research and data use, professional development of members, communications, and strategic alliances.

Betsy Kohler  
North American Association of Central Cancer Registries

See Also: International Agency for Research on Cancer; National Cancer Institute; National Cancer Registrars Association.

Further Readings

North Korea

North Korea (NK) claims it has a universal health care system for all citizens. However, the reliability of that claim is suspect. Health professionals working with contacts in NK say that adequate health services exist only for those who can pay. Most of
the information on NK’s health care system is outdated as access to the country is almost unavailable, and what is shown visitors is only the cream of the crop, so to speak. The latest statistics available (2001) indicate that NK spent 3 percent of its gross domestic product (GDP) on health care.

By contrast, the United States spent nearly 18 percent in 2013. The number of hospitals increased from 285 to 2,401 in 1986 and clinics from 1,020 to 5,644. For the last 30 years, there has been a greater importance placed on traditional Korean medicine, based on holistic treatment with herbs and acupuncture. NK did initiate a national telemedicine TV network in 2010. It connects the Kim Man Yu hospital in Pyongyang with 10 medical facilities in other provinces. In the 1990s, NK’s health care system, because of natural disasters and economic problems, experienced a sharp drop in health care services. In 2001, hospitals and clinics in North Korea were suffering shortages in medicines, equipment, running water, and electricity.

Surprisingly, in 2010, the World Health Organization (the United Nations public health arm) touted NK’s health care system as “the envy of the developing world.” At the same time, they cited “remaining challenges including poor infrastructure, a lack of equipment, malnutrition, and a shortage of medicines.” The organization was critical of an Amnesty International report that described “barely functioning hospitals” as outdated.

In an article by Margie Mason of the Associated Press in 2013, she intimates, after a guided tour of NK’s health facilities, that it is a “rehearsed picture of health the reclusive government wants the outside world to see, complete with spotless, granite corridors. But the reality of that image is clouded every time Chairman Mun takes a breath that explodes into icy wisps.” The hospital is so cold during this February visit that patients remain bundled in thick coats, gloves, and scarves during exams, while nurses swish with every step as they hustle through the halls in white snow pants and matching puffer jackets. Mun himself wears big, furry, teddy bear slippers. She says, “Even in the gleaming capital, some health facilities appear to be a throwback to another time. Hulking machines and antiquated equipment in exam rooms could have arrived decades ago, when there was still a steady flow of medical supplies from the former Soviet Union.” Despite this, NK touts its new breast cancer Institute in Pyongyang, the capital. It seems all the health care money is spent in the capital. The center is stated to be for “the prevention and treatment of mammary gland diseases and scientific researches.” However, like many facilities in NK, the hospital appears devoid of patients. Defectors and aid workers say hospitals everywhere are often eerily vacant. Bad roads, a lack of transportation, and no money make it impossible for many to access health centers. Medicine and care are supposed to be free. But in reality, everything has a price.

There’s a saying in North Korea: “If your relative has cancer, then your entire family is ruined because everything will go to getting that medicine,” says Jeon, a 24-year-old defector in Seoul who fled North Korea five years ago. “Some families who cannot afford the medicine have no choice but to watch their loved ones die.” Despite the new center, breast cancer is far from the top of the list of health problems gripping the country, revealing a disconnect between where the government spends and what the people really need, Mason describes.

Beijing, China, reports that NK has claimed to have developed a highly effective injection to cure liver cancer. The Injection Gallium-66 Microspheres developed by the NK Academy of Medical Science is able to treat liver cancers smaller than five centimeters. The medicine is guided by ultrasonic waves only to cancer tissues. The gallium substance was available in the country, and proper doses were obtained for the injection. It is normally effective in 20 days and can be in five. Giving of the injection to 50 patients since 2002 shows that it is effective in as many as 90 percent of patients.

Medicine is not a prestigious occupation in NK. This is because of earlier communist denunciation of all intellectuals, including doctors. As a result, 75 percent of physicians in NK are women. The country is perhaps 15 to 20 years behind in medical research, including cancer research. Nurses often have only a high school education or less.

NK highlights preventative care above all else. They have adequate inoculations when serum is available. All children get mandatory exercise in schools. There is a variation in the quality of medical care in the country. The best hospitals are found in Pyongyang, where government officials are afforded the best care. The predominance of cancer specialists are in the capital. Some facilities in Pyongyang are the only hospitals where patients may obtain
advanced cancer care. Cancer is the leading cause of death in the country, ahead of heart disease.

Assessing cancer care or health care, for that matter, in North Korea is severely hampered by the overly reclusive nature of the government. Suffice it to say that the biggest problem in NK is shortage—shortage of advanced treatment facilities, shortage of medicines, shortage of people's access to quality facilities, and alas, a shortage of food. Malnutrition is probably the most important factor in incidence of disease. Without needed nutrients, the body opens itself up to all manner of unfriendly disease. Also, the shortage of health education for all but the elite is another cause of disease.

NK has the trained doctors to treat cancer so long as patients are elite, live in the capital city, or can afford to get to where the treatment is. Many outlying hospitals do not even have doctors but are run by midwives. Nursing training is lacking. It is good that NK focuses on preventative medicine, and they have managed to increase longevity in the country significantly. However, NK basically is a repressed country with a repressive government, which in turn represses health care.

Bill Kte'pi
Independent Scholar

See Also: Australia; Disparities Within Nations (Elimination of Cancer); South Korea.

Further Readings


Mason, Margi. “North Korea Health Care: Freezing Hospitals Cast Doubt on Official Narrative.”


Norway

The northeastern European nation officially termed the Kingdom of Norway is thought to have first been settled by humans as long ago as 10,000 B.C.E. From this era to contemporary times, Norway has experienced numerous political renditions, from being under Denmark’s dominion from 1523 to 1814 to being unified with Sweden from 1814 to 1905. The Norwegian Parliament declared the nation and its peoples independent from Sweden in 1905, and thus the country has been the sovereign Kingdom of Norway ever since.

There is hardly any concrete data regarding specific rates of cancer in Norway previous to the year 1952 as this was the year that the country enacted a mandatory nationwide cancer registry. Consequently, little tangible information is available regarding precise trends of the disease in the country prior to the 20th century. Nonetheless, some things about the disease in the country pre-1952 can be certain, such as the fact that, like the rest of the globe’s population, the citizens of Norway have been dealing with cancer for centuries. In 2008, researchers at the University of Oslo conducted tests on a female body that was found aboard an ancient and buried Viking ship. After the test results were ready, the researchers discerned that the woman had died around the year 830 C.E. and that she had specifically suffered from bone cancer during the final years of her life. Subsequently, this is the nation’s first confirmed cancer casualty.

More than a millennium later, Norway was occupied by foreign forces during World War II, from 1940 to 1945. As the realities of being an occupied nation led to many lifestyle changes for Norwegians,
so too did these lifestyle changes seemingly affect cancer rates within the country. For instance, as the war progressed throughout the continent, Norwegians were forced to ration their food as a result of large-scale food shortages. It came to be that the majority of the Norwegian population began to catch and grow their own food, and so a regular Norwegian diet during this time frame usually consisted of fresh fish and fresh vegetables. Also, it was extremely difficult during this time for the average Norwegian to come across alcohol or tobacco, so usage of these substances was largely nonexistent. When Norwegian cancer data was analyzed in the years after war, there was a tangible dip in cancer incidences in the generation that lived through the war. This fact has led researchers to believe that the shift in the average Norwegian’s diet and behavior during this period strongly correlated to lower rates of cancer in the nation’s population.

Since the country mandated a nationwide cancer registry in 1952, Norway’s specialists have been able to precisely observe six decades of shifts and progressions in the incidences of specific cancers. Cancer rates have more than tripled in the country since its registry began, but this can partially be attributed to various factors such as the nation’s large populace of elderly citizens and its overall and sustained population growth. It is an unavoidable fact, however, that, since 1953, cancer rates in males have increased by 120 percent, while in females rates have increased by 60 percent. Currently, the most prevalent forms of cancer in Norway are bowel cancer, breast cancer, lung cancer, malignant melanoma, and prostate cancer. In recent years, incidences of lung cancer, malignant melanoma, and prostate cancer have been quickly increasing in Norway’s male population, while incidences of bowel cancer, breast cancer, lung cancer, and malignant melanoma have been increasing regularly in the nation’s female population. In general, incidences of stomach cancer and cervical cancer have been steadily dropping in the nation over the past several years.

Though currently survival rates are high in the country, cancer has been increasing in incidence in Norway recently, and many Norwegian citizens have had cancer over the years. The historic Norwegian Olympian athlete Grete Waitz succumbed to an undisclosed cancer at her home in Oslo in 2011, and also during the same year, the beloved Norwegian actress Wenche Foss lost her battle to breast cancer. More historically, the eminent and critically acclaimed Norwegian opera singer Kirsten Malfrid Flagstad passed away after a short battle with bone marrow cancer in 1962.

Norway is regarded in the international community as having good cancer specialists but conversely of having too few of them. The relatively small amount of specialists that the nation has are forced to work up to 60 hours a week in order to try and see as many patients as possible, and the Norwegian health care system will only become further strained as cancer rates are projected to steadily increase here over the next decade. Nevertheless, there is promising cancer research being conducted in the country at places such as the Institute for Cancer Research at Oslo University Hospital in Oslo and the Department for Cancer Research and Molecular Medicine at the Norwegian University of Science and Technology in Trondheim.

William M. Peaster
Independent Scholar

See Also: Breast Cancer; Lung Cancer, Non–Small Cell; Melanoma; Prostate Cancer.

Further Readings


Dan, I. “Norway Short of Cancer Specialists.” The Foreigner (December 2011).


Novartis Group
(Switzerland)

Novartis International is a leading Swiss multinational company with its headquarters in Basel, Switzerland. In 1996, after the merger of Ciba-Geigy and Sandoz businesses, Novartis was established, and in 2003, Novartis consolidated Sandoz’s generic drugs businesses into a single subsidiary and named it Sandoz.

Research and Development Focus

Novartis has almost 200 projects in clinical development, including 144 in its pharmaceutical division, and it has received three U.S. Food and Drug Administration (FDA) breakthrough therapy designations: LDK378 in lung cancer, RLX030 (serelaxin) in acute heart failure, and BYM338 (bimagrumab) in sporadic inclusion body myositis. Its portfolio includes a range of therapies for the treatment of cancer, hematology, pituitary, and other rare diseases. These include Afinitor/Votubia (everolimus); Exjade (deferasirox); Femara (letrozole); Gleevec/Glivec (imatinib mesylate/imatinib); Jakavi (ruxolitinib); Sandostatin LAR/Sandostatin SC (octreotide acetate for injectable suspension/octreotide acetate); Signifor (pasireotide); Tasigna (nilotinib); Zometa (zoledronic acid); and Zykadia (ceritinib). In 2014, the FDA approved the drug ceritinib from a new class of medicines known as anaplastic lymphoma kinase (ALK) inhibitors, which will be sold as Zykadia for non–small cell lung cancer patients who have a specific mutation of the ALK protein for which this drug will be used. The drug was developed based on the understanding of molecular pathways of a disease and its role in designing specific therapies.

In 2014, Novartis Group invested 17 percent of net sales or $9.9 billion in research and development. In pharmaceuticals, research and development investments were $7.2 billion or 22 percent of pharmaceutical net sales, focusing on the areas of greatest patient need and scientific promise. In 2013, Novartis has provided medicine worth $2.1 billion to more than 100 million patients and health education, infrastructure development, and other programs to another 8.1 million people worldwide. The company has 6,000 scientists working in the global research organization. The company recognizes that demographic transition affecting emerging countries and concerns around urbanization and high environmental pollution and chronic and age-related disorders are increasing along with cancer. This poses a serious challenge to public health resources, the economy, and the labor market.

Novartis's global research operations include the Novartis Institutes for Bio-Medical Research (NIBR), which has facilitated the development of the new products for the company. NIBR scientists collaborate with 300 academic and biotechnology partners worldwide to accelerate research and deliver the benefits of scientific progress to patients. Novartis Oncology of NIBR is a specialized part of the company that focuses on precision oncology treatment. Specifically, it aims to discern the genomic basis of cancer evolution and develop drugs to improve patient outcomes based on these
Novartis Group (Switzerland)

factors. They aim to provide precise cancer treatment by identifying pathways where cancer commonly occurs, screening compounds that can potentially impact the pathways, identify biomarkers, and create diagnostic tools that target patients most likely to benefit from therapy. Scientists at Novartis have gained insights into the complete genetic makeup of human cells, and the goal of functional genomics is to understand the function of each gene and its interaction with each of the nearly 30,000 others in the genome. Currently, several microexperiments have been undertaken to unravel each gene in the genome simultaneously. For instance, a single experiment can reveal the genes in high levels of lung tumors but not in healthy lung tissues. This research facilitates the identification of molecular targets and compounds to genetically profile tumors or patients and, in the future, to guide and customize therapeutic choices.

Novartis Oncology conducted a study titled Oncology Personalized Medicine: Global Professional Study (GPS) among 276 health care professionals (HCPs) in seven countries. Results indicated a positive attitude toward personalized medicine in oncology, and four key areas were narrowed down for successful implementation: professional capabilities to have data to support clinical decision-making, care processes that need to be improved with scientific advances in terms of clinicians being able to put them into practice while working with patients, systems and infrastructure in terms of lack of funding as a stumbling block for personalized care, and collaboration in terms of setting up of multisectoral teams vital for the delivery of personal care.

Dr. Ann Aerts was appointed head of the Novartis Foundation for Sustainable Development (NFSD) as of January 1, 2013, after Professor Klaus M. Leisinger, who led NFSD for more than 30 years. In India, the company has established its oldest social venture, Healthy Family (Arogya Parivar, in Hindi) that goes beyond its business interests toward developing a comprehensive approach to health care. Under this program, the company has increased available medicines from 28 to 109 to address the illnesses suffered by Indians living in rural areas. Under the Healthy Family initiative, the company organized 300,000 village health meetings and health camps attended by almost 11 million people.

The Access to Medicine Index, which ranks companies based on the accessibility of their products to the poor, ranked Novartis in 2012. In 2010, Novartis contributed $1.5 billion or 3 percent of net sales through access to medicine programs as well as investment in research targeting diseases that are prevalent in the developing world. They strive to eradicate in the midterm diseases such as malaria that can be prevented and treated to alleviate future suffering. In 2010, Novartis access-to-medicine programs reached 85 million patients in need, of whom 81 million were malaria patients.

Access Versus Monopoly

In India, Novartis suffered a setback owing to a Supreme Court judgment that rejected patent protection for Glivec, a cancer drug from Novartis. This judgment again highlighted the need to balance human interests vis-à-vis corporate profits, which are hidden in the guise of research and development, wherein drugs are modified in small proportions to allow continuous patenting and monopoly. The judgment allowed Indian companies making generic drugs to produce imitated versions of the drug Gleevec, which is spelled as Glivec in Europe and elsewhere. The drug provides treatment for leukemia and costs as much as $70,000 a year in developed countries, whereas in India, generic versions cost $2,500 a year. From the company’s perspective, it narrows down their profit margins, and as a result, they are less likely to invest in research in India.

Keerty Nakray
Jindal Global Law School

See Also: Daiichi Sankyo (Japan); Developing Countries; GlaxoSmithKline (United Kingdom); Johnson & Johnson (United States); Pfizer (United States); Pharmaceutical Industry.

Further Readings
Novo Nordisk (Denmark)

Novo Nordisk is a company that manufacturers and markets pharmaceuticals in the form of products and services. The company was created in 1989 by Nordisk Insulinlaboratorium and Novo Terapeutisk Laboratorium. Its primary products are equipment and medications for the care of diabetic persons. In addition to this, Novo Nordisk is involved with homeostasis management and hormone research. The company’s mission is to be the best supplier of pharmaceutical products in the world. This is to be achieved through supplying Novo Nordisk customers with high-quality products in regulatory compliance, with reliable delivery performance at a competitive cost, while remaining committed to operating in a clean, environmentally sound, and socially responsible way.

The company is currently researching pulmonary delivery systems for diabetic medications. It is also in the review of autoimmune and chronic inflammatory problems in the body with the intention of reviewing how antibodies may work.

Novo Nordisk’s headquarters are in Denmark. However, over time, the company has expanded to establish facilities and other offices in many places. The company has employed about 38,000 people globally and marketed its products in 180 countries. Novo Nordisk is the largest publicly traded company in the Nordic countries by market capitalization. It is part of the European Federation of Pharmaceutical Industries and Associations (EFPIA). In 2010, the company was ranked by Fortune Magazine 25th among the 100 best companies to work for. In January 2012, Novo Nordisk was named as the most sustainable company in the world by the business magazine Corporate Knights. In January 2014, the company was named on Fortune’s 100 Best Companies to Work For at position 72 within the U.S. state of New Jersey. Novo Nordisk’s B shares are listed on NASDAQ Copenhagen (Novo-B). Its American depositary receipts (ADRs) are listed on the New York Stock Exchange (NVO).

The company has a rich product line. It makes several drugs under various brand names. Even though the company’s main line is diabetes, it has diversified to other areas; therefore, it has drugs covering more than just diabetes. Some of the products from Novo Nordisk are NovoLog, Victoza, Novolin, NovoEight, Levemir, and NovoSeven. The company’s logo, which according to some has been the reason for penetration of markets like Egypt, is and has been since its inception, the Apis bull: one of the sacred animals in ancient Egypt.

The company is actively involved in publicly funded collaborative research projects with other industrial and academic partners. An example of this collaboration in the area of nonclinical safety assessment is the InnoMed PredTox. The company is expanding its activities in joint research projects within the framework of the Innovative Medicines Initiative of EFPIA and the European Commission.

Novo Nordisk is credited for founding the World Diabetes Foundation. The purpose of establishing the foundation was to save the lives of those affected by diabetes in developing countries and supported a United Nations (UN) resolution to fight diabetes, making diabetes the only other disease alongside human immunodeficiency virus (HIV) or acquired immune deficiency syndrome (AIDS) to have a commitment to combat at the UN level. The company was founded primarily to produce products targeting diabetes; therefore, products for the treatment of diabetes account for 85 percent of Novo Nordisk’s business. The company works with the various players in the health care system, doctors, nurses, and patients, for the purpose of developing products for self-managing diabetes conditions.

The company’s business model in the effort to deliver quality products and maintain the legacy established by the pioneers of the company is referred to as the triple bottom line. This model is founded on the belief that a healthy economy, environment, and society are fundamental to long-term business success. Through the model, the company is able to pursue business solutions that maximize
value to stakeholders as well as shareholders. In practice, the model requires people to review different studies: It has to be reviewed based on the responsibility points that come with the program at large. For solutions that meet the three considerations, the company is able to continuously optimize business performance and enhance contribution to the societies in which operations are available.

The company in 2001 conducted a study known as “Diabetes Attitudes, Wishes, and Needs” (DAWN). The study was a global survey on the psychosocial aspects of living with diabetes. The sample size was more than 5,000 persons with diabetes and about 4,000 caregivers. The purpose of the study was to identify barriers to optimal health and quality of life. In 2012, a similar study was done, and it involved more than 15,000 people living with, or caring for, those with diabetes. The second study was conducted in the United Kingdom (UK), and due to the findings of the study, a National Action Plan (NAP) was developed, with a multidisciplinary steering committee, to support the delivery of individualized, person-centered care in the UK. The purpose of the NAP is to provide a holistic approach to diabetes treatment for patients and their families.

Research in Novo Nordisk is a continuous activity. As a result, new and more-advanced products are produced every now and then. Currently, the company has quite a number of products awaiting approval. These include the following:

Tresiba is a type 1 and type 2 diabetes drug, a new-generation basal insulin with ultra-long duration of action of more than 42 hours administered through intravenous injection.

Liraglutide 3 Mg, commonly known as Victoza, is a one-per-day GLP-1 analogue. The drug serves as an adjuvant, intended for combination with lifestyle changes (including diet) to offer sustainable weight loss for people with severe obesity, including those at particular risk of developing diabetes.

Ryzodeg is a drug for persons with type 1 and type 2 diabetes. It is a soluble co-formulation of Tresiba and NovoRapid and is a rapid-acting meal-time insulin.

The board of directors of Novo Nordisk is made up of Goran Ando as the chair of the board as well as the chair of the nomination committee, Jeppe Christiansen as the vice chair, Bruno Angelici as a member, Liz Hewitt as a member, Liselotte Hyveled as a member and employee representative, Thomas Paul Koestler as a member, Anne Marie Kyraneland as a member and employee representative, Helge Lund as a member, Soren Thuesen Pedersen as a member and employee representative, Hannu Ryopponen as a member and chair of the audit committee, and Stig Strobaek as member and employee representative.

In March 2014, the company announced a partnership program to control the development of diabetes in many spaces around the world. The partnership is with the University College of London, the Steno Diabetes Center, and other local partners and health care professionals interested in diabetes.

Michael Fox
Independent Scholar

See Also: European CanCer Organisation; European Cancer Prevention; Pharmaceutical Industry.

Further Readings

Funch, D., H. Gydesen, K. Tornøe, A. Major-Pedersen, and K. A. Chan. “A Prospective, Claims-Based Assessment of the Risk of Pancreatitis and Pancreatic Cancer With Liraglutide Compared to Other Antidiabetic Drugs.” Diabetes, Obesity and Metabolism, v.16/3 (2014).


Nuclear Industry

The nuclear industry is a global enterprise that involves a variety of participants, including companies, industry associations, individuals, and governmental and intergovernmental bodies. The use of nuclear materials has numerous ramifications for public health, including an association with the development of cancer. Nuclear radiation emits subatomic particles in the form of ionizing
radiation that can enter the body and damage DNA and initiate cancer due to cell proliferation.

A Brief History
Henri Becquerel, who was a French physicist and Nobel laureate, discovered radioactivity in 1896. It was quickly recognized that ionizing radiation could adversely affect human health. For example, persons who handled radioactive materials often suffered burns on their hands. Perhaps the most famous case of someone suffering from radiation exposure is Marie Curie, who identified the radioactive element radium and eventually died from leukemia, suspected to be associated with radiation exposure. Furthermore, Wilhelm Roentgen, who discovered X-rays, died from cancer.

Young women in the 1920s were employed to use radium paint to paint the dials of some instruments. Some later develop jaw, bone, and head cancers. The exposure occurred when the women wetted their paintbrushes with their tongues. In addition, miners in an area of Czechoslovakia who were exposed to a pitchblende ore used for isolating radium, polonium, and uranium began suffering from lung problems. Many were later identified as cases of lung cancer, associated with the high radon gas levels in the mine. Since that time, lung cancer has been associated with uranium mining.

Uranium Mining
The nuclear industry is composed of two main segments. The nuclear power industry includes reactor builders and operators. The other segment focuses on mines, nuclear fuel, storage, and waste. This industry segment includes activities such as preparing fuel for use in reactors; management, reprocessing, and disposal of final wastes; and fuel supply.

The nuclear industry works with a radioactive form of the element uranium. Uranium radiation exposure can lead to chemical toxicity, with high levels of exposure leading to kidney failure. Uranium’s radiological toxicity also can lead to an increased risk of developing cancers. It has been difficult to trace cancers definitively with nuclear radiation exposure because these cancers typically occur many years after initial exposure. However, scientists agree that, the higher the exposure levels to radiation, the greater the risk of developing cancer.

Toxicity due to radiation exposure can develop due to breathing air containing uranium dust and eating foods containing uranium. When radioactive rock is pulverized during the mining of uranium, it produces a dust and fine radioactive particles that can be dispersed via wind and water, thus contaminating the air, water, and soil. A potent lung carcinogen is radon gas, which is created by the leftovers, or tailings, from the ground-up rock and effluents (liquid waste) created in the radium mining process, which includes drilling and blasting that have the potential to contaminate aquifers.

The uranium mining process also includes the use of water to control dust and create slurries for extracting the uranium. Contaminants in the tailings can lead to radioactive material occurring in waterways due to leaking and leaching or other mistakes in the mining process. In addition, different organisms, such as bacteria, can lead potentially to radioactive material being transported to areas far from the contaminated sites. Sites containing uranium mining waste products remain radioactive for thousands of years.

Refining, Storage, Transportation, and Nuclear Reactors
Those who work in the segment of the industry dealing with uranium refining or storage typically are exposed to uranium radiation from decay products, although these are considered low-level exposures. However, low-level exposure over a long period of time still can cause health problems, including cancer. In addition, refining and enriching facilities are known to release radioactive particles that have the potential to contaminate nearby populations.

Transporting radioactive materials by rail or truck also poses a threat of exposure if accidents, such as spills, happen and contaminate the surrounding air, water, and soil. A major concern associated with the nuclear industry stems from the operation of nuclear reactors for energy purposes. Although all nuclear reactors release some radioactive substances into the atmosphere, only relatively few studies have looked at the impact on health, including cancer.

One health risk stems from the toxic, spent fuel that nuclear reactors produce. This fuel remains radioactive for thousands of years. Reactors that use heavy water, which contains larger amounts of the hydrogen isotope deuterium than is normally found in water, release radioactive material into the atmosphere, as does the water used to cool the reactors.
These reactors release a carcinogen known as tritium, a radioactive isotope of hydrogen.

A major health concern is how to dispose of the spent fuel created by nuclear reactors. One plan is to bury the waste deep inside the earth. Nevertheless, there is the potential for this type of storage to contaminate both the atmosphere and water.

**Studies**

Various studies have shown a connection between chronic, low-level radioactive emissions from nuclear reactors and cancer. One of the highest concerns revolves around childhood leukemia. Some studies have indicated that the low levels of radioactive material released cannot be connected to cases of childhood leukemia. British studies dating back to the late 1980s revealed a statistically significant elevated rate of leukemia in children who lived within a 10-mile radius of nuclear plants and were under 15 years of age.

Other studies conducted around 15 nuclear power plants in Germany from 1980 to 1990 failed to find such a relationship. However, the studies did show that, within approximately a three-mile radius of reactors, an increase in leukemia occurred in the childhood population. Yet another British study released in 2005 has suggested that childhood cancers may increase in children living near nuclear facilities.

Despite these findings, there are studies that show limited to no risk associated with nuclear radiation and cancer. The National Cancer Institute studied the problem in the 1980s and stated that there was no correlation between cancer death and nuclear power plants. This study was based on the review of more than 900,000 cancer deaths that occurred from 1950 to 1984. Skeptics point out that not everyone who gets cancer dies from it. They also stress that the data gathered has not considered the fact that people move, meaning they can develop cancer in one place due to radiation exposure but end up moving and dying somewhere else.

**Reactor Accidents**

The health care community recognizes that every stage of the nuclear fuel chain is associated with potential human health impacts. In addition, nuclear reactor accidents or meltdowns, a term used to describe what happens when the nuclear reactor’s core is damaged from overheating, can release large amounts of radioactivity into the air. One such accident occurred in the United States at the Three Mile Island nuclear reactor in Pennsylvania in 1979.

Fortunately, studies conducted by the University of Pittsburgh, Columbia University, and others of the Three Mile Island accident showed that only low levels of radiation were emitted. Researchers determined the accident had negligible effects on human health or the environment. However, a far more serious accident occurred in what was then the Soviet Union.

The Chernobyl accident in the Soviet Union in 1986 caused an explosion that sent radioactive gas and dust into the upper atmosphere, leading to dispersion in places as far away as Finland, Sweden, and other parts of Europe. Although the long-term health effects of the accident are still being determined, studies have already linked the accident to the deaths of nine children from thyroid cancer. In addition, researchers have estimated that nearly 4,000 deaths may occur in the future from cancer and leukemia due to the accident, after factoring in cancer survival rates.

Further studies have made dire predictions concerning the future rate of cancer cases and deaths in Europe due to the Chernobyl accident, which already has been connected to 1,000 cases of thyroid cancer alone. In addition, another 4,000 cases of various cancers have been associated with the accident. Overall, scientists believe that approximately 16,000 cases of thyroid cancer and an additional 25,000 cases of other cancers may occur by 2065. Another major nuclear reactor accident due to a tsunami occurred in Fukushima in Japan in 2011. It is still too early to determine the long-term health effects of this accident, with the greatest effects expected to be seen in those who worked at the plant.

**Protection and the Industry’s Future**

Researchers have noted that many of the studies concerned with the nuclear industry, radiation exposure, and its health effects have limitations. Furthermore, studies have produced conflicting results in terms of health effects, including cancer. The nuclear industry stresses that, by far, the amount of radiation produced in the environment by their industry is negligible.
Some industry experts have stated the chance of nuclear core damage at a reactor as being at 1 in 10,000. Nevertheless, a 2003 study conducted at the Massachusetts Institute of Technology (MIT) and titled the “Future of Nuclear Power” noted that the number of nuclear reactors could triple worldwide in the not too distant future. In addition to accidents, there are concerns over terrorist attacks on nuclear reactor sites, which could lead to releases of significant amounts of radiation.

At all stages of the nuclear industry, there are known by-products associated with toxicity and potentially the development of cancers. Because radioactive contamination lasts for thousands of years, any contamination of the environment is, as of this time, considered to be permanent and irreversible. In order to protect populations from cancer and other health effects or exposure to radiation, acceptable limits or exposure have been reduced by various governing bodies over the years.

People are protected from radiation due to the nuclear industry in various ways. Workers in the industry are limited in the amount of exposure time to radiation. In addition, scientists have noted that the intensity of radiation decreases as the distance from its source increases. Shielding via lead, concrete, or water also provides protection from high levels of radiation, which is why radioactive materials typically are stored or handled underwater and by remote-control devices in facilities constructed of concrete or lined with lead. Furthermore, nuclear reactors work within closed systems that feature various barriers to make sure radioactive materials are safely contained.

Concerns about oil supplies and the health effects of fossil fuels such as coal and oil have led to a renewed interest in nuclear power stations. Evolving technologies in the nuclear industry indicate that the industry can operate much safer than ever before. Nevertheless, a 2005 study under the auspices of the National Academy of Sciences (NAS) concluded that there is a carcinogenic effect due to exposure that increases proportionately with dose, especially in the area of leukemia mortality. The report also noted that regulatory controls in the United States may not be strong enough. In 2010, the Nuclear Regulatory Commission asked that the NAS conduct a modern study to determine future research strategies on the effects of radiation exposure from the nuclear industry. Study results will take years to formulate.

David Petechuk
Independent Scholar

See Also: Leukemia, Acute Myeloid, Childhood; Lung Cancer, Non–Small Cell; Lung Cancer, Small Cell; Radiation, Gamma.

Further Readings
Obesity

The advent of technologies and the popularity of high-calorie foods in the 21st century have cultivated a sedentary lifestyle in which human beings engage in less physical activity and consume more calories than before. This has contributed to an unprecedented rise in the number of overweight and obese people in the world. Indeed, obesity has become one of the biggest health problems worldwide. According to the World Health Organization (WHO), obesity has doubled since 1980 throughout the world. In 2008, over 500 million adults suffered from obesity. In the United States, 35.9 percent of adults aged 20 and above are obese. High prevalence rates of obesity have also occurred in Europe. More than 20 percent of adults are obese in the European Union countries. For example, in the United Kingdom, over 25 percent of adults suffer from obesity, which are twice as many as in 1993. A projection suggests that four out of 10 adults in the United Kingdom will be obese by 2030 if existing trends persist. Obesity is not confined to Western countries, as the obesity rate in Asia is also creeping up at a dramatic rate. For example, China’s obesity rate is exploding at about 30 to 50 percent annually.

This phenomenon is not confined to adults. Obesity has more than doubled in children and quadrupled in adolescents over the last three decades. In 2012, over one-third of children and adolescents were overweight or obese. Obesity has become a global epidemic, which could lead to the problematic inflation of multiple health problems, such as diabetes, cardiovascular disease, and hypertension. Moreover, a growing body of evidence indicates an association between obesity and cancer risk of the breast, endometrium, kidney, esophagus, colon, and rectum.

To curb obesity, many antiobesity programs have been conducted by government sectors, civil society, and other stakeholders to encourage a healthy diet and physical exercise. Technology-based preventive strategies have also been implemented in recent years to combat obesity.

Definition and Measurements

Obesity is a condition in which a person has an excess of body fat that significantly increases their risk of ill health. The most common reference of obesity is the body mass index (BMI). BMI is a measure of weight adjusted for height. Specifically, BMI is calculated as weight in kilograms divided by the square of height in meters (kg/m²). According to WHO, a BMI that is between 18.5 and 25 indicates normal weight for an adult 20 years and older; a BMI that is between 25 and 29.9 indicates overweight; and a BMI of 30 or over indicates obesity. (There are international variations in some Asian countries in terms of the cutoff points for BMI.) Although BMI is considered an indicator of body...
Obesity technically measures excess weight rather than excess fat. For clinical purposes, diagnostic imaging such as dual-energy X-ray absorptiometry (DEXA) scanning, computerized tomography (CT), and magnetic resonance imaging (MRI) are usually used instead. DEXA refers to the use of two X-ray beams of different energy levels to develop estimates of bone mineral density, fat-free mass, and fat mass. Additionally, CT and MRI scans are two advanced imaging techniques that offer more precise measurements of body composition, including body fat, muscle, and bone mass. Although these scanning and imaging techniques are more accurate than BMI, they require expensive equipment and cannot be performed without the presence of professional medical personnel.

Causes and Consequences
Obesity can be caused by many different factors. More than 400 different genes play a crucial role in overweight or obesity. People are more likely to suffer from obesity if one or both of their parents are overweight or obese. Other than affecting people's appetite, satiety, metabolism, and body stress, genes could also affect the amount and location of fat stored in the body. Some studies have indicated that apart from genetics, parent-child resemblance in weight status might also be due to the fact that family members share similar food and physical activity habits.

Indeed, most cases of obesity result from unhealthy diet and inactivity. People who eat more high-calorie foods, such as sugary beverages, fried food, and processed meats, tend to have a greater chance of being overweight and obese. Meanwhile, doing little physical activity also contributes to overweight and obesity. Today, with the development of technologies, an increasing number of people are living a sedentary lifestyle. They spend a lot of time watching television or on their computers and smartphones instead of physically exercising. For example, people can easily engage in e-shopping on the Internet instead of walking to the nearest stores to purchase their goods.

The consequences of obesity include two main aspects—physical effects and psychological effects. Obesity contributes to deadly diseases, such as diabetes, cardiovascular disease, stroke, gallstones, and kidney stones. Although the relationship between obesity and cancer is not as clear as that for cardiovascular disease and diabetes, many studies have indicated that obesity is closely linked to several types of cancer. Additionally, obesity may also lead to psychological symptoms such as anxiety, depression, and isolation. Research has revealed that obese people are more likely to suffer from depression than those of healthy weight.

Obesity and Cancer Risk
Longitudinal observations of a large sample are required to examine the association between obesity and cancer. Over the past few decades, epidemiological studies have yielded evidence that increasingly supports the direct link between obesity and cancer. Excess body weight is now widely perceived as a major risk factor and is associated with increased incidence and risks of leukemia and cancers of the esophagus, endometrium, pancreas, thyroid, colon and rectum, kidney, gallbladder, and breast (for women who have gone through menopause). Studies have also pointed to the contribution of obesity to other types of cancer, including cancer of the liver, prostate, and ovaries.

A comprehensive review of findings regarding nutrition, physical activity, and obesity in relation to cancer conducted in 2007 found that a third of over 572,000 cancer deaths were related to obesity. Furthermore, 4 percent of nearly 34,000 new cases of cancer in men and 7 percent of over 50,500 new cases in women in the United States were attributed to obesity. Obesity is further expected to lead to around 500,000 new cases of cancer in the United States by 2030, which will increase the burden on the economy and health care system. Although the percentage of cancer cases that can be attributed to obesity is varied among the different cancer types, the percentage can reach as high as 40 percent for some, such as endometrial and esophageal cancer.

Various biological mechanisms have been proposed and investigated as mediators between obesity and cancer, such as obesity-related hormones, growth factors, and inflammatory processes. Different mechanisms promote obesity-related cancer, particularly at different sites. Excess body fat cultivates an environment that facilitates carcinogenesis. Adipose tissue, particularly abdominal or visceral fat, produces estrogen in excess amounts. High levels of estrogen are associated with some types of cancer such as breast, endometrial, and kidney.
Insulin resistance and adipose tissue dysfunction are mechanisms believed to explain the link between obesity and cancer. Adiposity results in excess release of nonesterified fatty acids, proinflammatory cytokines, and hormones, which triggers the development of insulin resistance. The pancreas compensates for this resistance by producing and secreting more insulin, releasing increased blood insulin levels, or hyperinsulinemia. An emergent body of evidence suggests that chronically high levels of insulin or insulin-like growth factors can promote cancerous tumor growth and cell proliferation in the colon, prostate, pancreas, and breast. Chronic low-grade inflammation has also increasingly been recognized for its modulating effect between obesity and cancer.

Several studies have shown that adiposity affects cancer treatment and therapy, resulting in adverse effects on prognosis. Obesity hinders diagnosis and treatment due to difficulties and uncertainties in surgery, imaging, and chemotherapy dosing, which may lead to poorer outcomes. Excess body mass has been shown to reduce the rate of survival after cancer diagnosis and to increase mortality related to cancer. Obese patients are more likely to suffer from more comorbid conditions and aggressive forms of cancer. Cancer survivors may also be at greater risk of cancer recurrence.

Following the establishment of the link between obesity and cancer, research generally suggests that losing weight will significantly decrease cancer risk. A longitudinal study in the United States that tracked more than 65,000 postmenopausal women found that women who adhered to healthy cancer-preventive lifestyle behaviors experienced lower total, breast, and colorectal cancer risk and cancer-specific mortality. Shedding extra body weight can help reduce inflammation, which may cause cancer.

**Obesity Preventive Strategies**

There are various strategies available to prevent obesity, ranging from personal lifestyle changes to larger societal and structural changes, such as (1) diet and nutrition, (2) physical activity, (3) sleep, and (4) mood control, as well as the role of (5) mass media, (6) technology, (7) parents and schools, and (8) governments.

**Diet and Nutrition**

A balanced and healthy diet is generally recommended as one way to combat the risks and effects of obesity. High-calorie diets are increasingly the norm in developed countries, and it is important for people to be mindful and adopt changes in their food and dietary intake in order to maintain a healthy weight. Healthy nutritional choices include the consumption of more vegetables and fruits, lean protein, nuts, and whole grains. It is also advisable for people to cut down on foods that are high in sugar, saturated fat, refined carbohydrates, and sodium, such as sugary drinks and processed foods. Another factor associated with obesity and cancer is alcohol consumption, which increases the risk of developing several types of cancers in the liver, colon, rectum, throat, and oral cavity. Limiting alcohol intake will help in cancer prevention.

**Physical Activity**

Besides maintaining a nutritious diet, physical activity also influences health. There is strong empirical support for the association between physical activity and a decrease in cancer risk in several sites including lung, breast, prostate, and colon. Regular exercise promotes the maintenance of the body from muscles to joints, as well as psychological well-being. Studies in general show that any uptake of physical activity, or increase in frequency, duration, or intensity, is beneficial for decreasing cancer incidence.

High-intensity physical exercise, such as jogging or running in particular, appears to be most effective in protecting people from the risks of cancer. In particular, high levels of physical activity may help reduce colorectal cancer risk by 30 to 40 percent, and endometrial cancer risk by 20 to 40 percent. Similarly, women who engage in regular, vigorous physical activity have a lower risk of developing breast cancer than women who lead a more sedentary lifestyle. A cohort study of more than 87,000 women showed that weight loss of 10 kilograms (about 22 pounds) after menopause reduced breast cancer risk by 57 percent.

Research indicates that physical activity helps in the maintenance of body mass, energy balance, and metabolism and the prevention of excess body fat. Physical activity also helps to regulate levels of hormones, insulin, and growth factors, which in turn reduce cancerous tumor growth and development. Physical activity may aid in cancer survival in terms of restoring and maintaining energy balance, as well as hormonal and insulin levels. Maintaining regular
exercise after cancer diagnosis has been found to lead to better cancer prognosis and outcomes by increasing survival and decreasing the chances of recurrence. There is a need for further research to determine the optimal levels of physical activity to protect against cancer risk and the extent of the positive impact of physical activity on people of varying body mass indexes.

**Sleep**

Getting adequate, undisrupted sleep is essential in helping the body protect itself from cancer. Increasing evidence suggests that sleep deprivation is linked to obesity. Reasons cited for the link include tiredness curtailing physical activity and overeating because of more waking hours and hormonal imbalance. People who sleep less are also believed to have stronger cravings for unhealthy fatty and sugary foods. Consequently, obesity develops when energy intake exceeds energy expenditure.

Evidence has shown that lack of sleep also affects glucose metabolism and appetite regulation. Sleep deprivation increases the release of the hormone ghrelin and decreases the secretion of the hormone leptin. Ghrelin and leptin are responsible for inducing hunger and signaling satiety, respectively. Thus, a lack of sleep can alter the hormones’ capacity to accurately signal the need for calories, which may then lead to excessive energy consumption and caloric intake.

Several epidemiological studies have shown evidence that support the association between sleep duration and body mass index. This puts people who habitually suffer from sleep deprivation or irregularity at a higher risk of weight gain and cancer. Hence, improving the duration and quality of sleep is vital in warding off cancer-related risk and mortality.

**Mood Control**

Psychological health is closely associated with both obesity and cancer. Studies suggest that psychological stress and obesity may have a reciprocal relationship. Research shows that stress is linked to eating patterns and behaviors, and overeating has been shown to be a coping reaction to stress. People who suffer from chronic stress in their lives are prone to stress-induced eating and often turn to comfort foods that are high in sugar and fat. This may then lead to weight gain and the development of obesity.

Conversely, an observational study conducted in Australia found that the body releases stress hormones such as cortisol after eating, and obese individuals secrete higher levels of cortisol in their bodies after a meal. High levels of cortisol may in turn increase appetite and preference for sugary and fatty foods. Evidence about the mechanism behind the increased release of cortisol in obese and overweight people remains inconclusive. Nonetheless, having excess body fat may lead to greater exposure to the stress hormone cortisol, which is linked to the development of chronic diseases. More research can be done to shed light on possible mechanisms such as hormones that may explain the link between stress and appetite regulation.

Psychological stress is also linked to cancer. While research does not generally support stress as a direct cause of cancer, it may affect the growth and spread of cancerous tumors. Stress may also indirectly influence and lead to poorer outcomes. People may feel a sense of fatality and choose not to pursue proper treatment or turn to risky behaviors such as drug use in response to the emotional and mental pressure. This then affects their chances of survival.

**Role of Mass Media**

The influence of mass media on obesity may be both positive and negative. Researchers caution about media use as a risk factor in the development of obesity from childhood. In particular, television and computer use is believed to encourage a more sedentary lifestyle and curb engagement in physical activity, thus decreasing energy expenditure. Simultaneously, television viewing and computer use may result in excess caloric intake due to snacking. A study conducted with over 2,400 pairs of parents and children found that children who have a television in their bedroom were 1.3 times more likely to be overweight than children who do not. Children who watch more television are exposed to advertisements and product placements for unhealthy food such as fast food, which may alter their food preferences and choices from youth. Unhealthy eating habits that last into adulthood increase the risk of lifetime obesity. Finally, high levels of media use can contribute to obesity by disrupting normal sleep patterns.
On the other hand, the mass media provides a platform for health intervention and communication efforts to encourage desirable behavioral change among people. Public engagement campaigns aiming to reduce obesity among the population, such as promoting physical activity or healthier diet choices, are typically disseminated through the mass media. These campaigns are often strategically designed to target specific groups of people at risk of obesity or developing diseases as a consequence of excess body weight, for example, through the marketing of social norms to motivate uptake of physical exercise. Studies evaluating the effectiveness of campaigns against obesity in Australia, the United Kingdom, and the Netherlands showed they were able to raise public awareness about obesity and its risks and encourage intentions to prevent weight gain. A pilot study in the United States tested a community-based and family-centered intervention aiming to reduce and prevent childhood obesity. Results showed positive improvements in the rate of obesity, uptake of physical activity, regular TV viewing, and dietary intake among children. Parents also felt more empowered in encouraging their children to eat more healthily and engage in physical activity.

Role of Technology
Technology—from television and video games to the Internet and smartphones—has made people, especially children and adolescents, more sedentary. People spend a lot of time on sedentary activities such as texting, using social media, and playing video games instead of physical activities. Thus, technology has been criticized as one of the key causes of obesity.

Technology can be a double-edged sword. Since people are increasingly immersed in the use of technology, high-tech solutions such as exergaming mobile apps and tracking devices have been developed to combat obesity. Exergaming
represents an alternative to traditional exercise, which provides an initial situationally interesting environment such that people must use their bodies instead of just their thumbs to play the video games. Today, there are many ways to participate in exergaming through systems such as the Xbox, Kinect, and Wii Fit. A meta-analysis has revealed that exergaming can reduce individuals' sedentary time and increase their physical activity levels, particularly for children and adolescents. Additionally, many big-name brands have launched a wide range of wireless tracking devices connected to mobile apps to track users' health, fitness, and physical activity data and to create customized plans for users in order to prevent or curb obesity. In other words, some evidence points to the usefulness of exergaming in encouraging and promoting physical activities.

Role of Parents and Schools
Since the foundation for lifelong health is laid in childhood, parents and schools are responsible for curbing the obesity epidemic. Family members usually share similar food and physical activity habits. In order to protect children from obesity, parents can foster children's healthy eating habits by offering healthy foods at home and limiting fried food and sugary drinks. Moreover, parents can limit children's time spent using the Internet or watching television and encourage them to engage in regular physical activities. Some studies have shown that parenting behaviors play an effective role in regulating children's food consumption and engagement in physical activities.

Outside of their homes, children spend most of their time in schools, which suggests that schools play a crucial role in childhood obesity. Schools can offer a variety of healthy foods in the cafeterias to improve children's nutrition. Furthermore, schools can hold regular sports events and offer interesting physical education courses to foster children's interest in sports and to increase their physical activity levels throughout the school day. Some evidence has revealed that school-based obesity prevention programs are effective in helping students achieve healthy weight.

Role of Governments/Policy Makers
According to WHO, governments and policy makers play a pivotal role in public health, including the prevention of obesity. Governments could provide an activity-friendly environment to encourage and promote individuals' daily physical activities, for instance, by constructing more recreation facilities such as parks, stadiums, swimming pools, and gyms, and lowering the cost of sports programs or equipment. Meanwhile, infrastructure such as footpaths and cycling routes could be built to increase individuals' opportunities to be active. To encourage healthy eating, governments could introduce more policies to limit or reduce fast-food consumption.

Strategies to combat obesity require changes in individual lifestyles as well as support from parents, schools, and governments. Furthermore, technology is both a contributing factor to obesity and a means to combat obesity. In the future, more technologies can be developed as approaches to combat obesity.

Shirley S. Ho
Liang Chen
Youqing Liao
Nanyang Technological University

See Also: Daily Life; Diet and Nutrition; Exercise.

Further Readings

Occupational Therapy

Occupational therapists and occupational therapy assistants help people to perform their important everyday activities. Occupational therapy practitioners work in more than 70 countries around the world, and the U.S. Bureau of Labor Statistics
estimates there will be more than 145,000 occupational therapy practitioners in the United States by 2022. The largest number of occupational therapy practitioners work in the United States and are represented by the American Occupational Therapy Association (www.aota.org), which has over 50,000 members.

Occupations can be categorized as (1) activities of daily living (ADL) including grooming, toileting and hygiene, sexual activity, swallowing and feeding, bathing, and dressing; (2) instrumental activities of daily living (IADL) including care of others, shopping, meal preparation, driving and community mobility, and home and financial management; (3) rest and sleep; (4) education; (5) work, including volunteer activity; (6) play; (7) leisure; and (8) social participation. Occupational therapy practitioners work with persons across the life span to help them engage and participate in familiar roles such as student, worker, parent, family member, volunteer, hobbyist, and religious participant. Occupational therapy practitioners are experts at analyzing the relationship between the person, the occupation to be performed, and the factors that affect performance such as physical ability, cognitive ability, sensory and perceptual abilities, communication and interaction skills, psychosocial influences, and the environment.

Because persons of any age can have cancer, and because cancer and its treatments can negatively impact a person's ability to perform valued daily occupations, occupational therapy is highly relevant to the comprehensive treatment of persons with cancer. Occupational therapy practitioners work with persons at any point along the cancer care control continuum (e.g., prevention, detection, diagnosis, treatment, and survivorship). Common problems that are addressed by occupational therapy include (1) fatigue, (2) pain, (3) mild to severe cognitive impairment, (4) decreased strength, (5) decreased endurance, (6) visual deficits, (7) motor deficits (i.e., coordination, dexterity, praxis), and (8) decreased mobility.

Impact of Cancer on the Performance of Daily Occupations
Cancer and its treatments, which can include surgery, chemotherapy, and radiation, can negatively impact a person's ability to perform valued daily occupations. Occupational therapy practitioners work with persons at any point along the cancer care control continuum (e.g., prevention, detection, diagnosis, treatment, and survivorship). Common problems that are addressed by occupational therapy include (1) fatigue, (2) pain, (3) mild to severe cognitive impairment, (4) decreased strength, (5) decreased endurance, (6) visual deficits, (7) motor deficits (i.e., coordination, dexterity, praxis), and (8) decreased mobility.

Occupational Therapy Interventions for Persons With Cancer
Common occupational therapy interventions for a person with cancer include analyzing the demands of the occupations to be performed in order to identify gaps in the person's performance capability. These gaps can be closed through intervention at the person's home, in the hospital, in the workplace, and/or in the community. Specific interventions can be categorized by five approaches, which are to (1) create or promote through an intervention

Occupational Therapy Process
Occupational therapy services typically include the following:

- An individualized evaluation, during which the client/family and occupational therapist determine the person's goals through a client-centered approach. Occupational therapy services may include analysis of various environments including the home, school, or workplace.
- Customized interventions to improve the person's ability to perform daily activities and reach their goals. Interventions may include remediation of physical deficits or compensatory strategies to adapt to performance limitations such as the use of assistive/adaptive equipment or adapting the occupation to be performed or elements of the environment. While the person with cancer (i.e., patient) is the center of the evaluation, other persons such as family members, teachers, coworkers, or employers are included in the intervention.
- An outcomes evaluation to ensure that the goals are being met and/or to make changes to the intervention plan.
approach that does not assume any disability is present and can enrich the experiences of the person and the environments in which they perform, (2) establish the skills or abilities of a client that have been impaired or restore skills or abilities which have not yet been developed, (3) maintain performance capacities by providing supports to the client, (4) modify the occupations to be performed by changing task demands or providing supports to the client including techniques to compensate for deficits, and (5) prevent future problems with the performance of occupations by reducing or eliminating barriers and by changing the task or the environment or promoting change in the client.

In addition, occupational therapy practitioners often intervene through the provision of education and training to family members and other persons who provide social or functional support to the client. Occupational therapy practitioners also often assume an advocacy role for their clients or for organizations, communities, or populations at the community and societal levels. A focus on improving and maintaining quality of life is included at all levels.

Brent Braveman
Lauro A. Munoz
Vivianne Yang
Trina C. Henry
Corey Helm Swartz
University of Texas MD Anderson Cancer Center

See Also: Alternative Therapy: Manual Healing and Physical Touch; Cost of Therapy; Physical Therapy.

Further Readings
American Occupational Therapy Association.

Ohio State University Comprehensive Cancer Center

The Ohio State University Comprehensive Cancer Center—Arthur G. James Cancer Hospital and Solove Research Institute (OSUCCC–James), commonly known as the James Cancer Hospital, is a 306-bed cancer hospital and research institute located in Columbus, Ohio.

Founded in 1990, the facility is one of 41 centers in the United States to be recognized by the National Cancer Institute as a comprehensive cancer center. The new James Cancer Hospital opened in late 2014, leading to the closure of the original facility. The construction of the new center represents the largest expansion project in the history of Ohio State University.

History
Upon opening its doors in 1990, the James Cancer Hospital became the first freestanding cancer hospital in the Midwest.

The center is named in memory of two Ohioans who dedicated their lives to combatting cancer. The facility originally opened as the Arthur G. James Cancer Hospital in memory of the venerated physician and faculty member in Ohio State’s College of Medicine. James first met prominent Columbus-area real estate developer and philanthropist Richard J. Solove while treating Solove’s father’s thyroid cancer in the late 1950s. The two fostered a friendship and spearheaded an effort to construct the state’s first freestanding facility dedicated to cancer treatment and research. The facility’s research center was renamed the Solove Research Institute in 1999 after Solove bestowed a $20 million donation on Ohio State for cancer genetics research.

The New James
In 2009, the Ohio State University board of trustees approved a $1 billion expansion of the James Cancer Hospital and its medical center facilities, with the help of a $100 million grant from the U.S. Department of Health and Human Services’ Health Resources and Services Administration. The new James Cancer Hospital opened in December 2014 and is dedicated to fostering a new era of interaction...
and collaboration between researchers, doctors, and patients.

The new facility is the third-largest cancer hospital in the United States, with 21 floors, 1.1 million square feet, and 306 inpatient beds, including a 36-bed bone marrow transplant unit. Inpatient floors specialize in treating specific subtypes of cancer, and are staffed by subspecialist multidisciplinary teams of physicians, nurses, and pharmacists. Each room is equipped to provide patients with nearly all of their treatments, bringing an end to multisite and multifacility visits that are often required of cancer patients enduring the advanced stages of the disease. A cancer emergency department is scheduled to open in March 2015.

Inpatient floors will also contain translation research labs, where researchers will work to develop effective, targeted treatments. Past research at the center has ranged from work covering experimental cancer treatments to analysis of molecular carcinogenesis and viral oncology.

The Ohio State University Comprehensive Cancer Center is one of five centers in the United States with approval to offer both Phase I and Phase II clinical trials. The new hospital contains a cancer clinical trials unit dedicated to early-phase clinical trials.

In 2013, the hospital received one of the nation’s most prestigious nursing honors when it achieved Magnet designation as part of the American Nurses Credentialing Center’s Magnet Recognition Program. The center’s achievements, cancer awareness campaigns, fund-raising efforts, and medical staff are profiled in the organization’s quarterly magazine, Frontiers.

The center also includes five specialized medical facilities. Three of the facilities—the Stefanie Spielman Comprehensive Breast Center (SSCBC); JamesCare at Martha Morehouse Medical Plaza, which specializes in hematologic disorders; and JamesCare at University Hospital East, which works to provide home-based care for patients suffering from cancers and blood disorders ranging from colon cancer to melanoma—are located in Columbus. The Gynecologic Oncology at Mill Run facility is in Hilliard, Ohio, and the James Care at Stoneridge Medical Center is in Dublin, Ohio. In 2014, the SSCBC received the prestigious Breast Imaging Center of Excellence designation from the American College of Radiology.

The James Cancer Hospital also has ongoing affiliations with Ohio’s two major pediatric cancer centers, the Ohio State University/Cincinnati Children’s Cancer Consortium and the Nationwide Children’s Hospital in Columbus. The three facilities work together to share research and treatment methods for children.

**Pelotonia**

In 2003, Michael Caligiuri, the director of the OSU Comprehensive Cancer Center and a research physician, cofounded the Columbus-based nonprofit Pelotonia, an annual bike race whose proceeds go directly to research at the center. Caligiuri founded the annual race with friend and cancer survivor Tom Lennox. The two drew inspiration from their participation in a 2008 charity bike race for Boston’s Dana-Farber Cancer Institute. In the years since its founding, Pelotonia has become one of Ohio’s most popular charitable events, helping to raise over $40 million for the center’s research.

The Pelotonia organization’s efforts also include the Pelotonia Fellowship program, which grants $2 million annually to undergraduate, graduate, and postdoctoral students interested in dedicating their scholarship and careers to helping to cure cancer.

**ORIEN Network**

Funds from the hospital’s annual Pelotonia fund-raising drive were instrumental in the founding of its Oncology Research Information Exchange Network, or ORIEN. Established in May 2014 in conjunction with the Moffitt Cancer Center in Tampa, Florida, the network is the world’s largest cancer-research, patient-information, and tissue-sample database. The state-of-the-art system was designed to provide researchers and clinicians with a faster way to match eligible patients to clinical trials and to conduct larger and richer analysis of data for research.

John Pritchard III

*Independent Scholar*

**See Also:** Comprehensive Cancer Center at Wake Forest University; Dana-Farber Cancer Institute; Holden Comprehensive Cancer Center at the University of Iowa; Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins; University of Alabama at Birmingham
Comprehensive Cancer Center; University of Chicago Medicine Comprehensive Cancer Center; University of California, Los Angeles, Jonsson Comprehensive Cancer Center; University of California, San Francisco, Helen Diller Family Comprehensive Cancer Center; University of Michigan Comprehensive Cancer Center; University of Southern California Norris Comprehensive Cancer Center.

Further Readings

OHSU Knight Cancer Institute

Seventy-seven percent of patients over age 55 years of age will be diagnosed with a type of cancer. Five to 10 percent of cancers are hereditary. A man’s chance of developing cancer is 50 percent and a woman’s chance is 34 percent. Because of the large role cancer plays in worldwide healthcare, the Oregon Health Science University (OHSU) Knight Cancer Institute (KCI) was developed. The Knight Center, founded in 1986, is an international leader in the research and treatment of cancer. This includes advances in melanoma, prostate, breast, and colon cancer, as well as leukemia, lymphoma, gastrointestinal, and stromal tumors. Additional specialty areas are breast, brain, colon, esophageal, gastrointestinal stromal tumor (GIST), head and neck, lung, lymphoma, melanoma, myeloma, myelodysplasia, ovarian, and sarcoma cancers.

Public support and philanthropy provide most of the finances for continued research and treatment of cancer. Nike donated $100 million in 2008, and then pledged to match dollar-for-dollar equal to $500 million, if the Knight Cancer Institute could raise $500 million in its two-year fund-raising campaign. With the original gift of $100 million, the Institute changed its name from the Oregon Cancer Institute to the Knight Cancer Institute. There are additional corporations who provide support to the Knight Cancer Institute. Gert Boyle, Chairman of the Board for Columbia Sportswear, gave $100 million. Other corporate collaborators are Intel Corporation and FEI Co. The money raised goes toward research; patient support services such as wellness programs and patient assistance funds; community outreach for early detection and healthy lifestyles; and education programs.

The mission of KCI is to end cancer and to decrease Oregon State’s cancer death rate to the lowest in the nation. Currently, Oregon has the highest rate of melanoma diagnoses in the nation. At KCI more than 400 clinical trials and more than 1,000 research studies are managed each year. The end results are new cures are discovered, better standards of care are developed, and new treatments and therapies for cancer are found.

The Institute accomplishes its mission by focusing on holistic individualized healing featuring a multidisciplinary team made up of medical, radiation, and surgical oncologists, nurses, pharmacists, physical therapists, social workers, nutritionists, and nurse navigators. Each cancer physician is fellowship-trained in a specialty. This highly skilled team of specialists produces a customized treatment plan, individualized for every patient.
The team meets on a weekly basis to discuss every patient under their care.

Based on Brian Druker’s 1993 discovery that cancer cells can be shut down at the molecular level by disabling the tumor’s ability to grow without harming the body’s healthy cells, each patient’s cancer is targeted based on DNA and the specific cancer. Even the radiation therapy is designed to target only tumor cells. As part of the holistic focus, alternative medicines are offered to heal mind and spirit, otherwise known as personalized cancer medicine.

The Knight Cancer Institute was the first in the region to provide access to the Calypso image guidance system and the stereotactic body radiation system. These treatment options reduce radiation toxicity and side effects. They have the region’s largest bone marrow transplant program offering both autologous and allogenic marrow transplants.

The National Cancer Institute (NCI) was formed by the Cancer Centers Program as part of the National Cancer Act of 1971. The goal of a NCI is to be known as a leader in scientific excellence and the provider of diversity in cancer research. They are to be the major source of new knowledge regarding cancer, its diagnosis, prevention, and treatment. This designation was given to the Institute in 1997. It remains the only NCI within the state of Oregon and the only one between Seattle, Washington, and Sacramento, California.

As a result of the research completed at KCL, standards in cancer care have changed. The Prostate Cancer Program joined the National Cancer Consortium to share the breakthroughs in detection, treatment, prevention, and standards of care for prostate cancer. KCL provided the evidence that established a colonoscopy as the international gold standard of care for the early detection of colorectal cancer.

In 2005, with the aid of the Lance Armstrong Foundation, the Knight Cancer Institute established the first Adolescent & Young Adult cancer program in the United States. The Adolescent & Young Adult cancer program is a rarity in the United States and abroad, offering comprehensive, personalized services for patients between the ages of 15 and 39 years of age. Persons in this age-group have different needs than other cancer patients. Cancer therapy affects education, career, fertility, and many other aspects. In 2011 in the United States, there were 69,212 diagnoses of cancer in this age-group, six times higher than those ages 0 to 14. Leukemia, lymphoma, testicular cancer (germ cell tumors), breast, melanoma, and thyroid tumors are the most common cancers seen in this age-group. Cancer in this age-group is the leading disease-related cause of mortality in the United States.

In an effort to provide better treatment to all of Oregon’s residents, KCL works with local healthcare facilities around the state by providing access to research results and treatment options within the local community. This allows the patients to remain near their homes during treatment.

With the increased demand for beds, the Institute expanded in 2009. It now boasts more cancer beds in one location than any other facility in Oregon. This expanded facility includes specialized areas for bone marrow transplants, hematologic malignancies, and many more. There is a new radiation treatment facility and with additional clinics and more laboratory space, for a total of more than 200,000 square feet of space solely dedicated to cancer research and treatment.

Continuing the societal focus on cancer, KCL is involved in the state’s legislature. In 2009 Senate Bill 316, requiring health insurance plans to provide coverage of routine qualifying clinical trials with copays and cost sharing requirements and limiting the liability of the insurers in the event of adverse effects from the clinical trials, passed.

Justina D. Higgins
Independent Scholar

See Also: Bone Marrow Transplants; Brain Tumor, Adult; Breast Cancer; Breast Cancer, Male; Clinical Trials; Colon Cancer; Esophageal Cancer; Melanoma; Myelodysplastic Syndromes; Myeloma, Multiple; Radiation Therapy; Technology, Imaging.

Further Readings
Oncology Nursing Society

The Oncology Nursing Society (ONS) is a professional association of more than 35,000 members committed to promoting excellence in oncology nursing and to transforming cancer care. The group's mission is to promote excellence in oncology nursing and quality cancer care. The ONS national office is in Pittsburgh, Pennsylvania.

In 1973, a small group of oncology nurses attending the First National Cancer Nursing Conference in Chicago began discussing the need for an organization to support their profession. In 1974, communication regarding a formalized group continued at the American Cancer Society–National Cancer Institute National Conference on Advances in Cancer Management in New York. ONS was incorporated on July 17, 1975, with a charter membership of nearly 500 members.

Since then, ONS has provided a professional community for oncology nurses, developed evidence-based education programs and treatment information, and advocated for patient care, all in an effort to improve quality of life and outcomes for patients with cancer and their families. Together, ONS and the cancer community seek to reduce the risks, incidence, and burden of cancer by encouraging healthy lifestyles, promoting early detection, and improving the management of cancer symptoms and side effects throughout the disease trajectory.

Organization Activities
ONS has more than 230 local chapters throughout the United States and 27 special interest groups, communities of members who share ideas, information, and experiences with others in the same cancer care subspecialty. The society is involved in education and outreach around the world, both to nurses and to interdisciplinary audiences; priority topics for nursing education include chemotherapy and safe handling of cytotoxic drugs, clinical trials, pain control, palliative care, diseasespecific education, evidence-based practice, and leadership development.

ONS is active in health policy, working collaboratively with policy makers, cancer and nursing community advocates, and other stakeholders at the local, state, federal, and international levels to advance legislative and regulatory efforts and integrate the nursing perspective throughout the policy-making process. Society members are encouraged to join programs that connect them to decision makers who are educated on the importance of oncology nursing.

In addition to its annual meeting each spring, ONS offers numerous continuing nursing education programs both in the classroom and online to enable oncology nurses to stay current on the latest cancer treatments and symptom management techniques. ONS is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation. In 2013, ONS offered 1,567 chemotherapy/biotherapy courses that provided education to 19,161 nurses. In 2014, the in-classroom chemotherapy course was replaced by an online course.

ONS collaborates with the American Society of Clinical Oncology to develop standards for the safe administration of chemotherapy; the original standards were published in 2009, with revisions published in 2011 and 2013. As of December 2012, the society's Putting Research Into Practice (PEP) resources have summarized more than 1,700 studies and provided evidence for 466 discrete interventions for the 20 PEP topics.

Publications
ONS publishes two scholarly scientific journals, Clinical Journal of Oncology Nursing and Oncology Nursing Forum, as well as a news magazine, ONS Connect, all of which are published in both print and online formats and included in indices and databases such as MEDLINE, Cumulative Index to Nursing and Allied Health Literature (CINAHL), and Google Scholar, among others. ONS members
receive all three publications as a membership benefit. The *Oncology Nursing Forum* consistently ranks among the top impact factors of journals in the nursing category as determined by Thomson Reuters. ONS also publishes books, monographs, and other publications for the cancer care community, with more than 70 books in print and between eight and 10 new titles every year. In addition, the society produces patient-oriented books under its Hygeia Media imprint. ONS and Hygeia books are available in print and e-book formats. ONS publications have received awards from the American Society of Healthcare Publication Editors, Association Media & Publishing, the American Journal of Nursing, and numerous other organizations.

The society has a Web site at www.ons.org and is active in social media via Facebook, Twitter, LinkedIn, YouTube, and Pinterest. The national office has a library that is a full member of the National Network of Libraries of Medicine, as well as an archive with project files, photographs, oral history recordings, and other materials of historical significance to ONS and oncology nursing.

**Affiliated Corporations**

ONS has three affiliated corporations. The Oncology Nursing Certification Corporation (ONCC) was incorporated in 1984 for the development, administration, and evaluation of a program for certification in oncology nursing, and has met all standards established by the Accreditation Board for Specialty Nursing Certification and the National Commission on Certifying Agencies. As of April 2014, ONCC offered six certification examinations—Oncology Certified Nurse, Certified Pediatric Hematology Oncology Nurse, Certified Breast Care Nurse, Advanced Oncology Certified Nurse Practitioner, Advanced Oncology Certified Clinical Nurse Specialist, and Blood and Marrow Transplant Certified Nurse.
The Oncology Nursing Society Foundation is a nonprofit, tax-exempt, charitable organization established in 1981 with a mission to support oncology nursing in order to improve the lives of people with or at risk for cancer. Contributions from individuals, ONS chapters, corporations, and foundations enable the ONS Foundation to meet its mission; since its inception, it has provided more than $23 million in funding support for oncology nursing awards, grants, scholarships, and educational initiatives.

ONS:Edge is the for-profit subsidiary of ONS, and is a specialized advisory firm providing marketing communications strategy and execution as well as services such as live events, Web presentations, and market research for pharmaceutical, medical device, and other companies. Its purpose is the transfer of cancer knowledge to oncology nurses in order to improve patient outcomes.

Mark Vrabel
Oncology Nursing Society

See Also: American Society of Clinical Oncology; International Society of Nurses in Cancer Care.

Further Readings

"International Society of Nurses in Cancer Care (ISNCC).” *Oncology Nursing Society* (April 18, 2014).


Ono Pharmaceutical (Japan)

Ono Pharmaceutical Co., Ltd. is one of the smaller Japanese pharmaceutical corporations, with 2,858 employees worldwide as of early 2014. In “Medical Care & the Pharmaceutical Industry,” an overview of pharmaceutical corporations’ 2012 sales figures compiled by the Japanese company Astellas Pharma, Ono Pharmaceutical ranked number 13 in Japan.

History and Corporate Philosophy
The precursor to Ono Pharmaceutical was founded by Ichibe Fushimiya in 1717 and sold traditional medicines in Osaka. Ono Pharmaceutical Co., Ltd. was formed in 1947, and the company’s shares were listed on the Osaka Securities Exchange and on the Tokyo Stock Exchange in 1962 and 1963, respectively. Ono completed the world’s first synthesis of prostaglandin (PG) in 1968. In an effort to internationalize, the company opened a London office in 1982, followed by a Seattle office in 1990 and a Seoul office (later Seoul Branch) in 1994. Ono’s offices in the United Kingdom (UK) and the United States were later replaced with Ono Pharma UK Ltd., established in the UK, and Ono Pharma USA, Inc. In 2013, Ono Pharma Korea Co., Ltd. was established in South Korea.

Ono has implemented an environmental self-regulating action plan, which consists of six elements. One element, relations with the communities in which the company is located, includes participating in cleanup activities and striving for the prevention of workplace accidents that involve employees’ injuries. A low-carbon economy plan aims for carbon dioxide emissions in 2020 to be 23 percent less than the company’s emissions in 2005. The company is also working to control chemical substances by reducing its discharge of chemical substances, and aims to reduce its waste disposal in 2015 by 40 percent of the volume disposed in 2010. Within the plan there are also measures to combat air and water pollution and measures for environmental accounting in accordance with the guidelines of the Ministry of the Environment.

Key Products
Based on sales figures for fiscal year (FY) 2012, the best-selling products were Glactiv for the treatment of type 2 diabetes (34.8 billion yen) and Opalmon for the treatment of peripheral circulatory disorder (33.9 billion yen). Other key products include Recalbon for osteoporosis (7.7 billion yen), Onon for bronchial asthma and allergic rhinitis (16.1 billion yen), Foipan for chronic pancreatitis and postoperative reflux esophagitis (8.8 billion yen), Kinedak for diabetic peripheral neuropathy (8.7 billion yen), Staybla for treatment of overactive bladders (6.4 billion yen), Rivastach for Alzheimer’s disease (3.9 billion yen), Onon for bronchial asthma and allergic rhinitis (7.3 billion yen), Elaspol for certain
kinds of acute lung injury (3.9 billion yen), and Onoact for the treatment of tachyarrhythmia during and postoperation (3.7 billion yen).

One key product is related to oncology—a treatment for chemotherapy-induced nausea and vomiting (7.9 billion yen in FY 2012) marketed as Emend in the form of capsules and as Proemend in the form of intravenous injection. The capsule version had been developed solely by Ono in Japan, was launched in December 2009, and has been marketed in Europe and in the United States by Merck & Co. The injection was launched in December 2011.

Ono Pharmaceutical has additional oncology-related candidates within its pipeline of global development projects. The candidate with the development code ONO-4538 (nivolumab) is undergoing Phase III clinical trials for indications such as melanoma, renal cell carcinoma, non–small cell lung cancer, and head and neck carcinoma. Nivolumab is a drug that can block a protein called programmed cell death 1 (PD-1), and is therefore also referred to as an anti-PD-1 immuno-oncology drug. In July 2014, nivolumab was approved for sale in Japan as a treatment for unresectable melanoma.

Ono Pharmaceutical entered into a collaboration with the U.S. company Medarex in 2005, enabling Ono to secure the Japanese rights to nivolumab. Medarex, which had started development of nivolumab for therapeutic use, was later acquired by Bristol-Myers Squibb (BMS). Ono and BMS have since collaborated on several of the trials being conducted by BMS, and the two firms are jointly developing the drug for treatment of renal cell carcinoma.

Research and Development
Research and development (R&D) activities at Ono Pharmaceutical have two distinct characteristics. First, the corporation is known for its active investment in R&D, with R&D expenditures between 30 and 32 percent of sales revenue from 2011 to 2013. This amount is much higher than that of most other Japanese pharmaceutical corporations, such as Astellas Pharma, Daiichi Sankyo, Eisai Co., Ltd., and Takeda Pharmaceutical, which all spent between approximately 18 and 23 percent for R&D during the same period. Second, Ono has organized a compound-oriented R&D process. A library of novel compounds is at the heart of the firm’s research into bioactive lipids and enzyme inhibitors. Ono continuously updates its compound-oriented process and library with technologies that aim to accurately and quickly pinpoint compounds that may be suitable for further development.

Ono applies the concept of open innovation, in the sense that its own original drug discovery methods may be combined with technologies acquired through alliances with Japanese or foreign companies, as well as through collaborations with academic and research institutions. Ono’s research staff is organized into project teams comprised of members from different departments. Drug discovery research is coordinated at the firm’s three Japanese laboratories—the Minase Research Institute, the Tsukuba Research Institute, and the Fukui Research Institute. The Minase Research Institute focuses on medicinal chemistry research and on the properties and efficacy of compounds and formulations. The Tsukuba Research Institute analyzes disease-causing substances and conducts exploratory research for new compounds that can control these substances, as well as focusing on genomics, metabolomics, and pharmacokinetics. Much of the Tsukuba facility’s research is in collaboration with academic and research institutions. The Fukui Research Institute concentrates on issues related to the safety of compounds as well as on mass production and cost reduction for the clinical and commercial supply of pharmaceutical substances.

Terje Grønning
University of Oslo

See Also: Astellas Pharma (Japan); Bristol-Myers Squibb (United States); Daiichi Sankyo (Japan); Eisai (Japan); Merck & Co. (United States); Takeda Pharmaceutical (Japan).

Further Readings
Oral Cancer, Childhood

Childhood oral cancers are very rare and present normally as benign and sometimes as malignant forms. Although these age-specific cancers differ from many characteristics of adult oral cancers, they are similar in their pattern of onset. Both begin as precancerous regions and then advance to benign or malignant tumors, which are further identified as sarcoma or carcinoma. Sarcoma is a malignant tumor that arises from mesenchymal origin, while carcinoma is a malignant tumor that arises from epithelial origin. Childhood cancers also follow the same TNM staging system as in adult cancers, where T stands for the size of the tumor, N stands for regional lymph node involvement, and M stands for extent of metastasis.

Childhood oral cancers often have symptoms that are nonspecific and different in onset, making detection and diagnosis difficult. On the other hand, cancer types and risk factors for these cancers are very specific and often have additive effects. These conditions are difficult to diagnose because children are not always aware or expressive of changes in their oral cavity. This is especially worrisome considering the need to identify and prevent further tissue overgrowth as early as possible. With time, many complications may occur, especially during sensitive developmental growth periods consistent with the timing of childhood cancers.

Signs and Symptoms
Diagnosis is difficult because the symptoms that children experience are different from those relevant to adult-onset cancers. In this respect, childhood cancer patients may experience analgesia or chronic pain in the oral cavity, neck, or face, sometimes accompanied by ear pain and observable weight loss. These symptoms cause confounding symptoms including continuous sore throat and difficulty in actions that involve opening the mouth while chewing, speaking, and swallowing. At the later end of childhood cancers, adolescents who abuse alcohol and tobacco can acquire red and white patches of tissue and bleeding in the oral cavity. In some cases, these present as continuing lesions in the mouth, neck, or face that do not heal and bleed easily. Additionally, it can be difficult for children to communicate the cause of their discomfort, oftentimes delaying detection, diagnosis, and exacerbating symptoms.

Risk Factors
Cancer occurs most frequently as the result of interactions between a person’s genes and the environment. Among children, previous radiation therapy to treat childhood tumors may increase the risk for oral cavity cancer as well as many other secondary cancers. Additionally, genetic disorders such as Fanconi anemia can also predispose a child to develop oral cancer, as well as other risk factors that increase the rate of cancer occurrence. These additional diseases and conditions include dyskeratosis congenita, a mutation in connexin genes, chronic graft-versus-host disease, epidermolysis bullosa, xeroderma pigmentosum, and human papillomavirus infection. Recently, human papillomavirus has become increasingly common and is associated mainly with an increase in oral cancer incidence among teenage girls.

Cancerous Precursors
Dysplasia is a precancerous tissue that presents as white or gray patches called leukoplakia, or as red, flat, relatively raised areas called erythroplakia, and may lead to cancer. When both of these symptoms are present, the tissue is referred to as erythroplakia. Dysplasias are graded on their microscopic appearance as mild, moderate, and severe. Severe cases may become cancers, while mild conditions have a high chance of full recovery. It is very important to prevent the advancement of dysplasia to cancer, especially in adolescent teens since the most frequent causes of dysplasia include alcohol consumption and smoking, which are highly avoidable.

Benign Tumors
Benign tumors occur within skeletal and smooth muscles and are often surgically removed because
they are unlikely to recur. There are many different types of benign tumors that originate from cells of the mouth or throat. These tumors are not life-threatening and likely do not cause problems since they normally remain within their site of origin. Examples of the more common benign tumors include hemangiomas, hamartomas, and lymphangiomas.

Salivary Gland Tumors
Many salivary gland tumors arise in the parotid gland, with 15 percent of salivary gland tumors arising in the submandibular and other minor salivary glands. The majority of these cancers are benign and can include sialoblastomas, which are usually found within the first few months of birth. Malignant salivary gland tumors generally arise as a result of radiation therapy and chemotherapy, which might have been given to treat primary leukemia or solid tumors. The malignant salivary gland tumors include adenocarcinoma, undifferentiated carcinoma, acinic cell carcinoma, and mucopepidermoid carcinoma. As long as these tumors are treated with complete surgical removal in combination with radiation and chemotherapy, these patients’ prognosis is good.

Malignant Tumors
Malignant oral tumors in children, although rare, usually occur as lymphomas and sarcomas. Oral squamous cell carcinoma in children, unlike adults, is rare. However, if oral squamous cell carcinoma is found in the adolescent population, the affected should be screened for Fanconi anemia, which increases the risk of some cancers in this age-group.

Treatment
Cancer treatments are available in the form of surgical intervention, radiation therapy, chemotherapy, or a combination of these therapies. Treatment of these cancers depends on the specific site of incidence, as well as the advancement of the overgrowth defined by factors characteristic to the tissue’s staging classification including extent/depth of invasion, tumor size, and presence/absence of regional lymph node metastasis. Treatment interventions are different for benign and malignant tumors. Since benign tumors are not hazardous, they are normally removed through surgical procedures. On the other hand, malignant tumors are treated by an individualized, patient-centered approach including a combination of surgery, chemotherapy, and/or radiation therapy.

Complications
Childhood oral cancers normally overlap with developmental growth periods, which makes them especially sensitive to the adverse effects of radiation therapy. This combination results in developmental changes including microdontia (smaller than normal teeth), early loss of teeth, and dental root abnormalities and xerostomia (dry mouth), which directly results in an increased risk for dental caries. Further, surgical procedures may remove too much tissue or radiation therapy may lead to tissue necrosis, both of which ultimately decrease muscle function such as trismus (limited mouth opening) and complicate functions including eating, chewing, and swallowing.

After removal or treatment of cancerous tissue, cancer patients are at an increased risk of developing secondary cancers. More specifically, these patients are at an increased risk of secondary head and neck cancers including salivary gland tumors, thyroid cancers, and cancers of the bone. In children, this threat is especially increased because they will live longer than average cancer survivors and will, therefore, have an increased risk of developing these cancers. Especially in the oral cavity, where turnover rate is high, the risk of developing cancer is greater.

David Jourabchi

University of California, Los Angeles School of Dentistry

See Also: Childcare and Cancer Risk; Childhood Cancers; Esophageal Cancer, Childhood; Nasopharyngeal Cancer, Childhood; Salivary Gland Cancer, Childhood.

Further Readings
Oral Cavity Cancer, Lip and

The oral cavity, similar to most of the human body, is lined and defined by connective tissue and is highly susceptible to cancer. The oral cavity is a region encompassed by the lip anteriorly, below and posteriorly by the circumvallate papilla (taste buds) of the tongue, and above the junction of the hard and soft palate superiorly. The lateral borders of the oral cavity are the anterior tonsillar pillars and glossotonsillar folds, which is where the oral cavity meets the oropharynx. The oral cavity contains many sub-sites that differ in cancer prevalence including the lip, tongue, floor of the mouth, lower alveolar ridge and retromolar trigone, upper alveolar ridge and hard palate, and buccal mucosa.

Cancers begin as precancerous regions and then advance to benign and malignant tumors. When a tissue is identified as a malignant tumor, it is further subclassified by two main suffixes—sarcoma or carcinoma. Sarcoma is a malignant tumor that arises from malignancies of mesenchymal origin, while carcinoma is a malignant tumor that arises from malignancies of epithelial origin. Cancers are recognized on a basis of stage 0 through 4 classification, in which larger numbers indicate more advanced cancers.

Cancer treatments include surgical interventions, radiation therapy, chemotherapy, or a combination. Treatment of these cancers depends on the advancement of the cancerous tissue and is defined by characteristics including extent/depth of invasion, tumor size, and presence/absence of regional lymph node metastasis.

Cancer occurs most frequently as an interaction between a person’s genes and the environment. Additionally, risk factors may increase the rate of cancer occurrence. In an attempt to reduce risk factors and decrease the likelihood of disease assembly, cancer prevention focuses on adjusting patients’ environmental and lifestyle factors.

Cancerous Precursors
Dysplasia is a precancerous tissue that presents as white or gray patches called leukoplakia, or as red, flat, relatively raised areas called erythroplakia, and may lead to cancer. When both of these symptoms are present, the tissue is referred to as erythroleukopla. Dysplasias are graded on their microscopic appearance as mild, moderate, and severe. Severe cases may become cancers, while mild conditions have a high chance of full recovery. It is very important to prevent the advancement of dysplasia into cancer, especially since the most frequent causes of dysplasia, including alcohol consumption and smoking, are highly avoidable.

Benign Tumors
Benign tumors occur within skeletal and smooth muscles and are often surgically removed because they normally remain within their site of origin. There are many different types of benign tumors that originate from cells of the mouth or throat and are not life-threatening.

Cancer Prevalence
Within the oral cavity, cancer within various sub-sites occurs at different prevalence rates and manifests numerous disease advancements. Subsites that require focused attention include the floor of the mouth, oral tongue, buccal mucosa (cheeks), and lip. Cancer of the floor of the mouth has tendencies to be locally invasive. Advanced forms of this cancer invade the bone of the mandible and metastasize to the lymph nodes. Cancer of the oral tongue is the
most common subsite for cancer in the oral cavity and is associated with the worst prognosis compared to other subsites. On the other hand, cancer of the buccal mucosa has the worst survival rate and highest probability to recur in the same region. This cancer is often found in more advanced stages because it is misdiagnosed as an infection or trauma. Cancer of the lip is usually characterized as squamous or basal cell carcinoma and is often diagnosed at early stages because the cancer is freely visible.

Squamous cell carcinoma is the most common among cancers of the oral cavity. First, these cancers are classified as carcinoma in situ, which means it is only present in epithelial cells (the outermost layer of cells). These cells then migrate to deeper layers of the tissue and are considered invasive. Additionally, the location of infection is crucial. For example, squamous cell carcinoma originating in the upper lip has a worse prognosis than in the lower lip.

**Symptoms**
Cancer patients may experience analgesia or chronic pain in the oral cavity, neck, or face, sometimes accompanied by ear pain and observable weight loss. These symptoms cause confounding symptoms including continuous sore throat and difficulty in actions that involve opening the mouth while chewing, speaking, and swallowing. Adults who abuse alcohol and tobacco can also acquire red and white patches of tissue and bleeding in the oral cavity. In some cases, these present as continuing lesions in the mouth, neck, or face that do not heal and bleed easily.

**Treatment**
Treatment of oral cancers differs based on progression of the tumor and is mainly divided into early (stages I and II) and advanced (stages III and IV). Surgery is preferred over radiation therapy for early cancers because it preserves more functional tissue. Radiation therapy is suggested to patients who have advanced stages of cancer, where surgery would be too invasive and result in severe loss of function. Ultimately, treatments combining surgery with concurrent radiation therapy showed the best results for patients with advanced cancer.

There are some complications that arise from surgical intervention and radiation therapy. Surgical interventions affect speech and swallowing functionality; however, these deficits can be reduced by ideal reconstruction of tissues and avoided in early-stage cancers. Some complications can occur during surgery, including infection, aspiration, bleeding, fistula, and flap loss. On the other hand, radiation therapy results in complications associated with radiotherapy toxicities, such as secondary cancers, and dry mouth, which continues posttreatment.

**Risk Factors**
Risk factors include environmental influences, hygienic tendencies, consumption patterns, and predispositions of some infections and genetic factors. Exposure to influences, such as radiation, and materials commonly found in the workplace, such as asbestos and pesticides, increases the risk of cancer in the oral cavity. Furthermore, exposure to irradiation for tumor intervention has been associated with salivary gland tumors and squamous cell cancers.

Poor oral hygiene and periodontal disease have also been linked to oral cancers. Further, consumption of tobacco has been found to be a causative factor for oral cavity cancer. Even light alcohol consumption has been associated with an increased
risk of oral cancer, specifically oropharynx cancers. Additionally, consumption of preserved meats with high levels of added nitrates has shown increased risk of nasopharyngeal carcinoma. Viruses and genetic predispositions can also increase the risk of cancer occurrence. For example, human papillomavirus (HPV) and Epstein-Barr virus (EBV) have been associated with squamous cell carcinoma and nasopharyngeal cancers, respectively. Genetic factors also increase the risk of oral cancer, as seen between Fanconi anemia and squamous cell carcinoma. Prevention of cancer involves avoiding or decreasing exposure to these risk factors.

David Jourabchi
UCLA School of Dentistry

See Also: Future of Cancer; Head and Neck Cancer; Nasopharyngeal Cancer; Oropharyngeal Cancer; Salivary Gland Cancer.

Further Readings


Organisation of European Cancer Institutes

The Organisation of European Cancer Institutes (OECI) had its origins in the desire and recognized need for collaboration and cooperation among the leading cancer research and treatment centers across Europe. The organization was initially modeled after the Association of American Cancer Institutes, founded in 1959, which proved to be an efficient mechanism for bringing together the most current knowledge and practices from cancer research and treatment centers across the United States. Other regional cancer organizations had also been formed in Latin America, Asia, and the Middle East; thus, a European organization was seen as part of a necessary trend toward making the fight against cancer an international one.

Over the course of the last half century, all of these regional cancer organizations have worked collaboratively in order to stimulate oncology research and improve the quality of treatment and care for cancer patients worldwide. The benefits of such collaborative efforts have been many, including more efficient and far-reaching research methods, multicenter cancer research studies and clinical trials, speedier development and approval of cancer medications, and overall improved diagnosis and treatment for cancer patients as well as lower mortality rates for various types of cancer.

Origins
Prior to the founding of the OECI, the many cancer institutes that existed in Europe were local organizations with their own histories and traditions, languages, and economic and political problems. This fragmentation caused many difficulties for researchers, physicians, and patients who sought...
the most up-to-date information about and treatments for cancer. The need for more cooperation in the fight against cancer was apparent to many in the field. A few international agencies dedicated to the fight against cancer did exist during the first half of the 20th century.

One of the most prominent was the Union for International Cancer Control (UICC), and it was under its auspices that the idea of the OECI was first conceived and implemented. In 1977, Pierre Denoix, then president of the UICC, called a meeting of leading European cancer institute directors to celebrate the anniversary of the Cancer Research Institute in Vienna. Denoix told his audience of more than 60 leading oncology experts from all over the world that he wanted the UICC’s Committee on International Collaborative Activities (CICA) to develop a plan to promote more communication and cooperation between the world’s cancer centers and institutes. His idea was enthusiastically supported by those attending, and the CICA members—six cancer institute directors from Eastern and Western Europe—began mapping out a framework for the OECI. The next year their plan was presented to members of the UICC’s Business Committee who were meeting at the 12th International Cancer Congress in Buenos Aires. In May 1979, a second meeting of the European Directors of Cancer Institutes was held in Dubrovnik, Yugoslavia, and the OECI was formally established.

The requirements for membership in the Organisation of European Cancer Institutes are fairly simple. A cancer institute wishing to become a member has to be located in Europe and has to follow a multidisciplinary approach to cancer. At the Dubrovnik meeting, an executive board for the OECI was formed and it set up two committees—a program committee and a membership committee—to develop a mission statement and guidelines for future activities. From the beginning, the OECI decided to link its activities to those of the UICC in the belief that both entities would benefit from increased collaboration between themselves and with other cancer organizations around the world. However, the OECI has developed its own unique collaborative programs and activities while maintaining ties with other regional cancer groups and with its sister organization, the Association of American Cancer Institutes.

Organization and Activities
The structure and organization of the OECI have undergone some changes since its founding in 1979. Originally composed of nine working groups and an executive board, the OECI was reorganized in 2005 when it was designated a European Economic Interest Grouping (EEIG). The EEIG designation provides a business and legal framework for the OECI and enables it to operate within a unified set of regulations without having to adapt its policies and procedures to the laws of individual European countries. The OECI remains a nonprofit, nongovernmental entity, but as an EEIG its operation has been streamlined, and coordination of its research and other projects has become more efficient and therefore more effective.

There are now six working groups within the OECI: accreditation and designation, biobanking and molecular pathobiology, communication and dissemination, cost benefit, palliative care, and Central and Eastern European countries. The last two are currently under development, but the others are fully operational. The accreditation group is responsible for developing assessment tools to evaluate European cancer centers that apply for designation as comprehensive cancer centers. As of 2012, 10 centers had gone through the accreditation process and five have been designated comprehensive cancer centers. The communication and dissemination working group oversees all forms of communication both within the OECI and between it and other cancer centers worldwide. In 2010, the OECI was officially designated a publishing entity and now produces books, pamphlets, and scholarly articles in its online journal eCancermedicalscience.

Perhaps the most important working group within the OECI is the biobanking and molecular pathobiology group. Under its guidance, a number of activities and platforms have been established to further cooperation and collaboration in cancer research throughout Europe and worldwide. For example, using EuroCanPlatform, developed with funding from the European Commission and various European ministries of health and research, the OECI has established TuBaFrost, a digital repository of tumor samples collected, catalogued, and made available to researchers through an open access database. START is another project sponsored and developed through the OECI. A state-of-the-art online database of information about
various topics relating to cancer, START has links to information on cancer for both professionals and the general public.

Carin Halper
Independent Researcher

See Also: American Association for Cancer Research; European Association for Cancer Research; National Cancer Institute.

Further Readings

Oropharyngeal Cancer

The word oropharynx describes the middle part of the throat in the oral cavity that includes the base of the tongue, the soft palate, the tonsils, the side and back wall of the throat, and the epiglottis. Patients with oropharyngeal carcinoma, or cancer that starts in the oropharynx, may present with a persistent sore throat, sore tongue, earaches, pain with swallowing, changes in voice quality, hoarseness, and enlarged lymph nodes, although some patients do not have any signs or symptoms. Historically, oropharyngeal cancer was grouped together with other squamous cell carcinomas of the head and neck due to similar characteristics and risk factors including alcohol and tobacco use. Recently, with the discovery of human papillomavirus (HPV) involvement in oropharyngeal cancers, oropharyngeal carcinoma (OPC) has been divided into HPV-positive and HPV-negative subtypes. Although tobacco use is still the leading cause of oropharyngeal carcinoma in the world, HPV is believed to be the leading cause of OPC in many developed countries. HPV-negative OPC is mostly associated with older age and alcohol and tobacco use, and its incidence is declining in the United States as tobacco use becomes less prevalent. HPV-positive OPC (HPVOPC) is associated with a greater number of sexual partners and is becoming more prevalent in the United States. These subtypes differ in presentation, gene expression, prognosis, and management.

HPV Status and the Classification of Oropharyngeal Carcinoma

The presence of HPV infection is an important clinical feature of OPC, as it often drives the presentation, prognosis, and management of patients with oropharyngeal carcinoma. HPVOPC usually presents in younger patients of higher socioeconomic status, while HPV-negative OPC presents in older patients with a history of smoking and/or alcohol use. Worldwide, approximately 65 percent of oral cavity cancer and 66 percent of pharyngeal cancers can be attributed to tobacco smoking, although these rates are higher in developing countries and lower in developed countries. Recently, HPV-DNA was found in two out of three cases of OPC in the United States, implicating it as the leading cause of OPC in the United States as well as in other developed countries. HPVOPC has a significantly better prognosis, with the three-year survival rate for patients with HPVOPC being 82.4 percent, compared to only 57.1 percent for those with HPV-negative OPC.

The primary lesion in HPVOPC is usually smaller, located in the tonsils or at the base of the tongue, and has more advanced lymph node involvement. Histologically, it is composed of nonkeratinized, poorly differentiated cells. HPV-negative OPC can be found anywhere in the oral cavity, oropharynx, hypopharynx, or larynx and is composed mostly of keratinized epithelium. The human papillomavirus contains two oncogenes, E6 and E7, which inhibit
the tumor-suppressor genes p53 and Rb, respectively. The inhibition of Rb leads to increased p16 expression, a feature unique to HPVOPC. HPV-negative OPC, on the other hand, is associated with an increased epidermal growth factor receptor gene copy number.

The leading cause of mortality in survivors of head and neck squamous cell carcinoma (SCCHN) is the development of second primary malignancies (SPMs), which may develop synchronously or metachronously as the original lesion. The etiology of SPMs in SCCHN has experienced a significant change over the past 30 years. In the late 1970s and early 1980s, oropharyngeal cancer carried one of the highest risks of a synchronous SPM among SCCHNs. However, since the early 1990s, there has been a gradual but significant decrease in the risk of synchronous SPMs in OPC, while the risk has remained steady in other head and neck SCCHNs. This decreased risk coincides directly with the increased prevalence of HPVOPC, leading researchers to believe that HPV-positive OPC is much less likely to present with synchronous SPMs. This may directly contribute to the improved prognosis of HPVOPC compared to HPV-negative OPC.

Treatment of Oropharyngeal Carcinoma
Due to its nature and location, a physician must take into account many factors when considering the treatment for OPC; these include stage, grade, location, and HPV status of the carcinoma. In the past, low-stage OPC was generally treated by a combination of surgery and radiation therapy, but radiation therapy alone is now preferred due to the high number of complications affecting speech and swallowing. Radiation therapy alone in low-stage OPC has comparable locoregional control and survival rates as surgery and radiation with lower rates of serious complications. Among OPC subtypes, HPVOPC is more sensitive to radiation therapy and is linked to improved outcomes. The advance of robotic surgery in recent years has led to a renewed interest in surgical treatment of low-stage OPC. Early studies reveal promising findings regarding functional and quality-of-life outcomes, although further studies are needed to determine an advantage over radiation therapy alone.

In more advanced disease (lymph node involvement, large tumor size, or invasive disease), survival is improved with the use of a chemotherapy regimen in addition to radiation therapy. The chemotherapy drug cisplatin administered concurrently with radiation therapy is generally considered the standard of care. With the revelation of HPV involvement in OPC, and the improved prognosis of HPVOPC, there is interest in tailoring therapy to the HPV status of OPC. Due to the comorbidities associated with high-dose chemotherapy and radiation therapy, ongoing clinical trials are studying the deintensification of chemotherapy and intensity-modulated radiation in treatment of HPVOPC. Researchers are hoping to maintain the efficacy of treatments while reducing morbidity and improving long-term mortality.

A 2006 trial revealed a significant improvement in the treatment of SCCHN with the addition of cetuximab (an epidermal growth factor receptor inhibitor) to radiation therapy. Although the HPV status of patients in the trial is not available, patients who benefited most from concurrent cetuximab therapy were younger, had primary oropharyngeal involvement, smaller primary tumors, and more extensive lymph node involvement, factors all indicative of HPVOPC. Subsequent trials studying cetuximab therapy must include the HPV status of oropharyngeal carcinomas to confirm that the response to treatment is related to HPV infection.

As HPV-positive OPC has become more prevalent over the past three decades, the prognosis of HPV-negative OPC has gradually improved. However, this has obscured the lack of improvement in the treatment of advanced HPV-negative OPC. Locoregional failure is the most common cause of failure of combined chemo- and radiation therapy. Novel therapies specific to HPV-negative SCCHN are currently being studied. A trial studying the use of the chemotherapy drug nimorazole in addition to radiation therapy shows improved survival specific to patients with HPV-negative SCCHN.

Conclusion
Although oropharyngeal carcinoma in humans has been a known pathology since the introduction of tobacco to the Western world, the recent differentiation of HPV-positive and HPV-negative OPC provides an opportunity for potential breakthroughs in both mechanism of disease and treatment. Researchers and physicians together will continue
Ovarian Cancer, Childhood

Ovarian cancer is the seventh of the 18 most common cancers in women worldwide. The global five-year prevalence of ovarian cancer is 22.6 per 100,000 people. Ovarian cancer is normally misdiagnosed or diagnosed late because there are often no symptoms at its early stages of development. With appropriate treatment, ovarian cancer can be contained or survived without further incident, as research has shown that the five-year survival rate for ovarian cancer is 30 to 50 percent.

Unlike the majority of ovarian cancer in adult women, which usually emerges in the form of epithelial carcinomas that begin in the cells on the surface of the ovary, childhood ovarian cancer emerges as a malignant germ cell tumor (GCT), a neoplasm derived from primitive embryonic gonad germ cells that begins formation in the egg cells of the ovary. Although epithelial tumors compose approximately 90 percent of ovarian tumors in adults, these are rarely seen in children. Rather, GCTs are the most common ovarian tumors in children and young women, composing about 70 percent of all cases. Ovarian GCTs compose 15 to 20 percent of all ovarian neoplasms and are the second-largest group of ovarian neoplasms. Overall, less than 5 percent of ovarian cancers originate as germ cell formations. Incidence of GCTs decreases as the patient’s age increases.

In children, ovarian tumors (or pediatric ovarian tumors) usually occur at birth or in girls’ early adolescence. The cause of these tumors is unknown; however, having certain inherited and nonhereditary disorders can increase one’s risk of developing germ cell tumors. A common noninherited syndrome known to be related to ovarian cancer in children is Ollier disease, a disorder of the skeleton; other inherited syndromes known to be linked to ovarian cancer in children include pleuropulmonary blastoma (PPB) and multinodular goiter (MNG). Epithelial tumors in children have the same morbidity and mortality as in adults.

Epithelial tumors can be benign or malignant; the majority of ovarian tumors in children are benign because the malignancy level decreases as the ovary matures and grows. The most common malignant ovarian tumors in children are dysgerminomas, accounting for 24.5 percent of all cancerous childhood ovarian tumors.

Seven percent of dysgerminomas are found in children less than 10 years old, while 34 percent are discovered in children between 10 and 19 years old. Another type of GCT common in children is immature teratomas, which constitute 28 percent of GCTs and 19.7 percent of childhood ovarian cancers; there are also yolk sac tumors (composing 7.2 percent of ovarian cancers in children), primary choriocarcinomas (0.9 percent), mixed germ cell tumors (8.6 percent), sex-cord stromal cell tumors (17 percent), and surface epithelial-stromal tumors (7 percent).

Symptoms and Treatment

There is usually about a three- to four-month delay in the clinical onset of ovarian cancer in children and the diagnosis of the disease; this is a result of...
Ovarian Epithelial Cancer

the variety of symptoms that can be experienced. Observed symptoms vary depending on tumor type, rapidity of tumor growth, tumor location, or degree of malignancy, among others. However, pain or mass in the abdomen are the most common symptoms in children. Tests that can be conducted to diagnose and stage ovarian cancer include blood tests, physical examination, computed tomography (CT) scan, ultrasound, and biopsy, among others. Laparotomy is often conducted for both diagnosis and treatment.

Treatment options for ovarian cancer in children, which include surgery, radiation therapy, and combination chemotherapy, depend on where the tumor is located, type of tumor, and level of malignancy, among other factors. If the tumor has spread beyond the ovary, a total hysterectomy, bilateral salpingo-oophorectomy, appendectomy, and omentectomy need to be performed. However, if the tumor has not spread, unilateral salpingo-oophorectomy with a biopsy of the opposite ovary can be done. It is recommended that treatment options be individualized in order not to harm the reproductive potential of the child later in life.

It is difficult for researchers to obtain tissues for study purposes due to the uncommon nature of childhood ovarian cancer; thus, treatments have mostly been performed on mouse models. Further, a lack of funding for childhood ovarian cancer, and all childhood cancers, greatly limits research advancements. Nevertheless, recent improvements in research have led to a better understanding of the causes of ovarian cancer in children. One of the discoveries is that the presence of a genetic material from a Y chromosome is necessary for a germ cell to be cancerous; however, how this leads to ovarian GCT is still not known. Thus, more research and funding are essential.

Lara Lengel
Dinah Adjo Tetteh
Bowling Green State University

See Also: Age; Childhood Cancers; Ovarian Epithelial Cancer; Ovarian Germ Cell Tumor; Ovarian Low Malignant Potential Tumor; Unusual Cancers of Childhood; Women's Cancers.

Further Readings

Ovarian Epithelial Cancer

Ovarian epithelial cancer is a type of ovarian cancer that develops when cancerous cells form in the tissue covering the ovary. It accounts for about 75 percent of all ovarian tumors and about 90 percent of all ovarian malignancies. The global incidence of ovarian epithelial cancer varies greatly; Scandinavia, Israel, and North America have the highest incidence of the disease, while the lowest incidence rates are seen in developing countries and Japan. The five-year survival rate for the disease rose from 37 percent in the 1970s to 45 percent in the 1990s and early 2000s.

As is the case with ovarian cancer in general, the common risk factor for ovarian epithelial cancer is family history of ovarian or breast cancer;
family history accounts for about 5 to 10 percent of all cases of ovarian epithelial cancer. Specifically, women with at least one first-degree relative (mother, sister, or daughter) or at least one second-degree relative (grandmother or aunt) with ovarian cancer are at higher risks of ovarian epithelial cancer. Other risk factors include environmental and dietary factors including use of talcum powder that has asbestos, a high-fat diet, consumption of lactose, delayed childbearing, late menopause, and early menstruation, among others.

In the United States, since the 1970s talcum products for use in the home have been required by law to be asbestos-free; this requirement is based on the relationship between asbestos and ovarian cancer risks. Factors known to reduce a woman's ovulation cycle, including the use of oral contraceptives, breast-feeding, and multiple pregnancies, are also known to reduce the risk of ovarian epithelial cancer.

Women at high risk of developing ovarian epithelial cancer can undergo a procedure called prophylactic oophorectomy to have healthy ovaries removed so they do not become cancerous. Ovarian epithelial cancer is usually diagnosed in women of advanced age (median age is 63); between 3 and 17 percent of women 40 years old or younger are diagnosed with the disease.

Two main hypotheses have been advanced to explain occurrences of ovarian epithelial cancer. First is the incessant ovulation hypothesis, which holds that repetitive damage and repair of the ovarian surface as a result of continuous ovulation eventually leads to mutations in the epithelial cells. The other is the gonadotropin theory, which maintains that excessive stimulation of the gonadotropin strain the ovarian surface and leads to epithelial cell mutation.

Characteristics and Symptoms
Ovarian epithelial cancer can spread to other parts of the body through tissue, the lymph system, or the blood. Its histological classification (i.e., the type of tissue from which the cancer originates) includes serous cystomas, mucinous cystomas, endometrioid tumors, and clear cell tumors, among others. Each of these is further classified as benign, malignant (invasive), or borderline (low-malignant potential). The majority of ovarian epithelial cancers are benign (not cancerous); these include serous adenomas, mucinous adenomas, and Brenner tumors. The cancerous ones begin in the tissue that lines the ovaries, and about 70 percent of cancerous epithelial tumors are diagnosed late.

Ovarian epithelial cancer can be recurrent (meaning that it has come back) or persistent (meaning that it did not go away after treatment). Ovarian epithelial cancer does not show symptoms during the early stages. Common signs include pains or swelling in the abdomen; pain in the pelvis; and having gas, bloating, or constipation.

Detection and Treatment
To find out its level and specific location, ovarian epithelial cancer is normally staged through surgery. Blood tests to measure one's cancer antigen (CA 125) level are required as a follow-up test and to restage the cancer. A higher CA 125 level points to a higher likelihood of ovarian epithelial cancer; however, a negative CA 125 level does not indicate absence of the disease. Thus, CA 125 levels are used with histologic diagnosis to determine the presence of ovarian epithelial cancer.

The standard treatment for ovarian epithelial cancer includes surgery, radiation therapy, and chemotherapy; more treatment options are being tested through clinical trials. Treatment options may depend on the stage of the cancer and whether the cancer is recurrent or persistent. Research has shown that about 80 percent of ovarian epithelial cancer patients will relapse/recur after first-line platinum-based and taxane-based chemotherapy/treatment; thus, after completing treatment patients are closely monitored with follow-up CA 125 tests at intervals of one to three months.

When detected early, ovarian epithelial cancer survival has improved, given empirical optimization of chemotherapy combinations and surgery. Nevertheless, ovarian epithelial cancer is the fifth-leading cause of cancer-related deaths in the United States.

Lara Lengel
Dinah Adjo Tetteh
Bowling Green State University

See Also: Menarche, Early; Ovarian Cancer, Childhood; Ovarian Germ Cell Tumor; Ovarian Low Malignant Potential Tumor; Religion: Jewish Women and Cancer Risk; Women’s Cancers.
Further Readings

Ovarian Germ Cell Tumor

An ovarian germ cell tumor is a disease caused by tumors developing in the egg-producing cells. Ovarian germ cell tumors are rare and account for about 2 to 3 percent of all ovarian cancers; 3.7 per one million women are affected annually. Most germ cell tumors are benign (noncancerous), but some are malignant (cancerous); they can be recurrent (if the tumors return after initial treatment) or persistent (if the tumors did not go away after treatment). Cancerous germ cell ovarian tumors occur mostly in teenagers and young women in their 20s and often affect only one ovary.

Unlike the majority of ovarian cancer in adult women, which usually emerges in the form of epithelial carcinomas that begin in the cells on the surface of the ovary, childhood ovarian cancer emerges as a malignant germ cell tumor (GCT), a neoplasm derived from primitive embryonic gonad germ cells that begins formation in the egg cells of the ovary. Although epithelial tumors account for approximately 90 percent of ovarian tumors in adults, these are rarely seen in children. Rather, GCTs are the most common ovarian tumors in children and young women, composing about 70 percent of all cases. Ovarian GCTs compose 15 to 20 percent of all ovarian neoplasms and are the second-largest group of ovarian neoplasms. Overall, less than 5 percent of ovarian cancers originate as germ cell formations. Incidence of GCTs decreases as the patient’s age increases.

There are different types of ovarian germ cell tumors; each behaves differently and is treated differently. The World Health Organization (WHO) has classified ovarian germ cell tumors into dysgerminoma, endodermal sinus, teratoma, choriocarcinoma, embryonal carcinoma, polynembryoma, mixed GCT, and combo GCT/stromal. Of these, dysgerminoma is the most common, accounting for 40 to 50 percent of ovarian germ cell tumor cases; about 15 to 25 percent of dysgerminomas recur. Teratomas are classified as immature (malignant), mature (dermoid cyst), and specialized (struma ovarii and carcinoid tumors).

The mature teratoma is mostly benign and can contain noncancerous tissues including bone, hair, and teeth. Immature teratoma can contain tissues
Ovarian germ cell tumors are treated with surgery and chemotherapy; however, if the patient is young, fertility-sparing and fertility-preserving surgical procedures including unilateral salpingo-oophorectomy are performed. Following fertility-preserving surgery and adjuvant chemotherapy, girls and young women who have survived malignant ovarian germ cell tumors can experience normal menarche and menstruation.

Bilateral salpingo-oophorectomy and hysterectomy are performed if the patient has completed childbearing. Chemotherapy as a treatment option can lead to secondary malignancies (i.e., cancers caused by treatment with chemotherapy) such as acute myelogenous leukemia (AML).

There are no known causes of ovarian germ cell tumors; recent studies have indicated an inverse association between family history of ovarian cancer and ovarian germ cell tumors. Ovarian germ cell tumors are hard to diagnose, and thus are often diagnosed late because there are no symptoms in the early stages. The common symptoms are swelling and/or pain in the abdomen and vaginal bleeding after menopause.

Elevated cancer antigen (CA 125) levels can also indicate presence of ovarian germ cell tumors, but these can be nonspecific. A physical exam, pelvic exam, laparotomy, computerized tomography (CT) scan, and serum tumor marker are tests that can be used to diagnose ovarian germ cell tumors. Ovarian germ cell tumors secrete biologic markers such as β-HCG and a-fetoprotein (AFP); these can be used to monitor treatment results and recurrent incidences.

Ovarian cancer is the seventh of the 18 most common cancers in women worldwide. The global five-year prevalence of ovarian cancer is 22.6 per 100,000 people. Ovarian cancer is normally misdiagnosed or diagnosed late because there are often no symptoms at its early stages of development. With appropriate treatment, ovarian cancer can be contained or survived without further incident, as research has shown that the five-year survival rate for ovarian cancer is 30 to 50 percent. Chances of recovery and treatment options (prognosis) depend on the type of cancer, the size of the tumor, the stage of the cancer, and the person's general health status.

With improvement in research, about 90 percent of malignant germ cell tumors are now curable. However, if the disease recurs, this normally happens within one year after diagnosis. Recent developments in chemotherapy regimens, more precise staging of the disease, improved radiographic imaging, and improved supportive care, among others, have led to improved survival rates of ovarian germ cell tumors.

See Also: Age; Extracranial Germ Cell Tumor, Childhood; Extragonadal Germ Cell Tumor; Ovarian Cancer, Childhood; Ovarian Epithelial Cancer; Ovarian Low Malignant Potential Tumor; Religion: Jewish Women and Cancer Risk; Women's Cancers.

Further Readings


Ovarian Low Malignant Potential Tumor

Ovarian low malignant potential (LMP) tumor is a disease that occurs when tumors form in the tissue covering the lining of the ovary. These types of tumors usually remain in the ovary and do not become cancerous. Ovarian LMP tumors, also known as borderline tumors or atypical proliferative tumors, show features or characteristics that are between benign ovarian tumors and malignant ovarian cancers. The unique characteristic of borderline ovarian tumors is that they do not invade the ovarian stroma. Ovarian LMP tumors account for 10 to 20 percent of all ovarian epithelial cancers. The incidence rate is 1.5 to 2.5 per 100,000 people per year.

The risk factors of ovarian LMP tumors include delayed childbearing or not having children, infertility, and aging rapidly among others. Breast-feeding, use of oral contraceptives, and multiple pregnancies can decrease one's risk of developing ovarian LMP tumor. Research findings are inconclusive as to whether BRCA1 (breast cancer 1, early onset) and BRCA2 (breast cancer 2, early onset) mutations are related to ovarian LMP tumor risk. However, certain mutations in the TP53 (tumor protein p53), BRAF, and KRAS genes have been found to be associated in varying degrees with risk of ovarian LMP tumor. Ovarian LMP tumors are usually diagnosed in women in their reproductive years; about 27 percent of patients are less than 40 years old.

There may not be signs for ovarian LMP tumor; about 16 percent of patients do not observe any symptoms at the time of diagnosis. However, if there are symptoms, they are usually in the form of abdominal swelling or pains, pain in the pelvis, constipation, gas, or bloating. Ovarian LMP tumor is usually diagnosed at an early stage and because patients are usually young, treatment options should be mindful of preserving the fertility of patients. Tests performed to diagnose and stage ovarian LMP tumor include physical exam, pelvic exam, ultrasound, CT (computerized tomography) scan, CA 125 (cancer antigen 125) blood test, and biopsy, among others.

When seen under the microscope, the LMP tumors cannot be clearly identified as cancerous. A biopsy is usually performed to confirm that the tumor is low malignant. Ovarian LMP tumor is classified as Stage I, Stage II, Stage III, and Stage IV depending on how the mutated cell has spread in the ovary and to other parts of the body; it is important to know the stage of the disease in order to choose appropriate treatment options. The common types of ovarian LMP tumors are the serous and mucous subtypes; the serous type accounts for 43 to 53 percent of all LMP tumor cases, while the mucous type accounts for 42.5 to 52 percent. Serous ovarian LMP tumors affect both ovaries (bilateral) in one-third of the cases. Eighty-five percent of mucous ovarian LMP tumors are intestinal, while 15 percent are endocervical.

Surgical treatments for ovarian LMP tumor include unilateral or bilateral salpingo-oopherectomy and hysterectomy; the type of surgery performed depends on the stage of the tumor and whether the patient wants fertility to be conserved. Chemotherapy may be considered if the tumor was diagnosed at an advanced stage; however, some studies suggest that chemotherapy and radiotherapy are not effective for treating the disease. Also, there is evidence that hormone treatment can be used to treat ovarian LMP tumors. Research has shown that about 15 percent of ovarian LMP tumors may recur about 20 years or more after the initial diagnosis. Recurrence rates are higher if conservative surgical treatment was used; conservative surgery, which involves complete staging and preservation of the uterus and at least one ovary, is preferred for fertility-sparing and hormonal functional purposes. Radical surgery, on the other hand, has a lower recurrence rate. Thus, there is a need for patients to be aware of the advantages and
disadvantages of both the conservative and radical surgery treatment options. Recurrences can be treated if detected early.

The 10-year survival rate is about 95 percent; the survival rate can be even better depending on age at which patient was diagnosed, the stage, and the type of tumor.

It is recommended that the gynecologic oncologist collaborates with the reproductive endocrinologist to ensure preserving the fertility of the patient. Follow-up is recommended, especially, if the conservative method of treatment was used.

Lara Lengel
Dinah Adjo Tetteh
Bowling Green State University

**See Also:** Developing Countries; Disparities Within Nations (Elimination of Cancer); International Society of Paediatric Oncology; National Childhood Cancer Foundation; Ovarian Cancer, Childhood; Ovarian Germ Cell Tumor; Society of Gynecologic Oncology; Women’s Cancers.

**Further Readings**


Pain and Pain Management

During the past decade, video games have provided new ways to effectively alleviate the pain experienced during cancer treatment. Several theories explain how involvement in entertainment media reduces the experiences of pain. While the brain is engaged in entertainment, it has less capacity to process pain. This article discusses the recent pain management research that demonstrates how video games are rapidly becoming an important factor in cancer treatment.

Growth of Video Games

Since the first video game appeared on an oscilloscope screen in 1958, video games have rapidly proliferated to become an important part of popular culture. T. Baranowski and colleagues define a video game as “any game played on a digital device and encompasses a wide range of games played at arcades, over the Internet on personal computers, or on dedicated game consoles (e.g., Nintendo GameCube, Sony PlayStation, or Microsoft Xbox) or handheld units (e.g., Nintendo Game Boy, Sony PSP).” Active video games like Nintendo Wii and Xbox Kinect have become extremely popular among children and adolescents. In 2012, for example, Nintendo Wii sold 99 million game consoles worldwide. In a study of children and adolescents, D. Roberts, U. Foehr, and V. Rideout found that in 2005, the 8- to 10-year-olds in their study spent an average of 65 minutes per day playing video games; and the 11- to 14-year-olds spent an average of 52 minutes per day playing video games. A. Lenhart and colleagues reported that 97 percent of American youth between 12 and 17 years of age reported playing video games. In a study of seventh- and eighth-graders’ media use, 94 percent indicated that they had played video games within the past six months, and half of them said they had played a video game within the previous day. C. K. Olson and colleagues’ 2007 study of children’s video game use several years ago indicated that 94 percent of seventh- and eighth-graders played video games within the previous six months, and at least half reported playing games the day before they completed the survey. These studies demonstrate that video games reach large and diverse audiences of young people who spend a considerable amount of time and attention playing them. The long-term and widespread exposure to video games makes them a powerful potential motivator of behavior change.

Theoretical Foundations for Video Game Effects

Given the wide popularity of video games among youth and their potential to affect health beliefs and practices, their growing use in the fields of health
and medicine is of no surprise and is one of the most exciting new uses of communication technology in the 21st century according to W. J. Brown. There are several important communication theories that explain how video games influence video game consumers. One group of theories falls under the general heading of audience involvement, broadly defined as the degree of psychological response by a person to a mediated message or persona. Involvement is a dynamic process in which a motivational state of arousal forms and fluctuates both during and after media consumption. P. Vorderer distinguished two levels of audience involvement: a low-level involvement characterized by media consumers who are distant and analytical, and a high-level involvement characterized by cognitively and emotionally engaged media consumers. Drawing on entertainment media theory, C. Klimmt, D. Hefner, and Vorderer’s 2009 research of video game experiences shows video game users experience high levels of involvement, which increases their media enjoyment.

One specific form of audience involvement in media narratives is called transportation. M. C. Green describes the process of transportation as becoming “cognitively and emotionally involved in the story.” Green and T. C. Brock used the phrase transportation into a narrative world to describe the power of narratives to totally immerse audiences into a story, such as when a reader is “lost in a book.” Although originally focused on written fiction, the study of transportation into narrative worlds has evolved beyond audience involvement with novels and now encompasses all forms of media, including video games, according to Brown. Transportation theory provides a powerful explanation for understanding the potential for video games to decrease pain experienced during medical treatments. Closely related to transportation theory is the attentional hypothesis, which explains how the brain functions when people focus their attention. The attentional hypothesis explains that virtual reality reduces pain by creating an entertainment experience that captivates the attention of patients receiving medical treatment, thus diminishing the brain functions that register pain, as reported by H. G. Hoffman and colleagues.

Another important theoretical framework for understanding the effects of entertainment media is A. Bandura’s 2004 social cognitive theory. Bandura explains how media consumers role model the characters they engage in narratives and other forms of entertainment programming. His research shows that when positive characters reap beneficial outcomes in a story and negative characters reap negative consequences, then audiences are motivated to adopt the positive beliefs and behavior of those who are rewarded. Thus personae (virtual characters) in video games can provide exemplary role models for patients receiving medical treatment. One of the important components of Bandura’s theory is self-efficacy, or the belief that a person has that he or she can enact a specific behavior that is being advocated. For example, a cancer patient receiving chemotherapy must believe that he or she can develop the skills and confidence needed to manage the treatments successfully in order to minimize the potential negative side effects of chemotherapy.

In summary, video games create a high level of audience involvement, provide media enjoyment, present potential positive role models for beneficial health beliefs and practices, and transport those who play them into narrative worlds that can divert attention away from the pain experienced during medical treatments.

Video Games for Pain Management

Several video games that are commercially available have been shown to have beneficial therapeutic effects for cancer patients dealing with the negative side effects of their treatment, including nausea, vomiting, anxiety, and pain from chemotherapy and radiation treatments. B. A. Primack and colleagues’ 2012 review of the academic literature indicates that active interventions based on video games improved 59 percent of the physical therapy outcomes, 50 percent of the physical activity outcomes, and 42 percent of pain distraction outcomes. Their own study of the daily use of Nintendo Wii games by children for at least 30 minutes and during hospitalization for an eight-week period to manage the pain of cancer treatments is now in progress, with expectations that Nintendo use will significantly improve the pain management of the treatments.

One of the first video games used by doctors to lessen pain is called Snow World, the first virtual world custom-designed for burn patients. When patients play this game, they can cognitively
transport themselves into an immersive virtual world that reduces their pain experience. Patients are distracted from focus on their painful burn wounds by wearing a virtual reality (VR) helmet, which enables them to see themselves floating through an icy 3-D canyon where they can shoot snowballs at snowmen, igloos, and penguins. D. A. Das and colleagues found that playing *Snow World* can reduce patients’ pain ratings during severe burn wound care by 30 to 50 percent.

As noted above, virtual reality games can reduce experiences of pain by creating an alternate entertainment experience that captivates the attention of patients receiving medical treatment. M. Griffiths reported one case study of an 8-year-old boy with neurodermatitis and scarring due to continual picking at his upper lip. Conventional treatments had failed to help him, but after he was given a handheld video game, within two weeks the affected area healed. Medical researchers at the University of Maryland tested a 3-D underwater virtual reality video game called *Free Dive* during medical procedures for children. Their research indicated that children engaged in *Free Dive* were able to better manage painful medical procedures.

T. Baranowski and colleagues reviewed 27 articles in 2008 that reported the effects of 25 different video games on health-related behavior changes. Many of the games they examined exhibited three characteristics that contributed to their effectiveness in promoting positive health behaviors. First, they merged the immersive, attention-maintaining properties of stories and fantasy. Second, they provided engaging properties that generated a high degree of interactivity. Finally, the behavior-change technology enabled its users to engage in role modeling, vicarious identifying experiences, and learning a story’s “moral,” among other change possibilities.

**Effects of Video Games on Cancer Treatment**

The positive effects of video games in helping medical patients to divert their attention away from the pain of medical procedures and treatments makes them an important source of pain management for cancer patients receiving radiation and chemotherapy. Controlled studies using both treatment and control groups with random assignment show that video games can provide cognitive distraction for children during chemotherapy for cancer and treatment for sickle-cell disease. These studies indicated that distracted patients had less nausea and lower systolic blood pressure than control groups (who were simply asked to rest) after treatment and needed fewer analgesics. D. J. Kolko and J. L. Rickard-Figueroa assessed the effects of video games on three young male cancer patients aged 11, 16, and 17. All three patients had been distressed before their chemotherapy treatments, but after playing video games, their anticipatory symptoms decreased, as did aversive chemotherapy side effects that they had previously experienced. In two studies of cancer patients ranging in age from 9 through 20, W. H. Redd and colleagues found in 1987 that patients who played a video game for 10 minutes during chemotherapy induction significantly experienced less nausea compared with control group patients. Children assigned to the video game group condition could choose from 25 different games on an Atari 800 XL computer system. Another study by J. Vasterling and colleagues in 1993 explored cognitive distraction through video games in comparison to standard relaxation techniques with a control group of young cancer patients. The patients who played video games experienced less nausea prior to chemotherapy and had lower blood pressure following chemotherapy compared with the patients who used the standard relaxation techniques. There were no differences in the effectiveness of the cancer treatments between the video game group and the control group. However, the administration of the standard relaxation techniques, requiring a trained therapist, was substantially more expensive than making video games available to patients.

In a 2008 study, P. M. Kato and colleagues investigated the effects of *Re-Mission*, a video game designed for adolescents and young adults with cancer. The objective of *Re-Mission* is to improve cancer treatment by helping young people manage pain during their treatments. The game features a nanobot named Roxxi that navigates through the bodies of cancer patients to destroy cancer cells and tumors with chemotherapy and radiation. Roxxi also fights against side effects of cancer treatment such as pain, nausea, infection, and constipation. Their study of 374 cancer patients aged 12 to 29 from 34 medical centers in the United States, Canada, and Australia indicated that those who played
Re-Mission over a three-month period maintained higher levels of chemotherapy in their blood and took their prophylactic antibiotic medication more frequently as prescribed than patients in the control group. In addition, patients who played Re-Mission showed greater increases in knowledge about cancer and increased self-efficacy to manage their cancer than patients in the control group. The research showed that a video game made specifically for young people with cancer can significantly increase important health behaviors that are related to survival outcomes.

Kato’s 2010 review of video game medical research shows that tailor-made games for specific medical treatments go beyond the strengths of commercial games in their ability to increase specific disease-related knowledge about self-care. He found that even though commercial video games have superior graphics and gameplay, medical patients give high ratings of acceptability to video games designed for patients fighting specific illnesses and find them engaging.

Conclusion
The academic literature indicates that video games can have powerful positive effects on health beliefs and practices. In particular, the high degree of psychological involvement created when people become immersed in video games and transported into narrative worlds has made video games an important means of pain management for cancer patients. In addition to reducing the pain experienced during chemotherapy and radiation, video games also can increase patients’ self-efficacy in successfully dealing with the potential negative effects of cancer treatment. Video games increasingly will serve an important role in successful cancer treatment in the future.

William J. Brown
Regent University

See Also: Chemotherapy; Media; Radiation Therapy.

Further Readings


---

**Paint**

Paint is a liquid or liquefiable composition that dries into a solid film after being applied in thin layers, and is used to apply color, texture, or protective coating to objects. Paint is one of the oldest human technologies, dating back at least tens of thousands of years. The technology to make paints has changed over time, with different media used for the base (egg yolks, oils, and water are among the possibilities) and different methods used to obtain pigment.

Today, paint pigments are taken from both natural and synthesized sources. Many paints are toxic—lead-based paints were common in household use before their toxicity was well understood—and studies have found correlations between working in the painting trades or paint manufacturing industry and the development of cancers of the lung, bladder, liver, esophagus, larynx, and oral cavity.

The film-forming component of paint is called the binder or vehicle, and it provides the adhesive properties of paint, as well as contributing to the gloss, flexibility, and toughness of the dried product. Binders used today include oils, epoxy, melamine resins, polyesters, polyurethanes, vinyl-acrylics, acrylics, and alkyds. Casein, derived from milk, has been used in paint since ancient Egypt and remained the tempera paint binder of choice until the 1960s, though it is still used today. It has been found not only to be an allergen for a small percentage of the population but to promote carcinogenesis, according to one Chinese government study; however, the study focused on casein consumption through milk drinking, and it is not clear that even chronic exposure to casein in other contexts would have the same effect.

In addition to the pigment, which may be derived from calcium carbonate, mica, silica, talc, various clays, and even insect sources or from synthetic sources, paints contain fillers that thicken the film, such as talc, lime, or diatomaceous earth. Some
Paints may also include antifreeze additives or additives that affect the speed at which they dry or the effects of ultraviolet light or age.

Lead paints include lead chromate, or chrome yellow, and lead carbonate, or white lead. When added to paint, lead makes the resulting film more durable, resists moisture in order to avoid corrosion of metal surfaces, and speeds drying. It is also one of the most widely known environmental and health hazards and has been banned from household paints in the United States since 1978.

Lead paint continues to be used in some other countries, as well as on outdoor signs and other applications. Asbestos paint is less known, though the general public is aware of the dangers posed by asbestos in general. Asbestos exposure is linked to a large number of respiratory problems, including most seriously mesothelioma, lung cancer, and chronic obstructive pulmonary disorder (COPD). It was used in paints for a long time because of its fire resistance, which therefore was thought to add additional safety to whatever was being built and painted. It is not often found in this form in new paints but remains in use in old paints. The mechanism by which asbestos causes lung cancer seems to be mechanical: the very small fibers of asbestos irritate the lung tissue and may be small enough to actually cause gene damage mechanically. Many of the solvents used in paints are associated with a host of health hazards, in some cases applicable only in accidental ingestion or chronic exposure. Inhalation of large amounts of vapor from most solvents will lead to unconsciousness, for instance, which is sometimes exploited recreationally but which can lead to permanent blindness or even death. Methanol, or “wood alcohol,” is one of the most dangerous in this respect, and it is additionally dangerous because it burns with an invisible flame. Chronic exposure to solvents in the workplace, such as in the painting trades or the paint manufacturing industry, can lead to neurotoxic effects as well as to a host of cancers and hypotension. There is also a correlation between exposure to solvents and alcoholism.

Benzene, found in many professional paints and paint sprays, is strongly linked to aplastic anemia, bone marrow abnormalities, acute myeloid leukemia, myelodysplastic syndrome, acute lymphoblastic leukemia, and chronic myeloid leukemia. It can also lead to birth defects and damage to the liver, kidneys, lungs, heart, brain, and DNA strands. Asbestos is thought to cause as much as 80 percent of all mesothelioma cases.

Benzene is a volatile organic compound (VOC), and one of several that is often used in paint. Others include aliphatic hydrocarbons, ethyl acetate, glycol ethers, and acetone. In addition to several VOCs being carcinogens, they are believed to play a role in so-called sick building syndrome when they are used to paint and coat the interiors of buildings or are otherwise used in their construction and contents. They frequently cause allergic or immune system reactions in adults and children alike and they react with other airborne chemicals like nitrogen oxides to produce secondary aerosols that cause irritation; damage the liver, kidneys, and central nervous system; and can cause discomfort of the nose and throat, allergies, nausea, nosebleeds, fatigue, loss of coordination, and chronic headaches or dizziness. Historically, many traditional paints included a variety of heavy metals.

These are currently used less commonly, and when they are used, they are accompanied with health warnings. Cadmium, for instance, is associated with kidney damage resulting in excess protein in the urine, lung inflammation, osteomalacia, and lung cancer, as well as being used to make yellow paints. Arsenic, a well-known poison, can also cause hyperkeratosis, diabetes, and cancer. Chromium can cause lung cancer, acute renal failure, gastrointestinal hemorrhage, and lung cancer. Mercury is linked to diarrhea, fever, vomiting, and a variety of nerve disorders. Cobalt can induce cardiomyopathy, contact dermatitis, and intoxication. Nickel sulfide is a carcinogen, and some people are allergic to nickel in any form. Selenium, although an essential trace element in nutrition, is toxic in excess, leading to cirrhosis of the liver and death. Titanium dioxide, which is used in both paint and sunscreens, is a Group 2B carcinogen according to the International Agency for Research on Cancer, meaning “possibly carcinogenic to humans.” Titanium dioxide pigment is suspected to cause lung cancer and gene damage, although a link has not been found between carcinogenesis and occupational exposure.

Bill Kte’pi
Independent Scholar

See Also: Acrylic Rubber and Fibers; Chemical Industry; Lead.
Further Readings

Pakistan

The south Asian nation officially termed the Islamic Republic of Pakistan has historically been the location of numerous cultures, kingdoms, and peoples. In the decades before Pakistan declared its sovereignty in 1947, the nation was a part of India and thus, by extension, under British rule. After independence was declared in 1947, the people created a new constitution that instituted the Islamic Republic of Pakistan. The country is currently one of the top 10 most populated countries in the world, having over 180 million citizens. Pakistan is currently facing huge obstacles in its battle against cancer, and nowhere is this more apparent than in the nation’s struggle against breast cancer. Pakistan experiences some of the highest rates of breast cancer in the entire world, as it is estimated that over 10 percent of all Pakistani women will be diagnosed with the disease in their lifetime.

The problem is that there are extreme cultural obstacles impeding access to cancer care for Pakistani breast cancer patients; in the nation, which is very conservative culturally, even uttering the phrase breast cancer can be cause for public backlash as a result of its perceived sexual connotations. In light of the negative connotations surrounding breast cancer, many women in the country refuse to seek treatment for the disease, much less have themselves checked for a diagnosis. Because breast cancer is the leading cancer of women in the country, resulting in over 40,000 fatalities a year, much needs to be done to raise public awareness of the issue, though this will be difficult. A recent survey conducted at Pakistan’s Rawalpindi General Hospital revealed that nearly three-fourths of the women surveyed had no idea what breast cancer is, nor its health implications.

For Pakistan, there are many, more difficult issues related to cancer treatment in the country. For instance, Pakistan has no nationally representative cancer registry with which to track cancer trends in the country. Also, in general, Pakistan’s health care industry is internationally regarded as lackluster. The nation simply does not have the funding that is required to aggressively combat domestic incidences of cancer, which has led to the country’s not being able to afford advanced treatment facilities and the newest cancer drugs. Even the vast majority of the hospitals that Pakistan currently has are not outfitted with cancer screening or treatment equipment.

The lack of medical funding, specialist facilities, and cancer drugs has thus instigated the cancer crisis that the nation is currently facing. Due to cultural taboos and lackluster health care, a large portion of Pakistanis who are faced with a cancer diagnosis will first go visit their local tribal healers for treatment. Usually when Pakistani cancer patients are finally seen by medical experts, they have waited so long that their cancer has advanced to the point of it being virtually untreatable. Though Pakistan has no national cancer registry, inferences can be made from the Karachi regional registry with regard to incidences and trends in the country. Presently, data suggest that the most prevalent forms of cancer in Pakistan are breast cancer, laryngeal cancer, liver cancer, oral cancer, and ovarian cancer.

In light of the fact that over 40 percent of the male population of Pakistan smoke, lung cancer is the most common form of cancer in males in the country, followed by incidences of larynx cancer and oral cancer. For Pakistani women, breast cancer is by and large the most prevalent form of cancer incidence in females, followed by oral cancer and ovarian cancer. Regrettably, cancer is a taboo subject in Pakistan, and so it is not often talked about publicly in the country. The female Pakistani politician Fahmida Mirza has done her best to reverse this trend, however. After being
diagnosed with breast cancer in early 2012, Mirza continued to play an important and very public role in domestic and international politics. After aggressive bouts of chemotherapy, Mirza’s cancer went into remission, and she has since used her platform in the Pakistani government to help raise domestic awareness of and treatment options for the disease. She has recently been involved with legislative attempts to institute a national cancer registry in the country, as well as to mandate yearly breast cancer screenings for the entirety of the nation’s female population. With public figures like Mirza campaigning against breast cancer, there is hope that the cultural stigmas that have impeded treatment for Pakistani citizens may be reversed.

William M. Peaster
Independent Scholar

See Also: Breast Cancer; Breast Cancer, Sociocultural Differences and; Laryngeal Cancer; Liver Cancer, Adult (Primary); Oral Cavity Cancer, Lip and; Ovarian Epithelial Cancer.

Further Readings

Pancreatic Cancer

Pancreatic cancer is a highly aggressive malignancy that currently ranks as one of the major causes of cancer-related death in various countries around the world. Several chemotherapeutic regimens have shown great potential as treatment options for advanced stages of pancreatic cancer based on the results of phase III clinical trials that show an increase in patient survival. The standard of treatment of patients with pancreatic cancer is gemcitabine, which has been used for at least 10 years, replacing 5-fluorouracil. The benefits observed with the administration of gemcitabine included less pain, lower level of functional impairment, and a smaller risk of weight loss.

After the introduction of gemcitabine as the standard of care for patients with pancreatic cancer, additional randomized phase III clinical studies were launched to determine the efficacy of gemcitabine-based combinations compared to the use of gemcitabine alone. However, these studies have also sparked some controversy regarding gemcitabine-based drug combinations. For example, a couple of phase III clinical trials initially showed encouraging results of increased patient survival. However, two other phase III clinical studies generated the opposite results, wherein the study participants failed to achieve a significant improvement in survival rate after receiving gemcitabine-based drug combinations compared to those using gemcitabine alone. In addition, a subsequent clinical study that pooled the data collected from two phase III clinical trials as well as a phase II randomized clinical study showed that the gemcitabine-capecitabine drug combination resulted in a small but statistically significant improvement in survival rate. Furthermore, two additional independent meta-analyses also showed a small yet significant increase in survival.
rate using a gemcitabine-based drug combination compared to gemcitabine alone.

Another drug that has been used in combination with gemcitabine is erlotinib, which has resulted in a 23 percent survival rate of patients with pancreatic cancer, compared to the 17 percent survival rate in patients who received gemcitabine alone. It appears that erlotinib is the only drug that could consistently generate improved outcomes in patients with pancreatic cancer. The rest of the drugs administered in combination with gemcitabine still require additional clinical trials to verify their actual effect on the survival rate of pancreatic cancer patients.

Recent studies such as ACCORD 11/0402 as well as that conducted by T. Conroy and colleagues have thus examined the efficacy of other gemcitabine-based drug combinations for the treatment of pancreatic cancer. The cocktail consisting of 5-fluorouracil, folinic acid, irinotecan, and oxiplatin, collectively called FOLFIRINOX, has been combined with gemcitabine for the treatment of metastatic pancreatic cancer. The initial study showed promising results of higher response rates and extended progression-free survival, as well as enhanced overall survival rates. However, these positive patient outcomes were also strongly associated with a higher incidence of toxicity effects such as diarrhea, neutropenia, and vomiting. In addition, the combinations of gemcitabine-capecitabine, gemcitabine-erlotinib, and FOLFIRINOX have not been assessed directly against each other in a single clinical study. It would also be helpful to identify the most cost-effective gemcitabine-based drug combination for the treatment of pancreatic cancer. This need to identify a cost-effective treatment regimen is mainly based on the limited budget provided by insurance programs, amid the rapid rise in the price of cancer drugs over a short period of time.

In a more recent study conducted by C. L. Attard and colleagues, the cost-effectiveness of FOLFIRINOX as a first-line drug for the treatment of pancreatic cancer was assessed and compared with gemcitabine alone. Similar to the findings of previous clinical trials, FOLFIRINOX was associated with a higher number of life-years, as well as quality-adjusted life years. In terms of sensitivity, FOLFIRINOX showed >80 percent sensitivity compared to using gemcitabine alone. Calculation of cost-effectiveness included the expenses incurred based on the dosage of FOLFIRINOX compared to that of gemcitabine, as well as the duration of treatment and the positive outcomes observed in the patients with pancreatic cancer. The patients included in the study thus showed a significantly longer life expectancy compared to that observed using the standard of care, gemcitabine. Although gemcitabine extends the life expectancy of a patient with metastatic pancreatic cancer by six months, those who received FOLFIRINOX as a first-line treatment showed an increase in life expectancy of 11.1 months. Furthermore, the cost of using either gemcitabine or FOLFIRINOX was essentially the same and, therefore, the newer drug formulation is considered the more cost-effective approach in treating patients with metastatic pancreatic cancer.

Despite these promising results, some discrepancy continues to influence and possibly delay the establishment of a new standard of care for metastatic pancreatic cancer. For example, to date, the universal definition of a cost-effective treatment regimen for pancreatic cancer is uncertain. Some analysts have previously suggested that an intervention that costs less than $20,000.quality-adjusted life year should be considered as cost-effective, whereas those costing more than $100,000.quality-adjusted life year should be considered not cost-effective. It is important to note that these thresholds for cost-effectiveness were established in the early 1990s and thus might not be totally representative of the current quality of health care that the patients received.
In addition, the cost of these drugs varies among countries and continents around the world. Interestingly, even the two countries in North America, namely, the United States and Canada, have significantly different costs for the same drugs for the treatment of metastatic pancreatic cancer.

The World Health Organization (WHO) has also attempted to assist in defining the term cost-effectiveness. This international organization thus recommended that the threshold of a cost-effective treatment regimen for pancreatic cancer should be based on the gross domestic product per capita of each nation. Thus, in Canada, for example, the threshold for cost-effectiveness of a treatment regimen for metastatic pancreatic cancer is approximately $151,000 per quality-adjusted life year. Using this approach, FOLFIRINOX continues to appear to be the more cost-effective treatment for pancreatic cancer. Subsequent clinical trials assessing the cost-effectiveness of gemcitabine and FOLFIRINOX continue to generate different results; however, it appears that these discrepancies were mainly due to the exclusion of cycles of administering FOLFIRINOX to a pancreatic cancer patient. The earlier ACCORD trial supports this reason, as the study participants received FOLFIRINOX ranging from one to 47 cycles. Further evaluation is thus warranted for this new treatment approach.

Rhea U. Vallente  
PreventionGenetics, LLC

See Also: Chemotherapy; Pancreatic Cancer, Childhood; Pancreatic Cancer, Islet Cell.

Further Readings
pancreatic cancer in childhood. 85 percent of pancreatic adenocarcinomas will have metastasized (spread to other organs) at the time of presentation. Acinar adenocarcinomas generally present after metastasis has occurred and have been described in children as young as 3 years. Some of these patients present with a constellation of findings, including polyarthralgia (joint aches), extrapancreatic fat necrosis, and eosinophilia (elevation in the blood of a type of white blood cell). These tumors frequently demonstrate allelic losses on chromosome 11p and alterations in the APC/β-catenin pathway. Treatment is direct excision and prognosis is more favorable than that for ductal adenocarcinoma.

Pancreatoblastoma is more common in boys than girls and presents often as an incidental abdominal mass. A number of patients will secrete anti-diuretic hormone from their tumor. Serum alphafetoprotein will be elevated and can be useful to follow the course of disease. Primary resection is the treatment and prognosis is good in these children.

Islet cell carcinomas arise from functional pancreatic lesions and are associated with hypoglycemia, or can be part of the Zollinger-Ellison syndrome (caused by a tumor that secretes the hormone gastrin). These cancers are usually associated with multiple endocrine neoplasia type I syndrome. There is also an association between von Hippel-Lindau (VHL) disease and islet cell carcinoma, which is caused by a germline mutation of the VHL gene on chromosome 3p25.

In multiple endocrine neoplasia type 1 (MEN1), nonfunctioning pancreatic neuroendocrine tumors (NF-PETs) are considered the most prevalent PETs and represent the main cause of death in MEN1 patients in their second decade of life. With the increased ability to molecularly detect patients who present with insulinasms as MEN1-related PETs, practice guidelines on MEN1 have been revised to start screening as early as age 10 for MEN1 carriers with suspected clinical disease. Congenital anomalies of the pancreas-associated enteric small bowel duplications have now been associated with chronic pancreatitis and pancreatic cancer in a few rare case reports. While duplications are benign in children, malignant degeneration has been described in adults, and a minority of these demonstrated adenocarcinomas of the pancreas in origin. In one report, the small bowel cancer demonstrated over-expression of the HER2/neu oncogene, a gene involved in apoptosis. This discovery has led to chemotherapy treatments with antibodies directed against the HER2 protein. A variety of nonepithelial tumors of the pancreas have been described, although rarely in children. Rhabdomyosarcomas and lymphomas and primitive neuroectodermal tumors can sometimes present as primary tumors of the pancreas. Secondary involvement of the pancreas by tumors can result from hematogenous spread in malignant melanoma, renal and lung tumors, and leukemia.

Sherry C. Huang
University of California, San Diego
John M. Carethers
University of Michigan, Ann Arbor

See Also: Islet Cell Carcinoma (Endocrine Pancreas); Pancreatic Cancer; Pancreatic Cancer, Islet Cell.

Further Readings
Pancreatic Cancer, Islet Cell

Pancreatic islet cell tumors are also known as islet cell tumors, islet of Langerhans tumors, neuroendocrine tumors, pancreatic neuroendocrine tumors (pNETs), neuroendocrine tumors (NETs), pancreatic endocrine cancer, islet cell carcinoma, and pancreatic endocrine tumors (PETs). They comprise fewer than 4 percent of all diagnosed pancreatic tumors, with gastrinomas and insulinomas more common than the other types. This article includes an introduction to pNETs, descriptions of the different types and symptoms, risk factors, exams and tests to diagnose pNETs, treatments, and prognosis.

Introduction
Islet cell tumors form from the islet cells of the pancreas, which include hormone-secreting cells. As a result, islet cell tumors usually produce excess hormones, and most of the initial symptoms are the result of the actions of these hormones. pNETs that produce excess hormones are called functional tumors. A smaller subset of islet cell tumors, referred to as nonfunctional tumors, have no significant symptoms due to hormones or peptides that the tumor makes. Instead, symptoms of nonfunctional tumors are mainly caused by growth and spreading of the tumor. In addition, some NETs are not cancerous, and these benign tumors might or might not cause symptoms.

Types and Symptoms of pNETs
There are several types of pNETs that result in different symptoms depending on the hormones they produce. They are described below. Glucagonomas produce glucagon, a hormone that signals the body to raise blood glucose levels. The most distinctive feature is necrolytic migratory erythema (NME), a red, blistery rash on the face, stomach, legs, groin, or buttocks. Other symptoms can include high blood sugar resulting in hunger, thirst, fatigue, weakness, headaches, dry skin and mouth, and frequent urination, diarrhea, weight loss, and malnutrition; blood clots in the lungs causing shortness of breath, coughing, and pain in the chest; blood clots in an arm or leg resulting in swelling, warmth, and redness of the limb; glossitis (swollen tongue); or angular cheilosis (sores at the corners of the mouth).

Gastrinomas (Zollinger-Ellison syndrome, ZES) produce gastrin, a hormone that signals the stomach to make acid. Symptoms include abdominal pain that may spread to the back, diarrhea, ulcers in the stomach and small intestine, vomiting blood, gastroesophageal reflux, and decreased appetite.

Insulinomas produce insulin, which lowers blood glucose levels. Symptoms include hypoglycemia that can result in fatigue, weakness, shaking, sweating, headache, hunger, double/blurry vision, rapid heartbeat, nervousness, anxiety, irritability, lightheadedness, and confusion. If blood glucose levels become too low, the patient can experience fainting, seizures, or even coma.

VIPomas (Verner-Morrison pancreatic cholera, WDHA) produce excessive vasoactive intestinal peptide (VIP). Symptoms include watery diarrhea, weight loss, dehydration, low blood potassium levels that can cause muscle weakness, aching, cramps, numbness and tingling, low acid levels in the stomach resulting in problems digesting food, frequent urination, rapid heartbeat, confusion, or abdominal pain or cramps.

Somatostatinomas produce excessive somatostatin, which regulates the production of several other hormones. Symptoms include steatorrhea, diarrhea, weight loss, gallstones, gallbladder problems causing abdominal pain, nausea, decreased appetite and jaundice, and high blood sugar resulting in headaches, frequent urination, dry skin and mouth, hunger, thirst, fatigue, and weakness.

Carcinoid tumors produce serotonin (5-HT) or 5-HTP, a precursor of serotonin. Because these molecules are broken down by the liver, carcinoid tumors generally do not cause symptoms until they metastasize. After spreading to the liver, the tumors can cause carcinoid syndrome with diarrhea, flushing, wheezing, and rapid heartbeat and can eventually cause damage to heart valves.

Other types of pNETs include PPomas, GRFomas, ACTHomas, and PTHrPomas. PPomas make pancreatic polypeptide and cause an enlarged liver, abdominal pain, and watery diarrhea. GRFomas secrete growth hormone releasing factor. ACTHomas secrete adrenocorticotropic hormone (ACTH). PTHrPomas secrete PTHrP and cause hypercalcemia.

While nonfunctional NETs do not secrete hormones that cause significant symptoms, as the tumors grow and invade the liver they can cause
diarrhea, indigestion, a lump in the abdomen, pain in the abdomen or back, and jaundice.

**Risk Factors**

Risk factors for pNETs include multiple endocrine neoplasia, type I (mutations in MEN1), neurofibromatosis type 1 (von Recklinghausen disease, VRH, mutations in NF1), von Hippel–Lindau disease (VHL), and tuberous sclerosis.

**Exams and Tests**

Exams and tests include general physical exams, exams of the abdomen, and tests to look for altered hormone levels or the metabolic results of increased hormone levels. An initial physical exam could identify jaundice, masses or fluid buildup in the abdomen, an enlarged gallbladder or liver, and swelling of lymph nodes. Examinations of the abdomen might include an abdominal computed tomography (CT) scan, abdominal ultrasound, intraoperative ultrasound, endoscopic ultrasound (EUS, endosonography), magnetic resonance imaging (MRI) of the abdomen, and endoscopic retrograde cholangiopancreatography (ERCP). Sometimes surgical examination of the pancreas through laparoscopy is used. An angiography might be used to look for extra or abnormal blood vessels feeding a tumor or for compression of blood vessels by a tumor. Somatostatin receptor scintigraphy (octreotide scan, OctreoScan, SRS) using radioactive octreotide, a hormone that attaches to tumors, might be used to look for somatostatinomas. Biopsies of pancreatic tumors can be performed through fine needle aspiration biopsy (FNA) through the skin, or a biopsy might be performed during an endoscopic ultrasound.

Blood tests include a fasting serum glucose level, fasting serum gastrin level, fasting serum somatostatin test, glucose tolerance test, blood glucagon level, blood insulin c-peptide, blood insulin level, chromogranin A test (CgA; if this is high but other hormones are normal, it could be a sign of nonfunctional NET), serum VIP, sodium and potassium in stool (for VIPoma), pancreatic polypeptide level, neuron-specific enolase (NSE), or substance P. In addition, levels of 5-hydroxyindoleacetic acid (5-HIAA, a product of serotonin degradation) may be measured in the urine. Additional tests include a test of basal acid output from stomach contents after fasting or a secretin stimulation test, which measures the acid level of the small intestine contents after secretin is injected.

**Treatment**

The treatment of pNETs varies depending on the type of tumor and whether it has spread to other tissues. In general, treatment might include surgery to remove the tumor. This could be enucleation to remove only the tumor, pancreateoduodenectomy (Whipple procedure), distal pancreatectomy, total gastrectomy, parietal cell vagotomy, or, if the cancer has spread to the liver, liver resection. Hepatic arterial occlusion or chemoembolization might also be used. Radiofrequency ablation or cryosurgical ablation are other options. For gastrinomas, the nerve that causes cells to make stomach acid might be cut to relieve some symptoms. If the cancer has spread, chemotherapy might be included. Supportive care used to treat symptoms includes pain control, treating stomach ulcers with proton pump inhibitors, histamine blockers, or somatostatin-like drugs, treating diarrhea with IV fluids and somatostatin-like drugs, treating low blood sugar with frequent meals or drug therapy to increase blood sugar levels, or treating high blood sugar with oral drugs or insulin injections. If excess production of hormones is causing symptoms, hormone therapy or other medications to counteract their effects are used. For example, in treating gastrinomas, drugs are used that decrease stomach acid levels, and in treating insulinomas, drugs are used to decrease insulin production.

**Prognosis**

pNETs are less common than pancreatic exocrine tumors and often have a better prognosis. The prognosis depends on the type of cancer, in which part of the pancreas it is located, whether it has spread to other tissues, the age and general health of the patient, and whether it is a new or recurring cancer. If it is found early enough, there is the possibility that the cancer can be cured if the tumor is removed before it can spread to other tissues. In general, potential complications of pNETs can result from increased expression of hormones, including diabetes, hormone crisis, severe low blood sugar, and severe ulcers in the stomach or small intestine. If the tumors spread to the liver, symptoms can include enlargement of the liver with pain and poor
Paper Industry

Paper is produced by pressing moist fibers together and drying them into flexible sheets. The process of making paper from cellulose pulp (derived from grass, wood, or rags) was developed in ancient China, and China continues to be the leading paper producer today. The United States, with its vast natural resources and rapid development of mills during the Industrial Revolution, is the second-biggest country in the pulp and paper industry. In addition to wood, paper is made from fiber crops like jute, flax, hemp, kenaf, bamboo, cereal straws, cotton, and corn stalks. Paper applications include paper currency, writing and printing paper, the various papers of the publishing industry (for books, magazines, and newspapers, each of which uses distinctly different papers), packaging materials from wrapping paper to corrugated boxes, blotting paper, emery paper, electrical insulation paper, litmus paper, paper chromatography, sand paper, cat litter, paper towels, toilet paper, and tissues. From the Industrial Revolution until World War II, the sulfite process was the dominant method for making wood pulp into paper. Instead of mechanically grinding wood into pulp, sulfur and oxygen are burned, creating sulfur dioxide, which is combined with water to create sulfurous acid. This "cooking liquor" extracts lignin from wood in order to leave behind cellulose-rich pulp. Though the sulfite process is no longer dominant, it continues to be used for fine paper, tissue, and other specialty papers, as well as to produce cellulose from wood pulp for non-paper purposes.

The kraft process, however, has overtaken the sulfite process in most papermaking. It uses a cooking liquor called "white liquor," a mixture of sodium hydroxide and sodium sulfide, to break the bonds connecting lignin to cellulose in order to separate the two. The resulting paper is stronger than that created by the sulfite process, and it can be used with a greater variety of woods. When pine is used, it also results in a by-product of raw turpentine.

Paper can also be made from waste paper, including "mill broke," which consists of the trimmings and scraps left over from the papermaking process; pre-consumer waste, which is finished paper that for one reason or another never made it to consumers; and postconsumer waste, which includes used paper, corrugated containers, magazines, and newspapers. Paper recycling today is a relatively simple process, using chemicals to remove the ink from the pulp in a process called de-inking, before bleaching and wetting the pulp as normal. De-inking is done through pH controllers, bleaches, soaps and fatty acids, and other chemicals. The by-product sludge—a combination of ink, plastic, and filler—is burned at some mills as a fuel source but can also be used as a fertilizer.

Both papermaking processes involve many other steps to process, treat, and bleach the pulp and paper. Chalk or china clay may be added to the pulp to improve writing- and printing-related characteristics. The pulp is fed through a paper machine to form a web, and water is removed through pressing and drying through both air and heat. Sizing cuts the paper to suit various applications, and paper is frequently calendared (polished) and coated to make it more appropriate for high-resolution uses.
like photography or high-quality printing. Rollers add textures or watermarks if desired. Many of these chemicals contribute to the pollution contributed by the paper industry.

Some of them can be dangerous to human health as well. Ethylenediaminetetraacetic acid (EDTA), which is used in the bleaching process, is weakly genotoxic, whether consumed orally, inhaled, or contacted on the skin. Though sulfur dioxide is normally not considered a carcinogen—a single study on mice has found it to be carcinogenic—studies show that it is linked to lung cancer in pulp and paper industry workers. A 2002 study of almost 58,000 workers found a positive increase in lung cancer, non-Hodgkin’s lymphoma, and leukemia among pulp and paper industry workers exposed to sulfur dioxide in the course of their jobs, compared to workers of similar age and nationality who were not exposed to sulfur dioxide in their workplaces.

The risk for non-Hodgkin’s lymphoma increased with the dose of sulfur dioxide; no such increase appeared evident with the other cancers. An earlier study of workers in sulfuric acid plants had similarly found increases in mortality due to sulfur dioxide exposure, specifically in increased bladder cancer risk and cardiovascular disease. Organochlorides are also used in paper processing. These hydrocarbons are organic compounds that include at least one covalently bonded chlorine atom. Many are highly toxic to people, animals, or the environment; for example, the pesticide DDT is one such organochloride and it was the focus of Rachel Carson’s book *Silent Spring* (1962), which began the environmental movement. The greenhouse gas carbon tetrachloride is another organochloride used in the paper industry, and exposure to its vapor alone can cause damage to the central nervous system, kidneys, and liver; chronic exposure is linked to liver, kidney, and other cancers. Other organochlorides have been linked to breast cancer risk in numerous studies.

The paper industry is also a significant polluter. Wastewater contains lignin, alcohol, chlorates, transition metal compounds, and enough nitrogen and organic matter to accelerate the eutrophication of freshwater lakes and rivers and change the ecological balance. When the waste sludge is burned, many of the chemicals contained are carcinogenic, and because de-inking involves its own chemical waste products, there is some debate about the level of environmental remediation represented by paper recycling. (Paper recycling also consumes a great deal of clean water.) The papermaking process produces a large amount of dioxins in the bleaching stage, though this problem has improved considerably since the 1980s. Dioxin production results from the use of chlorine, but by 2005, 75 percent of papermaking mills using the kraft process had converted to the elemental chlorine free process, with minimal dioxin production, while 5 percent were using the totally chlorine free technique, with almost no dioxin production. The sulfur dioxide produced in both the kraft process and the sulfite process is a major contributor to acid rain, and other sulfur compounds like hydrogen sulfide, methyl mercaptan, dimethyl disulfide, and dimethyl sulfide are also released by these processes.

Bill Kte’pi
Independent Scholar

See Also: Chemical Industry; Pollution, Air; Pollution, Water.
Further Readings

Colonial Period and Early Independence
Cancer treatment among foreigners living in PNG in the 19th and 20th centuries relied upon Western medicine, namely surgical removal of tumors. Modern health services provided under Australian rule began to reach rural PNG after World War II; however, the people rarely had access to cancer diagnosis and treatment unless they were in walking distance of an urban hospital in Port Moresby, Lae, Goroka, or Rabaul. There was a significant lack of cancer incidence and treatment data.

Australia established the Territory Tumour Registry in 1958. Total registered cases from 1958 to 1970 were 3,926 (302 per year; 13.8/100,000). Analysis of registry data in 1962 and 1965 found significant incidence of oral and skin cancers in coastal lowland and island regions. Oral cancers of the cheek linings, lips, and tongue were linked to the cultural practice of chewing betelnut, which later spread in popularity among the Highland peoples. Skin cancers (primary non-melanomatous) arise from malignant changes to tropical ulcers and burns, usually occurring on the lower leg. Cancers of the stomach, liver, breasts, and cervix, leukemia and lymphosarcoma among children, and others were found. However, these data reflected cancer among only those persons who had access to an urban hospital (less than 10 percent of the people). Females often went untreated due to taboos about discussing gynecological functions and symptoms.
Papua New Guinea gained independence from Australia on September 16, 1975. Beginning in 1977, the South Pacific Commission’s Pacific Islands Cancer Registry began collecting annually standardized cancer data from Papua New Guinea as well as 21 other Pacific island countries and territories that agreed to participate. This agreement has permitted comparative analyses for better understanding of causes, treatment, and prevention among Pacific peoples. Cancer registration rates increased steadily in the following years.

Risk Factors
Risk factors for common cancers in PNG include the hepatitis B virus (liver); smoking tobacco (lung); betelnut chewing (oral); the sexually transmitted human papillomavirus (HPV) types 16 and 18, which may cause as many as 70 percent of all cervical cancers; and exposure to malaria and the Epstein-Barr virus (lymphoma). The majority of
males (56.9 percent) and a quarter of females (24.8 percent) smoke tobacco. Among males, high rates of oral and liver cancer are linked to smoking, chewing betelnut, and excessive drinking.

**Incidence and Mortality**
Cancer is the fourth most common disease in PNG, affecting up to 15,000 people annually, 75 percent of whom experience poor health outcomes due to lack of diagnosis and treatment. Total PNG cancer incidence and mortality according to the Pulitzer Center/PRI are 139/100,000 and 109.3/100,000, respectively. One-third of these are oral cancers (41.5), which account for 22.8/100,000 deaths annually. Cervical (23.2) and breast (18.9) cancers combined, which almost exclusively affect females, account for one-third (42.1) of all cancers in PNG, and result in 29.4/100,000 annual deaths. About two-thirds of breast cancer patients are premenopausal and experience metastasis before the cancer is identified. Prostate (11.7), liver (9.4), stomach (7.4), and lung (7.3) cancers cause 33.5/100,000 deaths combined. Current data on skin cancer incidence and mortality is lacking.

In contrast to Polynesian, Micronesian, other Melanesian, and aboriginal Pacific peoples, who have high rates of prostate, breast, and lung cancer, PNG and the Solomon Islands have higher rates of oral, liver, and cervical, as well as breast cancer. Fiji and Vanuatu (other Melanesian peoples) also have high rates of cervical cancer.

**Education and Prevention**
Four of the leading cancers in PNG are preventable, that is, oral, cervical, liver, and skin cancer. Efforts at education and prevention have had mixed results. For instance, the Tobacco Products (Health Control) Act of 1987 prohibited advertising of tobacco products and sale to persons under age 18, required labeling that stated the level of harmful substances contained in a product, and authorized the Health Ministry to implement regulations prohibiting tobacco use in public places such as public transportation. None of these provisions was effectively implemented or enforced. The same has been true regarding curbing the use of betelnut.

The HPV vaccination is available to children prior to sexual development in many developed countries. Only private hospitals in PNG, however, offer the set of three vaccinations, which cost about US$600. The hepatitis B vaccine became part of the national vaccination schedule in the 1990s and is expected to produce a measurable reduction in the incidence of liver cirrhosis and cancer in the future. Notably, greater awareness and treatment of tropical ulcers and burns appears to have resulted in skin cancer decline.

Cancer education and prevention services primarily operate from the capital, Port Moresby, including the PNG National Cancer Centre and the Port Moresby Cancer Relief Society. The National Cancer Centre manages the national cancer registry, but it is understaffed and under-supported.

**Treatment**
In 2013 only two hospitals (Port Moresby General Hospital and Angau Memorial Hospital in Lae) had specialized cancer services, including radiation treatment and chemotherapy. A new screening system, the Visual Inspection With Acetic Acid test, is being used at the Mt. Hagen and Goroka General Hospitals in the Highlands, specifically for the detection of HPV. It has reported the screening of over 2,000 women, and early detection in about 15 percent, some of whom are treated with cryotherapy.

Overall, diagnosis and treatment services in PNG are quite limited and usually are provided by a few physicians and surgeons with specific cancer management skills who work in the hospitals noted above. Histopathology services, which examine tissue samples for disease, lack specialized staff and support, creating significant delays in reporting cancer results. Training of oncologists is largely dependent on overseas medical schools and donor agencies.

William N. Myhill
_Burton Blatt Institute at Syracuse University_

**See Also:** Breast Cancer; Cervical Cancer; Liver Cancer, Adult (Primary); Lung Cancer; Oral Cavity Cancer, Lip and; Stomach (Gastric) Cancer.

**Further Readings**
Paraguay

Paraguay is a country in South America. It is bordered by Argentina, Brazil, and Bolivia in the central region of South America and therefore is often referred to as the Corazón de América—the “Heart of America.” The indigenous community in Paraguay are the Guaraní and they had been living in Paraguay for at least a millennium before the Spanish conquered the territory in the 16th century. Paraguay was a part of the Spanish empire but was not well populated. At its independence in 1811, the country was ruled by a dictator who tried to maintain restrictive and rough policies that were often hard to work with. The disastrous Paraguayan War (1864–1870) truncated the development that had been made since independence. During this war, the country lost 60 to 70 percent of its population to war and disease and about 140,000 square kilometers (54,054 square miles) of territory to Argentina and Brazil. Paraguay’s population as of 2009 was estimated to be around 6.5 million. The capital and largest city is Asunción, whose metropolitan area is home to nearly a third of Paraguay’s population. Paraguay has long been one of the region’s most isolated countries, although it has grown to have a 2013 gross domestic product of $45.9 billion.

Cancer in Paraguay is not considered a major health issue. In general, modern biomedical practices are combined with herbal and folk remedies not only for cancer but for the full range of health cases. Public health clinics and hospitals are inaccessible to many people, especially in rural areas, and the urban and rural working classes and the poor often depend on self-medication or private pharmacies for medical treatments. As a result of this, herbal remedies are used alongside various pharmaceuticals for medical treatments. Some herbal specialists exist, but most people are knowledgeable about the medicinal uses of common plants or resort to relatives or neighbors for advice on their use. However, because cancer is not yet known to be cured by herbal remedies, the majority of medicines used for the treatment of cancer in Paraguay are imported. Donations are also one of the ways these products are made available to cancer patients in Paraguay. On April 21, 2014, the National Cancer Coalition (NCC) announced the donation of $3 million worth of cancer medicines and essential pharmaceuticals to assist the needy in Paraguay.

The cancer scenario in the country got more attention when the immediate former president of the country, Fernando Lugo, was admitted to a hospital. Due to the limitations of the country’s hospitals to handle cancer patients, he was transferred to the Syrian-Lebanese Hospital in San Paolo, Brazil. Lugo, aged 59, was suffering from redness and swelling around the face and was diagnosed with non-Hodgkin’s lymphoma. Reports from the American Cancer Society state that non-Hodgkin’s lymphoma is common in Latin America, accounting for about 5 percent of all cancers. However, due to the changes in recording or even diagnosing these conditions, it is possible that these statistics are far lower than the actual situation.

The most prevalent cancer in Paraguay is breast cancer, with a rate of 18.96; second is lung cancer with a rate of 15.29, and third is prostate cancer with a rate of 11.54. These are followed by stomach cancer with a rate of 10.19, cervical cancer with a rate of 8.28, colon-rectum cancer with a rate of 8.10, leukemia with a rate of 5.12, pancreatic cancer with a rate of 4.41, lymphomas with a rate of 4.34, and, in tenth place, esophageal cancer with a rate of 4.06. Even though cervical cancer ranks fifth in Paraguay, it is among the highest rates in the world. A study was conducted by E. Kasamatsu and colleagues (2012) to see how human papillomavirus (HPV) spreads in women based on how serious cervical lesions are. The sample was composed of more than 200 women who did not have lesions, 164 with low-grade intraepithelial lesions, 74 with high-grade lesions, and 41 with cervical cancer. The procedure determined what forms of HPV may develop. The results showed 12 high-risk and 24 low-risk HPV types. HPV 16 was the most prevalent, followed by HPV 18 in cervical cancer (14.6 percent), HPV 31 in high-grade intraepithelial lesions (14.9 percent), HPVs 58/42 in low-grade intraepithelial lesions (9.1 percent each), and HPVs 31/58 (2.4 percent each) in women who did not have any of these lesions.
The risk for cancer in Paraguay is considered to include tobacco smoking, use of any tobacco product among youth, fruit and vegetable intake in adults, alcohol consumption, low physical activity in adults, obesity among adults, and HPV prevalence (women with normal cytology). One key risk factor specific to Paraguay, and Latin America by extension, is maté, an Ilex paraguariensis infusion. It is a key factor for the development of cell carcinoma. However, this remains a theory because no meta-analysis on the subject has been performed to date.

The only incidence of cancer screening that is well governed is cervical cancer. Physicians and oncologists are required to adhere to guidelines when screening patients for cervical cancer. The guidelines recommend tests to be performed per age-group per frequency; that is, Pap tests should be conducted for individuals between 25 years and 49 years of age every three years after several negative Pap tests. Support for screening and cervical cytology is generally available in the public and the private sectors while visual inspection with acetic acid is not open in the public and the private sectors.

Treatment for cancer—any type of cancer—can be done in a public health facility or in private health facilities. Radiotherapy is generally not available in public hospitals and only a few private hospitals offer the service. In the country, there are only seven radiation oncologists, four medical physicists, and three radiotherapy centers.

Michael Fox
Independent Scholar

See Also: Cervical Cancer; Developing Countries; HPV Vaccination.

Further Readings

Paranasal Sinus and Nasal Cavity Cancer

Inverted papilloma (IP) is considered one of the most prevalent benign tumors that occur in the nasal cavity. It is responsible for at least 4 percent of all cases of sinonasal malignancies. Although IP has a relatively high incidence rate and is strongly associated with squamous cell carcinoma, its treatment has mainly involved the minimally invasive technique of endoscopic resection. Differentiating IP from the rest of the malignancies involving the nasal cavity is therefore essential in order to prevent the application of chemotherapy for those cases that do not require such treatment. Distinguishing this specific type of cancer can also identify which patients should receive radiotherapy. It is important to understand that both chemotherapy and radiotherapy can increase the incidence of morbidity among patients, particularly when they do not require these treatments. One challenge is that the clinical features of IP prevent minimal diagnostic importance. In addition, the accuracy of diagnosing IP using a biopsy derived from an endoscopy incision might not be high because it is generally difficult to determine whether the collected tissue is indeed the correct specimen that should be used for the analysis. Based on these experiences in the clinic, distinguishing IPs from other malignancies occurring within the nasal cavity has been a challenge in a majority of cases.

Two techniques that have been evaluated in terms of their capacity to resolve the issue of differentiating IPs from other malignant tumors are computed tomography (CT) and magnetic resonance...
Paranasal Sinus and Nasal Cavity Cancer

imaging (MRI). CT presents limited information on the characteristics of a soft tissue mass because these often generate low contrast during imaging. On the other hand, contrast-enhanced MRI has been extensively used because it facilitates characterization of an unknown mass. Previous reports have shown that a convoluted cerebriform pattern generated on T2-weighted images, or in other cases, T1-weighted images with contrast enhancement significantly enhances the sensitivity in IP diagnosis. Despite this improvement, the diagnostic specificity of contrast-enhanced MRI has been relatively poor due to the presence of a convoluted cerebriform configuration that is observed in a significant number of malignant tumors.

Based on these discrepancies in the sensitivity and specificity of imaging techniques, it is therefore essential that the extent of use and the limitations of each technique be identified. In a recent study led by Mohammed Gomaa, the level of input, which reflects the actual value of a specific imaging system, was compared between MRI and CT. This comparative assessment was conducted using various imaging modalities in cases of sino-nasal neoplasms. Their study involved a total of 30 patients, of whom 16 were males and 14 were females, who presented with a chief complaint of sinonasal tract symptoms. After completion of both clinical and local assessments, the study participants underwent the following procedures: conventional radiography, imaging (both CT and MRI), and histopathological examination. The results of the study showed that the nasal cavity was the site most commonly associated with sinonasal malignancies. The maxillary sinuses were the second most common sites of sinonasal malignancies. The site showing the lowest frequency of involvement with sinonasal malignancies was the frontal sinuses. The study identified 14 cases of benign sinonasal tumors. In addition, the most frequent benign lesion was determined to be juvenile nasopharyngeal angiofibroma, which was detected in six cases. IP was observed in three cases. The study also showed that although malignant sinonasal tumors were observed in 16 cases, five of these cases presented squamous cell carcinoma, and three showed undifferentiated carcinoma. The findings of the study also showed that MRI allows high-contrast evaluation of soft tissues of the sinonasal cavity, which is superior to that provided by CT for the pretreatment assessment of malignant tumors.

In another recent study, E. Allegra and colleagues utilized CT in combination with positron emission tomography (PET) in assessing IPs prior to treatment. The proponents of the study were aware that CT and MRI are commonly used for the assessment of sinonasal tumors; however, these imaging techniques are often limited in their capacity to differentiate between IPs and squamous cell carcinomas. Based on this difficulty, the investigators examined the usefulness of F-18 fluorodeoxyglucose (18FDG)-PET in imaging the head region of patients with sinonasal malignancies. A total of 12 patients who were suspected to have sinonasal IPs were included in the research study. Using 18FDG-PET, the standard uptake value of each patient was estimated. The results of the study showed that seven of the 12 patients showed a standard uptake value that ranged from 1 to 8.1. In addition, the histopathological diagnosis post-operatively confirmed an IP diagnosis in five of the seven patients, who then presented the maximum standard uptake value of at least 3. On the other hand, the other five cases that did not show signs of 18FDG uptake were diagnosed to be without IP.

The findings of the research study conducted by Allegra’s group are timely and of great interest because reports on the diagnostic role of newer imaging techniques such as 18FDG-PET/CT are limited. Those that are currently available in the literature are generally case reports that require additional studies to validate those findings. Nonetheless, these earlier reports show that the standard uptake value of benign IPs was generally lower than that observed in IPs co-occurring with squamous cell carcinoma. The study conducted by Allegra and colleagues therefore provided additional information on the extent of decrease in the standard uptake value in benign IPs. Lesions that show a negative or diffused pattern of 18FDG uptake, particularly with standard uptake values of <3, are therefore classified as IP-negative. Although this recent study still requires additional investigations to verify the results described in the report, it directly shows that the combination of PET with CT is a promising approach in diagnosing and staging IP. The combined technique also shows advantages that could not be provided by CT or MRI alone. In addition, the use of PET in combination with CT allows
the analysis of morphological as well as metabolic data over a single session. The standardization of the PET-CT technique in cases of sinonasal malignancies and the establishment of a range for standard uptake values for this specific malignancy are essential in determining the reliability of the technique for IP diagnosis.

Rhea U. Vallente  
PreventionGenetics, LLC

See Also: Radiation; Radiation Therapy; Technology, Imaging.

Further Readings


Parathyroid Cancer

Parathyroid cancer is a rare malignancy, accounting for only 0.005 percent of all cancers. Due to its rarity, there are no consensus guidelines available. The disease frequently presents as primary hyperparathyroidism, is difficult to detect preoperatively, and is often fatal.

Epidemiology

Parathyroid carcinoma is an uncommon cause of primary hyperparathyroidism, accounting for only 1 to 5 percent of cases. Risk factors include prior history of thyroid cancer and CDC73 germline mutations that can present with the phenotypes of hyperparathyroidism–jaw tumor (HPT-JT) syndrome, CDC73-related parathyroid carcinoma, CDC73-related familial isolated hyperparathyroidism (FIHP), or, rarely, MEN1 syndrome. Its recurrence rate has been reported at from 49 to 82 percent, most commonly in the first two to five years after initial surgery, although as late as 21 years. Overall survival has been reported ranging from 78 to 85 percent at five years and 50 to 77 percent at 10 years, with a median survival of 14.3 years. Factors associated with worse outcome include male gender, advanced age, presence of distant metastases, and nonfunctioning tumors.

Presentation

Parathyroid cancer typically presents as primary hyperparathyroidism, apparent by the presence of hypercalcemia. Calcium levels are often higher and the patients more symptomatic in carcinoma compared to adenoma. Renal and skeletal symptomatology is present in 80 to 90 percent of patients with carcinoma and may manifest as polydipsia, myalgias, nephrolithiasis, bone pain, or pathological fracture. Occasionally a neck mass is present. Up to 10 percent of parathyroid carcinomas are nonfunctioning and thus will be asymptomatic until the tumor has reached an advanced stage, where local invasion causes pain, hoarseness, or difficulty swallowing. At presentation, up to 30 percent of cases will have regional lymph node involvement, and one-third will have distant metastases, most commonly in the lung, liver, or bone.

Diagnosis

It may be difficult to distinguish benign parathyroid disease from malignancy based on preoperative testing and imaging or even by routine pathologic examination of the excised tumor. Factors indicating high risk for malignancy include a palpable mass, local pain, recurrent laryngeal nerve palsy, higher PTH (3–15 times the upper normal limit) and calcium levels (>14 mg/dL), and more severe clinical symptoms, particularly renal, bone, and neurological symptoms, or a significant family history of hyperparathyroidism or its associated syndromes including MEN and HPT-JT. Preoperative ultrasound features indicating high risk for malignancy include size >3.0 cm, lobulated hypoechoic appearance, infiltration of surrounding structures, calcification, or suspicious vascularity. In patients with CDC73 mutation, a 3rd generation:2nd generation PTH assay ratio may be greater than 1.0. Mutations in CDC73 lead to its inactivation and higher levels of amino-PTH, which is measured by the 3rd generation but not 2nd generation PTH assays. Based
on these criteria, patients may be preoperatively categorized as high risk versus low risk. Preoperative workup may also include chest and abdominal computed tomography (CT) or bone scan if there is concern about metastatic disease. Intraoperatively, a high index of suspicion based upon gross findings of a firm, white mass or a parathyroid gland densely adherent to surrounding structures could direct the surgeon to perform a more extensive operation. Intraoperative frozen sections are rarely helpful.

Pathologic diagnosis of parathyroid cancer is difficult, as histologic features may not distinguish it from an adenoma or hyperplastic gland. Gross or microscopic invasion or lymphovascular invasion is helpful. Weak or complete loss of expression of parafibromin, the protein encoded by CDC73 is seen in the majority of HPT-JT-related tumors and sporadic parathyroid carcinomas. On genetic profiling of tumors, high risk features include differential expression of specific microRNAs or mutation in CDC73 or, rarely, MEN1. These mutations may also be present in benign parathyroid disease, but any lesion in the presence of these mutations should be treated with a high index of suspicion. However, this data is not typically available preoperatively, as it requires the tissue specimen for analysis.

Treatment
Surgery is the mainstay treatment for parathyroid cancer, with the intention being curative. Surgical approach varies from local excision, en bloc resection, or oncological resection including the lymphatic drainage. Positive margins predict recurrence. If a parathyroid cancer is suspected, this mandates a minimum of en bloc resection of all involved adjacent structures. There is debate on whether this should include ipsilateral thyroid lobectomy, which is practiced by many surgeons but has not been demonstrated to improve survival when there is no clear tumor involvement. Nonetheless, any adjacent structures that are involved (most commonly ipsilateral thyroid lobe, strap muscles, ipsilateral recurrent laryngeal nerve, esophagus, and trachea) should be resected if feasible. Prophylactic neck dissection is not recommended unless there is evident lymph node disease. A common scenario is to not identify malignancy until postoperative histopathology examination. In this case, there is still debate about whether reexploration for ipsilateral thyroid lobectomy and central cervical neck dissection is necessary.

Surgical treatment is the same for patients with known presence of genetic mutations. However, in these patients it is critical to explore all four glands to avoid missing additional cancers or benign parathyroid adenomas. In the setting of metastatic disease, resection of the metastasis is indicated. Although this may not be curative, resection can reduce hypercalcemia and potentially improve patient survival. For unresectable disease, hypercalcemia should be treated with cinacalcet, as the most common cause of death is severe hypercalcemia rather than tumor burden.

Adjuvant therapy with radiation is not routinely used. Data show mixed results on whether there may be benefit to prevent local recurrence in high-risk patients or those with positive surgical margins. Survival benefit has not been shown. Chemotherapy is not recommended, as there is limited data and no evidence of benefit.

Follow-Up
While there is no consensus staging by the American Joint Committee on Cancer, A. R. Shaha and colleagues and N. Talat and colleagues have both proposed potential tumor node metastasis staging systems. K. M. Schulte and Talat suggest staging can be divided into low risk and high risk categories based on recurrence and survival. Low risk is defined as invasion limited to the capsule and soft tissue. High risk is when there is vascular invasion, lymph node metastasis, or invasion of the trachea, esophagus, or major cervical vessels. Approximately 50 percent of cancers fall into each category. The high-risk group had disease-specific mortality of 50 percent at five years, whereas the low-risk group had no deaths.

Due to high rates of local recurrence, patients should be followed closely. In low-risk patients, calcium and PTH should be monitored every six months for the first five years and annually thereafter. High-risk patients should be followed more closely, with lab work every three months for the first 10 years. In the 1 percent of patients with non-secreting tumors, imaging follow-up should be obtained instead.

Conclusion
Parathyroid cancer is a rare cancer that presents insidiously with severe hypercalcemia and its
manifestations. En bloc surgical resection is the mainstay for treatment. It is necessary to consider malignancy in the preoperative setting, as failure to suspect malignancy is the main reason for failure to perform oncologic resection. Multiple recurrences are common and repeat surgical excision, although difficult, may be needed, including metastasectomies, as the primary cause of cancer death is not from disease burden but rather from hypercalcemia. With proper surgical technique and careful follow-up, survival can be a decade or longer for many patients.

Sonia L. Sugg
Jessemae L. Welsh
University of Iowa Hospitals & Clinics

See Also: Surgery; Thyroid Cancer; Thyroid Cancer, Childhood.

Further Readings

Passive Smoking

Smoking of tobacco products has produced a global health epidemic. In 2009, the mortality count from tobacco usage was more than 5 million people, and it is projected to exceed 8 million by 2030. Tobacco smoke has become one of the major causes of cancer mortality, accounting for approximately 30 percent of all cancer deaths. There have been more than 600,000 deaths each year attributed to secondhand smoke, with approximately 3,400 lung cancer deaths occurring among nonsmokers.

Secondhand smoke has also been associated with cancer of the respiratory, digestive, and reproductive systems, as well as the kidney and bladder in adults and the risk of leukemia, lymphoma, and brain tumors in children. The U.S. Surgeon General reported that exposure to secondhand smoke can result in an increase of up to 20 to 30 percent more lung cancer cases, particularly among individuals who live with a partner who smokes. Based on the fact that secondhand smoke has also been identified
as a carcinogen, with an increasing incidence of cancer among nonsmokers, it is therefore important that this topic be thoroughly investigated. This article highlights and explains the relationship between secondhand smoke and cancer and identifies strategies for reduction of this health hazard.

Several terminologies can be used to describe secondhand smoke, including passive smoke, environmental smoke, or involuntary smoke. Secondhand smoke is a combination of the “sidestream” smoke that is given off by a lighted tobacco product and the “mainstream” smoke that is exhaled by the person who is smoking. It consists of a mixture of gases and fine particles that tend to persist in the atmosphere. It therefore puts unsuspecting nonsmokers at increased risk of inhaling the tiny particles, which tend to have higher concentrations of carcinogens. Individuals can become exposed to secondhand smoke in a wide range of settings, including places of business, residence, employment, and recreational facilities. This smoke contains approximately 250 substances that have been identified as harmful, and about 50 of these have been confirmed as carcinogens. Several factors influence the makeup of secondhand smoke; these include the type and amount of tobacco, the chemicals added to the tobacco, the method of smoking, and the material in which the tobacco is wrapped. Some of the harmful substances that have been identified in secondhand smoke are arsenic, benzene, beryllium, cadmium, chromium, ethylene oxide, and nickel.

**Measurement of Secondhand Smoke**

The level of secondhand smoke exposure can be determined by testing body fluids such as blood, urine, and saliva for cotinine. Cotinine is a substance that is produced from the breakdown of nicotine. The average levels of cotinine have fallen over the past 20 years, which could be attributed to changes in the law that have prohibited smoking in workplaces and public places. Higher levels of secondhand smoke have been associated with persons of certain professions and ethnic groups.
Reports have suggested that although there is a general decline in cotinine levels, non-Hispanic African Americans tended to have higher levels compared to non-Hispanic white Americans and Mexican Americans. Persons in certain occupational groupings such as construction workers, blue-collar workers, and service providers have also been identified as having higher levels of exposure to secondhand smoke. There is no safe level of exposure, and so agencies such as the National Institute for Occupational Safety and Health and the Occupational Safety and Health Administration (OSHA) have instituted policy changes in smoking regulations for buildings, workplaces, and public spaces.

Different Types of Cancer
Secondhand smoke has been associated with many different types of cancers. Cancer is an abnormal malignant condition that can occur within any tissue of the body. It is characterized by uncontrollable replication of cells, which may result in abnormal growths and damage to surrounding tissues. The damage or change in the DNA results in failure to replicate in a normal manner. One of the substances that have been incriminated in causing damage to the DNA with subsequent malignancy is secondhand smoke. Some of the cancers include those of the respiratory tract such as the lungs, naso-pharynx, and nasal sinuses and those of the reproductive organs of the breast, cervix, and ovary. There is also evidence to suggest secondhand smoke may be linked with cancers of the brain, bladder, rectum, and stomach. The California Environmental Protection Agency has identified a causal relationship between secondhand smoke and cancers in younger women. Traces of secondhand smoke have also been identified in breast tissue and breast milk. However, based on the fact that a causal relationship was not identified among active smokers, the link remains inconclusive. The Surgeon General therefore reported that there was not sufficient evidence to link secondhand smoke with breast cancer.

Smoking accounts for 87 percent of lung cancer deaths in men and 70 percent in women. The U.S. Environmental Protection Agency, the U.S. National Toxicology Program, and the International Agency for Research on Cancer have classified secondhand smoke as a carcinogen, directly causing lung cancer. Exposure to secondhand smoke can increase the risk of lung cancer by 20 to 30 percent. Between 2005 and 2009, secondhand smoke exposure has been estimated to cause more than 7,300 lung cancer deaths annually among adult nonsmokers in the United States. Children are at particular risk for exposure to secondhand smoke. It is believed that children who are exposed to secondhand smoke are at increased risk of developing a malignancy such as lymphoma, leukemia, or brain tumor. In 2009, the International Agency for Research on Cancer reported that children of parents who smoked before and during pregnancy were more likely to have a child with hepatoblastoma, which is a rare liver cancer that may have started development in utero.

Reducing Secondhand Smoke
Although secondhand smoke may not be the cause of a number of cancers, there is evidence to suggest that it significantly contributes to morbidity and mortality associated with cancer. Governments in several countries have imposed a ban on the advertising, promotion, and sponsorship of tobacco products. These bans have resulted in reduced usage of tobacco products with subsequent reduction in the exposure to secondhand smoke. Some governments have also imposed increased taxes on tobacco products. The imposed taxes have also resulted in a decrease in tobacco consumption, which further contributed to a reduction in secondhand smoke. The World Health Organization (WHO) in its commitment to reduce secondhand smoke has established the WHO Framework Convention on Tobacco Control. The application of this convention was introduced in 2008 as MPOWER. This program seeks to help countries control tobacco usage, promote health education and prevention policies, and provide support for the enforcement of legislation and policy regarding tobacco usage.

Secondhand smoke is of particular concern within work environments. The Occupational Safety and Health Administration has issued guidelines for establishing and regulating smoke-free workplace policies. Local, state, and federal authorities have also passed clean indoor air laws in order to protect people from secondhand smoke. It is also important that homes and motor vehicles be kept smoke free. Based on the fact that
it is difficult to control ventilation by air cleaning or by separating smokers from nonsmokers, a smoke-free environment is recommended. Federal law has banned smoking in certain public areas; these include public buildings, malls, parks, parking lots, schools, colleges, hospitals, playgrounds, airline flights, buses, and most trains. The Pro-Children Act of 1994 also prohibited smoking in facilities that routinely provide federally funded services to children. The goal of the Healthy People 2020 program was to reduce exposure to secondhand smoke by 10 percent. The program also included a nationwide health promotion and disease prevention agenda that addressed reducing illness, disability, and deaths related to tobacco use and secondhand smoke exposure. Mass media campaigns with anti-tobacco advertisements and graphic warnings have contributed to a reduction in the numbers of children who begin smoking and increased the number of smokers who quit. Studies conducted in countries such as Brazil, Canada, Singapore, and Thailand show that the warnings have increased people's awareness of the harms of tobacco use.

**Economic Costs**

There are tremendous direct and indirect costs associated with tobacco usage. The direct costs are based on the costs required to address the morbidity and mortality associated with cancer. The indirect costs are those associated with reduced productivity or lost wages due to illness and death. Ten percent of the economic costs related to tobacco use are attributable to secondhand smoke. This is of great significance based on the fact that more than 94 percent of individuals in society are unprotected from secondhand smoke. In order to reduce these economic costs, it is important to establish and maintain smoke-free environments within society.

**Conclusion**

Secondhand smoke has become one of the major factors associated with several cancers. It has also been associated with cancer of the respiratory, digestive, and reproductive systems as well as the kidney and bladder in adults and the risk of leukemia, lymphoma, and brain tumors in children. Secondhand smoke is particularly dangerous because it contains particles with higher concentrations of carcinogens that can be more easily inhaled into the lungs. Although some reports indicate a causal relationship between secondhand smoke and breast cancer in younger women, other reports have been inconclusive.

Local, state, and federal agencies have established policy guidelines and legislation to reduce exposure to secondhand smoke. Strategies for reduction of exposure to secondhand smoke include restricting smoking in public places, such as parking lots, and instituting laws against smoking in public buildings, including schools, and in other enclosed spaces such as airplanes, buses, and trains.

Based on the fact that there are high levels of cancer morbidity and mortality among nonsmokers with increasing direct and indirect economic costs, it is of great urgency and utmost importance that strategies be put in place to protect society and that research continue to be conducted so that the true relationship of secondhand smoke and cancer can be conclusively determined.

Fay V. Williams  
*Northern Caribbean University*

**See Also:** American Cancer Society; Smoking and Society; Smoking Cessation; Tobacco in History; Tobacco Smoking; Workplace Wellness Programs.

**Further Readings**

Penile Cancer

There are many different forms of penile cancer, with the severity depending on the extent to which the cancer has spread. Early detection offers many advantages, and there are many treatment options, including surgery, radiation therapy, biological therapy, and laser therapy. Penile cancer usually begins as a small lesion on the skin of the penis and tends to grow very slowly, spreading the cancer. Malignancies are usually found in the head of the penis (the glans), with the foreskin (or prepuce) the next most common site. Tumors in the shaft of the penis are uncommon. Penile cancer usually involves squamous cell carcinomas (cancer not involving melanomas). One common type of penile cancer is epidermoid carcinoma (where the cancer develops in the skin of the penis). Another is verrucous carcinoma (a low-grade malignancy that may spread into surrounding tissue). Approximately 5 percent of penile cancer is caused by melanomas from pigment-producing skin cells, basal cell penile cancer (that is, cancer not caused by melanomas), and sarcomas (cancers of the connective or supportive tissue such as muscles and blood vessels). Another rare form of cancer that develops in the sweat glands in the skin of the penis is called adenocarcinoma.

The severity of penile cancer depends on whether the cancer is detected at the earliest stage (known as carcinoma in situ) and whether the carcinoma is localized or has spread to other areas. Early treatment can cure penile cancer, but there are no universally recommended tests for early screening. Penile cancer may be emotionally devastating, embarrassing, and shameful for men, and this may lead them to delay seeking treatment. Such delays in seeking appropriate treatment may exacerbate the problem. An important thing to remember is that with early detection, there is often little or no damage to the penis. Delaying treatment can mean that some (or all) of the penis may need to be removed.

Typically, penile cancer is treated with surgery, such as local resection for superficial carcinomas (partial amputation of the affected part of the penis, possibly treated with a penile reconstruction). It is important for patients to be aware of the kind of penile cancer they have, whether it has metastasized, and the treatment options. The treatment team usually includes a urologist, a radiation oncologist, and a medical oncologist. Such doctors can answer questions about whether the patient will be able to have sex, have children, or whether the cancer will affect their ability to urinate. When surgery occurs, a small incision is usually made until the surgeon reaches normal skin tissue. Such surgery usually does not prevent patients from being able to have sexual intercourse. However, in some cases, surgical removal of the penis and perhaps a lymph node may be necessary. Chemotherapy, radiation therapy, biological therapy, and laser therapy are other possible treatment options.

Risk factors for penile cancer include human papillomavirus (HPV) infection, age, not being circumcised, having phimosis or built-up smegma, smoking, having a history of being treated for psoriasis with a combination of psoralens and ultraviolet lighting, and having AIDS. The most common types of HPV (HPV 6 and HPV 11) are associated with genital warts but have a low risk of being associated with cancer. However, some types of HPV are considered high risk (HPV 16, HPV 18, and HPV 31, as well as some others). Usually, infection with a high-risk HPV has no visible signs until precancerous changes or cancer develops. Penile cancer usually affects older men (those over 60), although a small proportion occurs in younger men as well. Malignancies of the penis are rare among circumcised men: those circumcised as babies almost never develop penile cancer. Smoking also increases the risk of HPV infection, which is another risk factor for developing penile cancer.

Men who have the skin disease psoriasis are often treated with combinatorial psoralen drugs and ultraviolet lighting; because this treatment also increases the risk of penile cancer, men are required to cover their genitals when they use such treatments. Having AIDS is another risk factor for developing penile cancer, most likely associated with compromised immune systems.

The risk of mortality associated with penile cancer varies greatly according to whether there is carcinoma in situ (the earliest stage of squamous cell cancer) and whether the carcinoma is localized to a specific area or not. For men with stage I and stage II penile cancer, the five-year survival rate from penile cancer is approximately 85 percent. When the cancer has spread to lymph nodes and nearby tissues, the five-year survival rate is approximately 60 percent. If the cancer has metastasized
to distant parts of the body, the five-year survival rate is 11 percent.

Penile cancer is generally uncommon in Western countries. The American Cancer Society estimates that approximately 1,640 new cases will be diagnosed in 2014, and roughly 320 men will die of it in 2014. However, penile cancer is much more common in less developed countries and accounts for approximately one-tenth of all cancers diagnosed in men in Asia, South America, and Africa. Because penile cancer is relatively rare, it has been difficult to enroll sufficient numbers of men in new treatment options to test their efficacy. However, some new treatment options are being explored. For instance, laser therapy is being used to treat some men with penile cancer. Additionally, some new drugs are being tested, and researchers are exploring the possibility of gene therapy to treat various forms of penile cancer. Vaccines that prevent the development of HPV may also reduce the number of men who develop penile cancer.

Mark D. Sherry
University of Toledo

See Also: American Cancer Society; Biologic Therapy; Chemotherapy; Radiation Therapy; Sarcoma, Soft Tissue, Adult; Surgery.

Further Readings

Perfume

The word perfume comes from the Latin per fumare, “to smoke through,” originally in reference to the perfuming of the air through the burning of incense and resins. The science of fragrance dates to the 2nd millennium B.C.E., and in the ancient world people used almonds, citrus fruit, flowers, plant resins, and spices to prepare incenses, distillations, infusions, and scented oils in order to add scent to rooms, themselves, and objects. Norms of perfume use have varied considerably from culture to culture and time to time; the modern perfume industry originates from the use of perfume and cologne to mask body odor in the early Enlightenment period, when people bathed rarely, and the industry remains centered in Italy and France today as it was then.

Although we commonly use “cologne” to mean fragrance for men, and “perfume” to mean fragrance for women, in the industry the terms refer to the concentration of aromatic compounds in a neutral medium of ethanol or water. Perfume is usually 20 percent or as high as 40 percent. Espirit de parfum is usually 15 percent aromatic compounds, while the more common eau de parfum is 10 to 15 percent. Eau de toilette or toilet water is 5 to 10 percent. Eau de cologne has a concentration of 3 to 8 percent and refers specifically to a fragrance from the chypre family, characterized by the combination of citrus, oak moss, patchouli, and musk. Classically, chypre also included civet—an extract from the African civet's musk gland—but this is less commonly used today, and synthetic civets are noticeably different. Men's colognes today are usually eau de parfum or eau de toilette, formulated from scents deemed appropriate for men or, increasingly, relying heavily on aldehydes and calone for “fresh” or “aquatic” scents.

Individual fragrances are described using three terms: (1) top notes or head notes, the scents that are noticed first and form the initial impression, though because they consist of light molecules, they also dissipate the fastest and will often not be noticed by anyone except the individual wearing the scent at the moment they first apply it; (2) middle notes or heart notes, which emerge after the top notes disappear; and (3) base notes, which last the longest but may take more than 30 minutes to become noticeable. Much of a fragrance's power comes from the interplay between the middle notes and the base notes. Perfume formulation is much like cooking, in that it is not sufficient to combine various scents that an individual likes and assume that they will bring out the best in each other. Perfumes are traditionally grouped into families, although there can be considerable variation within
these families, and some of the smaller perfume houses have built their reputations on unusual outliers. The modern list of perfume families includes floral perfumes, which rely heavily on flowers, alone or in combination; oriental perfumes, which build on animalic scents by combining them either with woody scents, camphor, resins, or lighter scents like vanilla; woody perfumes, characterized by scents like sandalwood, cedar, and agarwood; leather perfumes, which alludes to leather through scents like tobacco, wood, and wood tar; the aforementioned chypre, named for the 1917 fragrance by François Coty; fougere, combining oakmoss, coumarin, and lavender; green, a chypre variant that includes bright scents like cut grass, green leaves, and cucumber; aquatic, oceanic, or ozonic, pioneered by the 1988 introduction of Davidoff Cool Water and dependent on the 1966 discovery of calone; citrus; and gourmand, coming into focus in the 1990s with a focus on vanilla, coumarin, and food flavors.

Traditional perfumes include animal-derived ingredients, and the oriental and chypre families were traditionally dependent on them. This practice fell out of favor, and synthetics were developed in the 19th and 20th centuries to replace them, most of which are called synthetic musks or white musks. White musks are also cheaper than animal-derived ingredients, and part of a larger trend of developing synthetic replacements for expensive ingredients, providing the foundation for department store fragrance products as well as the ability to cheaply add fragrances to deodorant, shampoo and conditioner, soap, air fresheners, laundry and dish detergent, and other products. One such white musk is musk xylene, which was the most widely used white musk until the 1980s. Discontinued in Japan in 1982 and no longer produced in Europe (though it continues to be imported and is legal for use in cosmetics products and perfumes), musk xylene fell out of favor in part because of its unexpected explosive properties—it is classified as an explosive under the European Union (EU) Dangerous Substances Directive—and its possible environmental damage, upon discovery that musk xylene is not completely removed by sewage treatment processes and thus enters the water system. Musk xylene has some toxic properties, especially to the liver, but its carcinogenicity, though widely reported in lists of consumer product components to be avoided, is not clear.

The International Agency for Research on Cancer (IARC) lists it as class 3: “not classifiable as to their carcinogenicity to humans.” A study on mice found an increase in liver cancer after oral exposure, but the study’s applicability to human health has been criticized.

Policyclic and macrocyclic artificial musks have overtaken musk xylene’s popularity. Like musk xylene, they are inefficiently removed by wastewater treatment processes (which they enter through bath and shower water, for example, when used as perfumes or to scent soaps), but there is as yet no indication that they are carcinogenic.

Coumarin is a common perfume component, and it is also used in pipe tobacco and fabric conditioners. It can be derived from a number of sources, including tonka beans and cassia.
cinnamon, and adds a sweet smell similar to that of new-mown hay. The carcinogenicity of coumarin is not yet established but is suspected by some authorities, and it is toxic to the liver and kidneys in animal studies. Coumarin is also one of the primary culprits in the allergic or sensitive reaction some people have to perfumes or fragrances; in such people it can induce or aggravate asthma-like symptoms as well as migraines with or without headache.

The modern perfume family of aquatics/oceanics relies heavily on aldehydes, especially associated with sharp and ozonic smells or fresh scents like Davidoff Cool Water or Christian Dior's Dune. However, different aldehydes have different scents, and most modern perfumes, regardless of fragrance family, include aldehydes in their formulation. In women's perfumes, for example, aldehydes are associated less with the aquatic family and more with Chanel No. 5, in which aldehydes provide a rich warmth rather than a sharp freshness. Aldehydes are also used in many “fresh laundry” or “fresh cotton” smells, both in perfumes and in detergent and air fresheners.

Aldehydes are organic compounds, at least some of which are believed to be carcinogenic. Acetaldehyde, for instance, is known to damage DNA and interfere with muscle development, and is classified as a Group I human carcinogen by the IARC. It is one of the carcinogens found in tobacco smoke, as well as a result of off-gassing from many building materials, including linoleum, wood varnish, pine flooring, and many water-based paints.

Studies have also found links between working in the fragrance industry and the development of prostate cancer or male breast cancer.

See Also: Breast Cancer, Male; Chemical Industry; Deodorizers; Prostate Cancer.

Further Readings

Perlmutter Cancer Center

The Laura and Isaac Perlmutter Cancer Center is a big name in cancer care. The center, which was founded in 1975 as the New York University Cancer Institute (NYUCI), is a National Cancer Institute (NCI)—registered group. The center gets its name from the New York University Langone Medical Center of which it is part. In 1983, the center was branded the Kaplan Cancer Center. In 1991, the NYU Cancer Center in New York City and the Cancer Center at the Nelson Institute of Environmental Medicine merged. Since its establishment, the mission of the NYUCI has been and still is to learn about how cancer is formed and to use that knowledge to control the development of this disease.

NYUCI is a translational cancer center and takes a team approach to cancer. The institution has over 250 members who come together from a variety of disciplines to create collaborative research endeavors and clinical care teams. The team at the center, the researchers and scientists, share a goal of understanding how cancer develops at the molecular level and how that knowledge can be harnessed to reduce the risk of cancer and to treat the disease. To achieve this, the center seeks and creates new opportunities for collaboration between investigators within and outside the institution.

For example, researchers at the center collaborate with others in the New York University network of campuses (such as the Washington Square Campus in Lower Manhattan) as well as with researchers at other academic, research, and medical institutions, including Smilow Cancer Research Center, Tisch Hospital, Kimmel Stem Cell Center, Skirball Institute, Rusk Institute, the Hospital for Joint Diseases, and the Nelson Institute for Environmental Medicine. The Perlmutter
Cancer Center also works in affiliation with other institutions, including Woodhull Medical Center, Bellevue Hospital Center, and the U.S. Department of Veterans Affairs.

The team structure adopted by the institution is based on the knowledge that cancer is a complex problem requiring complex solutions. Moreover, the solutions are not to be limited to a single study area. Therefore, to develop appropriate solutions for cancer, various experts from a variety of disciplines are brought in to create collaborative research endeavors and clinical care teams. The center offers a full continuum of personalized care, from prevention through diagnosis, treatment, and posttreatment support. This personalized care offers the most up-to-date treatments for all cancers, and the institution is accelerating the pace of research and clinical care for all types of human cancer to develop better, more sophisticated, and appropriate care strategies. In 2014, the Perlmutter Cancer Center launched key studies in cancer health care disparities, molecular research, lung cancer, melanoma, and genetic or cellular signals within the body.

The Perlmutter Cancer Center is part of the NYU Langone Medical Center. The NYU Langone Medical Center is a world-renowned academic medical center located in Midtown Manhattan. Patients in the Perlmutter Cancer Center who are also being treated for other non-cancer medical needs, for example cardiovascular disease, have access to expert medical staff in place to provide that specialized health care too. This means an individual seeking treatment at Perlmutter will receive treatment that focuses not only on cancer but a holistic kind of treatment that focuses on the person as a whole. Patients can get all the care they need in one facility.

Perlmutter Cancer Center serves a diverse patient population. Persons seeking health care here come from all cultural backgrounds, from a variety of socioeconomic levels, and from many different countries. According to research and as has been practically established, cancer patterns and outcomes may vary according to such demographics; this means doctors and other health care professionals at the center learn a great deal about cancer by observing its presentation and behavior in different patient groups. This knowledge can lead to the development of better diagnostic and treatment services for all patients, regardless of their backgrounds. This is a benefit not only to the health professionals at the center but also to the patients, because such knowledge is used by the professionals to offer better and more suited care according to the patient’s specific history.

In early 2014, the institution changed its name to the Laura and Isaac Perlmutter Cancer Center. Laura Perlmutter is a member of the advisory board of the Perlmutter Cancer Center and Isaac Perlmutter is chief executive officer of Marvel Enterprises; both are trustees of the New York University Langone. The institution was formally renamed to Laura and Isaac Perlmutter Cancer Center to recognize the remarkable gift by Laura and Isaac Perlmutter.

Perlmutter Cancer Center scientific research programs focus on either fundamental questions about the biology of cancer or disease-specific research questions related to various types of cancer. Some of the current research programs are in growth control, cancer immunology, epidemiology and cancer control, environmental and molecular carcinogenesis, genitourinary cancer, breast cancer, stem cell biology, thoracic cancer, melanoma, hematologic malignancies, sarcoma, and gastrointestinal cancers. The results of each research program are translated into improved and comprehensive care for patients.

In addition to research and health care for cancer patients, the Perlmutter Cancer Center offers a variety of outreach and education programs for both patients and members of nearby communities. These outreach programs take the form of community seminars, cancer screenings, special programs for diverse populations, and a speakers’ bureau. Through these activities, the center is able to educate the people it serves by making cancer care and education available to all.

Michael Fox
Independent Scholar

See Also: Education; Kimmel Cancer Center; National Cancer Institute.

Further Readings
Peru

The Republic of Peru is a South American country with extreme geographical differences within its territory, ranging from the high Andes mountain peaks to the vast Amazon Rainforest Basin to the arid plains of the coastal regions. For much of its history, Peru was home to the ancient Inca Empire, which built the colossal religious buildings that still today dominate the well-known touristic landscape of the Sacred Valley of Machu Picchu.

In 1532 Francisco Pizarro’s Spanish conquistadors defeated Inca Emperor Atahualpa and started the colonization period, exploiting Peru’s vast natural resources (mostly gold and silver), enslaving the population, forcing the Catholic religion with the Inquisition violence, and importing African slaves to increase the labor force. Peru revolted against the Spanish crown in 1824, defeating it in the Battle of Ayacucho and declaring its independence under the presidency of Ramón Castilla. Through the 19th and 20th centuries, Peru waged numerous wars against its neighboring countries (Chile, Ecuador, Colombia), and together with the negative influence on its economy of the Great Depression first and a series of political struggles and military coups later, the country bled to bankruptcy several times. In particular, Peru’s economic and social stability suffered much through the 1980s and 1990s because of the influence of chronic inflation and the terrorist campaign carried out by the Shining Pact and Túpac Amaru Revolutionary Movement (MRTA) leftist insurgent troops against the Alberto Fujimori government. Internal conflict provoked at least 70,000 victims, many human rights violations such as mass murder, summary trials, and use of torture, and it is still going on today. Today Peru is a multiethnic country struggling to improve its economy: while still suffering widespread poverty and wealth distribution disparity, it saw an economic boom during the 2000s and today continues to grow rapidly.

Despite the existence of a public system of primary care managed by the Ministry of Health of Peru (MINSA) and the EsSALUD social security program, the Peruvian health care system still shows significant disparities in care between middle-income and poor citizens. In particular, most of the rural or Amerindian indigenous population still seek medical treatment from traditional healers and shamans (the so-called curanderos), who mix modern medicine with a more philosophical and often nonscientific approach. However, many of the plant-derived medicinal products and even some insects from the Coleoptera family used in ethno-traditional Peruvian medicine show promising activities as anticancer agents, although more studies and clinical trials are still required to properly assess their real benefits. A total of 17 plant species are used in the preparation of herbal remedies used in cancer treatment by local healers, mostly coming from the Asteraceae and Gentianaceae families. Among those, three plants in particular have shown noticeable antitumor activity: cat’s claw (Uncaria tomentosa), maca (Lepidium meyenii), and dragon’s blood (Croton lechleri).

The first modern cancer treatment facility, the Instituto Nacional de Enfermedades Neoplasicas (INEN), was founded in 1932 under its original name Instituto Nacional de Radioterapia (National Institute of Radiotherapy), but it was reorganized in 1952 by Eduardo Cáceres. Today the INEN is still one of the most advanced cancer facilities in the country. Since then, many efforts have been made by the Peruvian government in terms of cancer prevention, such as introducing the human papillomavirus (HPV) vaccine, joining the international organization Union for International Cancer Control (UICC), implementing communication strategies to increase public awareness about cancer, and financing projects for massive population screening and early cervical cancer detection using acetic acid (VIA). In 2004 the Multisectorial Coalition Against Cancer was formed to write and implement a National Cancer Control Plan, and in 2011 a cancer control plan called Esperanza was launched to
provide cancer care for the low-income Peruvian population.

In Peru cancer is the second-leading cause of death, following cardiovascular disease as in most developed countries. According to data provided by the Health Ministry, the annual mortality from cancer is 107 per 100,000 population, with an incidence of 157 people per 100,000 population, a 75.9 percent lethality, and 45,000 new cancer cases diagnosed each year. In Peru, three national population-based cancer registries are available: the first two, the Registro de Cáncer de Lima Metropolitana and Registry of Cancer of Trujillo City were founded in 1968 and 1984, respectively, and the third, the Arequipa Poblational Cancer Registry, was inaugurated in 2000. In 2006 the System of Epidemiological Cancer Surveillance was established in an effort to unify population registries. The most common cancer types in Peru are stomach cancer for both sexes, cervical and breast cancer for females, and prostate and colorectal cancer for males. Risk factors are those most commonly found in well-developed countries: obesity, bad dietary habits, sedentary lifestyle, alcohol consumption, and smoking. Also, recent studies reported that elevated levels of heavy metals such as lead, copper, and arsenic have been found in Peruvian drinking water. In particular, in many samples collected from water around the entire country, arsenic concentration was found to be up to four times higher than the World Health Organization (WHO) recommended limit of 10 μg/l, probably the result of industrial pollution from smelters, mines, and refineries discharging wastewater in the Rímac river basin. Exposure to moderate-to-high (more than 50 μg/l) levels of arsenic in drinking water is associated with an increased risk of lung, bladder, and skin cancer.

Claudio Butticè
Independent Scholar

See Also: Alternative Therapy: Herbs, Vitamins, and Minerals; Cervical Cancer; HPV Vaccination; Stomach (Gastric) Cancer.

Further Readings

Pesticides

The U.S. Environmental Protection Agency (EPA) defines a pesticide as “any substance or a mixture of substances intended for preventing, destroying, repelling, or mitigating any pest.” Pests are living organisms that are prevalent in unwanted areas or that cause damage to crops, humans, animals, or buildings. Pesticides are most broadly classified according to their target organisms. For instance, herbicides are used for weeds; insecticides for insects, etc. Pesticides encompass a variety of chemical structures and can be grouped by their common elemental forms. Phenoxy herbicides, organochlorine insecticides, and organophosphate insecticides are examples of different chemical categories. This article provides an overview of
the history of pesticide development and its uses, sources and routes of human exposure, environmental and human health effects, and regulations and exposure prevention.

History of Pesticide Development and Uses
The first recorded purposeful use of pesticides occurred as early as 2500 B.C.E. when Sumerians rubbed odorous sulfur compounds on their bodies to repel insects and mites. Ancient civilizations in Egypt, China, Greece, and elsewhere similarly developed compounds based on mercury and arsenic to control pests on their bodies and in homes. Personal and home uses eventually extended to protect agricultural crops from damage. Roman scholar Marcus Terentius Varro discovered the first chemical herbicide in the 1st century B.C.E. when he observed that amurca (a substance naturally produced from crushed olives) was toxic to weeds, as well as to ants and moles. Sulfur, mercury, arsenic, and salt also continued to be used alone or as part of simple mixtures to control weeds and insects.

Although pesticides have been used for centuries, progress in pesticide development was minimal until recent times. The agricultural revolution in the 18th and 19th centuries in Europe sparked the need for greater crop protection. Increased scientific knowledge about insects, fungi, and plants led to the design of agents targeted to specific organisms, such as Paris green to control the potato beetle. International trade also promoted the discovery and use of the naturally occurring insecticide pyrethrum. The organochlorine insecticide DDT (dichlorodiphenyltrichloroethane) was developed by Swiss scientist Paul Müller in 1939 as the first synthetic organic chemical for selective control. It was used extensively during World War II to kill typhus-carrying lice and malaria-carrying mosquitoes, earning Müller a Nobel Prize in Medicine. Although DDT was eventually banned in the 1970s and 1980s due to its harmful effects on wildlife and human health, it is still used to treat bed nets in malaria-endemic regions. Pyrethroids are an alternative to DDT for this purpose.

Pesticides that were developed for the purposes of warfare in World War II were later redirected for use on farms. Parathion and the phenoxy herbicides 2,4-D (2,4-dichlorophenoxyacetic acid) and 2,4,5-T (2,4,5-trichlorophenoxyacetic acid) are examples of agents developed during this era. Since then, the agrochemical industry has developed synthetic pesticides that have been widely used, for example, to sanitize water supplies and to protect buildings from structural damage. Thousands of years after their first recorded uses, pesticides remain the frontline means of controlling disease, weeds, insects, and other organisms at home, work, and in the environment.

Sources and Routes of Human Exposure
Occupational exposure to pesticides may occur during pesticide manufacturing processes and from mixing, applying, and/or handling pesticides in agriculture and other industries. Around the world, the highest levels of pesticide exposure are found in farmworkers, pesticide applicators, and people who live near heavily treated agricultural land. Farmers and farmworkers directly handle about 70 to 80 percent of the pesticides that they use and are at the highest risk of exposure. Three-quarters of U.S. households use at least one pesticide product at home and approximately 80 percent of most Americans’ exposure occurs indoors.

Residential pesticide exposure can occur from treated kitchen and bathroom surfaces, insect and rodent baits and traps, lawn and garden treatments, and flea and tick products on pets. Respiratory exposure to pesticide vapors and very small particles pose the most serious risks, and pesticides can be rapidly and completely absorbed through the thin and permeable lung tissues. Since pesticides are ubiquitous in treated water and store-bought fruits and vegetables, contact can also occur through the mouth. Skin absorption is the most common route of exposure in typical work environments. Genital and head regions are the most vulnerable areas. Certain pesticides continue to be used for preventing and killing bodily pests, such as lindane, a topical insecticide for head and body lice. The duration, frequency, and intensity of exposure are important variables in determining total or cumulative lifetime exposure and bodily absorption. The selection of the method(s) to assess exposure to pesticides is often guided by feasibility and cost.

Pesticide
Pesticide exposure is associated with many known and suspected environmental and human health effects. One of the most prominent findings was documented in Silent Spring, a book by Rachel
Carson published in 1962 that described declines in bird populations believed to occur as a result of eggshell thinning from DDT exposure.

The book was met with some criticisms; however, it spurred discussions about national pesticide policy and led to a countrywide ban of DDT for agricultural uses, as well as a grassroots movement that eventually created the EPA. Recently, scientists have found potential linkages between honey bee colony collapse disorder and the spraying of certain pesticides on agricultural crops that may affect bees’ immune systems. Identifying other possible causes is currently an area of active investigation. Studies are also ongoing for assessing possible reproductive health effects of atrazine, a commonly used herbicide, on frog populations. The intensive, repeated use of pesticides over time has contributed to insecticide resistance. Nearly every insecticide is now associated with insects that are genetically no longer responsive to its intended purpose. This often leads to more frequent insecticide applications until another agent becomes available. The risks of evolving resistance and cross-resistance are related concerns.

Children exposed to high levels of pesticides over a short period of time can experience neurological effects, nausea, and weakness; in the long term, exposure may cause learning disabilities, asthma symptoms, and birth defects, among other potential effects. Children are more vulnerable than adults to the adverse health effects of pesticides due to their smaller size, greater hand-to-mouth and outdoor activities, higher respiration rate, and active cellular development. Unintentional and intentional pesticide poisonings occur among children and adults worldwide, and these acute exposures are associated with illnesses and death.

Some of the human health effects that have been investigated over several decades of population-based research are immune suppression, neurological effects, skin and eye irritation, hormone disruption, and cancer. In a case-control study of Canadian men, there was a 30 percent increased risk of non-Hodgkin’s lymphoma among those who used 2,4-D and an over twofold risk associated with the use of mecoprop. In this population there were also higher risks of multiple myeloma observed for 2,4-D, glyphosate, mecoprop, malathion, carbaryl, and chlordane based on days per year of use. The small number of cancer cases is a major limitation of these analyses; nevertheless, they do provide important leads for further research.

The International Agency for Research on Cancer (IARC) has assessed the carcinogenicity of certain pesticides. To date, the pesticides that IARC has evaluated have been mostly categorized as “possible human carcinogens” (Group 2B) based on limited human and animal evidence. These include 2,4-D, DDT, 2,4,5-T, lindane, chlordane, mecoprop, and dicamba. Many were evaluated in the 1980s and 1990s. Evidence published since then confirms these findings and has identified additional pesticides that could be associated with specific cancers.

**Regulations and Exposure Prevention**
Countries have developed legislation and regulations that govern pesticide import and export, uses, and handling. For instance, in Canada, the Pest Control Products Act and Regulations is a legal document intended to ensure the acceptability of the risks, merit, and value of pest control products. Related laws, such as the Fertilizers Act and the Fisheries Act, are also involved in Canadian pesticide regulation. In the United States, pesticides are regulated federally by the EPA and by state-level agriculture offices. Some countries have developed bilateral agreements for trading pesticides and pesticide-treated products. The European Union has several pieces of legislation that set data requirements for active substances, plant protection products, sustainable pesticide use, implementation rules, and approval of active substances.

The International Code of Conduct on Pesticide Management provides a global framework for pesticide management, particularly for countries that use highly hazardous pesticides banned in other regions for health reasons. The known and potential harms of pesticides can be best addressed by preventing exposure. Eliminating, substituting, or reducing pesticide use can make meaningful impacts on lowered risks for some adverse health outcomes. The use of pesticide alternatives can also mitigate environmental concerns, save money spent on pesticides, and meet growing demands for organic food. Alternatives include but are not limited to integrated pest management and organic farming. Environmental health research organizations, such as the Environmental Working Group, aim to inform consumers about potential ways to reduce exposure through initiatives like Dirty Dozen
Plus and Clean 15. As a last resort, the correct use of personal protective equipment can reduce pesticide absorption and is especially relevant for occupationally exposed populations.

**Conclusion**

Pesticides have been used for centuries and play an important role in protecting human health, food and water supplies, and infrastructure. The history of pesticide development demonstrates a marked transition from localized use of elemental compounds to global application of complex, mass-produced synthetic mixtures. Exposure is widespread in workplaces, homes, and the environment and may occur dermally, orally, and through inhalation. Increasing evidence about adverse environmental and health effects associated with pesticides has prompted regulatory agencies to critically evaluate their use and make recommendations to reduce exposure. The advantages and risks of pesticides need to be carefully weighed in current and future uses.

Manisha Pahwa  
*Occupational Cancer Research Centre*  
Ann Del Bianco  
*York University*

**See Also:** Chemical Industry; Herbicide; Insecticides.

**Further Readings**


---

**Pfizer (United States)**

Pfizer Inc. is the world’s largest research-based pharmaceutical company, with five primary areas of focus, including oncology. Pfizer’s independent business unit, Pfizer Oncology, focuses on the discovery and development of innovative cancer treatments. Over the years, the company has developed and/or marketed drugs to treat breast cancer, prostate and other male cancers, and lung cancer. Pfizer’s drug lines include therapies for leukemia, lymphomas, and other hematologic cancers; colorectal and other gastrointestinal (GI) cancers; bladder, kidney, and other urologic cancers; respiratory and thoracic cancers; and pancreatic, thyroid, and other endocrine cancers.

German immigrants and cousins Charles Pfizer and Charles Erhart founded Pfizer in 1849 as Charles Pfizer & Company. Based in Brooklyn, New York, the company called itself a fine-chemicals business. The company’s offices, laboratory, factory, and warehouse facilities were housed in one building. Over the years, Pfizer developed into a large pharmaceutical company that focused primarily on developing drugs for chronic diseases, such as hypertension. These patients numbered in the millions and typically had to take drugs for the rest of their lives. Pfizer’s later growth was based on drugs such as Lipitor (atorvastatin) for cholesterol and Norvasc (amolodipine)
for blood pressure. In contrast, Pfizer and some other large pharmaceutical companies were less inclined to focus on cancer therapies. Since most cancer cases were terminal, some pharmaceutical companies saw little promise for profit in developing cancer drugs. In 2012, cancer drug sales accounted for only 5 percent of the Pfizer's revenues.

Pfizer, along with other large pharmaceutical companies, eventually turned more attention to developing cancer drugs. The company has experienced falling profits from some of its major drugs, such as Lipitor. The price of cancer drugs, however, began rising dramatically in the 21st century. As a result, developing cancer drugs has become economically attractive. In 2013, some cancer drug therapies cost $100,000 a year or more. Ongoing, extraordinary discoveries of how to target cancers via genome and other biological mechanisms have also spurred drug research.

Pfizer increased its commitment to developing new cancer drugs when it established its Oncology Research Unit. With their primary cancer research facilities based in San Francisco, California, Pfizer has committed 1,000 scientists to focus on cancer drug research. These researchers are developing compounds aimed at customizing treatment options for cancer patients and extending survival rates.

Pfizer researchers are studying potential cancer compounds for multiple tumor types. The company has four cancer biology areas: anti-angiogenesis, signal transduction, cell cycle, and metabolism. The research is often conducted collaboratively with other researchers outside Pfizer. These collaborators include academic researchers, cooperative research groups, and governments. Pfizer places a special focus on researching compounds in early clinical development that have shown promise following randomized controlled multicenter trials.

Pfizer is expanding several key cancer areas, including renal cell carcinoma, lung cancer, hematologic malignancies, and breast cancers. In terms of emerging areas of cancer biology, Pfizer researchers are conducting studies in areas such as epigenetics and antibody-drug conjugates. The latter is a class of biopharmaceuticals and targeted therapies that combine the specificity of an antibody to distinguish between healthy and diseased tissue. The therapies involve combining antibody-drug conjugates with the cell-killing power of chemotherapy.

In 2010, Pfizer began a small clinical trial at the Dana-Farber Cancer Institute to study crizotinib, a drug that targets a specific gene alteration that can cause certain types of cancer. Pfizer received approval from the U.S. Food and Drug Administration (FDA) in 2013 to market crizotinib under the trade name Xalkori. Initially, the drug was marketed for certain non–small cell lung cancer patients. Non–small cell lung cancer is the most common type of lung cancer. Pfizer is also developing a drug called palbociclib for breast cancer. The drug targets certain proteins in the body called CDKs. In February 2014, the company started a Phase 2 clinical study of palbociclib that showed promising results for certain advanced breast cancers. Pfizer also started petitioning the FDA in 2014 to allow it to market palbociclib. The company based its case on a 165-patient study showing that palbociclib, combined with another current treatment for breast cancer, stopped tumors from growing for a median of 20-plus months, twice as long as the other treatment alone. In addition, Pfizer is evaluating palbociclib in other tumor types, including melanoma, lung cancer, and head and neck cancer.

Pfizer's immune-oncology program includes studies on how to harness the immune system to treat disease, specifically by targeting a protein involved in immune cell proliferation and survival. One such research area focuses on a smoothened protein inhibitor (SMO) that has potential to treat a wide range of hematologic diseases. The SMO works by blocking cancer cell growth and survival. Pfizer has also developed the first canine cancer drug in the United States approved by the FDA. The oral therapy is called Palladia and is used to treat mass cell tumors in dogs. Approved for use in 2009, the drug showed in a clinical trial that approximately 60 percent of the dogs given Palladia had their tumors stop growing, shrink, or disappear. Pfizer also seeks to collaborate with other institutions and drug companies in its cancer research efforts. For example, in 2014, the company entered into an agreement with GlaxoSmithKline Inc. (GSK) to research the anticancer efficacy and safety of GSK's trametinib combined with Pfizer's palbociclib. The study features Phase 1 and 2 clinical studies of patients with advanced metastatic melanoma.

In 2014, Pfizer and Merck began collaborating in Phase 1 and 2 clinical studies to test the safety and efficacy of Merck's MKp3475 in combination with
Pfizer’s axtinib (Inlyta). The Merck drug is an investigational anti-PD-1 immunotherapy (PD-1 stands for programmed death receptor 1, an immune-cell pathway). The clinical trial enrolled patients with renal cell carcinoma.

Pfizer also offers patient and prescription assistance programs, including cancer patients. These special programs are designed to help patients with limited incomes and those without insurance to obtain the drugs they need. Among the services are insurance counseling, co-pay assistance, and providing some medicines at increased savings. Pfizer also offers help in finding other assistance programs, both government and private programs. In 2013, the company saw a 29 percent operational growth in oncology.

David Petechuk
Independent Scholar

See Also: Food and Drug Administration; GlaxoSmithKline (United Kingdom); Lung Cancer, Non–Small Cell; Lung Cancer, Small Cell; Prostate Cancer.

Further Readings

Pharmaceutical Industry

Because cancer refers more accurately to a type of disease than a single disease, it is not likely that there will ever be a single “cure for cancer.” Some cancers are caused primarily by genetic factors; others, primarily or exclusively by viruses. Environmental factors loom large. Some cancers are more likely to metastasize than others, or are more resistant to some kinds of treatment than others. The existence of a great variety of cancers has made the pharmaceutical industry's role important insofar as it develops pharmaceutical remedies for specific cancers or the side effects of cancer and cancer treatments. The oncological specialty dealing with drug therapies is medical oncology, which encompasses chemotherapy, hormonal therapy, and targeted therapy, but other specialties—notably gynecologic oncology and pediatric oncology—necessarily rely heavily on drugs as well, and even other modalities of treatment like radiation therapy and surgery still require considerable knowledge of drugs to deal with side effects and comorbid conditions. Frequently, cancer patients are treated by a multidisciplinary team for this reason.

Standard Modalities of Cancer Treatment
Chemotherapy is the most obvious area in which the pharmaceutical industry is involved. A chemotherapy regimen used to treat cancer usually consists of a number of drugs selected for the synergistic effects of their use in combination. Chemotherapy drugs come from a variety of types, including antifungals, antiprotozoals (drugs for infection by protozoans), antibiotics, antituberculars (antituberculosis drugs), antileprotics (antileprosy drugs), antihelmintics (vermicides designed to kill parasitic worms), antivirals, corticosteroids (hormones produced in the adrenal cortex, involved in inflammation and immune response), and cytostatics (cell growth inhibitors) as the most common categories. Alkylating antineoplastic agents are drugs that transfer alkyl groups to a molecule, which can cause DNA damage. This is useful in damaging cancer cells, but like many chemotherapy treatments, alkylating agents can themselves be carcinogenic to healthy tissue. Nitrogen mustard, related to the mustard gas used as a chemical weapon in World War I, was the first modern chemotherapy treatment for cancer after experiments with the gas were conducted during World War II. There are dozens of different standardized combinations, many of which are associated with specific cancers. For instance,
COPP—cyclophosphamide (a nitrogen mustard alkylating agent), Oncovin (the mitotic inhibitor vincristine), procarbazine (an antineoplastic alkylating agent), and prednisone (a corticosteroid)—is used to treat Hodgkin’s lymphoma, while VAD—vincristine, Adriamycin (an antibiotic), and dexamethasone (a corticosteroid)—treats multiple myeloma. Chemotherapy is often used in conjunction with other therapies, including surgery, radiation therapy, targeted therapies, photodynamic therapy, and hyperthermia therapy. Adjuvant chemotherapy follows local radiotherapy or surgery in order to reduce the risk of recurrence.

Most chemotherapy drugs are administered intravenously, though a small number are available only in oral doses. Special catheters and other systems have been developed for chemotherapy patients in order to avoid the need for repeated insertion while also offering low infection risk. In a small number of cases, non-melanoma skin cancer can be treated with topical chemotherapy. Chemotherapy usually is performed in several rounds or cycles, partly because only a fraction of the tumor cells are killed with each treatment and partly because of the often severe side effects experienced by the patient. Dosage is usually calculated based on body surface area (BSA), though recent work has suggested that factors like obesity, genetics, age, gender, disease state, and drug interactions have a significant impact on drug absorption, which may result in different therapeutic outcomes for BSA-identical chemotherapy patients.

The pharmaceutical industry also develops hormones for the treatment of cancer, in order to control gene expression in cancer cells. This is particularly true for treating breast, prostate, endometrium, and adrenal cortex cancers, and to treat side effects of cancer or chemotherapy such as anorexia. Tamoxifen is a hormone treatment used in breast cancer treatments.

Aromatase inhibitors are some of the best known hormone treatments. These drugs block the production of estrogen in postmenopausal women, arresting the growth of hormone-receptor breast cancer. Aminoglutethimide similarly treats adrenal gland cancers, and the side effects of adenocortical carcinoma. While many aromatase inhibitors can promote osteoporosis in women, exemestane is an aromatase inactivator that lacks that side effect. It is used to treat metastatic breast cancer that is resistant to tamoxifen.

Another hormone treatment used is gonadotropin-releasing hormones, which induce chemical castration by suppressing the production of estrogen and progesterone in women or testosterone in men. This can be an effective approach to treating prostate cancer, the growth and survival of which is assisted by exposure to testosterone. Prostate cancer is also treated with anti-androgens, which inhibit the androgen receptor in order to block the effects of testosterone on the tumor.

The term targeted therapy is used for pharmaceuticals that are formulated to be more selective than chemotherapy regimens, and may include both drugs and biologics. Most targeted therapies are either monoclonal antibodies, a biologic treatment that binds to a specific targeted substance associated with a particular cancer, or small molecules—organic compounds with a molecular weight below 900 daltons. Targeted therapies include imatinib mesylate, Gefitinib, Erlotinib, Sorafenib, Sutinib, Dasatinib, Lapatinib, and Nilotinib, all of which are small molecule tyrosine-kinase inhibitors; Torisel, Afinitor, Mekinist, and Tafinlar, all of which are
small molecule serine/threonine kinase inhibitors; and a host of monoclonal antibodies. Tamoxifen is perhaps the best known targeted therapy. Developed by AstraZeneca's predecessor Imperial Chemical Industries, it targets the estrogen receptors in breast tissue in order to treat hormone receptor positive breast cancer in premenopausal women and is one of the most important and commonly used anticancer drugs.

**Experimental Cancer Treatments**

There are always numerous cancer treatments in various stages of experimentation. The Pharmaceutical Research and Manufacturers of America lists 771 drugs in development for cancer, either in clinical trials or awaiting review by the U.S. Food and Drug Administration (FDA).

A small clinical trial of dichloroacetate as a treatment for brain cancer seems to have been successful in killing off tumor cells by reactivating suppressed mitochondria. It has the benefit of being an inexpensive pill, compared to the costs and rigors of chemotherapy. The antioxidant quercetin has shown promising results in treating oral cancers, leukemia, skin cancer, and prostate cancer.

The first human trials of BI811283, a small molecule kinase inhibitor, were conducted in 2010 as a treatment for acute myeloid leukemia and solid tumors. There is sometimes a fine line between experimental treatments that are not yet proven and alternative therapies that have been proven ineffective.

Another possible treatment is HAMLET (Human Alpha-lactalbumin Made LETHal to Tumor cells), a complex of alpha-lactalbumin and oleic acid that acts selectively to kill cancer cells without harming healthy cells. It is derived from human breast milk and has been used successfully as an antibiotic adjuvant to treat MRSA infections and benign skin tumors. It is being studied for use in the treatment of numerous cancers.

**Treating the Side Effects of Cancer and Cancer Treatments**

Almost every use of chemotherapy results in a weakening of the immune system, typically through the decrease of white blood cells. This can lead to an increased likelihood of infection while receiving treatment. More than three-quarters of such infections come not from external sources like contact with contagions in public places but from microorganisms residing in and on the patient’s own body that the immune system is ordinarily able to resist. There is actually a cascading effect here, often leading to a series of interrelated treatments and illnesses:

1. Chemotherapy treats the patient’s cancer but weakens the immune system.
2. The patient becomes ill due to resident microorganisms such as bacteria on the skin.
3. Both the symptoms and the cause of the secondary illness are treated with a course of antibiotics prescribed to deal with the bacterial infection(s).
4. Just as chemotherapy weakens healthy systems in its efforts to kill off cancer, antibiotics kill off good bacteria in the attempt to kill off the bad bacteria.
5. No longer held in check by the bacteria with which they compete, fungal life that resides on and in the patient’s body thrives, resulting in one or more fungal infections, such as a yeast infection, thrush, rashes, or dandruff.
6. Antifungal medications are prescribed, either internal or topical, which in some cases can result in bacteria thriving once more.

Chemotherapy alone taxes the patient’s system, but it is these secondary and tertiary illnesses, and the toll exacted by adding these medications to those taken as part of the chemotherapy regimen, that can further exacerbate the patient’s exhaustion, weakness, and accumulation of side effects. It is not inconceivable for the above cycle to play out just in time for the patient’s next round of chemotherapy to begin, starting the pattern over again.

As difficult as this can be to experience, it needs to be pointed out that the alternative is still worse, and that the availability of these medications to deal with each stage of the process is key to the survival rate of modern cancer patients.

One of the most common side effects of chemotherapy and radiation therapy is nausea, which is worst with certain chemotherapy drugs and regimes and which tends to be exacerbated if the patient is female, under 55, experiences anxiety or
depression, or has a history of motion sickness or pregnancy-associated nausea. Nausea can also be caused by the cancer itself, by physical side effects of the cancer like bowel obstruction, by ongoing constipation, by radiation therapy, and as a side effect of other maladies caused by cancer or cancer treatments, like dehydration, electrolyte imbalance, aspiration pneumonia, or anxiety. More than half of patients with advanced cancer experience nausea or vomiting, as do about two-thirds of patients undergoing radiation therapy.

Chemotherapy-induced nausea can be treated through a number of drugs, many of which were developed for the purpose. There are both prophylactic drugs to prevent the nausea and rescue treatment to deal with nausea once it has occurred: 5-HT3 inhibitors such as dolasetron, granisetron, and ondansetron, which act as receptor antagonists to a type of serotonin receptor in the vagus nerve, have been approved for treating chemotherapy-induced nausea as rescue treatments, usually administered in the first 24 hours, and are available orally and as injections and transdermal patches. Newer NK1 inhibitors, which work on a receptor found in the central and peripheral nervous systems, are sometimes administered with setrons and together can control nausea almost entirely, often with few other side effects.

Antipsychotics like olanzapine have also been tested for treating nausea and can achieve complete prevention on their own in some patients, or with setrons or dexamethasone (a corticosteroid) in others. (Despite the name, antipsychotics—sometimes called neuroleptics and referred to as tranquilizers in older texts—are increasingly used to manage nonpsychotic conditions.) Medical marijuana is also a common remedy, and synthetic THC (tetrahydrocannabinol) has been developed under the brand name Marinol. Some nausea can also be treated with antihistamines that block the H1 receptors in the vomiting center of the medulla, or with anticholinergic agents that relax smooth muscle, which also helps in managing bowel obstruction. Anticipatory nausea, which is likely a learned response, develops in about 20 percent of chemotherapy patients. The only drugs shown to be effective in counteracting it are benzodiazepines like clonazepam and lorazepam, which become less effective with frequent use.

Chemotherapy can also induce peripheral neuropathy, a progressive pain, numbness, tingling, and/or sensitivity to cold in the hands, feet, and esophagus. This happens to about one-third of chemotherapy patients, though it is more likely to be induced by some drugs than others. Neuropathy increases in severity and extent with each round of chemotherapy, leveling off when treatment is completed—though with cisplatin, oxaliplatin, and carboplatin, all of which are based on platinum, neuropathy continues to worsen until several months after treatment has ended. Some chemotherapy-induced peripheral neuropathy (CIPN) is permanent, and the numbness in particular is treatment resistant. In other cases, pain can be managed, and several types of treatments have been developed to inhibit the development of CIPN. Two antidepressants—velafaxine and duloxetine—have shown promise here, as has intravenous administration of calcium and magnesium. Valproate, an anticonvulsant that is effective in diabetic neuropathy, has worked prophylactically in tests on rats.

One of the most serious side effects of chemotherapy is myelosuppression, also called myelotoxicity or bone marrow suppression. This condition results from damage to normal cells—specifically leukocytes, erythrocytes, and thrombocytes—by the drugs used to kill or suppress the cancer cells, and for this reason the risk varies according to the kind of cancer and the chemotherapy regimen being applied. Bone marrow is where blood cells, including the white blood cells of the immune system, are produced, so causing a deficiency of marrow and thus of blood cells puts the immune system in serious jeopardy. Normally minor infections can become life threatening due to the body’s inability to fight them, and a reduction of red blood cells leads to anemia. In some cases this is treated by changing the chemotherapy regimen. In others it is treated through the aggressive use of intravenous antibiotics in order to quickly stop any and all infections.

Almost all high-dose chemotherapy patients experience mucositis, the inflammation and ulceration of mucous membranes in the digestive tract or the mouth, as do many low-dose chemotherapy patients and radiotherapy patients with head or neck cancers. Bone marrow transplants increase the odds of developing mucositis as well. Oral mucositis is treated with medicinal mouthwashes, often containing a viscous preparation of topical analgesic lidocaine for pain relief. Episil, marketed by Can- gene, is approved for pain management caused by
oral lesions, including oral mucositis, and the FDA has also approved MuGard, an oral protectant that has some success in preventing the development of oral mucositis. Untreated, oral lesions can become severely infected, postponing the next round of chemotherapy.

“Chemo fog” or post-chemotherapy cognitive impairment is suffered by about a quarter of chemotherapy patients and involves difficulties in thinking, reasoning, memory, attention, and/or motor control. This may last a few days or as long as 10 years after the final chemotherapy treatment. The mechanisms are not well known, and oncologists do not always adequately prepare patients for the possibility that life after cancer may not be a full return to normal. Most treatments are either off-label or in clinical trials. Clinical trials and experimental treatments include stimulants and antioxidants, while modafinil, which improves alertness and is approved for narcolepsy, is sometimes prescribed off-label.

**Major Pharmaceutical Companies**
The largest pharmaceutical companies in the oncology field, by 2013 sales, are Roche (with sales more than twice as high as Amgen's), Amgen, Novartis, Celgene, Johnson & Johnson, Lilly, AstraZeneca, Merck & Co., Bristol-Myers Squibb, Takeda, Pfizer, GlaxoSmithKline, Bayer, Astellas, Sanofi, Merck (Germany), Biogen Idec, Eisai, Kyowa Hakko Kirin, Otsuka, AbbVie, Teva, Ipsen, Gilead Sciences, and PDL BioPharma.

Bill Kte'pi
Independent Scholar

**See Also:** AstraZeneca (United Kingdom); Celgene (United States); Chemoprevention; Chemotherapy; Daiichi Sankyo (Japan); Estrogen, Steroidal; Experimental Cancer Drugs; GlaxoSmithKline (United Kingdom); Johnson & Johnson (United States); MedImmune (United States); Merck (Germany); Merck & Co. (United States); Novartis Group (Switzerland); Pfizer (United States).

**Further Readings**

**Pheochromocytoma**
Pheochromocytomas are rare catecholamine-producing neuroendocrine tumors originating from the chromaffin cells of the adrenal medulla. In some cases, tumors arise from within the extra adrenal chromaffin tissue and are called paragangliomas (PGL). They are also commonly associated with several metabolic and physiologic disorders, including the risk for hypertensive shock due to catecholamine secretion, including adrenalin, noradrenalin, and dopamine. The leading symptoms of pheochromocytoma—headaches, palpitations, anxiety, and diaphoresis—are caused by sporadic release of catecholamines into circulation.

Paroxysmal and persistent hypertension is also a common symptom in patients, while blood pressure is found to be elevated in over 10 percent of patients. There is no gender bias, and clinical signs vary, making diagnosis particularly difficult. Individuals may present first symptoms at any age; moreover, the age of presentation has been shown to provide insight into the affecting mutation and tumor phenotype. We know that individuals with the heritable syndrome often present at earlier ages than those with sporadic disease. Additionally, epinephrine-secreting tumors are shown to present later in life. Pheochromocytomas are most likely to be sporadic and without signs or symptoms in elderly populations. Patients demonstrating adrenergic spells, episodic palpitations, diaphoresis, pallor, and tremors should be evaluated for pheochromocytoma. Additionally, resistant hypertension in patients under the age of 20, alongside abnormal blood pressure during surgery or anesthesia in the presence of adrenal masses, should raise red flags. Individuals likely have a family history of pheochromocytoma and additionally clinical features of catecholamine-secreting tumors.
Tumors commonly arise within the adrenal glands, abdomen, and pelvis. Mutations in the following genes have been linked to tumorigenesis: SDHA, SDHB, SDHC, SDHD, SDHAF2, TMEM127, MAX, EGLN1, HIF2A, and KIF1B. Germline mutations in at least one of these genes accounts for almost a third of all paragangliomas in most individuals. Somatic mutations in genes encoding RET, VHL, NF1, MAX, HIF2A, and H-RAS have also been detected. Chromaffin cells, the underlying catecholamine-secreting tumor cell types, originate from neural crest tissue during development. Failure to diagnose and treat pheochromocytoma can have devastating consequences, such as adrenergic crisis and death. Adrenergic crisis is triggered by release of catecholamines from pheochromocytoma tumors at excessive levels. The release of hormones also occurs in response to drugs, particularly dopamine receptor agonists, sympathetic nervous system agonists, anticholinergic drugs, and catecholamine-sensitizing anesthetics. Physical deformation of tumor mass due to physical repositioning, tensile pressure, and straining or direct manipulation during procedures may also promote adrenergic storm.

Patients who are pregnant and are experiencing uterine contractions and fetal movement and those in delivery may also induce adrenergic crisis. While 24-hour urine tests have been used to make diagnosis, more sensitive methods of measurements include plasma-fractionated metanephrines by HPLC. Diagnoses are confirmed by the presence of plasma normetanephrine and metanephrine above reference values. These often include fourfold elevations in patients. Pheochromocytoma occurring in individuals with MEN 2 has been shown to produce predominantly epinephrine and metanephrine, whereas those in VHL syndrome produce principally norepinephrine and normetanephrine. PNMT, the enzyme that converts norepinephrine to epinephrine, has been found to be over-expressed in MEN 2–associated tumors, while under-expressed in VHL-associated tumors.

Elevated tyrosine hydroxylase activity has been found in patients with pheochromocytoma compared with those occurring in patients with VHL, leading to higher levels of catecholamines and metabolites in patients with MEN 2. Surgical resection remains the primary treatment option for patients with pheochromocytoma, though it is not routinely recommended for the treatment of acute adrenergic crisis. Complications occur, particularly in the context of lacking preoperative evaluation and medical management. These complications include infection and adrenergic crisis. Critical evaluation is recommended in patients undergoing tumor resection to mitigate risk of complications. Appropriate medical management significantly reduces morbidity and mortality risk during surgery. Laparoscopic adrenalectomy (LA) is a well-approved operative technique. The indications for LA include primary hyperaldosteronism, pheochromocytomas, and glucocorticoid-secreting adrenal tumors. A standard treatment regime for patients prior to surgery includes α-adrenergic blockade, and, subsequently, additional β-adrenergic blockade, is required to treat any associated tachyarrhythmias. Arterial blood pressure, heart rate, and arrhythmias are also followed closely.

Godfrey Ilonzo
Independent Scholar

See Also: Adrenocortical Carcinoma; Adrenocortical Carcinoma, Childhood; Surgery.

Further Readings

Philippines

Cancer is the third leading cause of death in the Philippines. Prominent cancer types are lung, breast, cervix, liver, colon and rectum, prostate, stomach, oral cavity, ovary, and leukemia. Medical personnel, facilities, and organizations are acutely aware of this fact and are attacking cancer on several fronts. This entry reviews the efforts toward cancer prevention in and comments on their effectiveness.
The Republic of the Philippines consists of 7,107 islands, a total area of 111,830 square miles, located on the Pacific Rim of southeast Asia. Two thousand of its islands are inhabited. There are no boundaries. It is bordered on the west by the South China Sea, on the east by the Philippine Sea, on the south by the Celebes Sea, and on the north by the Luzon Strait, which separates the country from its neighbor Taiwan. The closest nations to the south are Malaysia and Indonesia. Vietnam and China are the nearest neighbors on the mainland of Asia.

Thirty million employed persons work in agriculture, forestry, and fishing. The unemployment rate is over 9 percent. Fifty percent of the population live below the poverty line. The employed work seven days a week and may take additional jobs to make ends meet. Eight hundred thousand citizens work overseas in Saudi Arabia, Hong Kong, and Taiwan. Over Seas Workers (OSWs) have a governmental agency that looks after their interests. There are laws governing overseas workers but workers may be exploited and mistreated.

Prevention and Treatment of Cancer
The Philippine Society of Medical Oncology, Inc., is a scientific professional organization of oncologists committed to the ethical and holistic practice of medical oncology. According to their definition of “medical oncologist,” there is no separate certification for oncology. Most physicians are internal medicine specialists with extra training in the treatment of cancer. It appears patients are treated in a holistic manner with herbs and traditional remedies as well as advanced modalities. On the subject of preventing cancer by herbal supplements, authorities say that despite the lack of scientific evidence about their efficacy, high doses of vitamins and herbal remedies can be legally administered by medical practitioners. However, they are aware that the applicable standard of care is treatment by chemotherapy and radiotherapy. Before administering alternative remedies, the treating doctor must advise the patient of this. They admit that many of the supplements are without or with only limited scientific evidence as to effectiveness. Nevertheless, there are supplements that are supported by high-level scientific evidence. These supplements include fish oil, vitamin D, medicinal mushrooms, beta-glucans (immune boosters), bioavailable curcumin (powerful antioxidant), green tea polyphenols, pomegranate, acetogenin molecules (shrinks cancer cells), and bioavailable silymarin phytosome (milk thistle plant). Another organization actively engaged in cancer research and treatment is the Philippine Cancer Society (PCS). It is involved in activities dedicated to the prevention and control of cancer. Its advocacies and programs are in cancer registry, education and information for prevention and early detection, patient services, and hospice and palliative care. Registered since 1956, the PCS pioneered in such innovative programs as cancer registry, tobacco control, hospice care, and patient navigation.

The Philippine Department of Health (DOH) is active in fighting cancer. It offers Packages of Services, including free cervical cancer screening every year in 58 DOH hospitals to screen women 30 to 45 years of age, free adjuvant chemotherapy in four pilot hospitals for women diagnosed stage 1 to 3A breast cancer, and free chemotherapy for acute lymphatic leukemia for children with cancer. It also offers various free programs in promotion of a healthy lifestyle for cancer prevention.

Causes of Cancer Deaths in the Philippines
As stated above, cancer happens when normal cells have an abnormal change and grow and spread within the body. These abnormal cells then transform into tumors that can be benign (not cancerous) or malignant. Seventy-five percent of cancer patients in the Philippines are at least 50 years old. The rate decreases for children up to age 14 to 3.2 percent. Unfortunately, cancer still ranked third on the list of leading causes of death in the country in 2010. According to the World Health Organization (WHO), the number of cancer deaths worldwide will increase from 7.6 million to 17 million deaths by 2030. Thirty percent of cancers can be prevented by avoiding smoking, exercising regularly, and eating the right diet. Discussed below are the top causes of cancer deaths in the Philippines for 2010.

Breast cancer is the most common cancer, with 16 percent of 50,000 cases resulting in death. It is the most common cancer among Filipino women. As for prevention, physicians advise women to frequently do breast self-examinations so the disease can be more easily treated in its beginning stages. The Philippine Cancer Society has promised to provide more free mammography services, fine-needle aspiration biopsy, and education campaigns
to help more Filipinas in combating the disease. The Department of Health is leading the way in providing these free services. Lung cancer is the leading type of cancer in Filipino men. It formerly caused more deaths than breast cancer. Lately, more women are contracting lung cancer. Experts advise against cigarette smoking, as nine out of 10 smokers die from the disease. Nonsmokers are also vulnerable due to second- and thirdhand smoke.

Liver cancer appears to be more common in the Philippines than in the United States. Doctors postulate that the higher rate for liver cancer is due to the fact that chronic hepatitis B affects one-tenth of all Filipinos. Chronic hepatitis B causes cirrhosis of the liver, and cirrhosis is a leading cause of liver cancer.

Statistics indicate that 12 Filipinas die of cervical cancer each day. This type of cancer often strikes women between ages 30 and 55. Twenty-two in 100,000 women will get cervical cancer; only 44 percent will survive. Doctors urge women to begin screening for cervical cancer three years after their first sexual contact. There is a cervical cancer (human papillomavirus) vaccine available that should be taken by Filipinas aged 10 years and above.

The remainder of the top cancers common to the Philippines are colon cancer, thyroid cancer, rectal cancer, ovarian cancer, prostate cancer, and non-Hodgkin’s lymphoma. Philippine people are spread out over a large area. Yet there is no shortage of competent physicians and hospitals. It would appear that the people exercise unhealthy lifestyles that lead to disease, especially cancer. Preventive programs are urged by the cancer associations, societies, and the Health Department. Should the Philippine citizens take the advice of experts, cancer rates can come down. Philippine citizens are prone to taking supplements and herbs for treatment, which may work to a degree but not like the care recommended by competent physicians.

Kenneth B. Alexander
Independent Scholar

See Also: Alternative Therapy: Herbs, Vitamins, and Minerals.

Further Readings


**Photodynamic Therapy**

Photodynamic therapy, or photochemotherapy, combines phototherapy with the use of nontoxic light-sensitive chemicals that, when exposed to light, become toxic to targeted cells such as tumor cells or microbes. Photodynamic therapy is best known as an acne treatment, but because of its minimal toxicity and invasiveness, it has also become a useful cancer treatment. Pioneered as a cancer treatment in the early 20th century (though some skin cancers were treated similarly by ancient physicians), photodynamic therapy was clinically tested in the 1970s and has gained ground since.

Phototherapy, or light therapy, is the use of daylight or specific wavelengths of light for therapeutic purposes, usually exposing the patient or parts of the patient to the light for a prescribed amount of time. This has long been useful in treating skin conditions like psoriasis, vitiligo, and eczema, and seasonal affective disorder and some sleep disorders are treatable with light therapy of the eyes. Low-level light exposure may even be a useful adjunctive treatment for wounds.

Phototherapy for skin conditions often involves ultraviolet light exposure. Psoriasis, for instance, is caused by localized inflammation because of immune system responses, which can be suppressed
by exposure to ultraviolet B (UVB) light, and UVB is also useful in repigmentation of patients with vitiligo. However, ultraviolet light is also a key cause of skin cancer because of the genetic damage it causes, and direct exposure—whether via tanning bed or light therapy—exposes the patient to much more ultraviolet light than exposure to sunlight. That said, light therapy typically involves a much shorter period of exposure than do tanning beds, and has a clear therapeutic benefit that may balance out that risk. (Phototherapy lamps for sleep disorders and seasonal affective disorders do not emit ultraviolet light, which is not necessary to their therapeutic mechanisms, and so sustained use does not pose the same risk.)

Photodynamic therapy (PDT) relies not just on light but also on light-sensitive chemicals. Photochemical processes are chemical reactions that involve the absorption of light by molecules or atoms. Familiar examples include the way vitamin D is formed by the skin's absorption of sunlight, or the way plants create nutrients through photosynthesis. Light provides the activation energy necessary for the chemical reactions. Photodynamic therapy uses photosensitizers—molecules that photochemically produce chemical changes—in combination with a light source and oxygen available in the tissues. The resulting chemical reactions produce reactive oxygen species—chemically reactive oxygen-containing molecules. Though reactive oxygen species may be responsible for significant health problems when they overpopulate and cause oxidative damage (believed, by proponents of the free radical theory of aging, to be the fundamental cause of the degenerative effects of age, which is the logic behind the promotion of antioxidants as “anti-aging” substances), they are constantly created and destroyed by normal processes of the body. A wide variety of photosensitizers can be used, including dyes, porphyrins, and chlorophylls. Important characteristics are chemical stability, low dark toxicity, and high absorption. For skin cancer and skin conditions, they are applied topically; in treatment of internal cancers, they are administered intravenously, while the light is delivered by endoscope and fiber-optic catheter. The combination of light exposure and a topical photosensitive ointment for the treatment of skin conditions and possibly skin cancer has been used since ancient times.

Reactive oxygen species are deeply involved with cancer in the body in several ways. At low levels,
and can suppress tumor growth as well as killing off other species, however, activate cell-cycle inhibitors cells once they develop. Higher levels of reactive oxygen species in order to kill cancer cells. Normal cells are generally better able to survive this stress than cancer cells do, but chemotherapy and radiation therapy still both have the same problem—they kill large amounts of normal cells as part of a necessary sacrifice in order to kill even larger amounts of cancer cells.

Oxidative stress results from the imbalance of reactive oxygen species and the body’s ability to detoxify reactive intermediates or repair the damage they cause. Reactive oxygen species can damage every part of the cell, including the DNA, contributing to cancer growth. Oxidative stress is also thought to be implicated in sickle-cell anemia, Alzheimer’s disease, Parkinson’s disease, atherosclerosis, heart failure, autism, vitiligo, myocardial infarction, and chronic fatigue syndrome. The reactive oxygen species created by photodynamic therapy include free radicals in Type I PDT, and singlet oxygen in type II PDT. Photofrin, the trade name of porfimer sodium, was the first photosensitizer approved for use in photodynamic therapy in the West. First approved in 1993 in Canada for bladder cancer, it was subsequently approved by the U.S. Food and Drug Administration (FDA) in 1995 for esophageal cancer and later was approved for early non–small cell lung cancer. Concurrently, photodynamic therapy was intensively developed in Russia, with a photosensitizer called Photogem approved for clinical trials in 1992. China and Japan have made advances in PDT as well, with Chinese oncologists having particularly successful results in developing techniques of using photodynamic therapy on difficult-to-reach tumors.

In most photodynamic therapy, if the photosensitizer is not applied topically, 24 to 72 hours are allowed to pass after it has been injected in order to give the agent time to be absorbed by both normal and cancer cells and to be flushed from normal cells; cancer cells retain it longer. Ideally, the tumor is exposed to light during the period in which the cancer cells still retain the photosensitizer but the normal cells do not. Once activated, the photosensitizer not only kills cancer cells directly but damages blood vessels in the tumor in order to block the flow of nutrients to surviving cells and encourages the immune system to attack remaining cells. PDT is usually an outpatient procedure (overnight hospitalization is not required) like chemotherapy or radiation therapy and is often combined with those adjuvant therapies.

Some studies suggest that light therapy may activate certain hormones associated with reproduction, including testosterone, estradiol, and luteinizing hormone. In some cases, phototherapies should be avoided or side effects prepared for: if the patient is bipolar or is otherwise predisposed toward manic episodes (which can be triggered by intensive light exposure) or photosensitive as the result of a medical condition or medication. Side effects otherwise are usually limited to headache, nausea, and jitteriness. The photosensitizing agent used may have additional side effects, most commonly accompanied by a recommendation to avoid unnecessary exposure to direct sunlight or bright indoor light for six to 10 weeks following treatment. One of the greatest advantages of photodynamic therapy is its lack of long-term side effects, compared to chemotherapy and radiation therapy. Further, it is less invasive than surgery and easier for older or weakened patients to undergo. Unlike radiation therapy, multiple applications to the same site do not have cumulative damaging effects or become less effective; they are also much less costly than other new cancer therapies, such as gene therapy or biologics.

If a topical photosensitizing agent is used in the photodynamic treatment of skin cancer, the crust and scale is first removed from the skin cancer. The agent is applied in the form of a cream that remains on the applied area for three to six hours in order to ensure that the skin has time to absorb it. This makes the skin very sensitive to light; patients often report feeling a stinging or burning sensation (relieved by over-the-counter painkillers or even cool air from a fan) when light is shone on the skin. This is not serious. The area will form a scab after treatment and remain scabbed for at least a week,
Photodynamic Therapy usually three weeks. Thicker skin lesions require multiple treatments, usually spaced a month apart.

Because of the way the light is administered, photodynamic therapy is not useful for large tumors or those that lie far from the surface of the tissue or lining of the organ or cavity where the light can reach. More than one centimeter of tissue will block the light. This is one reason why the first photodynamic therapy approved by the FDA was for esophageal cancer, which is easily accessible to the implements used to expose the tumor to light. With topical applications, such as in treating skin cancer, this is not a concern. Similarly, PDT is not useful for metastasized cancer.

There are several journals devoted to photodynamic therapy, including Photodiagnosis and Photodynamic Therapy, published by the International Photodynamic Association.

Variants of Photodynamic Therapy

PUVA therapy is Psoralen UVA therapy, and uses the photosensitizing drug psoralen in conjunction with ultraviolet A (UVA) light exposure. The use of psoralen allows a lower dose of UVA to be administered. PUVA is useful in treating skin conditions like eczema and psoriasis, but is also a helpful therapy for cutaneous T-cell lymphoma. Further, PUVA therapy may be administered to patients suffering from graft-versus-host disease, such as following a bone marrow transplant. Long-term PUVA therapy is associated with higher risks of skin cancer and squamous cell skin cancer.

Photoimmunotherapy was developed at the National Cancer Institute and combines photodynamic therapy with biologic therapy in the form of a monoclonal antibody (mab). The mab targets human epidermal growth factor receptors associated with breast, pancreatic, and other cancers, while a photosensitizer is activated by near-infrared light. The combination of the two was able to destroy 80 percent of tumor cells in test mice. It has not yet (in 2014) been approved for clinical trials on humans.

Photopheresis (sometimes called extracorporeal photopheresis) is a form of photodynamic therapy incorporating apheresis, the technique of separating out a particular component from blood (the patient's or a donor's) before returning the blood to circulation. In photopheresis, buffy coat (part of a blood sample containing most of the white blood cells and platelets) is separated from the blood, treated with 8-methoxypsoralen, and exposed to UVA light before being returned to the patient. The UVA activates the photosensitive 8-methoxypsoralen, which induces cytotoxic effects on T-cell formation. This process was first described in 1987 and has been approved to treat cutaneous T-cell lymphoma. Side effects include hypotension. Photopheresis is in trials as a treatment for allograft rejection and graft-versus-host disease, which could help cancer patients receiving bone marrow transplants. It is related to the practice of blood irradiation therapy, which exposes blood to light radiation via an intravenous catheter or the blood vessels of the nose, a practice more common in Russia and China.

Photothermal therapy uses electromagnetic radiation—typically infrared light—to excite the photosensitizer to the point that it releases heat in order to kill targeted cells. It does not require the oxygen that standard photodynamic therapy requires. It can be used for various diseases, including cancer, and usually makes use of recent discoveries in nanoscience, particularly nanoparticles. Particles at the nanoscale have special properties, including preferentially accumulating in tumor tissue. For instance, gold nanoparticles can be delivered to the tumor and then heated with infrared light. The gold absorbs most of the light energy and releases it as heat, which destroys tumor cells. Gold has been explored in the form of nanorods and hollow nanospheres, which are absorbed more easily in the SPR region than are solid gold nanoparticles. Graphene nanoparticles in photothermal therapy have been tested on mice. Photothermal therapy is a type of hyperthermia therapy, which uses intense heat to denature cellular proteins and kill cancer cells through various means. Other types of hyperthermia use microwave heating, ultrasound, or induction heating.

Magnetic hyperthermia uses nanoparticles similarly to photothermal therapy, specifically magnetic nanoparticles. When magnetic nanoparticles are exposed to an alternating magnetic field, they produce heat, which in turn kills tumor cells. Clinical trials have been performed in Germany, treating prostate cancer with magnetic hyperthermia followed by radiotherapy.

Ineffective Therapies

In addition to the clinically proven and well-supported uses of phototherapy and photodynamic
therapy discussed above, there are some alternative light therapies for cancer that lack evidential support. One of these is called chromotherapy, color therapy, or colorology, and it purports to use different colors to balance energy levels in a person’s body in order to treat various conditions. Chromotherapy was popularized in the 1930s by Dinshah Ghadiali, who claimed different colored lights had different therapeutic benefits corresponding to different chemicals and organs.

The Dinshah Health Society founded by his son continues to promote chromotherapy, but there are many supporters of the basic concept whose approach is different from and not derived from Ghadiali’s. Often the color used to treat a given cancer is determined not by the fact that cancer is the disease being treated but by the part of the body in which it is found, each area of the body being assigned a different color. One form of color therapy is colorpuncture, which combines color therapy concepts with those of acupuncture in order to apply pressure to “acupoints” with colored quartz and which is predicated on the idea—developed by Peter Mandel in the 1980s—that illness results from poor choices by the individual.

A more recent form of cancer therapy pseudoscience is the use of a light box, emitting either much brighter light than a traditional lamp or lower-intensity light of a specific wavelength, in order to strike the retina and stimulate serotonin production and inhibit melatonin production. This is a reasonably effective treatment for seasonal affective disorder, though not all light boxes marketed for such purpose use the optimal wavelength or intensity. It has absolutely no demonstrated effect on cancer, however, any more than quartz crystal pendants or magnetic bracelets do. Light boxes may seem superficially similar to photodynamic therapy, which lends credence to the claims of their effectiveness, but the differences are important.

Bill Kte’pi
Independent Scholar

See Also: Biologic Therapy; Clinical Trials; Radiation Therapy.

Further Readings

Physical Therapy

Physical therapy is a vital health care profession that assesses and treats individuals with medical or health-related conditions affecting their ability to move, function, and participate in daily activities. Physical therapists, also known as physiotherapists, are engaged in the restoration of movement and promotion of overall health and fitness, quality of life, and improved physical function. It is a dynamic and growing profession with 277,700 physical therapists and 100,700 physical therapist assistants expected by 2022. Physical therapists (PTs) and physical therapist assistants (PTAs) work with individuals who may be in all stages of life—from newborns to the elderly—in a variety of settings, including in oncology with cancer patients. With the
American Cancer Society reporting that nearly 14.5 million Americans are living with or have a history of cancer, and an aging population with increased cancer risk, the need for specific rehabilitation measures for cancer patients will continue to grow.

Cancer is a disease process that may involve body structures such as nerves, bones, blood, and muscles that may alter individuals’ ability to move. Cancer treatment can include surgery, chemotherapy, and radiation, each of which may have significant side effects. These include decreased joint and limb range of motion, diminished muscle strength, difficulty with balance and movement, pain, fatigue, poor endurance, and cognitive changes. Such effects in turn can limit activities such as walking, driving, working, and participating in recreational and social events.

Cancer patients can work to overcome the side effects of cancer treatment with physical therapy. Physical therapy in oncology rehabilitation focuses on helping persons with cancer optimize their physical, social, vocational, and recreational abilities within the limits of their disease. Cancer rehabilitation also aims to improve the quality of life for patients’ families and caregivers. It is a dynamic process, relevant at any stage of the disease process, including any of the five paradigms of health, namely, prevention, restoration of previous function, supportive and palliative care, and survivorship.

Physical therapists’ role in cancer prevention involves screening for risk factors, education, and lifestyle modification. A physical therapist may investigate factors that increase a person’s risk of cancer, such as smoking, use of tobacco and alcohol, unprotected sun exposure, and family history. A major risk factor for cancer on which physical therapists can have a large impact is in the area of obesity, weight management, and physical activity. Having an increased amount of body fat is a known risk factor for several types of cancer, including breast, colon, endometrial, kidney, and pancreas, among others. It is also recognized that physical activity is associated with a reduced risk of cancer. A physical therapist’s knowledge in this area of energy balance is vital to teaching individuals to reduce their overall risk of cancer. Because cancer and its treatment can affect body structures and function, PTs and PTAs work to restore patients to pre-illness levels of function without disability. Patients are examined to determine problems, and interventions are designed to resolve and limit impairments.

Examination may involve a review of the patient’s medical history, a body systems exam, and specific tests and measures. PTs determine impairments in the body systems that may limit an individual’s mobility and ability to participate in activity.

After a PT performs an examination and writes patient-centered treatment goals, either a PT or a PTA may treat patients according to a plan of care. Treatments may include exercise, balance work, gait training, manual therapy, work retraining, or any other specialized technique within their scope of practice. One of these specialized techniques may be manual lymphatic drainage used to treat lymphedema. Lymphedema is a complication of cancer and cancer treatment wherein the body’s lymphatic system is unable to transport lymph fluid from an area of the body. If untreated, the affected body part will swell, often very large, feel heavy, become fibrotic, and can interfere with daily activities such as getting dressed and walking. A physical therapist specially trained and certified in care of lymphedema patients is a very important member of the patient’s cancer treatment team. Physical therapists use special massage techniques, wrapping, and specialized garments, as well as education and exercise, to treat and manage lymphedema.

The supportive and palliative care of patients involves teaching patients to limit functional loss, reduce complications, and help caregivers to participate in managing patients’ symptoms and providing comfort. Survivorship includes patient care from the time of diagnosis throughout life. Because many patients experience long-term side effects, special considerations, programs, and follow-up are required. Exercise and physical activity is an integral part of survivorship care for cancer patients. Physical therapists’ knowledge in the area of exercise, pathology, and body systems place them in a position to provide a broad spectrum of care to cancer patients and survivors.

PTs and PTAs must have a degree from an accredited physical therapy program before taking a state licensure examination required for them to practice. After obtaining a bachelor’s degree, a typical physical therapy program takes three years, culminating in a doctor of physical therapy degree (DPT). Physical therapist assistant programs are two years in length, with several prerequisite courses, leading to an associate’s degree. Both degrees consist of didactic and clinical education. Class content includes but
is not limited to anatomy, physiology, biomechanics, kinesiology, neuroscience, pathology, pharmacology, ethics, management, and clinical reasoning. Therapists are required to renew their licenses every two years, including continuing education.

Susan Lilly
Marifel Malacara
Yvonne Valdecanas
University of Texas MD Anderson Cancer Center

See Also: American Cancer Society; Occupational Therapy.

Further Readings

Pineoblastoma and Supratentorial Primitive Neuroectodermal, Childhood

Pineoblastomas and childhood supratentorial primitive neuroectodermal tumors (CSPNTs) are extremely rare and highly malignant soft tissue tumors affecting children. Pineoblastomas are malignant brain tumors arising in the pineal gland in the brain. The pineal gland, which is a tiny endocrine gland in the middle of the two brain hemispheres, produces the hormone melatonin, responsible for the sleep-wake patterns and circadian rhythms. Pineoblastoma accounts for about 0.05 to 2 percent of all brain tumors in children under 5 years old. CSPNTs are some of the most aggressive brain tumors in children, originating in the cerebrum, which is the largest part of the brain controlling processes such as thinking, learning, problem solving, speech, emotions, voluntary movements, reading, and writing. Less common origins of CSPNTs are the diencephalon and basal ganglia. CSPNTs are congenital tumors, and are also referred to as cerebral neuroblastomas or cerebral medulloblastomas. They were first described in 1973, and account for 3 to 7 percent of pediatric brain tumors, with around 65 percent of cases reported in children less than 5 years old. The current classification segregates them from medulloblastomas because the molecular origin and progression of pineoblastomas and CSPNTs is believed to be considerably different from that of medulloblastomas.

The duration of symptoms is short, and common symptoms include nausea, vomiting, headaches, ataxia with nausea, seizures, and personality changes. Increase in head size and lethargy may be observed in children less than 1 year of age. Seizures, along with signs of intracranial hypertension from hydrocephalus (collection of cerebrospinal fluid in the brain) and neurologic deficit are common symptoms associated with pineoblastomas and CSPNTs. Hydrocephalus can be life threatening, and requires immediate medical attention to release the pressure to the brain by removing the excess cerebrospinal fluid. Children diagnosed with pineoblastoma may also have changes in vision because the tumor may be located in proximity to a region in the brain that regulates movements. Pineoblastomas are currently classified by the World Health Organization as grade IV tumors. Because they are poorly differentiated, they are often studied along with other undifferentiated embryonic neuroectodermal tumors.

CSPNTs can be further classified according to the cellular subtype making up the tumor. Because CSPNTs are tumors of embryonic origin, they are generally phenotypically poorly differentiated, or
Pineoblastomas are malignant brain tumors arising in the pineal gland in the brain. Pineoblastomas and childhood supratentorial primitive neuroectodermal tumors are congenital tumors and are some of the most aggressive brain tumors in children. (Wikimedia Commons)

may exhibit differential degree of differentiation of neuronal, astrocytic, and ependymal cell types. Tumors with neuronal cell type differentiation are called central nervous system neuroblastomas. Tumors with features of embryonic neural tube formation are named medulloepitheliomas, and those with ependymoblastic rosettes are termed ependymoblastomas. Some CSPNT patients show cytogenic alterations, including deletions or translocations of chromosome 10q22-26 and translocations involving chromosome 6q. Although significant advances have been made in the diagnosis and management of CSPNTs, the prognosis remains poor.

Pineoblastomas are diagnosed after biopsies following computer tomography (CT) imaging or magnetic resonance imaging (MRI) that indicate the presence of a lesion. Treatment in children under 3 years old is restricted to chemotherapy to delay the development of tumors, whereas children over 3 years old may be subjected to radiation therapy, depending on the degree of advancement of the tumors. Because pineoblastomas and CSPNTs are extremely rare forms of tumors, the treatment options are normally based on therapies appropriate for metastatic high-risk medulloblastomas. Such treatment modality includes high-dose chemotherapy and radiation to the head and spine regions. Significantly inferior outcomes have been reported both prospectively and retrospectively with these treatment regimens in comparison to more localized treatment modalities. Several retrospective and prospective studies have consistently reported worse outcomes, even for localized CSPNTs treated with treatment modalities opted for high-risk medulloblastomas.

Survival rates for patients with pineoblastoma and other CSPNTs widely vary, depending on the type of treatment, whether the disease has metastasized at the time of diagnosis, and the age of the patient. Current standard treatment modality for pineoblastoma includes a gross total resection of the tumor, which is subsequently followed by radiation and chemotherapy. Complete recovery can be achieved if the tumor is completely resected. In
most cases, however, recurrent tumors are seen because of incomplete removal of pineoblastomas. Chemotherapy is an attractive modality to minimize the necessity for radiation therapy for treatment of children, and may be combined with autologous stem cell transplantation. Traditionally, pineoblastomas have a higher rate of unfavorable outcomes in comparison to CSPNTs.

Poonam Balani
Independent Scholar

See Also: Brain Tumor, Cerebral Astrocytoma/ Malignant Glioma, Childhood; Brain Tumor, Supratentorial Primitive Neuroectodermal, Childhood; Childhood Cancers.

Further Readings

Pinkel, Donald

Donald Pinkel is one of the pioneers of pediatric oncology, particularly recognized as the clinician who developed a “Total Therapy” for children with acute lymphoblastic leukemia. This combination chemotherapy plus radiation for the first time in the late 1960s achieved a “cure” or long-term remission in 50 percent of patients. Pinkel was also the first director of the cancer program at St. Jude Children’s Research Hospital in Memphis, Tennessee. Perhaps Pinkel’s greatest contribution to the field of pediatric cancer was his commitment to the idea that cancer could be cured. In the days of Pinkel’s training, cancer in children was almost certainly fatal, particularly leukemia. Pinkel has recounted in interviews how fatalism prevailed among doctors and hospital staff about dying leukemia patients and how they were reluctant to “torture” them by giving them drugs that would cause terrible side effects. Other than blood transfusion, there was not even supportive therapy, and children usually could not live long enough to benefit from the few drugs that could produce short remissions in the 1950s. As a medical student and resident, Pinkel made it his personal mission to know these patients and dedicate his career to their care and hopefully cure.

Pinkel was born in Buffalo, New York, in 1926. Even as a child, he was fascinated with science. His decision to study medicine came from his deep empathy for people. His older sister was a nurse and often discussed science problems with him at home after work.

As a medical student, Pinkel decided to enter residency in pediatrics and work with children with cancers. In 1951 he graduated from the University of Buffalo School of Medicine. He initiated a clinical cancer program in 1953 at Buffalo Children’s Hospital. His study of childhood cancer was interrupted by Army service. While working as chief of pediatrics at an Army hospital in Massachusetts, he contracted polio during an epidemic. During his rehabilitation in Boston, he worked with Sidney Farber, who developed the first effective drug against childhood acute lymphoblastic leukemia.

Pinkel returned to Buffalo in 1956 to develop and direct a pediatric research and treatment service at Roswell Park Cancer Institute. There he joined James Holland and Emil Frei and Emil J. Freireich of the National Cancer Institute. Their goal was to develop systematic comparative evaluations of chemotherapy of acute leukemia in children and adults. Although prolonged survival of children with acute lymphoblastic leukemia (ALL) was achieved by sequential or combination therapy with the five anti-leukemia drugs that became available between Farber’s 1948 discovery and 1961, the disease remained fatal. In addition, a new problem had emerged. Most of the children eventually succumbed to leukemia in the central nervous system because anti-leukemia drugs could not pass from the blood into the cerebrospinal fluid in effective doses.

After pioneering the program at Roswell, Pinkel moved to the newly established St. Jude Children’s Research Hospital, becoming its first director. There he served also as chief executive officer (CEO) from 1962 to 1973. His work focused on
childhood ALL. He and his colleagues identified four major obstacles to its cure: drug resistance, drug toxicity, meningeal relapse, and, most important, pessimism. They instituted a treatment program aimed at permanent cure of ALL. Called “Total Therapy,” it was based on all the available relevant research and experience at the time. There were four phases: remission induction, remission consolidation or intensification, specific preemptive meningeal treatment, and continuation chemotherapy for three years. Both radiotherapy and intra-thecal drug therapy were used for meningeal treatment. Eventually, a 50 percent cure rate was achieved in the 1967 to 1968 study V. This was the first significant cure rate for generalized cancer and for primarily drug treatment of cancer. This four-phase treatment plan is still used, with numerous modifications. Better use of chemotherapy drugs has generally replaced the need for prophylactic central nervous system therapy.

Pinkel and his colleagues also pioneered the multidisciplinary approach to children with solid tumors, the use of adjuvant chemotherapy to prevent metastases and of neoadjuvant chemotherapy prior to surgery or radiation.

Donald Pinkel has received many awards for his work and contributions in pediatric cancer, particularly that in the “cure” of childhood leukemia. His national and international awards include the Lasker Award for Medical Research, the Kettering Prize for Cancer Research, the Polin Prize for Pediatric Research, and the Zimmerman Prize for Cancer Research. From the American Cancer Society he received the Annual Award in Clinical Research, and from the Leukemia-Lymphoma Society of America he received the Return of the Child Award.

Robin L. Rohrer
Seton Hill University

See Also: Childhood Cancers; Leukemia, Acute Lymphoblastic, Childhood.

Further Readings


Pituitary Tumor

Pituitary tumors account for an estimated 9 to 15 percent of all intracranial growths and the overall majority of pituitary disorders. Recent estimates indicate that pituitary adenomas are common in the general population, occurring in from 14.4 percent to 22.5 percent of people (with an overall estimate of 16.7 percent). Pituitary carcinomas are much more rare, however, representing less than 0.2 percent of pituitary tumors.

Pituitary tumors are normally discovered as a result of pituitary hormone production symptoms, presentation of visual or neurological conditions stemming from mass effect, or incidentally in the course of using radiographic imaging to investigate unrelated questions. Once discovered, they are distinguished by size, functional status, and immunohistochemical characteristics. Treatment options vary according to the size and functional status of the tumor and include neurosurgical, pharmaceutical, and radiological options.

The Pituitary Gland

The pituitary gland is a small endocrine gland attached to and controlled by the hypothalamus. It is located below the hypothalamus, inside the sella turcica, a bony, saddle-shaped cavity. The posterior section of the gland is normally considered an extension of the hypothalamus, and it is where vasopressin (i.e., antidiuretic hormone) and oxytocin are stored. The anterior section of the gland is composed of glandular tissue and is responsible for the synthesis of six hormones: growth hormone (GH; somatotropin), thyroid-stimulating hormone (TSH; thyrotropin), adrenocorticotropic hormone (ACTH; corticotropin), luteinizing hormone and follicle-stimulating hormone (LH and FSH; gonadotropins), and prolactin. Most pituitary tumors begin in the anterior section of the pituitary gland and can emerge out of the sella.
turbica, exerting pressure on nearby tissue and possibly causing mass effects as they grow.

**Types of Pituitary Tumors**

Pituitary adenomas are classified according to size, functional status, and immunochemical characteristics. Adenomas smaller than 10 mm are referred to as microadenomas; those larger than 10 mm are called macroadenomas. Tumors larger than 4 centimeters (cm) are described as giant pituitary macroadenomas. Both micro- and macroadenomas can be functional, meaning they secrete hormones. Whereas functioning pituitary adenomas are hormonally active, nonfunctioning pituitary adenomas are those that do not secrete a detectible or clinically significant level of hormones.

Nonfunctioning pituitary adenomas account for approximately 28 to 37 percent of all pituitary growths. Functioning pituitary tumors are classified according to the hormone they secrete. Corticotrophs secrete ACTH and are clinically indicative of Cushing’s disease. Gonadotrophs secrete LH or FSH, lactotrophs secrete prolactin, somatotrophs secrete growth hormone and are associated with acromegaly, and thyrotrophs secrete TSH and relate to hyperthyroidism. Alternative diagnoses to pituitary tumors include pituitary hyperplasia, sarcoidosis, pituitary abscess, Rathke’s cleft cyst, germ cell tumors, and metastatic carcinoma, among others.

**Sources of Pituitary Tumors**

Most pituitary tumors emerge outside a family history of them, although about 5 percent occur in the context of a family history of multiple endocrine neoplasia type 1 (MEN-1). Nonetheless, pituitary tumors are believed to occur as a result of either inherited or acquired genetic mutations. Generally speaking, increased expression of tumor suppression genes and/or increased activation of oncogenes appear to be the primary routes by which pituitary tumors begin and/or grow.

The specific genes involved in the initiation and development of pituitary tumors depend on the type of tumor, but they are generally monoclonal, meaning that they initiate and progress from genetic changes in only one cell. Very little research has investigated the role of possible environmental or micro-environmental contributions to those mutations in humans.

**Presentation and Diagnosis**

The main clinical features of pituitary tumors are hormonal and neurologic, although approximately 10 to 20 percent of them are discovered incidentally, due to increased capability and use of neuroimaging to investigate other, unrelated questions. Nonfunctioning, intrasellar microadenomas that do not extend from the sella turcica are the most common incidentalomas, as they are normally asymptomatic.

When either functioning or nonfunctioning adenomas become parasellar, they can exert pressure on nearby tissue, leading to neurological mass effects stemming from pressure on cranial nerves III (oculomotor nerve), IV (trochlear nerve), and VI (abducens nerve). Effects on cranial nerve V (trigeminal nerve) have also been observed but are more rarely encountered than effects on nerves III, IV, and VI. Mass effects on these nerves can occur individually or in combination, and with varying degrees of severity depending on the tumor’s size, location, and growth rate. Mass effects on the oculomotor nerve are the most common, resulting in visual field changes that associate and progress as the tumor enlarges up and out of the sella turcica. Mass effects on the other cranial nerves result from lateral extension of the tumor outside the sella, into the cavernous sinus. Headaches are also a common complaint, although it is not believed that they associate with tumor size.

Functioning pituitary tumors normally present as a function of the hypersecretion of a specific hormone and the patient’s sex. Female menopausal state is an additional factor influencing the presentation. Hyperprolactinemia, stemming from prolactitrophs (prolactinomas), can relate to decreased libido, infertility, and milk production in both men and women. Corticotrophs (secreting ACTH and clinically identified as Cushing’s disease) associate with suppressed mood, skin changes, and weight gain. Gonadotrophs are associated with hypopituitarism, hypogonadism, and/or neurological mass effects. Somatrophs are typically recognized as a result of increased growth in hands and feet and change in facial features, particularly an enlarged mandible. Thyrotrophs are associated with symptoms of hyperthyroidism.

**Treatment Options**

Surgery is the main treatment for clinically significant pituitary adenomas, with the exception of
prolactinomas, which can be effectively treated pharmacologically with a dopamine agonist, such as a low dose of cabergoline or bromocriptine. In some other cases, functioning adenomas secreting ACTH are also potentially treatable with pharmaceuticals that reduce ACTH secretion, but the acceptability and effectiveness of such treatments for functioning adenomas other than prolactinomas is complicated and somewhat tentative at this time.

Unless the tumor is particularly large or accompanied with additional complicating morbidities, pituitary tumors can be effectively removed via transphenoidal surgery. In most cases, the tumor can be accessed transnasally, using endoscopic or microscopic procedures. The transphenoidal (transnasal) procedure is minimally invasive, has a quick recovery rate, and has very low complication and intraoperative mortality rates when conducted by a skilled surgeon. Patients with functioning adenomas may benefit from both surgical and pharmaceutical treatments, in addition to or apart from radiotherapy. Radiotherapy is often applied when surgery is not possible, when a tumor has recurred or was only partially removed, or when medications have effectively failed. Advances in Gamma Knife and Cyber Knife technologies are becoming the typical means by which radiotherapy is applied and have increased the possible effectiveness of this treatment.

Nonfunctioning microadenomas are often not immediately treated, especially when they are not causing any neurological symptoms. Rather, the recommendation is to follow the progression of the tumor growth and function through serial, annual, or bi-annual neuroimaging and through periodic endocrinological testing.

Stephen M. Yoshimura
University of Montana

See Also: Brain Tumor, Adult; Radiation Therapy.

Further Readings

Plasma Cell Neoplasm/Multiple Myeloma

Molecular investigations have confirmed that multiple myeloma is a highly heterogeneous disease that consists of subtypes, each characterized by specific clinicopathological symptoms and treatment outcomes. Based on this genetic heterogeneity, it is therefore difficult to develop a universal treatment scheme for multiple myeloma because patients generally harbor different features. The best treatment approach would then be personalized therapy using targeted strategies. The RAG (red, amber, green) model is technically a simplified representation of the genetic data commonly generated from sequencing tests and, instead, presents an aggregate risk score. The RAG model was designed to integrate gross and molecular genetic modifications that occur in the DNA of a multiple myeloma patient. Gross genetic modifications include trisomies, deletions, and translocations, whereas molecular changes encompass missense substitutions.

Whole genome or exome sequencing analysis of a multiple myeloma patient’s DNA sample can generate an extensive amount of genetic information on this particular patient. More importantly, these DNA sequencing techniques can also yield mutational information that can be strongly associated with the disease. Unfortunately, the clinical significance of these genetic mutations is apparently lagging behind the improvements in the DNA sequencing technology. To circumvent this obstacle, a genetic information–based risk stratification scheme for multiple myeloma, known as the RAG model, has been proposed. The RAG model is technically a simplified representation of the genetic data that are commonly generated from sequencing and, instead, presents an aggregate risk score. The RAG model was designed to integrate gross and molecular genetic modifications that occur in the genome of a multiple myeloma patient. Gross genetic modifications include trisomies, deletions, and translocations, whereas molecular changes encompass missense substitutions. The RAG model utilizes a scoring system that ranges from 1.0 to 3.0, which in turn can be included in the diagnostic, treatment, and prognostic algorithms of the multiple myeloma patient.

Molecular studies have shown that multiple myeloma can present various genetically different
subtypes; therefore, a universal treatment scheme will be ineffective for this disease. The genetic heterogeneity of multiple myeloma is largely due to the capacity of plasma cells to undergo clonal proliferation, resulting in a variety of clinical subtypes. The most effective option for the treatment of this disease would therefore be based on the specific genetic subtype of each multiple myeloma patient. In order to achieve this personalized treatment approach, a combination of conventional and molecular cytogenetic analyses is necessary. Conventional cytogenetic analysis would include karyotyping of G-banded chromosomes, whereas molecular chromosomal analysis entails the use of fluorescent in situ hybridization (FISH) using DNA probes. In addition to these cytogenetic assays, it is also essential that DNA sequencing analysis be performed as a standard test for multiple myeloma. The integration of the data generated from these three genetic assays facilitates the development of an algorithm for the treatment of the multiple myeloma patient. The risk stratification system of RAG was designed to simplify the genetic data gathered from various genetic analyses, thus allowing the clinician to infer the disease risk of a patient.

The development of the RAG model was also based on the delay in the establishment of the clinical significance of most of the results of whole genome or exome sequencing. It should be understood that although the results of these high-throughput DNA sequencing assays are rapidly generated using computerized systems, the direct implications of the results to the clinical setting have not been fully established. Most of the reports published to date are disease associations, or a relationship of observing a specific genetic feature in a particular disease or disease subtype. However, the functional consequences of these genetic features have not been validated in terms of whether these indeed are the causative factors for a specific disease. The association of a genetic feature or mutation with a specific disease is therefore not very informative for the clinician because it does not indicate that it directly causes a specific disease. Nonetheless, genetic information generated by these tests continues to accumulate at a rapid pace, and its clinical power will eventually be realized over time.

The RAG model was developed based on the concept of risk stratification, wherein multiple myeloma patients could be grouped into specific clusters that would totally, partially, or minimally benefit from a specific treatment regimen. This model also includes information on whether a specific patient, based on the genetic features that were detected during analysis, would elicit toxic responses to a particular medication for the treatment of multiple myeloma. The specific drug response of a patient is mainly due to biomarkers present in his or her cells, which are often the molecular targets of cancer drugs. Without this information, it is possible that a multiple myeloma patient would not respond to a specific treatment regimen because the target molecule of the administered drug is absent or of a different form.

The first staging system employed for multiple myeloma was presented in 1975 and used standard laboratory values coupled with imaging data. This initial system was therefore based on the stage of the disease; however, the genetic heterogeneity of multiple myeloma was not well characterized at that time. This discrepancy often led to variable responses to treatment, wherein some patients responded to the administered medications but others did not. Subsequently, additional prognostic factors such as serum β2-microglobulin (Sβ2 M) and albumin were used. These factors provided more information on the condition of the patient, including the disease stage and renal function; these were then applied to the development of the international staging system (ISS) for multiple myeloma. Although the ISS system is readily accessible and simple to use for prognostication, there was yet more detailed information that needed to be integrated into the system, such as the genetic information of the patient. Molecular genetic studies since then have shown that high-risk patients for multiple myeloma could be identified using DNA sequence signatures and mutations. Coupling the ISS system with genetic data thus further strengthens the results generated by whole genome association studies.

By 2009, a consensus FISH algorithm was presented by the International Myeloma Working Group that could be used for prognostication of multiple myeloma patients. This algorithm indicated that a FISH panel that would screen for the chromosomal rearrangements t(4;14), t(14;16), and del(17p) significantly helps in the diagnosis of myeloma. These chromosomal aberrations have been documented to be indicative of patient survival
and risk. A second FISH panel screening for +1q as well as t(14;20), on the other hand, further helps in risk stratification. Because multiple myeloma is commonly associated with gross chromosomal rearrangements such as trisomies and translocation, these FISH panels, together with conventional karyotyping, can supplement the information generated by clinical tests.

Rhea U. Vallente
Prevention Genetics, LLC

See Also: International Myeloma Foundation; Multiple Myeloma/Plasma Cell Neoplasm; Myeloma, Multiple.

Further Readings

Plastics Industry

Occupational exposure to chemicals in the plastics industry may contribute to an increase in breast cancer and reproductive problems, because the chemical substances in the industry either function as mammary carcinogens or disturb the function of the endocrine system or both. Most plastic products release estrogenic chemical substances. The plastics work environment contains endocrine-disrupting chemicals like phthalates, brominated flame retardants, and bisphenol A (BPA). Compounding the problem, a mixture of a large variety of the chemicals plus their combustion by-products exposes plastics workers to much higher levels of toxins, and the combined effect may be greater than the sum of the individual chemicals. Lung cancer also appears in association with the plastics industry, which might be related to the combinations of the chemicals.

A system of chaotic growth in the cells of the human body describes cancer. Both changes inside the body (i.e., genetic changes) and factors in the external environment (i.e., tobacco, asbestos) alone or together participate in the development of cancer. Exposure to cancer-linked particles over time weakens the body’s protective ability and the carcinogen overcomes the checks and balances in the body leading to cancer.

The Process of Making Plastic Products
Plastic products go through numerous steps in various occupational settings, and workers become exposed to cancer-producing chemicals at several stages of processing. In the first stage, monomers such as vinyl chloride, styrene, bisphenol A, acrylonitrile, butadiene, ethylene, and urethane come from processing crude oil and/or natural gas from a process the petrochemical industry dubs cracking. In the next stage, the ensuing monomers go to resin producers to undergo the procedure of polymerization. Polymerization encompasses a chemical reaction whereby molecules of a monomer such as vinyl chloride become interconnected to form large molecules with a molecular weight larger than the original monomer. Resin producers transform monomers into polymer products such as polyvinyl chloride, polystyrene, nylon, acrylonitrile-butadiene-styrene (ABS), and polyurethane. Resins travel to plastics merchandise manufacturers in the configuration of powders, liquids, or pellets. In the third and final stage, polymers move to downstream industries to create paints, adhesives, and plastics merchandise such as pipes, packaging, automotive components, toys, textiles, siding, medical devices, and tools.

Polymers consist of two primary categories of thermoplastic and thermoset. Thermoplastic polymers use heat and pressure to repetitively soften and reshape the items such as polyvinyl chloride (PVC), polyethylene, polystyrene, and acrylics. The other category, thermoset substances, go through a chemical process resulting in a permanent material that cannot be made pliable or restructured. Examples of thermoset products include polyurethane, phenolics, ureas, and epoxies. Resins take shape into diverse plastic products using one of these two categories of manner of development.

Worker Exposure to Chemicals
Every step in the plastic-making process exposes workers to different contaminants that are
discharged from mixing and processing of the plastic substances. The workers come into contact with gases, vapors, dust, and by-products. Unfortunately, thorough descriptions about worker exposures remained limited until recent qualitative studies conducted from 2008 to 2010. Example of comments gathered by R. DeMatteo and colleagues (2014) included statements like “lot of smells, a lot of fumes,” but no ventilation existed in workplace settings to dissipate the chemicals released into the air. The workers describe the effects: “You smell fumes, you taste [it] in your mouth, and then you get—it’s like a light-headedness, dizziness” and “We have skin and breathing problems.” Government agencies tested the air, but the contaminants failed to exceed the regulated levels. Even when inspectors found problems in plants, companies never followed up on clearing the violations.

Environmental studies measuring acrylonitrile, styrene, phthalates, and BPA found chemical body burdens in plastics workers significantly higher than those in the general population; even so, air sampling detected only levels far below exposure standards.

**Plastics Industry Toxins**

Massive amounts of toxic chemicals are used in plastics production. DeMatteo (2012) describes contaminants left by residual monomers, polymers, and additives to include plasticizers, stabilizers, pigments/colorants, flame retardants, activators, lubricants, and fillers. Many of these materials are known mutagens and known to cause cancers in humans, whereas others are suspected of producing cancer, and still others are identified as endocrine-disrupting chemicals. D. Lithner and colleagues (2011) found workers exposed to residual monomers that included vinyl chloride, styrene, acrylonitrile, BPA, formaldehyde, butadiene, ethylene, and urethane. Of these monomers, the ones with the highest hazard level consisted of polyvinyl chloride, styrene-acrylonitrile, and acrylonitrile-butadiene-styrene.

The carcinogen vinyl chloride causes angiosarcoma, testicular cancer, and male breast cancer,
whereas formaldehyde showed links to female breast cancer. Acrylonitrile demonstrated an association with genital abnormalities from mothers exposed during pregnancy, whereas research showed styrene as an endocrine disruptor.

Neeti and colleagues (2011) describe the phthalate chemicals in the form of polyethylene terephthalate (PET) that encompasses the material used to make the clear plastic containers for water bottles, soda beverages, sport drinks, and condiments (e.g., salad dressing, vinegar, catsup). Manufacturers of PET assert that the phthalate used in this product is chemically dissimilar from other plastics that cause endocrine disruption and cancer, but the research suggests the concentration of phthalate in these clear plastic containers varies depending on the contents of the bottle. Phthalates leach into lower pH products like soda or vinegar over bottled water. Elevated temperatures cause leaching of phthalates and antimony from PET (e.g., water bottle sitting in a hot car or at a picnic in the hot sun). The findings of studies even suggest that salad dressing stored in a warm warehouse for a month can potentially reach toxic levels.

Disposal of plastics by incineration results in the release of carbon dioxide, a greenhouse gas, and the carcinogenic substances polycyclic aromatic hydrocarbons (PAHs) and dioxins. North and Halden (2013) describe the negative environmental and health effects of the released carcinogens. Plastics revolutionized medicine with the switch from glass, metal, and wood, but the negative effects of plastic only arose in the last 20 years. In 2012, the Food and Drug Administration (FDA) amended its regulations to no longer use BPA-based polycarbonate resins in baby bottles and sippy cups. The FDA took this action based on a petition from the American Chemistry Council’s data. North and Halden (2013) report on the use of di-(2-ethylhexyl) phthalate (DEHP), another plasticizer used in PVC. This substance can leach out readily from any item made with it. Studies in animals show harmful health effects to the female and male reproductive systems and insulin resistance.

### Human Illness

A 1998 study by S. A. Petralia and colleagues initially identified breast cancer in women exposed to organic solvents and benzene in the plastics and rubber industry. The women demonstrated a nearly doubling rate (odds ratio [OR] = 1.8) of breast cancer. Occupational exposures to synthetic textile fibers, acrylic fibers, and nylon fibers prior to age 36 show an excess risk of breast cancer. Labreche and colleagues found in 2010 OR of 7.69 in these end products of the plastics industry. So, these women have nearly eight times the risk of developing breast cancer. This study supports the theory that younger women face higher vulnerability before breast tissue reaches full differentiation.

Research by D. G. Kern and colleagues found in 2011 exposure of workers to plastics carcinogens in the nylon flock industry caused lung cancers. The study showed a threefold increase in lung cancer risk.

Also in 2011, J. T. Brophy and colleagues found women in the automotive plastics industry developed breast cancer prior to menopause at a doubling rate (OR = 2.68) over the females in the control group. Food canning workers exposed to BPA in the plastic lining of cans also showed a doubling rate (OR = 2.35) of breast cancer.

A 2011 New Zealand study looked at occupations with high risk of lung cancer. M. Corbin and colleagues found multiple occupations with high rates of lung cancer after controlling for age, gender, socioeconomic status, and smoking. The occupations of a priori interest included rubber and plastics products machine operators (OR = 4.27); electric and electronic equipment assemblers (OR = 3.61); petroleum, coal, chemical, and associated product manufacturing (OR = 1.80); and loggers (OR = 4.67). Occupations not identified ahead of time but showing increased risk for lung cancer consisted of nursing professionals (OR = 5.45), enrolled nurses (OR = 7.95), car retailing (OR = 3.08), and road freight transport (OR = 3.02).

S. Villeneuve and colleagues conducted a 2011 population-based case-control study of 1,230 breast cancer cases and 1,315 healthy controls. The researchers found elevated rates of breast cancer in the occupational groups of textile workers, rubber and plastics product makers, nurses, and tailors/dressmakers. These workers face exposures in the workplace related to solvents, endocrine disrupting chemicals, nonmetallic mineral products, and night-shift work. Researchers found that agricultural workers displayed a significant decrease in breast cancer.
Pleuropulmonary Blastoma

Conclusion

The plastics industry exposures really came to light in the last two decades. Therefore, research only recently identified chemicals in this industry that cause major cancers of breast and lung. Further research is needed to ascertain the molecular details of the process in order to apply preventive measures.

Sharon A. Takiguchi
Independent Scholar

See Also: Breast Cancer; Breast Cancer, Male; Chemical Industry.

Further Readings


Pleuropulmonary Blastoma

Pleuropulmonary blastoma (PPB) is a rare and highly malignant cancer originating in the lung or pleural cavity, accounting for less than 1 percent of all primary lung tumors in children. PPB was first described in 1988, and is known to occur most often in infants and young children. PPB begins in the lung tissue or the tissue lining the lung cavity (pleural tissue). PPB arises during fetal and/or infant lung development. PPBs are composed of both immature epithelial cells and mesenchymal cells, and the early stages have a cellular presentation resembling fetal lung tissue.

PPB is classified into four different types. Type I PPB is composed of cysts with early evidence that it is cancerous. Type I PPB is difficult to diagnose early, and is known to occur in infants. Type I PPB has a better chance of being treated successfully than Types II and III PPB. Type Ir (regressive) PPB has diagnostic features similar to Type I PPB and is devoid of cancerous cells. Type II PPB is a combination of cystic and solid neoplasm, with a high risk of cerebral metastasis. Type II PPB may exhibit signs of hemorrhage or necrosis, whereas Type III PPB is a completely solid neoplasm, with cerebral metastasis occurring in more than 50 percent of the patients. Types II and III PPB are known to occur in children aged 3 to 4 years. PPB may also spread to the bones, lymph nodes, liver, pancreas, kidneys, and adrenal glands. These are cancerous tumors, and the treatment modality includes intensive chemotherapy.

Common symptoms associated with PPB include sudden and stressful breathing resulting from the air escaping from lung cysts into the chest cavity. This phenomenon is known as pneumothorax. A careful diagnosis is necessary because pneumothorax
can result from a number of other causes. Symptoms associated with PPB are similar to the symptoms of pneumonia, and include cough and pain in the chest, accompanied with fever. An initial chest X-ray may often be interpreted as pneumonia.

The exact cause of PPB is presently unknown, and it is known to randomly develop. There may or may not be a genetic risk attached to the development of PPB. The presence of cysts in the lung and a family history of PPB increase the risk of development of PPB. It has been shown that around 40 percent of children with PPB have a family history of lung or kidney cysts, Wilms tumor, thyroid lumps, and rare ovarian tumors, among other types of tumors. Gains of chromosome 8 is one of the consistent chromosomal aberrations associated with PPB. Additionally, trisomy 2 (presence of an extra copy of chromosome 2), unbalanced translocation between chromosomes 1 and the X chromosome, and mutations in the tumor suppressor gene p53 mutations have also been reported. More recently, a mutation in a gene called DICER1 has been found in families with PPB. Mutation of that gene, resulting in DICER1 syndrome, is found in 50 to 70 percent of patients with PPB. The DICER1 gene encodes instructions encoding a protein involved in the production of microRNA (miRNA), which blocks the production of proteins by attaching to their respective RNA templates.

Pleuropulmonary tumors are generally located around the lungs. Later stages of tumor may move, however. Radiological evaluation of the tumor to assess the spread to the circulatory system plays an important role in decisions regarding treatment modality adopted against the tumor. Surgery and removal of the tumor and surrounding tissue is a primary treatment modality for PPB. If, however, the tumor is too large to be surgically resected, chemotherapy may be performed to decrease the tumor size before resection. Type I PPB may be completely cured by surgical resection alone. Chemotherapy is particularly beneficial for patients with Type I PPB, and is almost always recommended for Types II and III PPB. The side effects of chemotherapy are dose dependent, and also depend on the individual. The side effects are temporary, and may include fatigue, increased risk of infection, nausea, vomiting, and hair loss.

Radiation therapy is only recommended if the cancerous cells are not completely removed after surgery and chemotherapy. Radiation therapy can have severe side effects by interfering with normal bone growth, as well as the development of secondary cancers. Historically, pleuropulmonary blastoma has a poor prognosis, especially for Grade II and Grade III tumors. Total surgical resection of the tumor is associated with a better prognosis. Cystic Type I and Ir PPB has a better prognosis when compared to Type II PPB, and Type II has a better outcome than Type III PPB. The five-year survival rates of around 30 percent are reported for patients with Stage I disease, and recurrences are reported in 30 to 40 percent of cases. Metastasis to surrounding tissues is also commonly reported.

Poonam Balani
Independent Scholar

See Also: Childhood Cancers; Lung Cancer, Non–Small Cell; Lung Cancer, Small Cell.

Further Readings

Poland

The history of cancer as an important problem in Poland goes back at least 400 years. The first hospital for cancer patients was established in Warsaw in 1591–1592. This was the first hospital treating
cancer patients in Europe and possibly in the world. Another milestone is the Radium Institute of Warsaw, inspired by Marie Skłodowska Curie and the result of a nationwide effort, opened on May 29, 1932. Curie personally brought the first gram of radium to the institute, purchased by Polish organizations in the United States and Canada. The Communist government from the late 1940s to 1989 oversaw further industrialization in Poland but did not invest sufficiently in public health. As a result, the incidence of cancer in the population increased. In 2011, the institute, presently known as the Marie Skłodowska Curie Memorial Cancer Centre and Institute of Oncology, served 28,000 patients in inpatient clinics; 26,000 patients in the One Day Chemotherapy Section; and more than 340,000 outpatients. The center is presently the nation’s most significant research, oncology data collection, prevention, and treatment facility.

Cancer, after cardiovascular disorders, is the second-highest cause of mortality in Poland. Every fourth death in Poland is caused by cancer. Although the incidence of cancer (about 20,000) in Poland has increased in recent decades, this increase must be considered alongside several other trends in public health. First, the increase in mortality among cancer patients is related mostly to the aging of the population. Mortality of men under 64 years of age decreased. The significant increase in mortality is only for older men. The effectiveness of cancer treatment actually improved significantly from 30 percent to 42 percent. At the beginning of the 2010s there are about 150,000 new incidences of cancer per year and about 100,000 deaths due to cancer. Each year about 360,000 people live diagnosed with cancer. It is estimated that in 2025 the new incidences of cancer in Poland will reach 180,000 annually. There are differences in cancer prevalence between genders. In 2012, the incidence of cancer for men was highest when detected in lungs (20 percent), prostate (15 percent), and colorectal (13 percent). For women the highest occurrence was breast cancer (23 percent), colorectal cancer (10 percent), and lung cancer (9 percent).

These four types of cancers are very common, accounting for half of all cancer problems in Europe. Lung cancer was the most common cause of death for men (31 percent) and women (15 percent) in Poland. For years, the role of environmental pollution and bad nutrition in the development of cancer were known. During the period of Communist rule from the late 1940s to 1989, ideological attitudes made it difficult to address questions of public health, especially those affected by nutrition and pollution. However, this situation changed after 1990. Poland now has a well-organized system of cancer-related reporting, data collection, research, and health care. As a member of the European Union (EU) and the World Health Organization (WHO), the Polish national program against cancer must respond to the requirements of those two international organizations. The guidance for national policies is delineated by the WHO formalized strategy “Health for All in the 21st Century” and the European Cancer Code. To improve the overall health of society the following action is advised and encouraged: decrease tobacco smoking, improve nutrition by increasing vegetable and fruit consumption and obesity control, increase exercise, limit alcohol consumption, and avoid sun exposure.

In 1990, the National Health Program was formulated to decrease mortality rates of the most critical health threats. Because the outcomes of this program were insufficient, the Polish government created in 2005 the National Program Against Cancer Diseases (NPACD), using significant financial and administrative resources. Several institutions coordinate efforts in responding to the threat of cancer. The Ministry of Health is responsible for policies and the coordination of programs. The National Health Fund finances programs and cooperates with health care providers. The Polish Union of Oncology cooperates with institutions outside the health sector such as public media and nongovernmental organizations. The National Cancer Registry (Institute of Oncology) collects national data. All these organizations support the main goals of the NPACD: prevention, improvement in early diagnosis and treatment, application of research findings, and monitoring programs' applications and effectiveness.

Polish media today offer more information to increase public awareness and knowledge concerning prevention and screening of cancer. Education about the critical role of tobacco smoking and diet in the development of cancer has led to a decrease in smoking among men and improvement in healthy choices in food consumption. There is ongoing education concerning breast and cervical screening that can significantly affect mortality among women. There are already measurable effects of these efforts.
Research performed in Poland has shown that the changes in diet have had a significant impact on the incidence of gastric cancer despite other negative health factors. Poland has a high prevalence of *Helicobacter pylori* infection, affecting up to 73 percent of the population. This infection is connected with the development of many gastric cancers. From 1950 to 1989 the national diet was based on the growing consumption of animal products and sugar. There was no import of fruits and vegetables that could be eaten throughout the year. This trend in consumption changed in 1990 and people began to eat relatively more fruits and vegetables. In 2006 morbidity related to gastric cancer was twofold lower than in 1960. That is a significant difference in spite of the high level of *H. pylori* infection.

Similarly there is an increase in the effectiveness of treatment for other kinds of cancer. There are, however, regional variations. The best results are achieved in the Mazowsze region (46 percent of patients survive) and the worst in the Lublin region (36 percent). The rate for survival after five years improved: 37 percent for men and 53 percent for women. To improve treatment effectiveness, there is a growing effort to apply molecular diagnostics to use a targeted, specific treatment for different types of cancer. Too often new treatment methods are used without regard to the type of cancer that needs to be treated.

The new national plan calls for each patient to have an individualized treatment plan created by a group of medical specialists. Patients will have their own oncological treatment cards that will have all relevant medical information that can be used by any health care provider. The main focus of the new government health program is to improve early detection and begin treatment as early as possible. It is recognized that when a cancer patient has identified symptoms, it may already be too late for successful treatment. To improve detection, the following action is advised: doctors will have incentives for establishing early diagnosis, there will be no financial limits for cancer treatment, and more medical personnel will have the necessary resources for cancer diagnosis. With a long history of national struggles with cancer, Poland is now able to use its best resources to decrease the rate of incidence and mortality due to cancer.

See Also: Diet and Nutrition; Pollution, Air; Smoking and Society; Stomach (Gastric) Cancer.

Further Readings

Polishes
Nail coloring practices date back to ancient Egypt and China. The materials used for nail polish came from natural substances (e.g., egg whites, flowers, henna, and wax). The history of artificial nails began about 600 B.C.E. in China with nails constructed from gold, silver, and precious stones. More recently, the Charles Revson Company (today known as Revlon) put together the first contemporary nail polishes in 1920 and the nail industry emerged onto the commercial market after 1932, motivated by enamel paint on cars.

Overview
Nail polish provides a means to beautification, a process to strengthen weak nails, and a means to cover surface irregularities or discolorations. The formulation of nail polish consists of the following:

- Film-forming elements (nitrocellulose used most routinely)
- Resins (e.g., tosylamide-formaldehyde) for adherence
- Plasticizers (e.g., dibutyl phthalate) for flexibility
- Solvents (butyl stearate and acetate compounds) for maintaining the polish in a fluid state and to assist in fast drying upon application
- Thixotropic agents (e.g., bentonite) to keep the ingredients in the polish uniformly suspended
- Variety of mineral pigments (calcium carbonate, zinc oxide, titanium dioxide,
Iron oxides) and synthetic pigments (D and C red 6/7/19, FDC yellow)
• Natural agents (guanine, bismuth, oxychloride, and micatitanium) to add color and shine to the nail polish

As noted above, nail polish represents one of the product categories that use the chemicals formaldehyde, toluene, and dibutyl phthalate (DBP). These specific chemicals show direct links to cancer. Other groups using formaldehyde, such as medical examiners and embalmers, show an elevated risk of leukemia and brain cancer compared to the overall population. Research indicates that these chemicals (called endocrine disruptors) probably disrupt the natural balance of hormones in the human body to produce cancer. Consequently, many smaller nail polish manufacturers eliminated these chemicals from their product line in 2005. The information below explains why other companies continue to use these three chemicals.

**Food and Drug Administration Regulation**
Nail polish falls under regulation by the U.S. Food and Drug Administration (FDA). As part of the FDAs’ wide-ranging authority, it can confiscate any cosmetic product found to be poisonous, harmful, lethal, adulterated, misbranded, or otherwise posing a health risk. The FDA as well as the Consumer Product Safety Commission and the Federal Trade Commission have responsibility for regulating cosmetics, including packaging, labeling, and advertising. The FDA expects the manufacturers of nail cosmetic products to list the ingredients on the package and to alert consumers to potential hazards if the product is used improperly. Since Congress decided in the early 1900s that risks caused by cosmetics remain low, the FDA does not require premarketing approval of cosmetics. The resources and tax dollars are diverted to the more harmful products of medicine and devices instead. Likewise, most other countries around the world also do not require premarketing approval of cosmetics.

**Risk Assessment**
Risk assessment refers to the ability to ascertain the health risks associated with a chemical. Many chemicals may produce an adverse impact at a high measurement dose so scientists set exposure limits for consumers and industry workers. The scientists look for the lowest level that produces an adverse health effect; then these professionals take into account how people become exposed and how frequently and to what degree. Based on this information, the scientists set the exposure limit at a level that will not harm people.

**Cosmetic Ingredient Review Expert Panel**
An independent group of leading scientists and medical doctors from colleges and universities comprise the U.S. Cosmetic Ingredient Review (CIR) Expert Panel. This group evaluates the safety of cosmetic components and carries out measurements of risk. Since the CIR was formed in 1976, it has reviewed thousands of cosmetic products. The Food and Drug Administration and the Consumer Federation of America take part in the panel's determinations of risk assessment.

The CIR has analyzed all the major elements in nail polish and proclaimed them safe. The organization states that keratin, a solid and primarily impermeable substance, forms the foundation of fingernails and toenails. Once the nail polish dries, the elements in the polish remain in the solidified film coating and fail to be taken up by the body or liberated to the environment.

**Occupational Safety and Health Administration**
The Occupational Safety and Health Administration (OSHA) requires companies that produce nail polish to provide material data safety sheets to employees and to nail salons. Plants that produce nail polish must give employees working in the manufacturing process adequate training and personal protective equipment for handling toxic chemicals.

**OPI Products**
The biggest producer of nail polish and nail treatment products in the world is OPI Products, Inc. Headquartered in California, the company delivers products to more than 70 countries, predominantly to nail salons, specialty spa salons, and beauty supply stores. Despite being a frontrunner in nail care, the company lingers behind in removing hazardous elements from its products. Industrial chemicals associated with cancer and reproductive impairment include formaldehyde, dibutyl phthalate,
Polishes

and toluene. OPI eliminates these chemicals from products in Europe but continues to sell the products containing the contentious components in the United States.

**Formaldehyde**

Formaldehyde or methylene glycol works as a nail hardener for nail polish. The FDA allows formaldehyde provided its weight does not exceed 0.2 percent of the total weight of the product. By avoiding the vapors, a person reduces the chance of inhaling it and exposing him- or herself to allergies or cancer risk. The International Agency for Research on Cancer (IARC) categorizes formaldehyde as a known human carcinogen. Formaldehyde, a strong-smelling chemical, appears in many building materials, in household products, and in nail polishes. It acts as an industrial fungicide, germicide, and disinfectant. Therefore, formaldehyde represents a good preservative in medical laboratories and in mortuaries. Other industries continue to use formaldehyde to manufacture furniture, wallpaper, carpets, and ceiling tile, despite its carcinogenic effects.

**Phthalate**

Phthalate exists as a variety of chemicals used primarily at concentrations below 10 percent in nail polishes. As plasticizers, the phthalate lessens cracking by making the nail less brittle, helps prevent chipping, and adds a moisturizing sheen to the nail.

In 2004 H. J. Koo and colleagues analyzed the amount of dibutyl phthalate (DBP) in nail polish and found that 19 of the 21 nail polishes tested positive for dibutyl phthalate. The median level of exposure to phthalates came to 22.917 g/kg bw/d, which represents a level far lower than the amount set by the International Programme on Chemical Safety of 66 g/kg bw/d. DBP continues to be used in food packaging, medical devices, blood bags, breast pumps, and toys.

In 2005 G. Latini reviewed the current monitoring techniques used to determine the exposure to phthalate in humans. A review of the toxicology of phthalates indicated that a limited number of studies exist on the sources and conduits of human exposure to phthalates. Since few studies report levels of phthalates, regular biological monitoring of phthalates in body fluids and tissues is needed to assist physicians in completing health risk evaluation for exposure in the general population and in directing government regulations to set the upper limit of acceptable levels in the environment, cosmetic products, and medications.

In 2009 J. L. Lyche and colleagues described the widespread use of phthalates in consumer products like nail polish and the constant contact of these chemicals with humans. Animal studies in rodents demonstrated an endocrine-disrupting effect that leads to developmental and reproductive toxicity. Furthermore, the research on exposure data shows inconsistent results suggesting that secondary metabolites may be more accurate indicators of internal contact with phthalates. The review by Lyche and colleagues shows insufficient human toxicity data to appraise developmental and reproductive effects in humans. The fact that phthalates occur in mixtures with other compounds represents a secondary problem to study. Therefore, future research must be initiated to address these issues.

**Toluene**

The National Highway Traffic Safety Administration reports that toluene acts as a solvent in various products like nail polish, nail hardeners, and nail polish removers. The toluene in the polish provides a smooth finish on the nail along with uniform color. The CIR Expert Panel rated toluene as safe for cosmetic use in 2005 if used in concentrations below 50 percent. It is best not to breathe in the fumes. Toluene can be found in ink, paint, glue, and detergents.

Exposure to toluene can occur by inhalation of vapor or by skin contact. Exposure to toluene in high doses produces neurological effects of drowsiness, confusion, fatigue, memory loss, delusions, and hallucinations; physiological symptoms of irritation to the nose, throat, and eyes, headache, nystagmus, slurred speech, impaired color vision, vigilance, nausea, vomiting, respiratory depressions, convulsions, severe organ damage, coma, and death can occur.

**Gel Manicures**

Gel nail polishes used in manicures provide a manicure enduring two weeks or longer without cutting the nail. Compared to standard nail polishes, gel polishes consist of much stronger content. A. F. Chen and colleagues (2012) describe the use of the ultraviolet lamps employed to seal the polish and
also the use of acetone to remove gel manicures. This small study reported problems with nail thinning, fragility, flaking, and breaking as the negative issues related to the gel polish. The researchers could not ascertain whether the nail problems related to the polish or to the use of the acetone to remove the gel manicures.

**Conclusion**

Modern nail polish arose in the early 1900s and continues to be part of the beauty routine to this day. The CIR Expert Panel started reviewing cosmetics in 1976 and ascertained the main cancer concerns with formaldehyde, dibutyl phthalate, and toluene. The FDA, the Consumer Product Safety Commission, and the Federal Trade Commission participate in the regulation of nail polish. These organizations concur with the CIR. The few studies to date show individuals have contact with very low concentrations of the three chemical substances. Because of the lack of studies, scientists raise the concern that little research supports these claims and therefore ongoing monitoring of the levels of these chemicals in humans is needed.

Sharon A. Takiguchi
*Independent Scholar*

**See Also:** Chemical Industry; Cosmetics; Plastics Industry.

**Further Readings**


**Pollution, Air**

Air pollution is one of the most serious challenges the world faces. Air pollution refers to contamination of the outdoor or indoor environment by any chemical, physical, or biological agent. Air pollution therefore can be classified as outdoor and indoor pollution. The air quality around and within buildings and structures is known as indoor air quality. Some of the common indoor air pollutants include radon, molds, carbon monoxide, carbon dioxide, asbestos fibers, and the burning of biomass. An air pollutant is a substance in the air that can have adverse effects on humans and the ecosystem. This article explains air pollution—its types, causes, and health impacts, and especially its linkages to cancer.

**Sources of Air Pollution**

The sources of air pollution can be natural or man-made. The air pollutants can be solid particles, liquid droplets, or gases. Air pollutants are usually classified as suspended particulate matter (PM; e.g., dusts, fumes, mists, and smokes) or gaseous pollutants. Particulate matter is particles in the air that are a mixture of solids and liquid droplets of varying size. Some particles are visible; others are invisible. Very small particles with a diameter of less than 2.5 micrometers are called fine particles, and these are suspended in air. They are produced mainly by burning of fuels and wood. The suspended particulate matter includes diesel exhaust particles; coal fly ash; wood smoke; mineral dusts, such as coal, asbestos, limestone, and cement; metal dusts and fumes; acid mists (e.g., sulfuric acid); and pesticide mists. Dust particles with size from 2.5 to 10 micrometers in diameter are called coarse particles.

Natural processes that can release substantial amounts of pollutants into the air include volcanic eruptions, biological decay, and forest fires. Carbon dioxide, sulfur dioxide, and nitrogen oxide are the main pollutants released by these processes into the atmosphere.
Human or anthropogenic sources of air pollution include the combustion of fossil fuels such as petroleum or coal by motor vehicles and railways, industry, and thermal power stations; the release of chemical by-products from industrial and agricultural processes; and the incineration of waste. Human causes of air pollution also include vehicles, domestic heating and cooking, and aircraft pollution. Motor vehicles emit nitrous and nitric oxides, carbon monoxide, organic compounds, and lead. Toxic fumes come from factories, machines, and automobiles. The combustion of wood or agricultural waste is another major source of air pollutants. Globally, about 3 billion people cook and heat their homes using open fires and burning biomass (wood, animal dung, and crop waste) and coal.

Gaseous air pollutants include sulfur compounds such as sulfur dioxide, carbon monoxide, nitrogen compounds such as nitrous and nitric oxide and ammonia, organic compounds such as hydrocarbons, and halogen derivatives. Carbon dioxide is one of the major air pollutants, and it is mainly emitted from thermal power plants, vehicles, and burning of fossil fuels. Another major air pollutant is methane, which comes from raising livestock, decomposition of wastes, and chlorofluorocarbons (CFCs).

Dangerous indoor pollutants that can usually be found in the home include cleaning solvent, pollen, pet dander, glue from composite wood furniture, mold, bacteria, fungi, viruses, cosmetics, and plastics. Studies have shown that pets with fur or feathers (e.g., cats, dogs, birds) can be contributors to indoor air pollution. Air pollutants can also be classified as primary or secondary. Primary pollutants are usually produced from a process, such as ash from a volcanic eruption or carbon monoxide gas from motor vehicle exhaust. Secondary pollutants are not emitted directly; rather, they are formed in the air when primary pollutants react or interact.

**Impact of Air Pollution on Health**

Air pollution has serious effects on human health. It is one of the biggest global killers. Pollution saturates the air with toxic particles and other irritants, which creates poor air quality. Air pollution has both long-term and short-term health effects. Short-term health effects include eye, nose, and throat irritation; headache; and allergic reactions. Some long-term health effects include damage to the brain, kidney, and liver; heart and respiratory diseases; and cancer. Air pollution can cause diseases such as asthma, bronchitis, pneumonia, emphysema, chronic obstructive pulmonary disease (COPD), and cardiovascular diseases. Particulate matter may cause chest pain, palpitations, and fatigue. High levels of toxicity in the pollutants can impair the body’s defense mechanism, rendering it incapable of fighting off infection.

Indoor air pollution is often much worse than outdoor air pollution. About 4.3 million people die every year from exposure to household air pollution. Nearly half of them die prematurely from illness attributable to household solid fuel use. More than 1 million people die every year from chronic obstructive respiratory disease (COPD) that develops due to exposure to indoor air pollution. Exposure is particularly high among women and young children who spend most of their time indoors. The U.S. Environmental Protection Agency (EPA) has revealed that indoor air is one of the top five public health threats in the United States. This is alarming when one considers that most people spend 90 percent of their time indoors and approximately 65 percent of their time at home.
Fine and coarse particles in the air are more health hazardous, causing serious health problems. In poorly ventilated dwellings, indoor smoke can be 100 times higher than acceptable levels for small particles. Nearly half of deaths among children under 5 years of age from acute lower respiratory infections (ALRI) are due to particulate matter inhaled from indoor air pollution from household solid fuels.

**Air Pollution and Cancer**

Studies have shown there is a link between air pollution and increased incidence of cancer. Lung, skin, breast, nasopharyngeal, and laryngeal cancers are caused by air pollution. The International Agency for Research on Cancer (IARC) has classified outdoor air pollution as a cancer-causing agent (carcinogen). The main carcinogenic pollutants include diesel engine exhaust, solvents, metals, and dust. Another major component of outdoor air pollution is particulate matter—as a carcinogen on its own that increases the risk of lung cancer. Studies show people who live in places with high levels of air pollutants have a 20 percent higher risk of death from lung cancer than people who live in less polluted areas. Exposure to PM 2.5 and sulfur dioxides is associated with an increased risk of mortality from lung cancer. Studies show people who lived in areas with high nitrogen oxide concentrations have an increased risk of lung cancer. The EPA in its report estimated the concentrations of air pollutants across the United States of America. The report covered over 181 air pollutants, 80 of which are thought to contribute to cancer formation in humans. For example, benzene is a toxin released from car exhaust that may lead to cancer. According to the EPA report, about 30 percent of the cancers caused by air pollution are due to car exhaust and another 25 percent are due to local industrial activity.

Several types of air pollutants may increase the risk of cancer. Apart from lung cancer, air pollution also increases the risk of breast and bladder cancer. Air pollution is also linked to other forms of cancer, including cervical and brain cancer.

Approximately 17 percent of annual premature lung cancer deaths in adults are attributable to exposure to carcinogens from household air pollution caused by cooking with solid fuels like wood, charcoal, or coal. Women exposed to indoor smoke thus have double the risk of lung cancer compared to those not exposed.

Chlorofluorocarbons (CFCs) released from air conditioners, refrigerators, and aerosol sprays rise to the stratosphere, damage the ozone layer, and create ozone holes. As a result, harmful ultraviolet rays reach the earth’s surface and cause skin cancer.

**Conclusion**

Air pollution is preventable. Indoor air quality can be improved by proper ventilation, filtration, and control of sources of pollutants. There is a need to install a high-quality air filter or air purifier system to trap the allergens and pollutants indoors. Toxic household cleaning supplies, paint, chemicals, lawn and garden supplies, and other products with noxious fumes are to be used at home with utmost care.

Manoranjan Mohanty

*University of the South Pacific*

**See Also:** Asbestos; Bladder Cancer; City of Hope; Coal Industry; Diesel Exhaust; Kidney (Renal Cell) Cancer; Liver Cancer, Adult (Primary); Lung Cancer, Small Cell; Paint; Skin Cancer, Melanoma; Transportation; War Gases and Chemicals; Wood Dust; World Health Organization.

**Further Readings**


Pollution, Water

Water pollution is one of the greatest threats to humankind. Water pollution refers to contamination of water bodies (e.g., rivers, streams, lakes, oceans, and groundwater) by pollutants. Pollutants are the particles, chemicals, or substances that make freshwater contaminated. Water pollution occurs when pollutants are discharged into water bodies without adequate treatment. Water pollution is a reflection of poor quality of environment. This entry explains water pollution—its types, sources, and health impacts, and especially its links to cancer.

Sources of Water Pollution

The sources of water pollution can be natural or man-made. With increasing world population and growing demand for water, sources of water are stressed and contaminated. Pollutants are very often added to water bodies by anthropogenic activities. Water pollution can be of two broad types: surface water pollution and groundwater pollution. Sources of surface water pollution are generally grouped into two broad categories based on their origin: point and non-point sources. Point source usually refers to pollutants that enter a waterway from a single and identifiable source, such as a ditch or a pipe. These sources of water pollution include discharges from an industry, a city storm drain, or a sewage treatment plant. On the other hand, non-point source refers to contamination that does not originate from a single source but often is the cumulative effect of contaminants accumulated from a large area.

An example is nitrogen compounds leaching into water sources from fertilized agricultural lands. Surface water pollution generally occurs by the discharge of wastewater from commercial and industrial sources, discharges from untreated municipal and domestic sewage, and contaminants flowing into water bodies from urban and agricultural runoff. Water bodies are often contaminated by seepage, leaks, spills, and accidents. Water pollution can be broadly classified as chemical, metallic, or biological pollution, based on its composition. Water gets polluted with toxic chemicals such as pesticides, herbicides, and vehicle fluids. Industrial chemical wastes, especially plastics, are major pollutants that often do not break down easily and remain a long time in the water bodies. It is estimated that about 14 billion pounds of garbage, mostly plastic, are dumped into the ocean every year.

Additives to water are another form of pollutant. All additives together, known as flocculants, are sources of water pollution. Chlorine and fluoride are the most common additives in drinking water. Chlorine is recognized as the most cost-effective method of purification of water supplies. However, chlorination is extremely volatile and combines with organic, carbon-based pollutants to form dangerous chemicals called tri-halo-methanes (THMs). Radioactive wastes are also added to water bodies as a result of inadequate disposal mechanisms.

Hydrocarbons also cause water pollution. These are the main ingredients of the chemical industry and are added to water bodies as industrial waste. They enter water supplies through agricultural runoff, sewage, and chemical dumps. Metals such as arsenic, aluminum, cadmium, lead, and mercury are the main water-polluting substances that originate from industries, electrical generation, mining, and vehicles. Arsenic contamination results from leaching from waste dumps, mines, or pesticides. Industrial pollution is one of the major sources of arsenic. Nitrates are another water pollutant commonly associated with the increased use of commercial fertilizers, animal waste, and human waste.

Biological pollution includes pathogens such as bacteria, viruses, protozoa, and worms that enter sewage systems and untreated waste. Parasites such as, for example, cryptosporidium are a form of biological water pollutant. Water bodies are polluted by natural phenomena as well. Events such as volcanic eruptions, algal blooms, storms, and earthquakes cause changes in water quality. Pollution of freshwater can also be caused by eutrophication, which is a process of excessive growth of nutrients in water bodies that promotes excessive plant or algal growth. The enrichment is often increased by human activities such as agriculture. It occurs mainly due to presence of nitrates and phosphates added by fertilizers through agricultural runoff and by untreated sewage effluents through urban runoff. The excessive plant growths cause low oxygen levels in freshwater and make it difficult for species to live; many aquatic organisms, especially fish, die when the dissolved oxygen level falls below 5 ppm (parts per million).

Groundwater is the source of drinking water for the vast majority of the global population.
Groundwater water pollution occurs when water below the earth’s surface becomes contaminated by seepage and by the presence of arsenic. Landfills are a major source of groundwater contamination. Buried chemical waste can seep into the groundwater. Groundwater pollution is much more difficult to abate than surface pollution because groundwater can move long distances through unseen aquifers.

Impact of Water Pollution on Health
Water pollution affects drinking water, rivers, lakes, oceans, and groundwater. It has adverse effects on human health. Water pollution is, in fact, one of the biggest global killers of human beings and animals. Over 1 billion people worldwide lack access to safe drinking water. Nearly 14,000 people die each day due to drinking dirty water. In addition, over 1 million seabirds and 100,000 sea mammals are killed by water pollution every year.

Arsenic is one of the water pollutants most hazardous to health. Arsenic in drinking water harms the central and peripheral nervous systems as well as the heart and blood vessels, and causes serious skin problems. Another contaminant is Escherichia coli (E. coli), which is a common, nonpathogenic bacterium. Its presence in water is an indication of fecal contamination. E. coli infection from water can cause dysentery. Contaminated water mainly causes diseases such as cholera, typhoid, diarrhea, and hookworm. Gasoline is one of the elements causing water contamination and is hazardous to health. It is estimated that one gallon of gasoline can contaminate 5 million gallons of drinking water. Water-soluble radioactive compounds cause cancer, birth defects, and genetic damage. Parasite pollutants can cause acute and chronic cases of diarrhea, cramps, fever, and vomiting.

Water Pollution and Cancer
Contaminants found in polluted water are known to have an effect on the DNA of reproducing cells. Water pollution adds toxins to the human body that may overwhelm the immune system. The drinking water contaminants that have carcinogenic risks include chlorination, arsenic, asbestos, fluoride, hazardous wastes, pesticides, tetrachloroethane, and nitrates. Trihalomethanes (THMs) in water have mutagenic and carcinogenic effects. These toxins are cause for concern as they are causing cancer. THMs increase incidence of rectal, bladder, and pancreatic cancer. Studies suggest fluoridated water presents an increased risk of bone cancer. Arsenic in drinking water causes bladder, lung, and skin cancer, and may cause kidney and liver cancer as well. Studies show that exposure to arsenic in groundwater causes cancer, and indicate that 1 in 10 people who drink water containing 500 μg of arsenic per liter may die from cancers. Fertilizers, insecticides, and herbicides also contain carcinogens that can filter down into water supplies, causing cancer. Atrazine, an herbicide used on crops, contaminates drinking water and is suspected of causing breast cancer. Studies have found a connection between polluted drinking water and ovarian cancer. Nitrates are contaminants that enter the water through the soil and are a suspected carcinogen. Studies also show that talc, a chemical often used in baby powder, feminine products, and cosmetics, has carcinogenic effects. Talcum powder has been suspected to increase the risk of ovarian cancer by 50 percent.

Conclusion
Minimizing the amount of contamination in drinking water is a topmost priority. People need to be aware of the quality of the water they drink and how to protect themselves. Various methods have been used to improve water quality. For instance, Floating Litter Traps and Boom Systems have been designed to collect floating litter, vegetation, and other debris in waterways. One of the main keys to preventing cancer is to limit the amount of harmful toxins that enter into the body. Drinking pure water helps the immune system to flush out the toxins and mutated cancer cells. Reverse osmosis filtering is one of the few effective ways to remove potential cancer-causing chemicals from water. A good water filtration system for clean water can prevent illnesses and diseases. A quality water purification system can remove up to 99 percent of harmful contaminants that cause illness and cancer.

Manoranjan Mohanty
University of the South Pacific

See Also: Battery Acid; Dyes and Pigments; Insecticides; Kidney (Renal Cell) Cancer; Lead; Liver Cancer, Adult (Primary); Meat Processing; Paper Industry; Pesticides; Plastics Industry; Radiation, Ionizing; Water Treatment; World Health Organization.
Portugal

The Portuguese Republic is a coastal nation of the European continent bordering with Spain. During the Middle Ages, Portugal was a Moorish Muslim caliphate, until their defeat during the Reconquista. With the Renaissance, Portugal became one of the most prosperous colonial empires of the age, with dominions spanning the world, from Africa to North America and South America, giving birth to some of the most audacious explorers of all time, men like Vasco de Gama and Ferdinand Magellan. Today, Portuguese is still the sixth most spoken native language in the world, and Portuguese culture has influenced many populations, especially in South America. In 1910, the Republican Revolution deposed King Manuel II, founding a short-lived republic that was later overthrown by a right-wing dictatorship that eventually allowed António de Oliveira Salazar to establish his power in 1933.

During the second half of the 20th century, Portugal lost much, if not all, of its colonial and transcontinental power, as many overseas provinces declared their independence one after the other. In 1974 a bloodless leftist military coup called the Carnation Revolution restored democracy, and during the 1980s, Portugal followed a modernization process by rewriting its constitution and joining the European Union (EU). Today Portugal is an advanced developed country with a very broad-minded, peaceful, and globalized culture, although its economy has suffered since the beginning of the 21st century.

The Portuguese National Health Service (NHS) is a decentralized system funded through general taxation to provide every citizen with free universal health care. In addition to this, a series of special social health insurance schemes for certain professions (health subsystems) and voluntary private health insurance act to provide additional services. To improve population awareness and knowledge of cancer, many sensitization campaigns and projects are promoted every year by national and international associations and organizations, such as the European Colorectal Cancer Awareness Month sponsored by EuropaColon, or the annual breast cancer charity fund-raising sponsored by the Liga Portuguesa Contra o Cancro (NRS). Following World Health Organization (WHO) global guidelines on cervical cancer prevention in women, in 2007 Portugal launched a human papillomavirus (HPV) vaccination program by including it in the National Immunization Program (NIP), and in 2010 it was the only European country together with the United Kingdom to reach a coverage rate of more than 80 percent of total population.

Although a national cancer registry system comprising three regional registries (northern, southern, and central regions) was established in 1960, it is only since 1988 that cancer registration has been mandatory in Portugal. Cancer is the second leading cause of death in Portugal, following cardiovascular disease. The cancer forms that showed the highest incidence in men were prostate cancer (95.1), colorectal cancer (61.4), and lung cancer (49.1); for women, the cancers with the highest incidence were breast cancer (85.6), colorectal cancer (33.8), and cervical cancer (18). Cancers showing the highest estimated mortality in 2012 for both sexes in Portugal were lung cancer (22.8), colorectal cancer (21.4), and prostate cancer (19). Common risk factors for cancer in Portugal are those often seen in developed countries, such as sedentary lifestyle, obesity and bad dietary habits, tobacco smoking, alcohol consumption, and environmental pollution in highly urbanized settings. Specific genetic alterations in the human epidermal growth factor Receptor 2 (HER2) in local Portuguese populations seem to double the risk of breast cancer in women who
Poverty is defined as not having adequate resources (wealth) to purchase basic human necessities such as food, shelter, and clothing. But it is much more
than simply not having enough money. People who live in poverty often do not have access to societal services such as education and health care. Poverty is measured differently around the world. In the current economic climate, many individuals live at or just above the official “poverty level” and even people with middle-class incomes are struggling to meet basic needs. Such individuals may be only a paycheck away from poverty, and the loss of employment can quickly affect their quality of life. In such circumstances, people must decide which of their essential needs are primary, as all are not affordable.

Others, living above the poverty level, are also affected by living in stricken neighborhoods. Such communities are defined as having more than 20 percent of households living below the poverty level. In such cases, many of the environmental effects of poverty may affect all who live in these neighborhoods: unsafe housing, a high density of fast-food establishments and bars, and the lack of grocery stores with healthy (and fresh) food options.

Poverty affects health in numerous ways. Affected individuals may engage in unhealthy habits, reside in environments that pose health risks, lack access to recommended and preventive health care screenings, be unable to identify potential illness signals, and are deprived of affordable and accessible health care. And while poverty does not cause cancer, it is linked in myriad ways to behaviors, environmental factors, and social structures that may increase a person's cancer risks or the options available to them for prevention, detection, and/or treatment.

Poverty as a Risk Factor for Cancer
In 1991, Samuel Broder, then director of the U.S. National Cancer Institute (NCI), declared “poverty is a carcinogen.” It is not the poverty itself that causes cancer but rather the environment or behaviors engaged in by individuals living in poverty that increase their chances of developing cancers. The World Health Organization (WHO) suggests maintaining a healthful diet, avoiding tobacco, leading an active lifestyle, and limiting alcohol intake can prevent a significant percentage of cancers. Individuals living in poverty are less likely to engage in these preventive behaviors.

In 2011, the American Cancer Society (ACS) highlighted the role of poverty in cancer. Using education as an indicator of socioeconomic class, researchers found people with lower levels of education are more likely to have higher rates of cancer. The greatest difference was found in lung cancer, which had a morbidity rate four to five times higher in people with less education compared to the most educated. The ACS (2011) found persons with a lower socioeconomic status are more likely to engage in behaviors that increase cancer risks, such as tobacco use, physical inactivity, and poor diet. Tobacco and alcohol companies create products specifically marketed to poverty populations, often targeting the youngest consumers.

Youth, who may see limited opportunities, are often attracted to the use of these products and also illicit drugs as ways of coping or improving their social status. Older individuals, who may be unemployed or work at low-paying and/or low-status jobs, use substances as a way of dealing with stress. In addition, many with mental health issues who cannot afford care or medication or may be culturally discouraged from addressing or telling of their symptoms may be using alcohol, tobacco, and other substances to self-medicate. Access to health insurance and care is limited among the poor. While many may qualify for governmental assistance, the care may be hard to access, require long waiting periods, and be demeaning or substandard. Those without health insurance are less likely to utilize health care and are more likely to present for treatment when their illness is advanced and their prognosis poor.

While there may be differing cancer rates among various racial and ethnic groups, this is likely to be associated with cultural, behavioral, and economic dynamics rather than membership in a racial or ethnic group. Race/ethnicity is less of a factor than poverty when looking at cancer prevalence. The ACS (2011) indicates that “among African Americans, eliminating socioeconomic disparities has the potential to avert twice as many cancer deaths as eliminating racial disparities.”

Alcohol Use
Alcohol consumption increases the risk of cancer of the mouth, throat, esophagus, liver, and colon in men. In women, it also increases the incidence of breast cancer. Consuming more alcohol regularly over time increases one's risk of developing an alcohol-associated cancer. Based on NCI data from 2009, an estimated 3.5 percent of all cancer deaths in the United States were alcohol related.
For a variety of social reasons, people living in poorer neighborhoods are more likely to use alcohol, an established risk factor for cancer. Unemployed individuals are similarly inclined, but it is unknown which is the precipitating factor: using alcohol to deal with the stress of unemployment or alcohol use as a factor in unemployment. Unemployed individuals are also at risk of living in poverty. Stress, a factor in both unemployment and poverty, is also associated with increased alcohol use.

E. M. Berke and colleagues (2010) looked at the geographic density of retail alcohol locations within U.S. census tracts. Poorer neighborhoods were more likely to have more alcohol retailers. Alcohol access within poor communities may create social influences in which drinking behavior is observed and seen as a normal aspect of everyday life. Easy access and familiarity may increase alcohol use and, ultimately, cancer risks.

**Tobacco Use**

Tobacco continues to be the single greatest cause of preventable cancer mortality worldwide. The use of tobacco products increases risks for a variety of cancers (lung, stomach, neck, throat, and bladder). People who live in poverty are more likely to engage in cigarette smoking despite the cost and health promotion campaigns. According to the Centers for Disease Control and Prevention (CDC), in 2014, 18.1 percent of all U.S. adults regularly smoked cigarettes. Many more individuals who live in poverty are regular smokers (27.9 percent) and are at increased risk for cancer. In addition, the combination of tobacco and alcohol use among those living in poverty multiplies cancer risk.

**Diet and Exercise**

The ACS (2011) suggested approximately one-third of cancer deaths are preventable and related to obesity, physical inactivity, and poor nutrition. These factors are much more prevalent among poverty populations and are interrelated. Obesity is associated with increased risks of cancers of the esophagus, breast (postmenopausal), endometrium (the lining of the uterus), colon and rectum, kidney, pancreas, thyroid, and gallbladder.

Children living in poverty are more likely to be obese than children in higher socioeconomic classes. In addition, such children are at higher risk for obesity in adolescence. Numerous studies have documented the relationship between poverty and obesity. Multiple factors associated with poverty, such as the cost of fresh fruits and vegetables, access to grocery stores carrying healthy foods, and the prevalence of fast-food retailers, create a matrix of social and behavioral factors increasing opportunities for inadequate diets among the poor. “Value sizing” of convenience foods offers high caloric meals at lower prices attractive to individuals with fewer economic resources. The poor may be unaware of other dietary recommendations for the reduction of cancer risk, such as avoiding red and processed meats and grilled, broiled, and fried meats, which are major components of fast-food diets. Maintaining a healthy diet requires knowledge, effort, access, and economic resources. Diet is related to the use of alcohol and tobacco, and all three, together, increase the potential for cancer and other health complications among the poor.

**Health Care and Access Disparities**

Health disparities, according to the CDC, “are differences in the incidence, prevalence, mortality, and survival of a disease and the related adverse health conditions that exist among specific population groups.” According to the ACS, poverty is the overriding factor in creating obstacles to prevention, early detection, and treatment of cancer. In practice, the elimination of disparities should result in a reduction in cancer incidences and deaths and an increase in cancer survival among socioeconomically disadvantaged people to levels comparable to those in the general population. Individuals living in poverty are more likely to be unable to access health care or prescriptions due to the cost of such services. In 2012, among all American adults, 9.6 percent delayed or did not receive medical care because of cost, and 6.8 percent were unable to fill prescriptions. Those living below the poverty level were more likely to delay or not receive medical treatment (22.4 percent) or were unable to fill prescriptions (19.4 percent). The lack of access to health care has serious consequences for cancer detection, prevention, and treatment. Higher screening rates for three types of cancer (breast, cervical, and colorectal) are positively associated with education and the availability and use of health care. Those who are most poor often do not participate in early cancer screenings and present for treatment when they are much sicker and have less successful treatment outcomes.
Conclusion
For a variety of social, behavioral, and environmental reasons, people living in poverty are at greater risk for cancer and other serious medical problems. The Affordable Care Act expands access to many individuals living near or at the poverty level and offers opportunities for prevention, education, screening, and care. Public health efforts need to increase education to reduce risks, while creating opportunities for early detection and access to health care.

Adele Weiner  
*Metropolitan College of New York*  
Kim Lorber  
*Ramapo College of New Jersey*

See Also: Alcohol; Diet and Nutrition; Disparities Within Nations (Elimination of Cancer); Exercise; Smoking and Society; Tobacco-Related Exposures.

Further Readings


Prostate Cancer

Prostate cancer is the most common non-melanoma malignancy among men in the United States and is the second most common cause of cancer-related death among men. In 2013, 238,590 new cases and 29,720 deaths related to prostate cancer were estimated. Currently, one in six men will develop prostate cancer during their lifetime, which is higher than the ratio observed for breast cancer in women. Between 1969 and 1990, the incidence of prostate cancer increased steadily in the United States at an average annual rate of approximately 3 percent. The incidence rate was increased to 12.7 percent in 1990–1993, and decreased to 8.4 percent in 1993–1996. The highest incidence rate was observed in 1993, at 140.4 cases per 100,000 men.
Annual age-adjusted mortality rates from prostate cancer in the United States for white males were increased 0.7 percent from 1969 to 1987, 3 percent from 1987 to 1991, then decreased 1.2 percent from 1991 to 1994, and 4.5 percent from 1994 to 1999.

Changes of incidence rates in the 1990s reflect the increase in early detection of prostate cancer due to the introduction of the prostate-specific antigen (PSA) blood test. PSA is a glycoprotein generated exclusively by prostate tissue and present at low levels in blood from healthy men. The PSA's tissue specificity enables detection at an early stage of prostate cancer by a simple blood test. However, other abnormal conditions, such as benign prostatic hyperplasia (BPH) or prostatitis may also increase the PSA level. Therefore, this notoriously low specificity of the PSA test for prostate cancer has been a main subject of debate, although early screening and detection has been used historically as a strategy for prostate cancer prevention.

A meta-analysis of the five independent randomized studies suggested no difference in prostate cancer–specific mortality between groups with and without the PSA screening. Two large trials, the European Randomized Study of Screening for Prostate Cancer (ERSPC) and the U.S. Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial provided inconsistent results. The European study showed a 20 percent relative reduction in the risk of death from prostate cancer (RR 0.84, 95 percent CI 0.73–0.95) by PSA screening, but not the American study (RR 1.15, 95 percent CI 0.86–1.54). Therefore, these results suggested a high risk of overdiagnosis and/or overtreatment of prostate cancer due to false-positive results from PSA-based screening. Overdiagnosis and overtreatment often cause infection, pain, erectile dysfunction, incontinence, and low quality of life. Currently, there is no convincing data in support of or against PSA screening for prostate cancer in healthy men.

The burden of prostate cancer in society is substantial and has increased since the PSA testing was introduced. In the United States, the total estimated expenditure on prostate cancer was approximately $10 billion in 2006. The mean annual costs per patient were $10,612 in the initial phase after diagnosis, $2,134 for continuing care, and $33,691 in the last year of life. Although prostate cancer–specific mortality has decreased, costs are likely to rise due to increased diagnosis at an earlier stage and increased survival. The economic burden of prostate cancer will continue to rise because of the aging of the current U.S. population.

**Risk Factors**

Unlike lung and cervical cancers, there is no established cause for prostate cancer. However, several risk factors have been established by numerous epidemiological studies.

**Age.** Age is a major risk factor for prostate cancer. The probability of developing prostate cancer sharply increases in the sixth decade of life (7 percent) and further increases after age 70 (15 percent). This contrasts significantly with the probability of 0.01 percent among men less than 40 years old and 2.7 percent among men 40 to 59 years old. The aging of the current population means that the disease will become an even greater public health problem in the future.

**Family History.** Men with a family history of prostate cancer have two to three times higher risk and typically are diagnosed earlier than men without a family history of the disease. Further, men with more than one affected relative have a 35 to 45 percent risk of developing prostate cancer. Family history may also be associated with a risk for aggressive prostate cancer. Prostate cancer patients with family history may have a worse outcome at five years after treatments by radiotherapy or radical prostatectomy compared with patients without family history (RR, 1.8; 95 percent CI, 1.3–2.4).

**Genetic Factors.** Genetic factors are responsible in 5 to 10 percent of prostate cancer cases. Numerous studies have examined potential genetic factors associated with prostate cancer risk. However, most studies reported inconsistent results. Recent genome-wide association (GWA) studies identified several genetic loci, including 8q24 and 17q12. A more recent large consortium study identified 77 genetic biomarkers of associated risk for prostate cancer using blood DNA samples from 25,074 prostate cancer cases and 24,272 controls. Several studies reported that mutations at BRAC and CHEK2 also increased risk for prostate cancer.

**Race/Ethnicity.** Significant variations in prostate cancer incidence and mortality are observed at the
international level. These striking variations may be in part due to genetic factors that vary in different populations of the world. The highest risk of prostate cancer is found in the United States, especially in African American men, while the lowest risk is found in Asian countries. Migration studies reported that the incidence rate for prostate cancer leaned toward those of the host country. For example, Asian men living in the United States have a lower risk of prostate cancer than Americans, but a higher risk than Asian men living in Asia. The results of these studies indicated that environmental factors may play a role in risk changes in the host country.

Conclusion
The burden of prostate cancer in the United States is significant and will increase due to the aging population. SEER data indicate that prostate cancer will be diagnosed in one out of six men and be fatal in one out of 36. A diagnosis of prostate cancer carries a significant burden, and a reduction in the risk of prostate cancer could be very valuable to society. However, value of screening for prostate cancer is debatable. A clear understanding of risk factors, including the endogenous (family history, hormones, race, and aging) and exogenous (diet, occupation, and environmental agents) and their interplay, will help to design strategies to prevent carcinogenesis and the progression of prostate cancer. In most cancer cases, early detection usually leads to better outcomes. However, prostate cancer may not be in this category. The direction of future studies may be toward identification of biomarkers for aggressive type, progression, and response to treatments.

Jong Y. Park
Moffitt Cancer Center

See Also: Age; Penile Cancer; Sex.

Further Readings


Proton Therapy
Proton therapy is a type of external beam radiation therapy that uses a proton beam to destroy cancer cells by irradiation. The physics of penetration of energetic protons through the tissue allows more precise delivery of the radiation dosage to the treatment area than with other types of external beam radiotherapy. Proton beam is characterized by higher relative biological effectiveness (RBE) when compared with conventional megavoltage (MV) photon radiation therapy. Recent progress in the proton beam technology makes this radiation therapy modality more affordable. A number of new proton therapy centers will open in the near future in the United States and around the world.

History of Proton Therapy
The use of the energetic protons in cancer therapy was proposed by Robert Wilson in 1946. The first clinical use of proton beam was in 1954 at the Lawrence Berkeley Laboratory (LBL) in California. European proton treatment history started in 1957 with the program in Uppsala, Sweden. In the 1960s, 1970s, and 1980s, proton programs were opened in Russia (St. Petersburg and Moscow), Japan (Chiba and Tsukuba), Switzerland (Villigen), and England (Clatterbridge). The first hospital-based proton center was established at the Loma Linda University Medical Center (LLUMC), California, in 1990. Today there are 43 operating proton centers worldwide; of this number, 14 are in the United States.
Particle Therapy Co-Operative Group statistics state that 93,452 patients were treated with protons worldwide (March 2013; http://www.ptcog.ch). Within the next five years, 10 to 20 new centers with proton beam will be opened in the United States and 10 to 15 will be opened around the world.

**Physics of Proton Therapy**

The potential of the proton beam for cancer treatment is defined by the physics of the proton interaction with the tissue. The tissue consists of relatively low atomic number chemical elements. The proton beam has weak scattering in the tissue. The ionization density of protons is very high at the end of their range. These factors lead to forming the Bragg peak at the end of the proton beam that entered the tissue. The protons stop close to one another and deposit a large amount of their energy within a 1 centimeter (cm) area. The dose at the shallow depths is lower than for the MV photons. The combination of the proton beams of different energies creates spread-out Bragg peak (SOBP) to cover the tumor. Protons deliver the dose only to the depths of the Bragg peak. These properties of the protons reduce the undesired dose delivered to healthy tissue in cancer treatment with proton beam therapy. The mechanisms of proton interaction with the tissue depend on the energy of the protons. The primary mechanisms are the ionization energy loss and multiple scattering. Energetic protons will produce secondary neutrons in the tissue and a small amount of induced radioactivity in nuclear reactions. The fraction energy loss in nuclear interactions is considerably less than for ionization energy loss by protons.

The cross sections of the nuclear interactions are nonlinear with energy, and this channel of energy deposition plays a different role along the proton penetration to the depth of its stop. The proton beam energies used in clinical applications are from 60 to 230 MeV (million electron volts) that cover all possible proton ranges to deliver the dose to the tumor. The proton therapy operates with the term of the proton range. The proton beam range is defined from proton fluence measurements as the depth of material at which half the protons that undergo only interactions have stopped. The value of the range well corresponds to the 80 percent of the dose at the distal edge of the Bragg peak. Therefore the range can be determined from the dose measurements.

**Technology**

The proton therapy facility consists of the major components, which are the source of the proton beam, systems, the beam transport system, treatment rooms, and treatment head. The source of the proton beam is the accelerator producing the protons between 60 and 250 MeV. Statistical analysis of the typical treatment depths for MV shows that 200 MeV proton facilities could cover 95 percent of the possible depths of the treatment, while 230 MeV will cover entirely all 100 percent. The operating facilities use cyclotrons or synchrotrons or SynchroCyclotrons. New solutions for the proton facilities are under testing currently. There are the linear accelerators of the protons, laser-plasma accelerators on the base of high-intensity lasers and dielectric wall accelerators. The typical beam today has from a 6 millimeter (mm) to 1 cm size with about 2 percent peak energy variation.

Until recently, the proton beam facility utilized a passive scattering technique. A proton beam passes through a set of scattering foils and propellers or ridge filters to create a SOBP. Although this technology is still in use, the main focus of the design for
facilities today is to use active electromagnetically scanning proton beams. The scanning beam facility utilizes the range modulator approach wherein thin plates made of the low atomic number materials are used to reduce proton range or accelerator capability of proton beam energy variation. Another possibility is an energy variable source of protons. There are two main approaches in scanning technology: one is uniform scanning and the second is spot scanning. The dose field shaping is performed with patient-specific devices called apertures, and depth pattern is achieved with compensators. Typically, the aperture material is brass. There is a discussion in the literature about the usage of the multi-leaf collimator (MLC) to replace the aperture. The MLC could advance the facility and increase the patient throughput.

However, the solution to use the same MLC technology as for MV photon therapy where tungsten is the material of choice will create unnecessary secondary neutrons. The alternative solution to select a material of low atomic numbers for the proton beam MLC has been proposed. The narrow, pencil beam could be deflected in the magnetic field. The active scanning technology has the possibility to reduce the secondary neutrons. Moreover, the narrow proton beams, once achieved, will have potential for the intensity modulated proton therapy. The tumor could be irradiated point by point. However, the physical limit imposed on the spot size that could be achieved in the tissue is approximately 5 percent of the initial proton range. There is also an undesired effect on the increase of the entrance to Bragg peak dose ratio for narrow beams. These factors implement the necessity of modifications for treatment planning and treatment strategies.

Two treatment room types are utilized now; one is a fixed beam room with a possible robotic arm treatment table and the other one is a gantry room. Although the dosimetrical properties of proton beams offer an ability to confine dose to those regions targeted, these properties can magnify the effects of any errors that may occur in the process of delivery. There are ongoing research and development studies to advance the control over the planned delivery of the proton beam. The primary focus is to develop the method of the dose and proton range verification. Three primary methods are considered: the positron-emitting tomography post treatment, prompt gamma method, and ultrasound tomography utilizing the thermo-acoustic effect from a proton beam. Another focus is image-guided proton therapy, control of the delivery depending on organ motion, beam gaiting, and intensity modulated proton therapy.

**Radiobiology of Proton Beam Therapy**

Protons have different relative biologic effectiveness (RBE) from photons due to higher ionization density. The established correction factor for dose modification is 1.1 relative to 60Co gamma radiation. Multiple studies have shown that the RBE increases close to the end of the range of the protons. Recent data has shown that RBE will be higher than 1.1 at the distal edge of Bragg peak. The SOBP has higher RBE close to the distal edge where the bio-effective dose increases.

**Treatment Planning**

Proton dose calculations for treatment planning are performed with a treatment planning system (TPS) based on computed tomography (CT) data acquired from the CT scanner. The CT scanner and the CT image interpretation are specifically customized for proton therapy. The CT numbers calibration is associated with the relative linear stopping power function of protons. The CT images acquisition, treatment planning, and treatment of the patient are performed with site-specific immobilization devices. There are specific procedures of the commissioning and quality assurance (QA) of the treatment planning and CT scanner for radiation treatment using a proton beam that includes validation of TPS calculations with the phantom measurements.

The treatment planning is typically performed with the dose computational algorithms based on a pencil beam approach. Analytical algorithms are based on measured dose distributions and include all contributions to dose deposition. The important method of dose calculation is the Monte Carlo technique of the particle transport simulation. There are remarkable differences between pencil beam algorithms and Monte Carlo simulation. The progress in computer technologies makes possible implementation of fast Monte Carlo–based algorithms for proton beam therapy planning or plan verification. Future progress in this direction will improve the accuracy of the planning, especially for intensity modulated proton therapy.
There were a set of studies on comparative treatment planning to investigate the dosimetric properties of the proton beams for various treatment sites. It has been shown that protons in comparison to photons produce dose distributions with better conformation of around-the-target volume, more homogeneous dose distribution in the target, and lower integral dose in healthy tissues. There are a few groups who are developing a bio-effective approach for treatment planning utilizing the increasing of the RBE at the distal edge of the Bragg peak. This research may create a new treatment approach and technique.

Dosimetry and Quality Assurance
The Report 78 of the International Commission on Radiation Units and Measurements (ICRU) and the protocol for dose calibration contained in Technical Report Series No. 398 published by the International Atomic Energy Agency (IAEA) are currently the guidelines for the dosimetry of the proton beams. The basic dosimetry standards require annual verification of the dose and credentialing by the Radiological Physics Center (RPC). The quality assurance (QA) procedures are developed to assure safe operation of the proton therapy system. The proton therapy machines are significantly different from the photon machines. This makes some QA procedures definite for the proton facilities and includes machine-specific procedures for mechanical components, beam calibration, TPS, and patient-specific components, such as patient-specific devices.

Clinical Experience and Perspectives
The main advantages of proton therapy are the physical properties of the proton beam, which enables the delivery of a high dose to the target volume while reducing the dose to the surrounding normal tissues, as well as ensuring higher conformity of the dose shaping around the tumor. Hence, proton therapy has established itself as ablative therapy and organ preservation therapy. In recent years the major cohort of the patients treated with the protons were prostate cancer patients, who accounted for up to 80 percent of treatments at some facilities.

Over the last five to seven years, the fraction of prostate patients has decreased to 20 to 30 percent due to an increase of patients with other treatment sides. The dosimetrical properties of the proton beams delivering a lethal radiation dose to the tumor tissue while sparing surrounding normal tissue make this modality attractive for a pediatric patient cohort. The limited accessibility of proton therapy is reflected in the number of treated patients (less than 100,000). New emerging centers will allow establishing more baseline data for clinical outcome of proton therapy.

During the last decade, a number of clinical evidences were established. In particular, proton therapy for uveal melanoma has shown over 90 percent for local controls over the five-year period of time. The reports from various groups indicate they were able to achieve local control between 70 percent and 100 percent for chordoma, and 89.8 and 100 percent for chondrosarcoma. In comparison, the conventional photon methods give the local control rates between 17 percent and 50 percent for chordoma of the skull base.

There are also data on improvement in local control for head and neck tumors, non–small cell lung cancer (NSCLC), esophageal carcinoma, hepatocellular carcinoma (HCC), pancreatic carcinoma, extracranial sarcoma/chordoma and chondrosarcoma, and prostate cancer.

The studies have shown the advantage of the higher RBE from protons in the case of radioreistant tumors. The dosimetrical properties of the dose deposition allow confining the dose within the target area and minimize the dose to healthy tissue in the case of HCC. One of the prospective future directions is a combination of systemic therapy and radiation. Though the potential of the combination of chemo- and radiotherapy, chemo-radiation, approach is not fully evaluated for photons yet, nevertheless it is a therapeutic gold standard in many diseases. The chemo-radiation approach has shown a higher local control rate and reduced distant failure for photons. There are few groups in proton therapy working toward establishing combined chemo-proton radiation therapy. There is ongoing discussion in the radiation oncology community on proton therapy perspectives and its advantage over photon therapy. There is also a discussion on necessity to establish clinical trials to compare the proton and photon treatments.

Side Effects
Proton therapy, like photon radiation therapy, may cause side effects. The accumulated experience
Proton Therapy

shows the side effects from proton therapy are milder, compared with photon therapy. The advantage of the dosimetrical properties of the proton beam in sparing tumor and normal tissue allows organ preservation from radiation damage. There is ongoing research to reduce the side effects from proton therapy, in particular, acute skin reaction.

Secondary neutrons are considered one of the possible risk factors of secondary malignancies, presenting possible long-term effects. This is an important aspect for deliberation for the pediatric cohort of patients whose life expectancy may exceed the latent period of secondary malignance. However, the yield of the nuclear reactions and neutron production is relatively small.

The main sources of the undesired secondary neutrons are the elements of the treatment machine. Published studies on the level of secondary neutron production show that the 16 and above MV linac machines could produce more neutrons than those in today’s proton treatment machines and modern approaches in proton treatment. The implementation of uniform scanning and spot-scanning pencil proton beams will reduce the secondary neutron contamination even further.

**Economic Considerations**

The major limiting factor for wide usage of proton therapy is the start-up cost of the proton facility. The typical price of the two-treatment-room facility is about $100 million. The capital cost of the facility includes real estate, a cyclotron/synchrotron and beam line, a number of treatment gantries, shielding, manpower, power supply, and patient specific devices (compensators and apertures). The estimate of the cost of a proton treatment facility totals about double the cost of a photon treatment facility, considering the initial investment and the operating costs. The capital costs will be distributed among a larger number of patients with the increase of patient throughput. That will reduce the cost per patient once the facility is operating at full capacity.

There are strong efforts in research and development in the field of medical physics, accelerator physics, and engineering, which form the basis of modern, cost-efficient proton facilities. Currently, vendors are proposing a single-room solution for a reduced price. The operational cost of the facility could be reduced with implementation of the pencil beam spot-scanning and multi-leaf collimator from optimized material for neutron contamination reduction. An analysis of the treatment facilities, patient statistics, and treatment planning statistics has shown that combination of fixed beam treatment rooms with gantry rooms in one facility can reduce the capital cost of the facility. The progress in acceleration technology over the last decade creates the basis for new, less expensive solutions for proton beam therapy. In particular, the linear accelerators of protons with the modular design or laser-plasma accelerators can reduce start-up costs of the proton facility. The cost of proton treatment trends toward reduction as the technology is further developed.

**Patient Education**

Accidents in the nuclear industry formed some pre-judgment against radiation applications among the general public. There is an important need to provide patient education on the benefits of radiation therapy and especially on proton therapy. The independent nonprofit National Association for Proton Therapy (NAPT; http://www.proton-therapy.org) was founded in 1990 for public education on proton therapy. NAPT provides information on the therapeutic benefits of proton therapy for cancer treatment in the United States and abroad. Thirteen operating centers are among the supporting members and nine centers are under development. Practically each established proton therapy center provides patient education resources on proton therapy as well.

**Future Development**

Today, research and development in beam delivery technology is focused toward more compact, more efficient, and less expensive accelerators. In the next few years new types of accelerators will become the source of the proton beam at treatment facilities. There is ongoing development of new treatment strategies such as spot-scanning techniques and intensity modulated proton therapy (IMPT) as well as more accurate TPS algorithms like Monte Carlo simulation.

More clinical trials and protocols are under development to expand proton therapy to different treatment sites and to increase efficacy of the therapy. The efforts to improve inter- and intrafractional motion management, beam delivery control
techniques, and image-guided proton beam therapy will improve the treatment outcome. It has been shown also that proton beam could be used for imaging purposes, and it has potential for proton-based CT. Bio-effective treatment planning may reduce the dose to achieve the same treatment effect. This could lead to reduction of side effects.

Conclusion
Proton therapy, invented four decades ago, is still a rapidly developing radiation therapy modality. The proton beam deposits most of its dose in the tumor volume, improving the tumor and sparing the surrounding normal tissues in comparison to conventional photon modalities. Proton therapy offers benefits of its physical and radiobiological properties (increased RBE) to improve the local control and reduce side effects of the treatment. Thousands of patients have been treated effectively with proton therapy for localized tumors. There is evidence in the clinical literature of the success of proton therapy for many types of cancer. Several clinical trials are under development for evaluation of proton beam therapy for new application sites. New technologies in accelerators and treatment delivery techniques make the future very promising for proton beam therapy.

Vadim P. Moskvin
Indiana University–Purdue University Indianapolis

See Also: Clinical Trials; Head and Neck Cancer; Radiation Therapy.

Further Readings

Psychosocial Care/Support
Cancer has a profound impact on a person's emotional, psychological, and social well-being, and psychosocial care and support are central to health outcomes. Rates of clinically diagnosed anxiety and depression among those with cancer have been reported to be at least 30 percent, with caregivers and family members also experiencing distress, anxiety, and depression at similar levels. It is estimated that up to 70 percent of people across the cancer trajectory will experience some level of emotional and social distress.

A cancer diagnosis may bring feelings of denial, grief, and shock for those diagnosed, their families, and the wider community. These feelings quickly intensify when the practical realities of diagnosis disrupt all aspects of daily life. Social and professional roles and family functioning become compromised as people struggle with treatment side effects and the implications of illness in their everyday lives.

For a parent diagnosed with cancer, there are concerns about children's well-being and the practical realities of maintaining a functioning family home in the face of a life-threatening illness. For a single person, fear of being alone and concerns about how they can cope without daily support are paramount. For a child diagnosed with cancer, the impact on parents, siblings, friends, teachers, and the broader community are far reaching.

Parents of children with cancer have been identified as having a particularly high risk of developing symptoms consistent with a diagnosis of post-traumatic stress disorder. For older people, a cancer diagnosis is an additional burden in the presence of other co-morbidities.

As people move beyond initial diagnosis, the impact of cancer treatment and associated adverse effects, or the reality of progressive illness, and facing one's mortality, intensify feelings of anger, grief, helplessness, hopelessness, loss of control, and dependency.

The impact of cancer on the ability of people to maintain social functioning has been well documented. For young children, treatment, treatment side effects, and periods of hospitalization interfere with normative developmental stages. Physical changes resulting from the disease and treatment
adversely impact children’s social functioning, and reentering school can be particularly stressful. Adolescents often experience schooling interruptions, where diagnosis and treatment constrain future aspirations and limit normal adolescent experiences and the development of social skills and relationships. For adults, occupation and employment can be affected, with a loss of income and economic security. Career disruption or unplanned early retirement add to feelings of loss of purpose and worthlessness. Relationships become strained as the practicalities of ongoing support and caregiver roles are realized. Issues with body image, changes in sexual function, low self-esteem, and mood disturbances create challenges for the person with cancer and those with whom they interact.

The pervasive psychosocial impact of cancer on patients and their families extends to the survivor phase, as concerns about recurrence cause long-term stress. The financial burden of cancer can have long-lasting consequences; studies have demonstrated that savings can be exhausted through loss of income and the costs associated with treatment. In the United States, it has been estimated that approximately 5 percent of those who declare bankruptcy cite cancer as the underlying reason. The psychosocial burden of cancer traverses age, diagnosis, culture, socioeconomic status, and gender, but geography also creates adverse psychosocial outcomes. For rural people with cancer, the risk of serious psychological distress is higher than for their urban counterparts, as they are challenged by geographic isolation and lack of access to services. Additionally, delays in diagnosis can result in advanced disease and poorer survival rates.

Globally, there is recognition of the need for effective psychosocial care and support for people with cancer, caregivers, and families, but also there is acknowledgment that psychosocial needs are frequently not identified and often are unmet. People across the cancer trajectory indicate that they lack information to guide complex decision making and how to access the practical supports available to them. While there are a myriad of reports, studies, and trials that identify the importance of support from health professionals and the efficacy of psychological interventions and treatments, there is a growing body of evidence that indicates the people who would most benefit from support and interventions do not receive them.

The Provision of Care to Support Good Psychosocial Outcomes

Emotional and practical support provided by family and friends of people with cancer is considerable, and the patience, adaptability, and flexibility required can result in emotional exhaustion and substantial levels of stress. Rates of depression and anxiety among caregivers and family members highlight the need for psychosocial support to be targeted at all affected by cancer, not only those with a diagnosis. While family and friends informally provide the majority of psychosocial care and support, the role of health professionals in addressing emotional, familial, social, financial, and informational needs is also well documented. Psychosocial care by skilled health professionals is viewed as central to well-being across the cancer trajectory, with effective care linked to improved functional adjustment and quality of life. There is a demonstrable reduction in anxiety, depression, and cancer-related issues such as pain, fatigue, nausea and vomiting, and physical impairment.

Clear, honest communication by health professionals, opportunities to ask questions, information and choice surrounding treatment options, preparation for procedures and treatments, and emotional support and continuity of care by health professionals have all been identified as important for improved psychosocial outcomes. Optimally, psychosocial care provided by health professionals should occur from diagnosis, through the treatment trajectory and into the survivor period, or from curative to palliation, death, and bereavement. Active listening and empathy of health professionals, using a person-centered communication style, and skills in delivering information in ways that can be understood and retained have been consistently demonstrated to improve psychosocial outcomes for people with cancer, their caregivers, and friends and families.

Consistent with policy across most countries, there is increasing emphasis on involving the patient in all aspects of decision making. Shared decision-making models emphasize partnerships between clinicians, the person diagnosed with cancer, and his or her family and have been shown to consistently result in high levels of service user satisfaction. Strong partnerships between the health professional team and families are particularly important if the cancer patient moves to noncurative stages, where information and support can prepare people
to cope with anticipatory loss, grief, and bereavement. Reduced rates of depression and anxiety among people with cancer and their families have been reported, with targeted psycho-educational and psychosocial interventions deemed successful. Specific psychological therapies, such as cognitive behavioral therapy, have been shown to improve emotional adjustment and social functioning, and reductions in cancer-related symptoms and adverse effects have been reported. Other interventions such as support groups and drop-in centers (including Web-based), psycho-educational information, community-based programs, retreats and camps, and activities such as dragon boat race teams and expressive writing groups have all been documented as successful in improving psychosocial outcomes.

**Barriers to Effective Psychosocial Care**

Treatment side effects, fatigue, pain, emotional exhaustion, stress, anxiety, and depression all impact a person’s receptivity to psychosocial care. Lack of education and information influence a person’s ability to make decisions and fully understand treatment and treatment options; but even when good information is provided, timing is crucial. Information needs and receptivity to this information change over time.

Studies have shown that even when people are provided with good, clear information and develop knowledge to support their psychosocial well-being, lack of service availability, transportation, and financial difficulties can further impede their receptivity to access the support they need. Large surveys have indicated that lack of transportation can be a particular barrier to accessing psychosocial care. Lack of social support from family, friends, and the broader community significantly compounds psychosocial issues for people with cancer. Throughout the cancer trajectory there will be periods when caregivers, friends, and families become exhausted and face their own psychosocial issues, which in turn impact their capacity to continue to support their loved ones. For those people with cancer who enter the survivor period, there can be significant psychosocial challenges when their support network expects them to return to “normal” and reenter their life, grateful for surviving the cancer experience. Although supportive care by health professionals has been identified as central to the psychosocial well-being of people with cancer and their families, there is a wealth of research that identifies a lack of professional confidence and specialized knowledge of how to best address psychosocial needs. Inadequate education and training and lack of knowledge about services, techniques, and strategies for improving psychosocial care have been identified as professional shortcomings.

Lack of access to health professionals with the expertise to deliver effective psychosocial care has been identified as a major barrier to improving outcomes. In rural areas, lack of access to specialist staff and lack of confidence among health professionals, who are expected to be multiskilled generalists, have been consistently shown to impact the psychosocial outcomes for those with cancer and their families. Additionally, the impact of lack of confidence and skill among health professionals has been shown to impact their own well-being and create professional stress when they feel that the care they are delivering is inadequate. Despite the development of clinical practice guidelines to support psychosocial care of people with cancer and their families, there is evidence that these guidelines are often not implemented. Consistently, cancer patients and their families report that health professionals fail to assess, understand, and respond to their psychosocial needs, and that clinicians often lack awareness of existing services and resources. Overall, many health professionals fail to acknowledge psychosocial needs, care, and support as a central part of their role and integral to overall quality cancer care.

Amanda Kenny

Jan Pascal

*La Trobe University Rural Health School*

**See Also:** Childhood Cancers; Daily Life; Pain and Pain Management; Stress; Survivors of Cancer.

**Further Readings**


Kenny, A., R. Endacott, M. Botti, and R. Watts.

“Emotional Toil: Providing Psychosocial Care to
Purdue University Center for Cancer Research

The Purdue University Center for Cancer Research is a National Cancer Institute–Designated Cancer Center that specializes in translating lab findings as quickly as possible into new therapies. The center facilitates an understanding of the cancer cell, develops technology, creates diagnostic tools, and synthesizes chemical components utilizing the university’s core strengths in engineering, nutrition, pharmacy, veterinary medicine, chemistry, structural biology, and the biological sciences.

In 1975, a committee funded by a two-year grant from the National Cancer Institute (NCI) was established to plan the center. A year later the Purdue Cancer Center was created. Three years later, in 1978, the center was awarded an NCI Cancer Center Support Grant (which has been renewed ever since). In 1989, the center developed a scientific partnership with the Walther Cancer Institute. A partnership with the Indiana University (IU) Simon Cancer Center was established in 2004. The center officially became the Purdue University Center for Cancer Research in 2009. Membership in the Purdue University Center for Cancer Research is considered by the director and executive committee.

The committee consists of two associate directors, a deputy director, four scientific program leaders, four program co-leaders, and a managing director. Membership includes e-news and announcements regarding funding opportunities, sponsored retreats, symposia, and member discounts. Once approved, membership is granted for three years. Every three years, depending upon the recommendation of program leaders, members update their curriculum vitae and provide statements outlining their contributions to the center.

Several state and local organizations have supported the center for many decades. Since 1981, the Carroll County Cancer Association has funded a Summer Undergraduate Research Program. Beginning in 1948, the Indiana Elks Charities, Inc., has funded the Innovative Grants. These grants support faculty research.

The Lafayette Lions Club has honored a faculty member with a research award every year since 1978. The West Lafayette Sagamore Lions Club contributed $250,000 to establish an endowment fund to support an annual symposium on cancer research. Participants have included Purdue University, Indiana University, and the University of Notre Dame as well as other cancer organizations.

A Cancer Benefit Concert that is also sponsored by the Purdue Musical Organizations was established in 2005.

Since 2008, an annual 5K challenge has existed. The Jordan-Rieger Event supports pancreatic cancer research at the center.

The Purdue Center for Cancer Research has also established several endowments to expand funding resources. The Carl J. and Irene E. Dexter Fund was created in 1981 to support equipment and materials. The Bernice L. Anderson Cancer Research Fund established in 1989 supports general cancer research. The Melba M. Schumacher Cancer Research Fund created in 1993 also supports general cancer research. The Joyce Fox Jordan Fund created in 2001 supports cancer research at the center. The Jim and Diann Robbers Cancer Research Grant for New Investigators established in 2003 supports new researchers selected by the executive committee. The James R. Lowe Lung Cancer Research Fund created in 2004 supports lung cancer research. The Eva Bergstrom Cancer Research Fund created in 2005 supports postdoctoral research, with recipients and award amount determined by the executive committee. The Vision of Hope for Research in Women’s Cancer was established in 2006 to support research of women’s cancers. The Glenn A. and Marian J. Karch Cancer Research Fund was created in 2010 to support cancer research. The Indiana Extension Homemakers Association Cancer Research Fund,
also created in 2010, supports cancer research. The Darrel B. Sims Matching Fund doubles every donation, but the center must raise a total of $100,000 to be awarded funds in the amount of $200,000.

The Purdue University Center for Cancer Research has also identified six important areas of funding needs. The Scientific Research Fund assists with new imaging techniques, early detection tests, and new treatments. The Strategic Asset Enhancement Fund supports the development of innovative ideas that may not be typically funded or explored. The Women’s Cancer Fund sustains research in breast, ovarian, and cervical cancers. The Jordan-Rieger Fund for Pancreatic Cancer supports pancreatic cancer research specifically. The Prostate Cancer Research Fund supports research regarding prostate cancer specifically. The James R. Lowe Lung Cancer Research Fund supports research specific to lung cancer.

There are 18 departments, six colleges, and more than 90 scientists who gather at Purdue University to research, share ideas and insights, and promote cancer research. Faculty and researchers focus on one of the four research programs at the center. The Cell Identity and Signaling Program studies the key molecules and processes that distinguish normal cells from cancer cells. Program members rely on biochemistry, molecular biology, genetics, and developmental biology in their expertise. The Chemical and Structural Biology Program uses a wide variety of chemical, biochemical, and structural approaches to investigate the unique biological targets for chemotherapy and to develop new chemical treatment methods. This program develops an understanding of cancer molecules and their interactions, mutations, and modifications. In this manner, new inhibitors can be developed. The Drug Delivery and Molecular Sensing Program develops new initiatives, including nanotechnology and cancer imaging. This program researches cancer cell growth, cancer cell differentiation, cancer drug design, cancer drug discovery, chemical biology of cancer, and structural biology of cancer. Finally, the Medicinal Program focuses on the development of cancer chemotherapeutic agents. Research in this program includes chemical, biochemical, cellular, and animal methods to discover and design chemotherapy drugs.

The Purdue University Center for Cancer Research currently organizes cancer forums in breast cancer research and prostate cancer. Three clinicians (oncologist, radiologist, and pathologist) and a nationally renowned physician scientist will present information about building partnerships among scientists, engineers, and clinicians. The first breast cancer forum is scheduled in November of 2014. The first prostate cancer forum is currently being developed and is scheduled to take place in March 2015. Both events will be free to faculty and research scientists at Purdue University. The center also offers seminars and an annual scientific retreat.

Jessica Anne Hammer
Independent Scholar

See Also: Mayo Clinic Cancer Center; Ohio State University Comprehensive Cancer Center; University of California, Davis, Comprehensive Cancer Center; University of Chicago Medicine Comprehensive Cancer Center; University of Minnesota Masonic Cancer Center.

Further Readings
Purdue University Center for Cancer Research.
Radiation

Radiation is energy released as either particles or electromagnetic waves. The average United States citizen receives a total dose of about 360 millirems of radiation per year through a combination of man-made and natural sources. There are five types of radiation that pose a serious risk to human health, which are alpha and beta particles, gamma and X-rays, and neutrons. Ionizing radiation makes these types of radiation a significant risk to human health because the energy transferred is high enough to disrupt chemical bonds (radical formation or ionization), including living tissue. In contrast, nonionization radiation, such as radio waves, microwaves, and cellular devices do not have enough energy to disrupt the chemical bonds, but can cause other biological effects on humans. Ionized radiation also provides benefits to humans in regard to the application of medicine, especially in the treatment of cancer.

The main sources of man-made radiation in humans are three medical procedures, which are diagnostic examination (predominately X-ray images), malignant disease treatment (radiation oncology), and nuclear medicine (radiopharmaceuticals for diagnosis and treatment of diseases). Man-made radiation accounts for about 18 percent of the annual radiation dose, of which 11 percent comes from medical X-rays, four percent from nuclear medicine, three percent from consumer products, and less than one percent from various radiation sources that include occupational (0.3 percent), fallout (< 0.3 percent), nuclear fuel cycle (0.1 percent), and miscellaneous (0.1 percent). Commonly utilized radioactive isotopes by the medical community include cesium-137, colbalt-60, iodine-131, iridium-192, strontium-89, and technetium-99m.

Natural background radiation has three main sources (cosmic, terrestrial, and internal) accounting for 82 percent of the natural sources of radiation, specifically, radon (55 percent), internal (11 percent), terrestrial (8 percent), and cosmic (8 percent). The Earth is constantly receiving a steady trickle of mostly beta and gamma radiation from space (cosmic source—the Sun and stars). Significant terrestrial sources of radiation are from uranium and thorium and their decay products (e.g., radium-226, -228, -224 [and radium's decay product is radon]) which are found everywhere on Earth and thus are in the water, soil, and vegetation. Humans have a number of naturally occurring radionuclides within our bodies from birth, such as potassium-40, uranium-238, thorium-232, and their decay products, as well as carbon-14, rubidium-87, and lead-210.

Radioactivity

Radioactivity is the spontaneous decay of the nuclei of particular radioactive atoms (radioisotopes) with the emission of ionizing radiation. Nuclei exhibiting
Radiation

Radioactivity are unstable and in a continual process of gradual breakdown (i.e., disintegration), which is referred to as radioactive decay. The effect of radioactivity is to produce a more stable state. The decay is typically of three main types, alpha and beta particles and gamma radiation, accompanied by the emission of ionizing radiation in the form of high-energy particles or rays. The rate of breakdown or decay is calculated by the half-life, or the time it takes for a given number of atoms to decay by half, which can range from milliseconds for short-lived isotopes to billions of years. The amount of radioactivity exhibited is measured by the number of disintegrations per second (dps); 1 becquerel (Bq) = 1 dps, and 1 curie (Ci) = $3.7 \times 10^{10}$ dps = $3.7 \times 10^{10}$ Bq.

**Alpha and Beta Particles, Gamma and X-rays, and Neutrons**

Alpha particles are positively charged, high-energy particles emitted from the nuclei of a radioactive atom. They are the largest in mass and the slowest traveling at less than one-10th the speed of light. Alpha particles are produced following the decay of radioisotopes of heavy nuclei such as americium, actinium, radium, radon, thorium, plutonium, and uranium. The process of alpha decay transforms one element into a different element that has a lighter nucleus than the original radioisotope by emitting an alpha particle, which consists of two protons and two neutrons. The total energy (including the masses of the new element and the alpha particle) is the same as before, but some of the nuclear binding energy is converted into kinetic energy of the alpha particle. Naturally occurring alpha particles are generally not harmful to humans, unless they enter the body via a cut or are inhaled or ingested where they are potentially dangerous to human health. Alpha particles from cosmic rays are the exception, which can emit very high amounts of energy.

Beta particles are electrons emitted from the spontaneous decay of unstable nuclei when one of its neutrons turns into a proton and emits an electron and an electron antineutrino. Tritium, carbon-14, cobalt-60, cesium-137, iodine-129 and -131, phosphorus-32, and strontium-90 all decay by beta emission. Beta particles travel at a high velocity, which can be as fast as 98 percent of the speed of light and are fast enough to travel a few feet before losing most of their initial energy. Beta particles are electrons and thus have only have about 1/2,000 the mass of a proton or neutron, and their emission does not affect the mass number, and no new element is created. Since beta particles travel farther than alpha particles they are capable of penetrating living tissue more easily and causing health damage, especially phosphorus-32. Exposure to a beta particles source, if intense, is capable of causing redening of the skin (called "beta burn") and/or eye damage. As alpha and beta particles penetrate matter they bump electrons out of atoms or molecules, thus ionizing them.

X-rays, like gamma radiation, are composed of high energy electromagnetic rays (photons) and are identical in physical characteristics and biological effect. They do not have an electric charge or mass. The difference between the two is their origin. Specifically, X-rays originate outside of the nucleus (commonly a shell of electrons bending around the nucleus), while gamma rays originate from within the nucleus during fluorescence and radioactive decay. As the X-rays’ electromagnetic rays collide with atoms, the energy of the electromagnetic ray is absorbed by the atom, typically resulting in a higher orbital level. If the electromagnetic ray is very energetic, it can bump an electron out of the atom, causing the atom to ionize. More dense materials, like bones, absorb the electromagnetic rays more readily than smaller atoms found in soft tissue material (skin, organs, muscles) resulting in dark shadows being visible on photographic film (an X-ray image). An X-ray machine utilizes this difference in absorption resulting in images of human structure through the skin. Medical diagnostic procedures, such as dental, chest, or mammography are where people are exposed. Gamma rays are produced following spontaneous decay of radioactive material, such as cobalt-60 and cesium-137. They are similar to ordinary visible light but differ in their wavelength. Gamma rays have a wavelength that is far shorter than visible light and thus higher in energy, greater than 100 keV. Gamma decay generally occurs simultaneously with an alpha or beta decay and does not affect the atomic number or the mass number of a nucleus, and no new element is created.

Neutrons are electronically neutral (uncharged) and heavy particles that interact with atomic nuclei and are more deep penetrating than alpha or beta radiation (sometimes more than gamma radiation). They have both particle-like and wave-like
properties. Today, neutrons primarily come from nuclear power plants and cosmic rays. There is also limited use of neutrons in radiotherapy, industrial radiography, and explosives. Neutrons do not damage living tissue cells by ionizing them directly, but instead disperse atoms as a result of colliding with protons (hydrogen nucleus, principally). The colliding with other atoms scatters the atoms resulting in the scattered atoms emitting alpha, beta, gamma, or X-rays that in turn produce ionization (called indirectly ionizing radiation). Neutrons being heavy and uncharged only lose energy from interactions with nuclei, which results in a sudden large loss of energy from a single event that is not uniform. Therefore, neutrons are more carcinogenic than electromagnetic waves (gamma and X-rays) because they release more of their energy in clusters of ionizing events and thus cause a variety of DNA damage with lower reparability than gamma and X-rays. When comparing the same absorbed dose, neutrons are more efficient at causing gene mutations, chromosomal aberrations, and decreasing cell survivability than gamma and X-rays. Thus, the calculation of the effective dose of neutrons is weighted more heavily than X-rays or gamma rays.

Alpha, beta, gamma, and X-ray radiation each produce differing amounts of ionization radiation called low linear energy transfer (low LET) radiation. Ionizing radiation is used in radiation therapy. Its principal effect is its capacity to shrink tumors, damage or stop cancer cells from replicating, or sever their DNA strands. The damaged cancer cells are broken down by the body and expelled naturally. The damage to cancer cells from photon beams (electron and proton radiation) is by activating radicals from the atomic interactions. Alpha particles produce the most ionization because they are heavy, slow moving, and carry two positive charges. Gamma and X-rays produce the least because they are photons that carry no charge, while beta particles have an ionizing potential in between alpha and gamma rays. The ionizing potential of alpha and beta particles and gamma radiation causes damage on contact or proximity with living cells and can
result in radiation sickness. In contrast, neutrons are high linear-energy-transfer (high LET) radiation. The damage from neutrons is essentially from nuclear interactions. Low LET tumor cell damage is not complete and the cells can repair and thus continue to grow, while high LET radiation-damaged tumor cells’ ability to repair is significantly limited. Fast neutrons are able to treat large cancerous tumors regardless of their stage and do not require oxygen to destroy cancer cells like low LET radiation.

**Radiation Therapy**

Approximately half of cancer patients experience some form of radiation therapy. The type of radiation therapy is dependent on the cancer, its size, location, proximity to normal tissue, and the general health and social dimensions (age, gender, etc.) of the patient. Radiation therapy damages not only cancer cells but also normal cells. There are several processes for radiation therapy, such as outside the body (e.g., external-beam radiation therapy), placing a radioactive material inside the body near the cancer cells or tumor (internal radiation therapy, also called brachytherapy), or by mouth or injecting radioactive materials into the bloodstream (systemic radiation therapy) for targeting and destroying cancer cells.

External-beam radiation therapy commonly uses photon beams (either X-rays or gamma rays) targeted at a specific part of the body with a cancer tumor or cancerous cells. Gamma rays have a higher amount of energy than X-rays. The amount of energy used is based on the cancer tumor or cancerous cells targeted. The photon beam is commonly delivered by various machines, such as a linear accelerator (LINAC), Intensity-Modulated Radiation Therapy (IMRT), 3-dimensional conformal radiation therapy (3D-CRT), etc.

Internal radiation therapy involves radioactive materials placed inside or on the body to shrink a tumor or destroy the cancer cells. The delivery device emits radiation causing the tumor or cancer cells to shrink or be destroyed. One type of internal radiation therapy is called “brachytherapy” where a radiation source is sealed inside tiny pellets (called “seeds”), capsules, or ribbons and placed in the body by needles, catheters, or another delivery device. The seeds can be temporary or permanent and deliver a continuous low-dose (several days) or high-dose (conducted one session at a time via a device/machine that places the radioactive source(s) in or near a tumor and is removed after the session) of radiation. The advantage of brachytherapy is that it can be targeted to a smaller part of the body with a high dose of radiation than external-beam radiation therapy resulting in less normal tissue damage. The delivery device can be left in the patient for few weeks or even months where the radioactive isotopes decay and the seeds are rendered harmless. The seeds can be left in the body or removed. Brachytherapy can be used as a stand-alone treatment or in conjunction with external beam radiation, chemotherapy, surgery, or as an increased dose of radiation. Internal radiation therapy can be in liquid form (e.g., taken orally, IV drip, or pill) resulting in the liquid radiation traveling throughout the body killing the cancer cells.

Systemic radiation therapy is when the patient takes a radioactive substance orally or receives it by injection. Common examples are radioactive iodine or a laboratory made protein that binds to substances in the body including cancer cells (called monoclonal antibodies). The monoclonal antibodies are critical in enabling the radioactive substance to target the specific area and/or cells in the body. These antibodies are coupled with the radioactive substance which travels around the human body locating and killing tumor or cancer cells. Radiation therapy is also used to relieve pain (palliative) from the cancer treatment, such as in cases of metastasized cancer, cancer of the esophagus that prevents food or water intake, or when tumors are pressing against the spine or growing in the bone. Systemic radiation therapy can be used to reduce pain for patients with bone metastases. Some radioactive drugs to treat pain are strontium-89 chloride, radium-223, and samarium-153-lexidronam.

The side effects of radiation therapy range from acute to secondary malignancies many years later. The side effects are based on the type of cancer, the length and type of the treatment (type of radiation used, dosage, concurrent with other chemical therapy), and the damage to normal tissue or organs. Common acute side effects of radiation therapy include nausea and vomiting, damage to the epithelial surfaces, sores of the mouth, throat, and stomach, hydropsy, intestinal discomfort, infertility, and fatigue. Long-term side effects (occurring months to years after treatment) are primarily localized to
the area treated, such as damage to the blood vessels and the cells of the connective tissue. Other side effect conditions include hair loss (epilation), dry mouth (xerostomia), dry eyes (xerophthalmia), reduced elasticity of irradiated location (fibrosis), fluid retention and tissue swelling (lymphedema), heart disease, cognitive decline, and rectal problems (proctitis).

Andrew Hund
United Arab Emirates University

See Also: Radiation, Gamma; Radiation, Ionizing; Radiation Therapy.

Further Readings

Radiation, Gamma

Gamma radiation is probably the most well-known type of radiation thanks to Dr. Bruce Banner. Anyone familiar with the Marvel Comics character knows that gamma radiation was responsible for the mutagenic damage that turned the mild-mannered Dr. Banner into the Incredible Hulk. It is not as unusual as one might think that a comic book character is making an appearance in a cancer encyclopedia. In 1962, when the Incredible Hulk made his comic book debut, it was just over 15 years since the first atomic test bomb was detonated in the deserts of New Mexico, followed by the dropping of atomic bombs over Hiroshima and Nagasaki. A generation had grown up with increasing concerns about the long-term effects of radiation. While the real-world concern was directed at the possibility of nuclear war, and the more immediate possibility of cancer from radiation exposure, speculative fiction dramatized these concerns in the form of Godzilla and other irradiated, havoc-wrecking monsters in Japanese film. At the same time, Marvel comics capitalized on the science by creating a line of superheroes—Spider-Man, the Fantastic Four, the Incredible Hulk—all mutants who received their powers (and status as outcasts) in the aftermath of radiation exposure. Further expanding on the fears of the long-term effects of radiation exposure, Marvel’s X-Men were the result of increases in ambient levels of radiation which caused mutagenic changes at the germ line level, causing the creation of “gene X,” the mutant gene.

Gamma radiation is a type of ionizing radiation, with a very high frequency. These rays are named for their principal source of production, the decay of atomic nuclei from a high-energy state to low-energy gamma decay, and are the product of the alpha and beta rays of radioactive decay. Gamma decay is often a result of nuclear reactions like nuclear fission or fusion, though gamma rays can occasionally be produced in other lesser-known ways.

Gamma rays were first named in 1903, by analogy to alpha and beta rays, which had been discovered and named in the preceding decade. Unlike alpha and beta rays, gamma rays are not easily deflected by magnetic fields. Their wavelengths overlap with those of X-rays, and so they are distinguished by their origins, with gamma rays emitted by the nucleus, while X-rays are emitted by electrons.

While alpha and beta rays can be blocked by very thin materials, gamma rays can be blocked only by significant amounts of mass, preferably including materials of high density and high atomic number. This is one of the reasons Cold War fallout shelters were lead-lined and/or used exceptionally thick walls, for instance, and benefited from being built fully or partially underground. Shielding in nuclear power plants and fuel rod storage facilities is of course even more extensive and massive.

Alpha and beta rays produce only surface damage to living organisms, because they don’t penetrate further than the skin. Gamma rays can produce the same damage that alpha and beta rays do—radiation burns and other skin damage—but also result in radiation sickness, DNA damage and cell death, and very often cancer. Survivors of Hiroshima and Nagasaki, for instance, were a third more likely to die of cancer, while among nuclear
workers with chronic low-dose exposure, the risk of leukemia increases from between 2 percent to 10 percent, depending on the exposure level.

Gamma rays occur naturally in radioisotopes like the americium-241 used in household smoke detectors and the gadolinium-153 used in X-ray machines, as well as from interactions between the atmosphere and cosmic rays (the source of the Fantastic Four’s powers, incidentally). More rarely they occur from gamma-ray flashes or lightning strikes. Terrestrial gamma-ray flashes are produced in the atmosphere and have been recorded by the Compton Gamma Ray Observatory as well as terrestrial observatories. Most or all are caused by the electric fields of intense thunderstorms. A 2013 study found that passengers of commercial aircraft are occasionally exposed to gamma radiation as a result of these storms, in doses about the same or less than that of a full-body CT scan.

Gamma radiation is responsible for the “zone of alienation” surrounding Chernobyl, in the aftermath of the 1986 catastrophic nuclear accident that released nuclear particles into much of the Soviet Union and Europe. Though only 31 deaths were confirmed during the accident, the number of cancer deaths, birth defects, and other long-term effects is considerably higher; however, due to the handling of information by the Soviets and later the Russian government, the statistics are ultimately unknowable. (Chernobyl was evacuated before non-Soviet authorities were even notified of the event; the outside world discovered it only because radiation was detected in Sweden, prompting an inspection of the Forosmark Nuclear Power Plant and subsequent discovery that the source of the radiation came from much farther afield.) Four hundred times more radioactive material was released during the meltdown than in the bombing of Hiroshima. The handling of the disaster played a significant role—not understood until much later, due to the cloak of obfuscation over the matter at the time—in the dissolution of the Soviet Union, and created friction with Ukraine (which reported thousands more deaths than the Soviets would acknowledge), and remains pertinent today almost 30 years later.

Bodies of water surrounding Chernobyl, which was located on the Pripyat River that feeds into the Dnieper reservoir system, one of the largest surface water systems in Europe (and experiencing spring flooding at the time of the accident), were almost certainly contaminated, though the guidelines for acceptable levels of radioiodine were temporarily raised in order to permit the government to report the drinking water as safe, and authorities claimed that radioactive material had sunk to the bottom of aquatic systems in a form that would not dissolve for centuries. Contamination of fish became a concern throughout Europe in the short term and for years to come in Russia, Ukraine, Belarus, and Scandinavia. Groundwater, though, was not badly impacted, by comparison.

A large area of pine forest was renamed the Red Forest after it turned from green to reddish-brown in rapid death, and horses and cattle that were not evacuated died with massive thyroid damage. Wild boar in Germany in 2010, 24 years later, were found to be contaminated with radiation that could only be attributed to Chernobyl (through the boars’ consumption of radioactive mushrooms, in large part, or of animals that had eaten those mushrooms), leading to a ban on wild game meat. Norway has had similar trouble in the livestock industry, with plants used for grazing found to be contaminated with Chernobyl radiation. In the United Kingdom, restrictions on sheep farming were not lifted until 2012.

The primary long-term health impact of Chernobyl appears to be thyroid cancer, which was rampant in children in the aftermath, with at least 6,000 cases of thyroid cancer in children and adolescents attributed to Chernobyl radiation. Against expectations, there does not seem to be an increase in leukemia or solid cancers like lung cancer, according to the International Atomic Energy Agency, the Chernobyl Forum, the United Nations Scientific Committee of the Effects of Atomic Radiation (UNSCEAR), and the World Health Organization (WHO) Radiation Program. The International Physicians for the Prevention of Nuclear War has argued that the thyroid cancer figure is at least 10,000, with 50,000 more expected as a result of ongoing radiation exposure. Outside the highly contaminated zone, there are an estimated 5,000 cancer deaths and an unknown number of additional cancer cases that are attributable to Chernobyl gamma rays.

Radiotrophic fungus, appearing similar to black mold, has been discovered growing inside and near the Chernobyl Power Plant, having evolved the ability to convert gamma radiation into chemical energy. They thrive on radiation the way other
plants thrive on sunlight, and demonstrate once again the unbelievable versatility of life.

Bill Kte’pi
Independent Scholar

See Also: Radiation; Radiation, Ionizing; Radiation Therapy

Further Readings

Radiation, Ionizing

Ionizing radiation is any radiation that carries enough energy to ionize electrons by freeing them from atoms. It consists of ions, atoms, subatomic particles, and electromagnetic waves. Ionizing radiation includes the upper part of the ultraviolet spectrum, gamma rays, and X-rays. Radio waves, microwaves, infrared light, and visible light are nonionizing. Ionizing radiation occurs naturally through cosmic rays, radioactive decay, lightning, plasma discharge, the high temperatures of the solar corona, and phenomena like supernovae, and it is generated through a variety of means, including X-ray tubes, particle accelerators, nuclear power, and the detonation of atomic bombs.

Ionizing radiation is both important to the medical field and a source of serious health hazards. Different types of ionizing radiation vary considerably. Alpha, beta, and gamma rays all result from radioactive decay, for instance. While all three can be damaging, alpha and beta particles are stopped by fairly thin materials and don't penetrate further than the skin, and so they cause radiation burns — this damage can result in skin cancer as well. Gamma radiation, on the other hand — named because it is produced later than alpha and beta — not only penetrates the body, but can do so after passing through shielding that is 12 inches thick (depending on its intensity). The gamma radiation released as a result of the 1986 Chernobyl Power Plant meltdown has resulted in at least 10 thousand — and very possibly tens of thousands of — cases of thyroid cancer, and continues almost 30 years later to be a severe health hazard.

Ionizing radiation's most common and most serious health impact is in inducing cancer that develops years or even decades after exposure. Scientists understand how ionizing radiation causes cancer, but there is much less consensus about the frequency with which it happens. As a result, there is considerable disagreement about the risks of exposure, and about projections of future cancer rates related to Chernobyl and, more recently, the 2011 Fukushima nuclear disaster in Japan. Ionizing radiation can similarly cause cognitive decline and heart disease, again developing long after exposure.

The culprit in Chernobyl-related thyroid cancer, and in similar problems in the aftermath of the significantly smaller Fukushima disaster, is iodine-131, or radioactive iodine. A radioactive isotope of iodine, it's a major uranium, plutonium fission product, and causes mutation and death in penetrated organic cells. However, it's also used for medicinal purposes, to treat hyperthyroidism, Graves' disease, and some cancers, including thyroid cancer, neuroblastoma, and pheochromocytoma. The related isotope iodine-125 lacks beta radiation, emitting only low-energy but deep-penetrating gamma rays, and so is used in diagnostic testing as well as brachytherapy.

Brachytherapy is also called sealed source or internal radiotherapy, and is an important form of radiation therapy in the treatment of cancers. In brachytherapy, instead of being exposed to a beam of radiation originating outside the body, the patient is treated via a radiation source that is placed inside the body. Radioisotopes like iodine-125 and other sources of ionizing radiation (cesium-137, cobalt-60, iridium-192, palladium-103, and ruthenium-106 are all common) are enclosed inside a capsule or wire to prevent them from moving inside the body or being dissolved by body fluids. This allows for highly targeted radiation exposure in order to kill
off tumor cells, and for a faster course of treatment than external beam radiotherapy. The strength of brachytherapy is the ability to use a high dose of radiation on a very small area, ideally minimizing the destruction of healthy tissue associated with both radiation therapy and chemotherapy. Minimizing that destruction cuts down on side effects, and also reduces the extent to which the treatment interferes with and limits the body’s natural ability to heal and cure itself. Patients who have difficulty taking time off from work for treatment, or who live far from their treatment center, especially benefit from the convenience of brachytherapy. The treatment is also useful in cases where surgery isn’t technically feasible or doesn’t offer the best chance of a cure, though there are also cases combining brachytherapy with surgery.

Brachytherapy is most commonly used in treating breast, skin, cervical, and prostate cancer, but can treat tumors in many parts of the body. Contact brachytherapy puts the radiation source next to the targeted tissue, such as inside a body cavity like the cervix, on the surface of the skin to treat a skin cancer, or in the empty space of the trachea or esophagus. Interstitial brachytherapy, in contrast, is placed directly inside the targeted tissue, as with breast cancer.

Doses vary and are generally discussed in terms of four types: low-dose rate (LDR) brachytherapy, which is common for oral cancers, sarcomas, and prostate cancer; medium-dose rate (MDR), which is less common; high-dose rate (HDR), which is used for many interstitial applications of brachytherapy, especially in treating breast and prostate cancer; and pulsed-dose rate (PDR), which uses short pulses once an hour, to treat head and neck or gynecological cancers. Temporary brachytherapy applies the radiation source for anywhere between a few minutes (in the case of high-dose rate brachytherapy) to a 24-hour period for pulsed-dose rate, while permanent brachytherapy implants small radioactive pellets the size of rice grains, which are allowed to gradually but permanently decay inside the tumor tissue. This is the common form of brachytherapy used for treating prostate cancer.

For cervical cancer, LDR, PDR, or HDR brachytherapy are all possibilities, depending on the individual case. In prostate cancer, permanent brachytherapy is typically used for patients who have not metastasized and have a good prognosis.
erectile dysfunction in prostate cancer patients, ongoing digestive or urinary issues for prostate or cervical cancer patients, and fat necrosis (resulting in swollen tender breasts beginning some months after treatment) in breast cancer patients.

Bill Kte’pi
Independent Scholar

See Also: Broad-Spectrum Ultraviolet (UV) Radiation; Radiation, Gamma; Radiation Therapy.

Further Readings

Radiation Therapy

Cancer refers to the group of diseases that occur when cells from organs or tissues grow out of control. This growth can materialize as a mass or tumor, which can dislocate healthy cells. A tumor can spread to nearby tissues or organs as tiny cells detach and journey throughout the body, through the blood or lymph system, and begin growing in new locations. Radiation therapy uses targeted energy (e.g., X-rays, radioactive substances) to destroy cancer cells, shrink tumors, and/or alleviate certain cancer-related symptoms.

The medical field has utilized radiation therapy as a treatment for cancer for over a century, with its initial origins traced to the discovery of X-rays in 1895 by Wilhelm Röntgen. Emil Grubbe is recognized as the first American physician to use X-rays to treat cancer, beginning in 1896. The arena of radiation therapy began to grow in the early 1900s mostly due to the revolutionary work of the scientist Marie Curie, who discovered the radioactive elements polonium and radium in 1898. This discovery ushered in a new era of medical research and the development of new treatments. Radium was utilized in various forms until the mid-1900s, when cobalt therapy and cesium units came into use. Radium became medical linear accelerators, which have been utilized as radiation sources since the late 1940s.

In 1971, when Godfrey Hounsfield invented computed tomography (CT), three-dimensional planning became a possibility and created a shift from two-dimensional to three-dimensional radiation delivery. CT-based planning allows physicians to make a more precise determination regarding the dosage distribution, using axial tomographic images of the patient’s anatomy. Megavoltage linear accelerators, useful for their penetrating energies and lack of physical radiation source have essentially replaced Orthovoltage and cobalt.

Historically, the three leading classifications of radiation therapy are external beam radiation therapy (EBRT or XRT) or teletherapy, brachytherapy or sealed source radiation therapy, and systemic radioisotope therapy or unsealed source radiotherapy. These are distinguished by the position of the radiation source; external is external the body, brachytherapy utilizes sealed radioactive sources placed accurately in the treatment area, and systemic radioisotopes are given by infusion or oral ingestion. Brachytherapy can use temporary or permanent placement of radioactive sources. The temporary sources are usually placed by a technique called afterloading. In afterloading a hollow tube or applicator is placed surgically in the organ to be treated, and the sources are loaded into the applicator after the applicator is implanted. This minimizes radiation exposure to health care personnel who are administering the radiation therapy. Particle therapy is a special case of external beam
Radiation therapy where the particles are protons or heftier ions. Intraoperative radiation therapy or IORT is a special type of radiation therapy that is delivered immediately after surgical removal of the cancer. This method has been employed in breast cancer (TARGeted Introperative radiation therapy or TARGIT), brain tumors, and rectal cancers.

The introduction of new imaging technologies, including magnetic resonance imaging (MRI) in the 1970s and positron emission tomography (PET) in the 1980s, has led to the creation of more targeted treatment practices. Three-dimensional conformal radiation therapy has given way to intensity-modulated radiation therapy (IMRT) and image-guided radiation therapy (IGRT) tomotherapy which permit radiation oncologists to zoom in on tumors. The result is improved therapy outcomes, more organ preservation, and fewer side effects.

**Radiation Therapy Explanation**

Radiation therapy, also known as radiotherapy, or radiation oncology (frequently abbreviated RT, RTx, or XRT), is the medical utilization of ionizing radiation, commonly as part of cancer treatment, to manage or kill malevolent cells. Radiation therapy could be restorative in numerous forms of cancer if it is localized in a single area of the body. It could also be utilized as a portion of adjuvant therapy, to prevent tumor recurrence after surgery or to remove a primary malevolent tumor, such as in the early stages of breast cancer. Radiation therapy is cooperative with chemotherapy, and has been utilized before, during, and after chemotherapy in sensitive cancers. Radiation therapy utilizes targeted energy to abolish cancer cells, minimize tumors, and/or relieve specific cancer-related indications. In other words, this type of therapy could be utilized as a primary remedy to abolish cancer cells; in amalgamation with other treatments to impede the growth of cancer cells; before another treatment to minimize a tumor; after another treatment to impede the growth of any remaining cancer cells; and to relieve indications of progressive cancer.

Radiation therapy is commonly applied to the cancerous tumor because of its ability to control cell growth. Ionizing radiation works by damaging the DNA of cancerous tissue leading to cellular demise. To spare normal and healthy tissues such as skin or organs, which radiation must pass through to treat the tumor, shaped radiation beams are aimed from numerous angles of exposure to intersect at the tumor, providing an increased absorbed dosage at the site. The radiation fields could also include the draining lymph nodes if they clinically or radiologically involve with a tumor, or if there is a cause of subclinical malevolent spread assumptions. It is mandatory to include a margin of normal tissue around the tumor to allow for uncertainties in daily set-up and internal tumor motion. These uncertainties can be actualized by internal movement (for example, respiration, and bladder filling) and development of external skin blemishes relative to the tumor position. Radiation therapy has numerous applications in non-malevolent conditions, such as the remedy of trigeminal neuralgia, acoustic neuromas, severe thyroid eye disease, pterygium, pigmented villonodular synovitis, prevention of keloid scar growth, vascular restenosis, and heterotopic ossification. Utilization of radiation therapy in non-malevolent conditions is limited partly by worries about the occurrence of radiation-induced cancers.

Radiation oncology is the medical specialty concerned with prescribing radiation, and is distinct from radiology, the use of radiation in medical imaging and diagnosis. Radiation could be recommended by a radiation oncologist for curative or for adjuvant therapy. It could also be utilized as palliative treatment (where cure is not possible and the aim is for local disease control or symptomatic relief) or as a therapeutic remedy (where the therapy has survival benefit and it can be curative).

**Radiation Therapy Methods**

*External beam radiation therapy* is directed from a machine external the body onto cancerous cells within the body. Examples of this type of radiation therapy are 3D conformal radiation therapy, IMRT, IGRT, TomoTherapy, and stereotactic radiosurgery. External beam radiotherapy or teletherapy is the most common form of radiotherapy. The patient sits or lies on a couch and an external source of radiation is pointed at the affected part of the body. In contrast to internal radiotherapy (brachytherapy), in which the radiation source is inside the body, external beam radiotherapy directs the radiation at the tumor from outside the body. Kilovoltage X-rays are utilized for treating skin cancer and superficial structures; while megavoltage X-rays are utilized to treat deep-seated tumors (e.g., bladder, bowel, prostate, lung, or brain). Despite the fact that
X-ray and electron beams are by far the most widely utilized sources for external beam radiotherapy, a small number of centers operate experimental and pilot programs employing heavier particle beams, particularly proton sources.

Conventional external beam radiation therapy (2DXRT) is delivered via two-dimensional beams using linear accelerator machines. 2DXRT mainly consists of a single beam of radiation delivered to the patient from numerous directions: often front or back, and both sides. Conventional refers to the way the remedy is planned or simulated on a specially calibrated diagnostic X-ray machine known as a simulator because it re-creates the linear accelerator actions (or sometimes by eye), and to the usually well-established arrangements of the radiation beams to achieve a desired plan. The aim of simulation is to accurately target or localize the volume that is to be treated. This technique is well established and is generally quick and reliable. The apprehension is that some high-dosage remedies could be limited by the radiation toxicity capacity of healthy tissues, which lie close to the target tumor volume. An example of this problem is seen in radiation of the prostate gland, where the sensitivity of the adjacent rectum limited the dosage, which could be safely prescribed using 2DXRT planning to such an extent that tumor control could not be easily achievable.

Prior to the invention of CT, physicians and physicists had limited knowledge about the true radiation dosage delivered to both cancerous and healthy tissue. As a result, 3-dimensional conformal radiation therapy is becoming the standard remedy for a number of tumor sites. Worth mentioning, a new technique to reduce rectal radiation damage in prostate cancer patients involves the employment of an absorbable spacer placed between the prostate and rectum. It has been shown via MRI that a hydrogel spacer can push the rectum away from the prostate in the course of radiotherapy. Note that such spacers are commercially obtainable in some areas, and are a part of clinical trials in others. As a result of provisionally modifying the anatomy, these products have the capacity to allow for improved cancer targeting while minimizing risk to bordering healthy tissues. For all intents and purposes, prostate rectum spacers should be compatible with all prostate cancer radiotherapy treatments including 3D conformal, IMRT, stereotactic radiation, and brachytherapy.

Internal radiation therapy (brachytherapy) is a radioactive material placed directly into or near a tumor via a catheter or other carrier, such as a high-dosage rate brachytherapy. Brachytherapy is delivered by placing radiation sources inside or next to the area requiring remedy. Brachytherapy is commonly utilized as an effective remedy for cervical, prostate, breast, and skin cancer and can be utilized to treat tumors in many other body locations. As with stereotactic radiation, brachytherapy remedies are often known by their brand names. For example, brand names for breast cancer brachytherapy remedies include SAVI, MammoSite, and Contura. Brand names for prostate cancer include Proxcelan, TheraSeed, and I-Seed. In brachytherapy, radiation sources are precisely placed directly at the site of the cancerous tumor, which means that the irradiation affects are much localized. These characteristics of brachytherapy provide advantages over external beam radiation therapy: the tumor can be treated with very high dosages of localized radiation, at the same time reducing the probability of unnecessary damage to surrounding healthy tissues. A treatment of brachytherapy can frequently be completed in less time than other radiation therapy practices. This can help reduce the chance of surviving cancer cells dividing and growing in the intervals between each radiation therapy dosage. As one example of the localized disposition of breast brachytherapy, the SAVI device delivers the radiation dosage through multiple catheters, each of which can be individually regulated. This approach decreases the exposure of healthy tissue and resulting side effects, compared to both external beam radiation therapy and older methods of breast brachytherapy.

Systemic radiation therapy is a radioactive substance that is swallowed or injected and journeys through the blood to locate and abolish cancerous cells. An example of this type of radiation therapy is radioactive iodine therapy. Systemic radioisotope therapy is a form of targeted therapy; targeting can be due to the chemical properties of the isotope such as radioiodine. This process is specifically absorbed by the thyroid gland much better than by other bodily organs. Targeting can also be accomplished by attaching the radioisotope to another
molecule or antibody to guide it to the target tissue. The radioisotopes are delivered through infusion (into the bloodstream) or ingestion. Examples are the infusion of metaiodobenzylguanidine (MIBG) to treat neuroblastoma, of oral iodine-131 to treat thyroid cancer or thyrotoxicosis, and of hormone-bound lutetium-177 and yttrium-90 to treat neuroendocrine tumors, and peptide receptor radionuclide therapy. Another example is the injection of yttrium-90 radioactive glass or resin microspheres into the hepatic artery to radioembolize liver tumors or liver metastases. These microspheres are utilized for the remedy approach known as selective internal radiation therapy. The microspheres are approximately 30 μm in diameter (about one-third of a human hair) and are delivered directly into the artery supplying blood to the tumors. These remedies begin by guiding a catheter up through the femoral artery in the leg, navigating to the desired target site, and administering remedy. The blood feeding the tumor will carry the microspheres directly to the tumor enabling a more selective approach than traditional systemic chemotherapy. There are currently two different kinds of microspheres: SIR-Spheres and TheraSphere. A major use of systemic radioisotope therapy is in the remedy of bone metastasis from cancer. The radioisotopes move carefully to areas of damaged bone, and spare normal undamaged bone. Isotopes commonly utilized in the remedy of bone metastasis are strontium-89 and samarium (153Sm) lexidronam.

**Radiation Therapy Side Effects**

There are actually two kinds of side effects from radiation therapy; they are early and late. Early side effects, such as nausea or fatigue, are usually momentary. They cultivate during or right after radiation therapy treatments and last for numerous weeks after remedy ends, but then improve. Late side effects, such as lung or heart problems, could take years to develop and are often permanent when they do. The most common early side effects from radiation therapy are fatigue and skin problems. Other early side effects such as hair loss and nausea are typically specific to the site being treated.

Radiation therapy itself does not impose pain on the patient. Many low-dosage palliative remedies (i.e., radiation therapy to bony metastases) cause minimal or no side effects, although temporary pain outbreak can be experienced in the days following treatment due to edema compressing nerves in the treated area. Higher dosages can cause varying side effects during remedy, which are acute, in the months or years following remedy long-term side effects, or after remedy, cumulative side effects. The nature, severity, and longevity of side effects depends on the organs that receive the radiation, the treatment itself (type of radiation, dosage, fractionation, concurrent chemotherapy), and the patient. Most side effects are predictable and expected.

Side effects from radiation are usually limited to the area of the patient’s body that is under treatment. Modern radiation therapy aims to reduce side effects to a minimum and to help the patient understand and deal with those inevitable side effects. The main side effects reported are fatigue.
and skin irritation, like a mild to moderate sunburn. The fatigue often sets in during the middle of a course of radiation remedy and can last for weeks after radiation ends. The irritated skin will heal, but may not be as elastic as it was before.

**Early Side Effects.** This is not a general side effect of radiation therapy, and mechanistically is associated only with remedy of the stomach or abdomen that commonly react a few hours after remedy or with radiation therapy to specific nausea producing structures in the head during remedy of certain head and neck tumors, most commonly the vestibules of the inner ears. As with any distressing remedy, some patients vomit immediately during radiotherapy, or even in anticipation of it, but this is considered a psychological response.

Epithelial surfaces could sustain damage from radiation therapy. Depending on the area being treated, this could include the skin, oral mucosa, pharynx, bowel mucosa, and ureter. The rates of onset of damage and recuperation from it depend upon the turnover rate of epithelial cells. Typically, the skin starts to become pink and sore numerous weeks into remedy. The reaction could become more severe during the remedy and for up to about one week following the end of radiation therapy, and the skin could break down. Although this moist desquamation is uncomfortable, recuperation is usually quick. Skin reactions tend to be worse in areas where there are natural folds in the skin, such as underneath the female breast, behind the ear, and in the groin.

**Late Side Effects.** These occur months to years after remedy and are generally limited to the area that has been treated. They are often due to damage of blood vessels and connective tissue cells. Many late effects are reduced by fractionating remedy into smaller parts. Fibrosis is experienced; tissues, which have been irradiated, tend to become less elastic over time due to a diffuse scarring process. Epilation (hair loss) could occur on any hair bearing skin with particular dosages. It only occurs within the radiation field(s). Hair loss could be permanent with a single dosage of a precise amount, but if the dosage is fractionated permanent hair loss could not occur until dosage exceeds that specified amount. Dry mouth (xerostomia) and dry eyes (xerophthalmia) can become irritating long-term problems and severely reduce the patient’s quality of life. In the same way, sweat glands in treated skin for example of the armpit tend to impede working, and the naturally moist vaginal mucosa is often dry following pelvic irradiation. Lymphedema, a condition of localized fluid retention and tissue swelling, can result from damage to the lymphatic system sustained during radiation therapy. It is the most commonly reported complication in breast radiation therapy patients who receive adjuvant axillary radiotherapy following surgery to clear the axillary lymph nodes.

Radiation is a potential cause of cancer, and secondary malignancies are seen in a very small minority of patients—usually less than 1/1,000. It usually occurs 20 to 30 years following remedy, although some haematological malignancies could develop within 5 to 10 years. In the vast majority of cases, the empirical risk is greatly outweighed by the reduction in empirical risk conferred by treating the primary cancer. The cancer occurs within the treated area of the patient. Radiation has possibly excess imperial of demise from heart disease seen after some past breast cancer RT regimens. In cases of radiation applied to the head radiation therapy could cause cognitive decline. Cognitive decline was especially apparent in young children, between the ages of 5 and 11. Studies found, for example, that the IQ of 5-year-old children declined each year after remedy by numerous IQ points. Radiation proctitis can involve long-term effects on the rectum including bleeding, diarrhea, and urgency and is associated with radiation therapy to pelvic organs. Pelvic radiation therapy can also cause radiation cystitis when the bladder is affected.

**Cumulative Side Effects.** Cumulative effects from this process of radiation therapy should not be confused with long-term effects—when short-term effects have disappeared and long-term effects are subclinical, re-irradiation can still be problematic. During the first two weeks after fertilization, radiation therapy is lethal but not teratogenic. High dosages of radiation during pregnancy induce anomalies, impaired growth, and intellectual disability, and there could be an increased empirical risk of childhood leukemia and other tumors in the offspring. In males previously having undergone radiotherapy, there appears to be no increase in genetic defects or congenital malformations in
their children conceived after therapy. However, the use of assisted reproductive technologies and micromanipulation techniques might increase this risk.

Different people have different side effects with radiation. You could have little or only mild side effects from your remedy; someone else could have many or very severe side effects. Unfortunately, it is impossible to predict who will have what side effects. In addition, the specific side effects you could have depend on the type of radiation being utilized, the dosage of radiation, the area of the body that is being targeted, and the state of your health.

Conclusion
Cancer cells duplicate quicker than normal cells in the human body; radiation therapy focuses on these rapidly dividing cells. Radiation therapy involves the use of high dosages of radiation to kill cancer cells. New developments have made radiation therapy safer and more effective than ever. External radiation remedies are scheduled four or five days a week for numerous weeks. You must complete all sessions to achieve the best result. Internal radiation therapy is now being utilized for more types of cancer. Patients who experience side effects should contact their medical practitioner or nurse right away. Patients of radiation therapy are recommended to take good care of themselves by resting and eating properly. Skin in the treated area could become sensitive and easily irritated.

Approximately 60 percent of all cancer patients will require radiation therapy as part of their care. Radiation therapy can be utilized to help cure cancer or to relieve indications alone or in combination with other therapies, such as surgery or chemotherapy. Overall, patients who need radiation will have treatments four or five days a week. This regimen can last for five to seven weeks. Generally, cancer patients receive radiation therapy for one to five minutes per remedy.

Tamikia Lott
Old Dominion University

See Also: American Society for Radiation Oncology; Chemotherapy; European Society for Therapeutic Radiology and Oncology; Japanese Society for Therapeutic Radiology and Oncology; Oncology Nursing Society.

Further Readings

Raloxifene

Raloxifene was approved in 1997 for preventing bone loss in women after menopause. Subsequently, it was approved in 2007 for breast cancer prevention. On September 13, 2007, the U.S. Food and Drug Administration (FDA) approved raloxifene hydrochloride tablets (under the brand name Evista) to prevent and treat osteoporosis (bone thinning) in women past menopause. In bone cells, raloxifene acts like estrogen to prevent osteoporosis in women who have gone through menopause. It also helps to lower the fat in the blood, known as low-density lipids or “bad” cholesterol. Raloxifene can reduce breast cancer peril in these women, although it cannot entirely prevent it; it is not a cancer medication and is not considered a remedy for breast cancer.

Raloxifene is also utilized to reduce the peril of spinal fractures related to osteoporosis. In the course of studies, scientists noticed that among postmenopausal women who took the drug there was a lower rate of invasive breast cancer. After additional studies, the FDA approved the consumption of raloxifene for prevention of breast cancer. Raloxifene is a selective estrogen receptor modulator (SERM). SERMs have anti-estrogen influences on some tissues and estrogen-like influences on other tissues. To be clear, they are utilized to reduce the peril of invasive breast cancer in postmenopausal women that are at a high peril of developing breast cancer. However, women who have already
had breast cancer should not consume it nor should it be utilized in the treatment of breast cancer.

**Raloxifene Administration**

Raloxifene improves osteoporosis by decreasing bone breakdown and thinning. It works to help prevent invasive breast cancer by blocking estrogen in breast and uterine tissue. One out of every four cancer diagnoses in women each year is invasive breast cancer which can be deadly if not detected and treated early. Noninvasive breast cancer remains in the milk ducts or lobules (lobes of the breast) and does not spread to the surrounding tissue. Invasive breast cancer, however, spans outward from the milk ducts and lobules into the surrounding breast tissue, and ultimately, travels to other areas of the body.

Raloxifene is comparable to the drug tamoxifen, which also blocks estrogen in breast tissue. Since raloxifene does not act extensively like estrogen in the uterus, it has a significantly lower peril of causing cancer of the uterus than tamoxifen. It may also cause fewer blood clots. Studies found raloxifene to be just as effective as tamoxifen in reducing breast cancer risk (by up to 40 percent), however with fewer side effects.

**Raloxifene Studies**

Research studies of raloxifene include the Multiple Outcomes of Raloxifene Evaluation (MORE) trial, the Raloxifene Consumption for the Heart (RUTH) trial, and the Continuing Outcomes Relevant to Raloxifene (CORE) trial. All of the before listed studies compared raloxifene to placebo, also known as a sugar pill, in women past menopause. Taken together, these three studies revealed a qualified peril of invasive breast cancer in excess of half (59 percent). The studies revealed about a 70 percent qualified reduction in the peril of ER-positive breast cancer. These studies were not designed to find differences in death rates between the groups taking the SERMs and the placebos, and no differences were observed. So far, women who took SERMs had no survival advantage (did not live longer), although more follow-up is needed. There were other studies, such as the Study of Tamoxifen and Raloxifene (STAR) and the Selective Estrogen Response Modifier (SERM) studies.

*The Study of Tamoxifen and Raloxifene (STAR).* The largest study to look at the effect of raloxifene on breast cancer peril was the STAR trial. This study compared the influences of tamoxifen and raloxifene on breast cancer peril in more than 19,000 women past menopause who had an increased peril of breast cancer. Half were assigned to take tamoxifen and half were assigned to take raloxifene each day for five years. Both drugs reduced the peril of breast cancer, although tamoxifen seemed to reduce the peril more.

*Selective Estrogen Response Modifier (SERM) Studies.* A 2013 analysis put together the data from well-controlled studies, which (combining all of the studies cited above with a couple of contemporary ones) was an accumulation in excess of 80,000 women. The researchers concluded that SERM drugs lowered breast cancer peril by 38 percent over a period of 10 years—the five years of taking the drug plus the next five years. Based on the rate of breast cancer in the studies in the analysis, this would translate to about one case of invasive breast cancer being prevented for every 53 women taking a SERM drug. If you include non-invasive breast cancers such as ductal carcinoma in situ (DCIS), only about 42 women must take SERMs for five years to prevent one case of breast cancer with respect to a 10-year peril of breast cancer of around 6 percent. By definition, DCIS is a noninvasive form of breast cancer because the cancer cells are confined to the milk ducts of the breast. DCIS does not cause any symptoms. Rarely, a woman may feel a lump in the breast or have nipple discharge. However, most cases of DCIS are detected with a mammogram.

For a group of women with higher peril, the number that would need to be treated would be much lower. You would need to treat many more women to prevent one case of breast cancer if the group started out with a lower peril. Understand that some of the SERMs utilized in this large analysis are only available in Europe, but most of the women took tamoxifen and raloxifene. Studies continue to show that SERMs do not reduce the peril of endocrine receptor (ER) negative breast cancers. These cancers are more common in younger women and those with BRCA1 mutations. Although these drugs have not specifically been studied in women with BRCA mutations, it is not clear how helpful they are in those women.

*BCPT Trial.* In this trial, tamoxifen did not seem to help women with BRCA1 genetic mutations, but
it did seem to help those with BRCA2 mutations. BRCA1 and BRCA2 are human genes that produce tumor suppressor proteins. These proteins help repair damaged DNA and, therefore, play a role in ensuring the stability of the cell’s genetic material. When either of these genes is mutated, or altered, such that its protein products are not made or do not function correctly, DNA damage may not be repaired properly. As a result, cells are more likely to develop additional genetic alterations that can lead to cancer.

**RUTH, MORE, and CORE Trials.** Protection and efficiency for reduction in the peril of invasive breast cancer in postmenopausal women with osteoporosis were demonstrated in three clinical trials (RUTH, MORE, and CORE).

**The MORE (Multiple Outcomes of Raloxifene Evaluation) Trial.** This trial was a randomized, placebo-controlled, double-blind, multinational osteoporosis treatment study in 5,133 postmenopausal women. The effect of raloxifene hydrochloride on the incidence of breast cancer was assessed as a secondary safety endpoint. After a median of four years on treatment, raloxifene hydrochloride reduced the incidence of invasive breast cancer by 71 percent compared with placebo. There were 11 invasive breast cancers in 2,557 women on the raloxifene hydrochloride arm compared to 38 in 2,576 women on the placebo arm.

**The CORE (Continuing Outcomes Relevant to Raloxifene) Trial.** This trial was a follow-up study conducted in a subset of 4,011 postmenopausal women originally enrolled in the MORE trial. After a median of three additional years on treatment, raloxifene hydrochloride reduced the incidence of invasive breast cancer by 56 percent compared with placebo. There were 19 invasive breast cancers in 2,716 women on the raloxifene hydrochloride arm compared to 20 in 1,274 women on the placebo arm.

**The RUTH (Raloxifene Consumption for the Heart) Trial.** This trial was a randomized, placebo-controlled, double-blind, multinational study in 10,101 postmenopausal women at increased peril of coronary events. After a median of five years on treatment, raloxifene hydrochloride reduced the incidence of invasive breast cancer by 44 percent compared with placebo. There were 40 invasive breast cancers in 5,044 women on the raloxifene hydrochloride arm compared to 70 in 5,057 women on the placebo arm.

In the MORE, CORE, and RUTH trials, the reduction in incidence of breast cancer was primarily due to a reduction in the incidence of ER-positive invasive breast cancers. There was no reduction in ER-negative invasive breast cancers, and there was no difference in incidence of noninvasive breast cancers between the raloxifene hydrochloride and placebo groups. Most invasive breast cancers were stage I or II. The number of women required to be treated for one year to prevent an invasive breast cancer in one woman ranged from 323 to 862 in the three trials.

**Risks of Raloxifene**

Raloxifene is the second drug to be approved by the FDA to prevent invasive forms of breast cancer. The first drug, tamoxifen, has been on the market for several decades. Raloxifene works by blocking estrogen in the breast tissue of women at high peril. The medication helps prevent the spread of tumors that require estrogen to grow. Raloxifene is not effective, however, in women who currently have invasive breast cancer or who have had invasive breast cancer. It will not prevent cancer in these women, nor will it treat cancer once it appears. Although raloxifene can reduce the likelihood of invasive breast cancer, it is important to be aware of its serious side effects.

Those serious side effects include but are not limited to increased chance of blood clots in the lungs and legs; and increased chance of stroke in women with coronary artery disease. Other milder side effects include those of leg cramps; joint pain; swelling of the extremities; flu-like symptoms; sweating and hot flashes; trouble sleeping; and vaginal dryness and discomfort. Experts caution that some women who take raloxifene will still get invasive breast cancer. Therefore, women need to consider the pros and cons of taking a medication with very serious side effects.

As discussed previously, protection and effectiveness for decrease in the peril of invasive breast cancer in postmenopausal women at high peril of breast cancer were evaluated in the STAR (Study of Tamoxifen and Raloxifene) trial. The influences of raloxifene hydrochloride 60 mg/day versus
The results from a non-inferiority analysis are consistent with raloxifene hydrochloride potentially losing up to 35 percent of the tamoxifen effect on reduction of invasive breast cancer. Fewer noninvasive breast cancers occurred in the tamoxifen group compared to the raloxifene hydrochloride group. Raloxifene hydrochloride had a lower incidence of deep vein thrombosis, pulmonary embolism, cataract surgery, and hysterectomy than tamoxifen and there was a trend for a lower incidence of endometrial cancer.

Raloxifene hydrochloride is associated with an increased peril of deep vein thrombosis, pulmonary embolism, and retinal vein thrombosis. An increased peril of death due to stroke was observed in a trial in postmenopausal women with documented coronary heart disease or at increased peril for major coronary events. If you have heart problems or are at peril for a serious heart problem, it is recommended that a consultation occur with a physician to be sure that the benefits of using raloxifene outweigh the perils. Raloxifene may increase the peril of serious blood clots. It is recommended that individuals who have a history of serious blood clots (e.g., in the lung, leg, or eye) do not take raloxifene. Other adverse reactions (greater than two percent and more common than with placebo) include hot flashes, leg cramps, peripheral edema, flu syndrome, arthralgia, and sweating. Each individual postmenopausal woman’s peril/benefit ratio must be carefully considered.

**Indications of Raloxifene**

Hormones are chemical substances that are produced by glands in the body, which enter the bloodstream and cause influences in other tissues. For example, the hormone testosterone is made in the testicles and is responsible for male characteristics such as deepening of the voice and increased body hair. The use of hormone therapy to treat cancer is based on the observation that receptors for specific hormones that are needed for cell growth are on the surface of some tumor cells. Hormone therapy can work by stopping the production of a certain hormone, blocking hormone receptors, or substituting chemically similar agents for the active hormone, which cannot be utilized by the tumor cell. Their function and/or the type of hormone that is affected categorize the different types of hormone therapies.

Raloxifene is indicated for the reduction in peril of invasive breast cancer in postmenopausal women at high peril of invasive breast cancer. The effect in the reduction in the incidence of breast cancer was shown in a study of postmenopausal women at high peril for breast cancer with a five-year planned duration with a median follow-up of 4.3. Twenty-seven percent of the participants received drug for five years. The long-term influences and the recommended length of treatment are not known. High peril of breast cancer is defined as at least one breast biopsy showing lobular carcinoma in situ (LCIS) or atypical hyperplasia,
one or more first-degree relatives with breast cancer, or a five-year predicted peril of breast cancer ≥1.66 percent (based on the modified Gail model). Among the factors included in the modified Gail model are the following: current age, number of first-degree qualifies with breast cancer, number of breast biopsies, age at menarche, null parity, or age of first live birth. Currently, no single clinical finding or test result can quantify peril of breast cancer with certainty. After an assessment of the peril of developing breast cancer, the decision regarding therapy with raloxifene should be based upon an individual assessment of the benefits and perils. Raloxifene does not eliminate the peril of breast cancer.

Patients should have breast exams and mammograms before starting raloxifene and should continue regular breast exams and mammograms in keeping with good medical practice after beginning treatment with raloxifene. Imperative limitations of consumption for breast cancer peril reduction do exist. There are no data available regarding the effect of raloxifene on invasive breast cancer incidence in women with inherited mutations (BRCA1, BRCA2), which allows for specific recommendations on the effectiveness of raloxifene. Raloxifene is not indicated for the treatment of invasive breast cancer or reduction of the peril of recurrence. Raloxifene is not indicated for the reduction in the peril of noninvasive breast cancer.

**Raloxifene Administration**
The recommended dosage is one 60 mg raloxifene hydrochloride tablet daily, which may be administered any time of day without regard to meals with a full glass of water once a day. There is no intravenous (IV) preparation available. If a dose is missed, it is recommended not to take a double dose the next day. In addition to raloxifene, a health care provider may recommend that the patient take a calcium supplement with vitamin D (absorbs calcium better). The amount of raloxifene that is prescribed depends on many factors, including your general health or other health problems, and the type of cancer or condition being treated. A physician will determine the dose and length of time to take raloxifene. Before starting raloxifene treatment, it is recommended to alert the prescribing physician about any other medications (including prescription, over-the-counter, vitamins, herbal remedies, etc.). Recommendations suggest not to take aspirin, or products containing aspirin, unless your physician specifically permits this, since this medicine may increase your peril for developing blood clots.

Raloxifene may cause fetal harm when given to a pregnant woman. Raloxifene must not be given to a pregnant woman or a woman who intends to become pregnant. If a woman becomes pregnant while taking raloxifene, the medication must be discontinued without delay and the woman given appropriate counseling. Furthermore, it is recommended for both men and women, not to conceive a child (get pregnant) and to utilize contraception while taking raloxifene; nor should a mother breastfeed while on the drug. A physician should approve when it is safe to become pregnant or conceive a child after therapy.

Raloxifene self-care tips include but are not limited to wearing light clothing, staying in a cool environment, and putting cool cloths on your head to reduce symptoms if hot flashes are experienced. In addition, a physician should be contacted if the hot flashes worsen, or become intolerable. For flu-like symptoms, keep warm with blankets and drink plenty of liquids. There are medications that can help reduce the discomfort initiated by chills. Acetaminophen or ibuprophen may help relieve discomfort from fever, headache, and/or generalized aches and pains. However, be sure to talk with a physician before taking it.

Raloxifene causes little nausea. Nevertheless, if nausea is experienced, take antinausea medications as prescribed by your physician, and eat small frequent meals. Sucking on lozenges and chewing gum may also help. Exercise is recommended as often as possible. Light walking four or five times per week, for 20 to 30 minutes at a time will increase your energy level, decrease your chance of developing blood clots, and help strengthen your bones. Other self-care tips involve avoiding sun exposure by wearing SPF 15 (or higher) sunblock and protective clothing. In general, drinking alcoholic beverages should be kept to a minimum or avoided completely; as well as getting plenty of rest and maintaining good nutrition. Any symptoms or side effects experienced while taking raloxifene should be discussed with a health care provider, as he or she can prescribe medications and/or offer other suggestions that are effective in managing such problems.
Monitoring and testing occurs while taking raloxifene. A health care provider will want to do blood tests to see how well the patient is responding to raloxifene; as such, all appointments for tests and office visits should be carried out. Women will need a gynecologic examination before therapy, and in the course of therapy, at regular intervals; the appropriate schedule should be discussed with your health care provider. In addition, bone mineral density (BMD) should be done periodically to determine how strong your bones are; a patient may need this at least every two years or sooner if your health care provider suggests. Your physician may also monitor other types of blood work, to see if the medication is affecting other parts of your body.

Tamikia Lott  
Old Dominion University

See Also: American Cancer Society; Anticancer Drugs; Beta-Carotene; Breast Cancer; Cancer Drugs, Cost and Benefits of; Food and Drug Administration; National Cancer Institute; Tamoxifen.

Further Readings

Rectal Cancer

The international impact of rectal cancer has not been established due to the scarcity in the number of studies that investigate the epidemiology of this disease. Rectal cancer is considered as a malignancy that is strongly influenced by ethnicity, as well as geographic distribution. Based on the limiting features of this malignancy, the details of its etiology have remained uncertain.

The incidence of rectal cancer globally is generally very low, though in some parts of the world, the rates are relatively high. For example, in certain populations in southern China, north Africa, southeast Asia, and the Arctic region, rectal cancer is recognized as the most common type of malignancy. The unique distribution of rectal cancer in specific geographical areas indicates that its occurrence may be influenced by environmental and genetic factors.

To determine the impact of environmental and genetic factors on the incidence of rectal cancer, it is essential to initially establish the global incidence rate of this malignancy. However, previous reports have shown varying rates of rectal cancer due to the lack of integration in conducting epidemiological studies. Additionally, mortality data has not been established, as most of the areas afflicted by rectal cancer do not have a health registry to record deaths from the disease. The best source for statistics on rectal cancer both globally and on a country-by-country basis is the International Agency for Research on Cancer (IARC).

The IARC was established by the World Health Organization (WHO) to collect information on various cancers worldwide. The Section of Cancer Information maintains a large database that holds specific information on various cancers, such as incidence and mortality rates. The IARC lists international and national cancer registries. Unfortunately, the information on rates of specific cancers is limited to certain countries, and is therefore not a comprehensive record of less-common malignancies, including rectal cancer. In order to gather more comprehensive statistics on rectal cancer, scientists have begun integrating the data from various countries and reviewing the information for accuracy. The information collected in this database could be a starting point for further research on rectal cancer.
One of the major contributions of the IARC is GLOBOCAN, a database on the incidence of cancer in five continents. The data collected by GLOBOCAN is compiled into a report that represents information collected from 300 registries in a total of 61 countries around the world. Analysis of this data can then be used to identify countries showing the highest mortality rates for a specific cancer, as well as to determine the global trends in diagnosis. Epidemiologists utilize data from GLOBOCAN in order to develop preventive programs against specific cancers.

According to the GLOBOCAN data on rectal cancer, there are significant variations in the diagnosis of this specific disease around the world. Furthermore, the incidence of rectal cancer between males and females varied per country. For example, the incidence of rectal cancer in Central America was estimated as 0.2 per 100,000 person-years, whereas in southeast Asia the estimate was 6.5 per 100,000 person-years. The incidence rates for rectal cancer were lowest in Central America, South America, and western Europe. The highest incidence rates of rectal cancer were among males from southeast Asian countries such as Malaysia, Indonesia, Singapore, Cambodia, Brunei, and Myanmar.

The incidence rates of rectal cancer in females also varied per country. For example, among women in Central America the rate was 0.1, whereas in southeast Asia it was 2.8, reflecting at least a twofold increase. As with males, the highest incidences of rectal cancer among females were observed in the registries of southeast Asian countries, specifically Singapore, Myanmar, Indonesia, Bhutan, and Thailand.

Overall, statistics indicate that rectal cancer occurs at a higher rate among males than females, reaching a 200 percent increase. On the other hand, the low incidence rates of rectal cancer in both males and females in China were uniquely low, possibly reflecting a dilution in this specific population. However, in order to fully establish and validate this claim, additional investigations are warranted.

Another approach in studying the epidemiology of rectal cancer is through mortality rates. By comparing mortality rates between those of the World Health Organization and those collected by GLOBOCAN, it is possible to generate a more accurate estimate of this parameter within a five-year period. The mortality rates of rectal cancer varied across the globe, ranging from 0.1 among males in Central America to 4.2 among males in southeast Asia. Most of the registries showing the highest mortality rates involved males from counties in Asia, South Africa, and Micronesia. On the other hand, the lowest mortality rates were observed in countries of western and northern Europe, South Africa, Central America, and Melanesia. The mortality rates of rectal cancer in females ranged from 0.1 to 1.8 in Central America and southeast Asia, respectively. The highest mortality rates in females were observed in countries from Asia, South Africa, and Micronesia. However, in order to fully assess the severity of this particular malignancy on a global scale, additional studies covering more countries should be conducted.

Rhea U. Vallente
PreventionGenetics, LLC

See Also: Colon Cancer; Colon Cancer, Childhood; Latitude.

Further Readings

Religion

Religion, as a form of social structure, can serve the function of influencing attitudes toward health and illness among individuals. Religion not only affects the mind; religious beliefs and practices can affect the physical state and health in general. Hence, the role of religion in cancer control and prevention cannot be underrated. Religion often involves faithful devotion to a deity, ritual beliefs and observances, and a set of normative values and behaviors.

While there are mixed opinions on the relationship between religion and health, most
Religion generally show a positive relationship. Specific religious practices found to be beneficial to health include prayer, regular church attendance (community), and faith-driven beliefs and practices. However, religion alone is not the defining factor regarding overall attitudes toward disease and illness. Individuals are also influenced by other social structures such as ethnicity, race, marital status, education, and income.

Association with religious groups can provide not only spiritual support, but emotional and economic support for individuals with cancer as well. In addition, religion can act as a coping mechanism for those afflicted with disease. Church-based support is considered a source of material and psychological sustenance.

The role of religion in reducing cancer mortality has been documented. Studies found reduced risk of cancer among members of religious groups characterized by doctrinal orthodoxy and behavioral conformity. Frequency of church attendance and general commitment are important predictors of cancer mortality among those with some religious affiliation.

It is believed that religious beliefs affect attitudes and behaviors on two levels. Health attitudes are shaped by doctrine or teaching, while health behaviors are indicators of the strength of devotion. Doctrine may prescribe behavioral expectations that impose certain lifestyles that prohibit known health risks (for example, banning alcohol or tobacco use).

Evidence shows lower rates of cancer among some religious groups due in part to their dietary and hygiene practices. It is generally observed that behaviors influenced by doctrines are found more often among adherents of conservative rather than liberal religious groups.

Ellen Idler in her research has identified four areas where religion (whether practiced publicly or privately) can have positive effects on health.

- **Health Behaviors**: Religious belief helps reduce health-destructive behaviors.
- **Social Cohesiveness**: Participation in religion can create a social network for coping and support.
- **Cognitive Coherence**: Faith can lead to a belief system that helps one make sense of life.
- **Theodicy**: Religious belief modifies perceptions of distress associated with physical suffering, often giving hope to the individual.

Émile Durkheim examined religion as having a beneficial effect on human social life and individual well-being because it regulates behavior and integrates individuals into caring social circles. It provides stability and support. Religious belief systems may include prohibitions against certain high-risk behaviors such as smoking, excessive alcohol use, or sexual experimentation, lowering the incidence among religious group members of illness and disease.

During times of critical illness, such as cancer, people turn to religion for support. Religious groups can offer physical and spiritual assistance to the sick through prayers, visits, and meals, among other things. These help to reduce distress and restore hope. Prayers are seen as a cognitive and emotional resource immediately accessible to the sick and disabled.

Religion’s role in prevention includes greater access to services and health information, and motivation to maintain a healthy lifestyle. Studies have demonstrated that women who attended church regularly were more likely to be screened for cervical cancer than women who never attended church services. However, there is no clear research on the role of religious beliefs and denominations and the use of preventive health care services.

The positive influence of religion can be felt across age, gender and ethnic group. However, certain psychological factors have been found to mediate the relationship between health and religion. These include perception of personal control over events in one’s life, cognitive processes, acceptance of other people or God, attribution of purpose and meaning to negative life events, and perceiving negative events in life as having an external cause and positive events as having an internal cause.

Individuals with fundamental religious beliefs are typically more optimistic, hopeful, and socially involved than those with liberal beliefs. Belief in the superiority of spiritual or religious intervention by a deity through prayers or other means may help explain why some people delay medical treatment. For example, it may explain why some women delay seeing a doctor regarding noticeable breast lumps,
thereby contributing to advanced stage breast cancer at diagnosis. In some studies religion and spirituality were positively related to health care, leading one to seek medical help for minor illness; but religion became a barrier to seeking help for more serious conditions such as cancer.

To understand the complex relationship between religion and health, it helps to examine the functions that religion serves for the faithful. Jean Byrne identified at least 10 needs that religion fulfills, and that interact with health decisions, including providing a source of social support and strength in critical times.

Church attendance has been correlated with better health outcomes. Data suggest that weekly religious attendance is associated with longer life, lower physical disability, faster recovery from depression, and greater life satisfaction. Naguib Samir and colleagues noted that religious support or church attendance is linked to lower cancer pain, lower risk of cancer, lower instances of colorectal cancer, and decreased incidence of cervical cancer.

During times of great difficulties, such as being diagnosed with cancer, religious belief may help provide a greater sense of purpose, since death is seen not as an end to life but rather a time in which one will be judged for their actions and given either eternal life or eternal condemnation.

Religion can be seen as one important factor in understanding complex social phenomena. Since religion has demonstrated an impact on the reduction of unhealthy behaviors such as alcohol abuse, smoking, drug abuse, and an unhealthy diet, it is possible to view religion as a tool in cancer control. Additionally, the social network that is part of organized religious practice could be used as a way to reach out to those living with cancer and to encourage compliance with cancer management recommendations.

Samuel Ojima Adejoh
University of Lagos

See Also: Religion: Jewish Women and Cancer Risk; Religion: Meditation and Risk; Religion: Preventability Versus Preordained; Religion: Use of Interventions.

Further Readings


Religion: Jewish Women and Cancer Risk

In the United States, ethnic Jewish women demonstrate a greater risk of early-onset breast cancer than the general population. In 1990, genetic mutations to the tumor-suppressing genes BRCA1 and BRCA2 were discovered in a group of Ashkenazi Jewish families of eastern European descent. Harmful mutations in these genes can increase the risk of cancer incidence in both women and men. These genetic mutations can be passed from parents to children by both mothers and fathers, and about 2.5 percent of the ethnic Ashkenazi Jewish population carries the mutations. Norwegian, Dutch, and Icelandic peoples have also been found to have higher incidence of harmful mutations to these genes. People with a family history of cancer can be tested for mutations in the BRCA1 and BRCA2 genes.

The BRCA1 and BRCA2 genes produce proteins that help to repair damaged DNA. Mutations in these genes cause higher incidence of breast and ovarian cancers when compared with cancer rates in the general population. Studies show that women with mutations to the BRCA1 gene (chromosome 17q21-q24) have a 60 percent chance of developing breast cancer and women with mutations to the BRCA2 gene (chromosome 13q12-q13) have a 45 percent chance of developing breast cancer. In contrast, women in the general population have a 12 percent chance of developing breast cancer. Women with a mutated BRCA1 gene have a 40
percent chance of developing ovarian cancer and women with a mutation to the BRCA2 gene have a 17 percent chance of developing ovarian cancer. Men with the mutated BRCA2 gene have a 6 percent chance of developing breast cancer, representing a 100 percent higher chance than the general male population. BRCA2 mutations can also indicate a higher risk of colon cancer, prostate cancer, stomach cancer, pancreatic cancer, and cancer of the gallbladder.

The increased prevalence of mutations causing breast and ovarian cancer among American Ashkenazi Jewish families may have been caused by the migrations that resulted from World War II (1939–45) and the German Nazi Holocaust. Prior to World War II, approximately 9 million Ashkenazi Jews were living in eastern Europe. The Nazi genocide reduced this population by two-thirds, consequently reducing the overall genetic diversity of Ashkenazi Jews. Many of the surviving Ashkenazi Jews migrated to the United States during this period, becoming the “founders” of a new population of ethnic American Ashkenazi Jews. In population genetics, this is known as a founder effect: due to random chance selection, a smaller population is produced when it separates from a larger population. The result is a loss of genetic variations among the new, smaller population and specific genetic characteristics which are passed on to subsequent generations.

Genetic tests are available to screen for mutations of the BRCA1 and BRCA2 genes. A positive test result does not guarantee that the patient will develop cancer, but rather that he or she has an increased genetic predisposition for certain cancers. Some women with BRCA1 or BRCA2 mutations may choose to begin screening for breast cancers at an earlier age than the general population. Some experts recommend that women who test positive for these mutations begin annual breast examinations or mammograms at age 25 to 35. By screening at a younger age, breast cancers may be caught at an earlier stage and more successfully treated. However, women with the BRCA1 or BRCA2 mutations may be more susceptible to developing cancer due to radiation exposure during routine screenings from mammogram and X-ray machines.

The U.S. Food and Drug Administration has approved the drugs tamoxifen and raloxifene to reduce the risk of breast cancer in women. However, the efficacy of chemoprevention (the use of drugs to reduce the risk or delay the recurrence of cancers) in patients with BRCA1 and BRCA2 mutations remains unclear. Women with these mutations may lower their risk of developing ovarian cancer by taking oral contraceptives (birth control pills).

The significant genetic risk of cancers among families of Ashkenazi Jewish descent have prompted many otherwise healthy women to receive prophylactic surgeries to remove breasts and ovaries. Jewish women whose relatives have had cancer are more likely to view prophylactic surgeries as acceptable medical procedures. These surgeries are controversial because they cannot reduce all cancer risks in the patients who receive them and can cause side effects such as early menopause. Patients who undergo prophylactic surgeries can still develop breast or ovarian cancers, although their risk of mortality from these cancers is greatly reduced.

Within Israeli and American ethnic Jewish populations, Orthodox and Ultraorthodox (Haredi) Jewish women were found to have the highest risk of breast cancer incidence. In addition to the prevalence of BRCA1 and BRCA2 genetic mutations, other health factors might contribute to the higher incidence of breast cancer among Haredi women. Within this subset of the larger Ashkenazi Jewish population, Orthodox and Ultraorthodox women tend to have access to fewer health education resources, undergo cancer screening at lower rates, and are more likely to face other contributing health factors such as poor diet or obesity.

Haredi Jewish populations live in insular communities, maintain a strict religious way of life, and reject secular society. Haredi women express the belief that a religious lifestyle provides protection from harmful medical conditions and reduces the need for visits to physicians.

They often consult rabbis when making decisions about health care and health screenings in order to ensure compliance with religious practices. Some Haredi consider healthcare providers to be the means by which God heals people on Earth, rather than seeing them as trained medical experts or scientists. Among Haredim, illness is commonly seen as God’s indictment of the
community and an opportunity for atonement. For this reason, Haredi Jews often consider it their duty to pray for the health of ill community members and view individual instances of illness as the responsibility of the whole community.

Some preventative treatments for breast cancer and all available preventative treatments for ovarian cancer can result in reduced fertility in female patients. For religiously observant Jewish women, the canonical texts of Judaism (the Torah, Midrash, Mishnah, and Talmud) can provide ethical and moral guidance regarding fertility treatments. Jewish scholars have interpreted procreation as a duty based on the Book of Genesis. This duty is understood to fall primarily on men, making female infertility less of a religious transgression. However, following the deaths of 6 million Jews in the Holocaust, the religiously defined duty to procreate has taken on a new and historically related significance. While infertile Jewish women may not feel the pressure to procreate from religious doctrines, they may feel this pressure from family and community members.

Halacha (Jewish laws derived from religious texts) are rarely cited as objections to fertility treatments. In addition to the duty to procreate, Halacha also outlines a duty to heal which ethically aligns the religious doctrine with the goals of oncofertility (interdisciplinary research into the reproductive futures of cancer survivors).

Jessica A. Hutchins
Independent Scholar

See Also: Breast Cancer; Breast Cancer, Male; Chemoprevention; Colon Cancer; Drugs; Genetics; Israel; Ovarian Epithelial Cancer; Pancreatic Cancer; Prostate Cancer; Radiation;Raloxifene;Religion;Religion: Preventability Versus Preordained;Religion: Use of Interventions;Screening;Stomach (Gastric) Cancer;Surgery;Tamoxifen;United States;Women’sCancers;X-Rays.

Further Readings


Religion: Meditation and Risk

Meditation is an individual practice of mental training for the purpose of inducing a particular mode of consciousness. There are a wide variety of meditative practices requiring different levels of focus and concentration. While meditation is often discussed in the context of religious practice, meditation has evolved beyond its religious roots. In the West in particular, it is common to find many people practicing different forms of meditation outside of any formal religion, similar to the way practitioners of yoga often separate it from a larger spiritual belief.

In the West, “meditation” commonly refers to “meditation practices from the East,” which became of interest to Western intellectuals and New Age practitioners in the 19th century as new patterns of immigration, trade, and translation brought Eastern and Western ideas together. In 1893, the year of the
famed Chicago World’s Fair, or World’s Columbian Exposition, held to celebrate the 400th anniversary of Columbus’s arrival in the New World, the first Parliament of Religions was held concurrent with the fair. It was the first formal meeting of representatives of both Eastern and Western religions, including an Anglo-American convert to Islam, the first Zen Master to teach in the United States, the wandering Hindu monk Vivekananda, the Theravada Buddhist preacher Anagarika Dharmapala, and many others. This marked the start of Western interest in Zen practices, and in various meditative practices from the East, including India.

That said, meditation has a long history in the West under other names. Mysticism has generally not been embraced by the mainstream in either Christianity or Judaism, though in the late 19th century a wave of charismatic and born-again Christian movements began which embraced such mystical practices as snake handling, speaking in tongues, ecstatic dancing, and faith healing. Individual mystics like Saint John of the Cross have been revered, and their practices often included states of intense prayer that are identical to meditation practices in all but name. For that matter, the Catholic recitation of the Rosary, in which formulaic prayers are recited repeatedly, is essentially a meditative practice. And in both the Catholic and Orthodox churches, there is a 2,000-year history of religious figures engaged in deep contemplation that is likewise indistinguishable from a state of meditation.

Meditative practices originating in the West are typically devotional or scriptural, explicitly religious in nature, while meditation in the East, and Eastern meditative practices adopted by Westerners, are more likely to be pragmatic in nature. This is a generalization pertaining to overall trends, rather than the goals of any one individual. Another key difference is that Eastern religion has a long history of focus on proper posture, which can often become highly technical. Western traditions not only lack this, but Westerners are often cavalier about matters of posture in their adoption of Eastern practices.

Scientific research on meditation dates to the 1930s, and increased dramatically with the growth of neuroscience in the 1970s. Cross-cultural studies of meditation have often attempted to categorize different types of meditative practice, rarely with much satisfactory success. Even defining what exactly counts as meditation, in a way that excludes practices that are clearly non-meditative, is a challenge not yet met.

Among Eastern practices, Buddhist meditation is the most familiar, though it is misleading to speak of “Buddhist meditation” as though it is a single tradition or school of thought. Still, there are certain important commonalities, including a focus on breathing (which is also true of Hindu meditative practices) and the value assigned to tranquility and insight (vipassana, in Pali). Tranquility or serenity is the state or practice of calmness, which steadies and concentrates the mind during meditation and prevents it from turning into an opportunity to let one’s thoughts wander—or to fall asleep. By developing tranquility through practice, the meditator is able to avoid “hindrances”—distractions that prevent meditation—and in so doing, develops insight. (Actually, the Buddha’s disciple Ananda said that serenity and insight are developed in three ways: serenity is developed and leads to insight, insight is developed and leads to serenity, or serenity and insight are developed together.)

Buddhist meditation is often called mindfulness, which is similar to the Western psychological idea of mindfulness. In fact, Buddhism and psychotherapy share a lot of common ground, and are similar in their goals, in that they seek to understand the mind and the individual, and aim to free the individual from being overburdened by the world.

In the modern world, it is meditation’s putative “healing” power that is so often extolled. This can be a difficult topic to talk about without wandering into the New Age aisle and so-called alternative medicine. Meditation does not have the ability to cure cancer. Deep meditation, putting the individual into a mystical state, does have the ability to expel the awareness of pain, discomfort, and suffering from the individual’s mind—both the East and the West have a long tradition of mystics and martyrs who are transported into such states of mind and thus escape experiencing the unpleasantness of their violent ends. (This is not quite the same as the legendary yogi’s ability to walk on hot coals or pass nails through his palms, which involves a degree of body control that goes beyond the scope and intent of meditation, but the practices did develop side by side.)

But perhaps more important than limiting the suffering experienced by those few cancer patients
who have the time, attention span, and discipline to practice meditation at the level of an exalted master or who are natural-born mystics, meditation when properly performed has the scientifically proven ability to reduce stress. Heart rate, blood pressure, and breathing all slow during proper meditation, and the effects last longer than the meditative session itself. Experienced meditators have less need for sleep with no ill effects—though to be fair, a rephrasing of this might be simply that sitting very still in meditation for an extended period of time confers enough of the benefits of restfulness that the meditator is less tired at the end of the day—and experience less work stress. As a result, mindfulness-based programs have been put together in the medical community for dealing with the stress of illness and to reduce pain, though one of the benefits of meditation as a practice is to hopefully reduce the incidence of cancer.

Although studies attempting to establish links between stress and cancer incidence have had limited success due to the difficulties of design and implementation, there is general agreement in the oncology community that stress is a contributing factor to the development and metastasis of cancer, perhaps some cancers more than others.
example, suggest that the most frequently cited causes for developing cancer are God’s will, karma, and fate. In Buddhist and Hindu philosophy, karma is the belief that the deeds of one’s past lives are reflected in one’s current life. Therefore, suffering in the present life—such as being diagnosed with cancer—is attributed to misdeeds of a previous life. Similar beliefs about cancer diagnoses are also cited by Muslim patients who report that cancer is Allah’s punishment for one’s sins; embracing the disease is seen as a form of penance. Studies indicate that people who believe in karma, God’s will, or that human destiny is preordained are less likely to participate in cancer screening and are more likely to use complementary alternative medicine (e.g., Ayurveda, acupuncture, religious healing practices).

Cancer fatalism, by virtue of emphasizing an external locus of control (i.e., “God will cure me of cancer.”), engenders passive acceptance of the illness. On the other hand, the concept of Divine Providence focuses on internal locus of control (i.e., “I can cure myself of cancer.”) and free will. In Christian and Jewish philosophy, God is seen as benevolent, giving man an opportunity to correct wrongs and shape his or her destiny. As a consequence, the influence of religion on health beliefs and behavior may vary among religious groups.

In a study examining health beliefs and attitude toward breast cancer screening, it was found that Christian women reported more positive attitudes toward screening and were more likely to participate in breast cancer screening than Druze and Muslim women. Religious beliefs can sometimes override cultural norms. For example, Vietnamese women living in the United States were less likely to undergo cervical cancer screening if they were Buddhists as compared to being Christians.

Reflecting the important role that religion plays in health behavior, research also highlights variances in treatment choices and medical decisions based on religious backgrounds. In a study of patients with lung cancer, religious faith was found to be the second most important influence on treatment decisions after the oncologists’ recommendations. In a review of literature, it was found that a range of spiritual and religious factors influenced African American patients’ treatment preferences in cancer. Spiritual beliefs impacted healing, and patients were likely to feel that God is responsible for one’s health and that physicians carry out God’s will. Religious and spiritual beliefs are observed to influence attitudes toward other outcomes of cancer treatment such as pain management, handling side effects, and even end-of-life decisions.

Therefore, when public health and physician recommendations do not take religious beliefs into account it can result in nonparticipation or nonadherence. For instance, in a qualitative study, Muslim women reported that although they were aware of the benefits of breast cancer screening, they did not attend screening programs because they were designed in a way that was not in line with their Islamic beliefs and customs. Research recommends a culturally sensitive public health approach in order to gain maximum participation in cancer prevention programs.

In many countries where the religious and cultural beliefs about female modesty determine cervical cancer screening practices, the visual inspection with acetic acid (VIA) method is often used. This test involves swabbing the cervix with an acetic acid solution (usually vinegar), waiting for a minute, and then visually examining the cervix for any changes in color. White areas are suspected to be precancerous and treatment is recommended. The VIA is a simple, accurate, and inexpensive test that can be administered by trained health care staff such as midwives and nurses, thereby overcoming religious barriers for attending cervical cancer screening. Extensive research in developing countries has shown a positive response to the VIA method.

Recognizing the significant and influential role of religion on health, recent research emphasizes the inclusion of religious institutions as a channel for health promotion and risk prevention. Church-based health promotion (CBHP) interventions have gained increasing interest owing to the proven significant impact they have on a range of health behaviors. CBHPs have been effective in raising awareness about cancer prevention through screening (mainly colorectal, breast, prostate, and cervical cancers) and the benefits of physical activity and proper nutrition. Studies that used mosques as a site for health awareness programs reported similar positive findings, highlighting the importance of using religious institutions to target groups that are difficult to access.
The influence of religion on other cancer-related aspects such as mortality and adherence are inconclusive. In a review of studies it was found that the evidence was inadequate to support the link between religion and cancer mortality. Findings about adherence to cancer treatment, on the other hand, are conflicted with some studies reporting no negative impact of religion on compliance and a few studies evidencing a link between culture (not religion, specifically) and compliance.

**Religious Coping**

Numerous studies have examined coping in respect to religion when faced with a cancer diagnosis, treatment, and at end of life. Religious coping comprises three key processes: emotional (e.g., expression of fears), cognitive (e.g., finding a causal link to God), and behavioral (e.g., going to a religious shrine). Patients have reported reverting to their religious beliefs when diagnosed with cancer.

In a study of Hindu patients in India, it was observed that they discussed their faith in God, accepting God’s will, and praying. Taiwanese women diagnosed with breast cancer viewed their illness as an existential quest where they could find meaning in their experiences of illness and suffering. African American patients who were successfully treated for cancer reported that believing that healing was God’s work, praying, and letting God take over were their primary forms of coping. These patients believed that being diagnosed with cancer helped them attain increased spiritual awareness. Further, religious coping strategies were related to treatment preferences and end-of-life decisions.

Positive religious coping is observed to lower psychological distress, improve illness adjustment and quality of life, and encourage treatment choices that will extend life. Negative coping strategies, although less common, result from fatalistic attitudes toward the diagnosis, prognosis, and treatment of cancer. Some research indicates negative coping can result in increased levels of distress, poor illness adjustment, poor quality of life, and refusal to undergo treatment.

Religion has a significant influence on health beliefs and behaviors. Consequently, public health systems and physicians are beginning to take more culturally aware approaches to patient care. Adopting a method that is sensitive to religious backgrounds can increase participation in cancer screening programs, early detection, proper utilization of health resources, and treatment adherence.

**See Also:** Alternative Therapy: Mind, Body, and Spirit; Psychosocial Care/Support; Religion; Religion: Use of Interventions.

**Further Readings**


**Religion: Use of Interventions**

Religion and spirituality play an important role at various times during the cancer trajectory, such as when a patient is faced with the diagnosis of cancer, when they receive treatment, when cancer is in remission or cured, and at the end of life. While the primary goal of a doctor–patient consultation is to discuss a diagnosis and subsequent treatment modalities, patients may also have questions that are more existential in nature (e.g., Why me?...
What have I done to deserve this?). Research suggests that there are many benefits for using religion and spirituality (R/S) as a coping mechanism when diagnosed with cancer, especially in terms of acceptance, problem solving, and emotional regulation. In spite of the numerous benefits of R/S coping, it appears that R/S concerns and needs of patients are rarely met. Indeed, interventions that were focused on R/S needs of patients were reported to be preferred, helpful, and effective. This entry will describe key religion- and spirituality-centered interventions in cancer care and the outcomes and challenges of these interventions.

**Religion- and Spirituality-Centered Interventions in Cancer Care**

Effective R/S interventions are built on psychotherapy models such as those used by psychologists, counselors, or psychiatrists. These R/S psychotherapy interventions can be delivered to individuals, in a group, for a short term or long term. There is a growing interest in alternate models such as logotherapy (therapy developed by neurologist Viktor Frankl that attempts to help patients find meaning in their lives beyond their medical diagnoses) and dignity therapy (individualized, short-term therapy designed specifically for the terminally ill and their families).

A classic study by Brenda Cole and Kenneth Pargament used a psychotherapy and spirituality intervention for cancer patients. The intervention focused on helping patients adjust to their diagnoses, aiding in developing spiritual coping, and settling any spiritual conflicts. The framework of this intervention included four main existential issues individuals encounter when faced with a health crisis: finding one's locus of control, retaining a sense of identity, maintaining relationships, and finding existential meaning. Using a randomized control study design, the authors reported that after the intervention was completed and at two-month follow-up the patients in the intervention group had stable levels of pain and depression, whereas the group that received no intervention had higher levels of pain and depression.

Group psychotherapy is another form of intervention that includes a peer support framework wherein patients can share and get support for their cancer-related issues. William Breitbart developed Meaning-Centered Group Psychotherapy (MCGP), a spiritual intervention that was modeled after logotherapy. MCGP was used for advanced cancer patients with the goal of helping them develop and maintain a sense of meaning, peace, and purpose in their lives. This group therapy was delivered over an eight-week period and included a combination of a didactic approach, discussions, and experiential learning that was meaning-centered. Randomized controlled trials that used MCGP reported that the group therapy format was especially beneficial to cancer patients who were approaching end-of-life as it reduced their feelings of loneliness and anxiety. Further, these studies found MCGP to be effective for cancer patients at various stages of their disease, namely during treatment, advance stage, palliative stage, and during survivorship.

Dignity therapy is a novel, patient-centered intervention used for end-of-life patients that focuses on enhancing meaning, purpose, and a sense of worth. In this intervention, patients are encouraged to create a "generativity document" that is left for the patients' loved ones. Dignity therapy is believed to help patients establish their sense of worth through appraising their life with a therapist. Studies show that dignity therapy significantly decreases patients' levels of physical and mental suffering.

Recently there is a growing interest in including health care professionals such as nurses and doctors in delivering R/S interventions. Kristeller and colleagues conducted the Oncologist Assisted Spiritual Intervention Study (OASIS) in which oncologists were trained to deliver a semistructured and brief spiritual intervention to their patients during their consultations. The intervention is tailored to individual patient needs and involves inquiring after the patient's spiritual concerns, how they are adjusting to their illness, how they are finding peace and meaning, what resources they have available, and offering appropriate help. Patients who received the intervention reported decreased levels of depressive symptoms, improved health-related quality of life (HRQoL), and increased satisfaction with their care as compared to the control group that did not receive the intervention. Further, 85 percent of the oncologists rated the intervention as "quite" or "very" comfortable in delivering the intervention. Although the findings of OASIS need to be replicated in order to establish success of the intervention, these findings indicate that
OASIS may help in patients’ adjustment to cancer, especially in terms of their HRQoL, depression, and care from their oncologist.

This brings up the question of which health care professional should deliver R/S care and interventions to patients. Tom Gordon and David Mitchell suggested a multilevel framework for assessing and providing spiritual care for patients that is being implemented in Scotland. First, all staff who have regular, casual interactions with patients and their caregivers are expected to identify patients who have R/S needs and pass them on to the care team. The more senior the staff member, the greater the expectation that he or she will be better able to assess patients’ R/S needs. A recent study that examined the effectiveness of a short-term training intervention for health care staff in providing patients with existential support reported that the participants who received the intervention felt more confidence during patient communication. Hence, with appropriate training and referral, it is possible to improve health care staff’s sensitivity and skills in identifying and addressing patient R/S needs and concerns.

**Outcomes and Challenges of Religion- and Spirituality-Centered Interventions**

Religion- and spirituality-centered interventions are evidenced to have positive effects on patients in terms of their well-being and quality of life. The benefits of using R/S interventions for patients include increased levels of hope, optimism, resilience, self-esteem, and emotional bonding with others. Consequently, these feelings are believed to increase patients’ desire to survive the cancer which, in turn, results in patients being more actively engaged and compliant toward their treatment. The main emphasis of R/S interventions is on religious coping skills which, as research suggests, help reduce levels of stress that can arise from the lack of control and a sense of helplessness in the face of cancer. The central feature of religious coping strategies is to achieve a balance between those aspects of cancer that one can control and those that one cannot control (in other words, allowing God to take care of those that are out of one’s control). Therefore, through focusing on building religious coping skills of patients, R/S interventions help distressed patients attain a sense of inner peace by striking a balance between encouraging patients to be actively involved in their care and accepting the aspects of illness that cannot be controlled.

There are some challenges in delivering R/S interventions in clinical care that need to be considered. First, the professional boundaries of spiritual assessments in the clinical consultation need to be clear so the health care provider neither imposes his or her beliefs on the patient nor feels compelled to reveal what his or her beliefs might be. It may be helpful for both the staff member and the patient if there is a clear understanding from the beginning that the purpose of questions relating to religion or spirituality are in order to provide appropriate support to the patient. Second, there may be some role confusion between a psycho-oncologist and priest that should be addressed. It is important to understand that roles should be made clear; a psycho-oncologist may be trained to detect clinical depression but may not be trained in the theology or well-versed with sacred scriptures and vice-versa. Third, health care providers must understand the intersection between culture, religion, and spirituality. Religion and spirituality are very personal topics. Therefore, providers need to be sensitive, discreet, and open-minded in their queries about patients’ religious or spiritual philosophies.

---

Mahati Chittem  
*Indian Institute of Technology Hyderabad*

**See Also:** Alternative Therapy: Mind, Body, and Spirit; Psychosocial Care/Support; Religion; Religion: Preventability Versus Preordained.

**Further Readings**


Kaplar, Mary, et al. “The Effect of Religious and Spiritual Interventions on the Biological, Psychological, and Spiritual Outcomes of Oncology
Retinoblastoma

Retinoblastoma is the most common childhood cancer that develops inside the eye. It is a curable condition but can cause blindness and death if diagnosis and treatment are delayed. Effective treatments fortunately do exist, and promising new therapies and protocols are under investigation. This entry will discuss retinoblastoma's epidemiology, pathogenesis, clinical features, and management.

Retinoblastoma develops in approximately one out of every 15,000 live births. Three hundred to 350 children are newly diagnosed with retinoblastoma each year in the United States. The majority of children are diagnosed before 2 years of age, and the cancer does not discriminate between sexes and races. Seventy-five percent of patients develop retinoblastoma in one eye (unilateral), while 25 percent are affected in both eyes (bilateral). Unilateral cases usually occur from a spontaneous genetic mutation only in the child. Almost all bilateral cases signify a hereditary form of retinoblastoma, as do unilateral cases with multiple tumors in one eye. These patients usually have a germ-line mutation, meaning that every cell in the body carries the mutation, and the child is predisposed to develop other non-ocular cancers throughout life. The most common secondary cancers are bone and soft tissue, which are potentially life-threatening.

Retinoblastoma arises from retina cells that grow and proliferate uncontrollably. The retina is the light-sensitive layer comprising the innermost stratum of the eye that enables visual perception. Retinoblastoma develops when mutation of a gene located on chromosome 13 called \textit{RB1} occurs. \textit{RB1} is normally responsible for restraining cell proliferation, but mutations in its DNA sequence rendering it dysfunctional or deleting it altogether can result in tumor formation. The discovery of the \textit{RB1} gene was a seminal event in medicine, as it was the first identified genetic cause of cancer, and it revolutionized our understanding of many other diseases.

Leukocoria and strabismus are common signs of retinoblastoma. Normal pupils appear red when bright light is reflected off the retina, such as in flash photography, but patients with retinoblastoma frequently present with white pupillary reflexes sometimes referred to as “cat’s eye,” a condition called leukocoria. Strabismus is a misalignment of the eyes, which can occur if there is poor vision. Diagnosis by an ophthalmologist is made via an eye examination best performed under general anesthesia. Retinoblastomas appear as white masses inside of the eye. Ultrasonography, MRI, and other imaging modalities can confirm the diagnosis and help stage the disease. CT is usually not recommended since the radiation from the scan is thought to enhance second cancers in hereditary retinoblastoma. Patients and family members are also offered genetic testing and counseling.

Retinoblastoma is best managed by a multidisciplinary team of specialists experienced in the management of retinoblastoma, including ophthalmologists, pediatric oncologists, radiation oncologists, radiologists, pathologists, nurses, and social workers. Patient survival is the primary goal of retinoblastoma treatment, and although essential priorities, salvaging the eye and vision are secondary and tertiary concerns. The mainstay of treatment for advanced tumors is enucleation, which involves the surgical removal of the entire eye and a section of the optic nerve. This is the only method to completely remove cancer tissue from the eye to prevent recurrence and metastasis to other anatomical sites. The enucleated eyes are examined under a microscope to confirm the diagnosis and to identify features that increase the risk of metastatic spread such as involvement of the optic nerve beyond the excised margin and cellular invasion outside of the eye. After the surgery, patients are fitted for prostheses (“glass eyes”). Modern prostheses are made of plastic and have realistic appearances and promote motility.

Advances have been made over the years to allow many cases of retinoblastoma that have not spread outside of the eye to be treated without
enucleation. Small tumors can be treated with local therapies such as with photocoagulation and cryotherapy. Photocoagulation uses lasers to heat and destroy tumors and their blood vessels, while cryotherapy involves freezing tumors by placing cryoprobes on the sclera adjacent to the tumor. Patients are treated during examinations under anesthesia.

The current standard of care for most cases of retinoblastoma that cannot be controlled by local therapies alone is intravenous chemotherapy. This technique is called “chemoreduction.” Chemotherapy is provided systemically using drugs to disrupt the tumor cells’ ability to grow and replicate in order to shrink the tumors. Photocoagulation and/or cryotherapy are often used to augment the effects of the chemotherapies and to treat new smaller tumors. Commonly used chemotherapies include carboplatin, etoposide, and vincristine.

If tumors do not respond well to chemotherapy, radiation therapy is usually the next step. Retinoblastoma is very sensitive to radiation, and external beam radiation therapy (EBRT) used to be the primary treatment of choice prior to the advent of chemoreduction. However, EBRT fell out of favor, because approximately 35 percent of patients with hereditary retinoblastoma developed unique cancers in the field of radiation. EBRT has undergone many advances since then, and the delivery of radiation is now more precise. However, it is still reserved for cases that have failed chemotherapy due to the side effects.

Two better options for focal delivery of radiation are proton therapy and plaque brachytherapy. Proton therapy is available at several specialized medical centers, and allows for very targeted radiation while sparing surrounding tissues. Its main limitation is the lack of availability at most...
Rhabdomyosarcoma, Childhood

Rhabdomyosarcoma is the most common form of soft-tissue sarcoma, accounting for 4.5 percent of all cases of childhood cancer. Approximately 350 new cases of rhabdomyosarcoma are diagnosed annually in the United States. The incidence is 4.5 per 1 million children with 50 percent of cases seen in the first decade of life. It is the third most common extracranial solid tumor of childhood after neuroblastoma and Wilms’ tumor. It is included in the group of small blue round cell tumors of childhood along with neuroblastoma, lymphoma, and primitive neuroectodermal tumors. The tumor cells are thought to be derived from mesenchymal progenitors that are committed to muscle-specific lineages. Most cases of rhabdomyosarcoma occur sporadically. Genetic conditions associated with rhabdomyosarcoma include Li-Fraumeni cancer susceptibility syndrome, pleuropulmonary blastoma, neurofibromatosis type I, Costello syndrome, Beckwith-Wiedemann syndrome, and Noonan syndrome.

Subtypes

Rhabdomyosarcoma is classified into five subtypes depending on clinical and pathological characteristics. The “International Classification of Rhabdomyosarcoma” created by the Intergroup Rhabdomyosarcoma Study further associated these subtypes with disease prognosis.

Alveolar rhabdomyosarcoma. Generally seen during teenage years, this subtype has an incidence of about one case per 1 million children and adolescents. They are more commonly seen in the extremities, trunk, and perineum/perianal region and have a higher risk of metastasis. Histologically, this subtype has a key defining pattern in which fibrous septa composed of collagenous fibrovascular tissue provides a scaffold for rhabdomyoblasts (small blue round cells), and this organization forms alveolar-like structures.

Molecularly, most of these tumors express a constitutively active transcription factor, $PAX3$-$FKHR$ or $PAX7$-$FKHR$, resulting from chromosomal translocations $t(2;13)(q35;q14)$ or $t(1;13)$ (p36;q14), respectively. Patients with tumors that

---

Yoshihiro Yoneykawa
Shizuo Mukai
Harvard Medical School

See Also: Chemotherapy; Childhood Cancers; Radiation Therapy.

Further Readings


harbor these translocations have a poorer prognosis than those without.

**Embryonal rhabdomyosarcoma.** This is the most common rhabdomyosarcoma occurring in children. Embryonal rhabdomyosarcoma is 1.5 times more common in males with highest incidence (four cases per 1 million children) between birth and 4 years of age, followed by approximately 1.5 cases per 1 million in adolescents. These tumors occur mostly in the head, neck, and genitourinary region. On histology, this tumor recapitulates normal embryonal myogenesis, exhibiting cellular phases of muscle development, from undifferentiated mesenchymal cells to elongated myoblasts, multinucleated myotubes, and fully differentiated myofibers. Genetically, this group has no characteristic chromosomal translocations and its behavior resembles *PAX-FKHR* fusion-negative alveolar rhabdomyosarcoma with intermediate prognosis. These tumors may have a loss of heterozygosity at the 11p15 region.

**Spindle cell rhabdomyosarcoma.** These tumors are a variant of embryonal rhabdomyosarcoma and typically occur in young males. They occur most commonly in paratesticular soft tissue, followed by the head and neck. This neoplasm contains relatively differentiated spindle cells somewhat resembling smooth muscle tumors. They are *PAX-FKHR* fusion-negative tumors with better prognosis than the embryonal variant.

**Botryoid rhabdomyosarcoma.** A variant of embryonal rhabdomyosarcoma, this small-cell tumor abuts an epithelial surface, with condensation of tumor cells in the immediate subepithelial zone. The “bunch of grapes” appearance of this polypoid lesion led to its name as a *sarcoma botryoides*, from the Greek term *botryos*. Genetically, these are similar to *PAX-FKHR* fusion-negative rhabdomyosarcoma with good prognosis. This subtype is commonly seen in the walls of hollow, mucosa-lined structures such as the nasopharynx, common bile duct, urinary bladder of infants and young children, or the vagina in females, typically younger than age 8.

**Rhabdomyosarcoma, not otherwise specified.** Infants younger than 1 year have a higher incidence of undifferentiated sarcoma and tumors of the trunk and abdomen. This tumor is composed of poorly differentiated cells with no *PAX-FKHR* fusion and very poor prognosis.

**Diagnosis**

Rhabdomyosarcoma diagnosis is based on tumor morphology and the results of immunohistochemical stains. Rhabdomyosarcoma stains positive for desmin and muscle-specific actin but these markers are not specific for the tumors.

Myoglobin stains positive only in differentiated cells, and is hence not sensitive enough for diagnosis. Muscle transcription factors, MyoD and myogenin, are normally expressed during muscle development and are seen in high levels in rhabdomyosarcoma. These markers are both sensitive and specific for rhabdomyosarcoma. Molecular diagnostic tests such as reverse transcriptase PCR and fluorescent in situ hybridization can detect *PAX-FKHR* and chromosomal translocation status. These tests are not commonly used in practice yet.

**Prognostic Factors**

Presently, rhabdomyosarcoma is mostly curable in children with localized disease who receive multimodal therapy with greater than 70 percent five-year survival after diagnosis. Thereafter, relapses are uncommon with a 9 percent late-event rate at 10 years. Patients with metastatic disease at diagnosis have a poor 30 percent five-year survival.

The following factors are associated with favorable prognosis:

- **Age:** Children aged 1 to 9 years.
- **Tumor Site:** Cancer in head and neck along with non-bladder, non-prostate genitourinary areas.
- **Tumor Size:** Smaller tumors (<5 cm).
- **Tumor Spread:** Patients with localized disease and no lymph node involvement.
- **Tumor Resectability:** No residual tumor after surgery.
- **Histological Subtype:** Spindle, botryoid, and embryonal subtypes tend to have good prognosis.
- **Treatment Response:** Negative post-irradiation positron emission tomography (PET) scans predict improved local failure-free survival.
Stage
Staging assesses the extent of the disease before instituting therapy. This evaluation includes bone marrow aspirates and biopsy along with imaging modalities such as chest X-ray, chest computed tomography (CT) scan, bone scan, magnetic resonance imaging of the base of the skull, and abdominal/pelvis CT scan depending on the primary tumor site. PET with fluorine-18-fluorodeoxyglucose scans may help identify areas of possible metastatic disease. Rhabdomyosarcoma staging is relatively complex as it includes assignment of stage (1–4), local tumor group (i–iv), and risk (low/intermediate/high) group on a combination of various prognostic factors.

- **Stage**: Determined by primary site, tumor size (widest diameter), and regional lymph node involvement and/or distant metastases.
- **Local Tumor Group**: Determined by postoperative resection/biopsy status, with tumor margin and lymph node assessment.
- **Risk Group**: Determined by stage, group, and histology.

Treatment
All rhabdomyosarcoma patients require combined modality treatment with systemic chemotherapy, together with surgery, radiation therapy, or both to achieve maximum treatment response. Treatment strategies differ between the United States and Europe. In the United States, localized rhabdomyosarcoma is initially treated with surgery followed by chemotherapy (vincristine, dactinomycin, cyclophosphamide), with radiation reserved for residual disease. Addition of other agents such as topotecan, ifosfamide, and etoposide to date has not been shown to improve outcomes in metastatic disease. In Europe, chemotherapy followed by second-line therapy in the presence of poor response is delivered to avoid extensive surgeries. Surgical resection is preferred over radiation, which is given only for residual disease or when lymph nodes are involved. Current clinical trials are trying to target molecular alterations that are important for rhabdomyosarcoma pathogenesis.

Sheetal A. Mitra
*Children's Hospital Los Angeles*

See Also: Childhood Cancers; Genetics; Neuroblastoma.

Further Readings

Roche Group (Switzerland)
Roche, founded in 1896 by Fritz Hoffmann-La Roche, headquartered in Basel, Switzerland, is a globally leading pharma company. The company which is known as F. Hoffmann-La Roche Ltd. is a research-focused health care company. Its holding company, Roche Holding AG, has bearer shares listed on the SIX Swiss Exchange. The functions of Roche revolve around discovering, developing, manufacturing, and marketing innovative diagnostics and therapeutic products and services.

The company’s products and services address the prevention, diagnosis, and treatment of diseases, and improve the well-being and quality of life of patients. Roche specializes in in-vitro diagnostics and drugs for cancer and transplantation. The company classified its operations into two reportable business segments: Pharmaceuticals and Diagnostics. Roche has operations in various countries across North America, Latin America, Europe, Asia, Africa, Australia, and Oceania. The company’s main strategy for establishing itself in the market is through new product launches, network expansion, internal development, in-licensing of technology, and products, acquisitions, and strategic alliances.

Through acquisitions, Roche owns the Japanese biotechnology company Chugai Pharmaceuticals,
the American biotechnology company Genentech, and Ventana, based in Tucson, Arizona.

During the fiscal year 2013, the company's revenues were 46.78 billion Swiss francs. Roche is owned by three entities. Descendants of the founding Hoffmann and Oeri families own slightly over half of the bearer shares with voting rights: a pool of family shareholders 45 percent; and the Oeri family a further 5 percent. The Swiss pharma firm Novartis owns a third of the company's shares. Roche is the fifth-largest pharma company worldwide, as per 2013 rankings. It is one of the few companies increasing their dividend every year. The fiscal year 2013 was the 27th consecutive year of the company realizing increasing annual dividends.

Roche is a full member of the European Federation of Pharmaceutical Industries and Associations (EFPIA). Soon after its establishment in 1896, the company established itself as a leader in the market through the production of various vitamin preparations and derivatives. Roche was the first to produce, on large scale, synthetic Vitamin C with the brand name Redoxon. In 1957, the company introduced into the market the class of tranquilizers known as benzodiazepines, with Valium and Rohypnol being the best known brand names. In 1992, the company bought the patents for the polymerase chain reaction (PCR) technique. It has produced various HIV tests and antiretroviral drugs. In the field of cancer, Roche manufactures and sells several cancer drugs and is a leader in this field.

In 1982, the United States arm of the company acquired Biomedical Reference Laboratories located in Burlington, North Carolina, for $163.5 million. By the early 1990s, Roche Biomedical, which was formed after Hoffmann–La Roche mixed its laboratories, was one of the largest clinical laboratory networks in the United States, with 20 major laboratories and $600 million in sales. In 1994 and 2002, Roche acquired Syntex and Chugai Pharmaceuticals respectively. In 2009, the company acquired Memory Pharmaceuticals Corp. and Genentech. In 2010, the companies acquired were Medingo Ltd. and Biolimagene, Inc. In 2013, the company acquired PVT Probenverteiltechnik GmbH, mtm laboratories AG, and Anadys Pharmaceuticals, Inc.

Due to the wide infrastructure and firm grip on the market, the company has a wide variety of drugs in their product line. Some of these products include Avastin (bevacizumab) for certain malignant tumors, Erivedge (vismodegib) for basal-cell carcinoma, Herceptin (trastuzumab) for HER-2 positive breast cancer, Kytril (granisetron) for chemotherapy-induced nausea and vomiting, MabThera (rituximab) for lymphocytic leukemia, non-Hodgkin's lymphomas, rheumatoid arthritis, a number of solid tumors (including Kaposi's sarcoma), genital lesions, hepatitis C, Tarceva (erlotinib) for various cancers, Xeloda (capecitabine) for breast and colorectal cancer, and Vesanoid (tretinoin) for acute promyelocytic leukemia, among others.

Despite the obvious successes and achievement made by Roche, the company has had to overcome challenges too. In 1999 the firm pled guilty to participation in a worldwide conspiracy to raise and fix prices for vitamins sold in the United States and globally.

Roche undertakes intensive research and development (R&D). In addition to internal research and development activities the company is involved in publicly funded collaborative research projects, with other industrial and academic partners. One example is InnoMed PredTox in the area of non-clinical safety assessment. In joint research, Roche is expanding its activities within the framework of the Innovative Medicines Initiative of EFPIA and the European Commission.

In the area of oncology, Roche Group is the world's leading provider of cancer care products. (Some of the cancer products have been listed above.) The company's anticancer medicines are saving lives and significantly advancing the way some cancers are treated. Moreover, the company is developing new diagnostic tests that will have a significant impact on disease management for cancer patients in the future. This is being done through a broad portfolio of tumor markers as well as a range of molecular oncology tests. Through such advances, it is obvious that Roche will continue to be one of the leaders in providing cancer-focused treatments and diagnostics. As a show of its commitment in the field of oncology, the company has four oncology research sites (two in the United States and one each in Germany and Japan) and five development sites (two in the United States and one each in the United Kingdom, Australia, and Switzerland).

Roche's R&D in the area of oncology is focused on providing effective cancer therapies through the
discovery and development of novel therapeutics that target the specific molecular pathways associated with cancer. By understanding the molecular mechanisms of tumor development and how tumors spread, scientists are able to target the processes that lead to cancer. The area of oncology covered by Roche is one where a number of antibodies can be important. The objective of the company is to get more technologies ready to make all functions for treatments easier to manage.

According to the company, the key to successful treatment of cancer lies with precise diagnosis. Biomarkers enable doctors to determine which cancer type a patient has much more quickly and specifically. The company is also working to identify tumor markers that will detect tumor cells long before the first symptoms become apparent. In such a way, physicians will be able to initiate targeted and effective treatment without delay, therefore enhancing patient well-being and bringing down the cost to the health care system.

Michael Fox
Independent Scholar

See Also: Cancer Drugs, Costs and Benefits of; Drugs; Genentech.

Further Readings

Romania

Located in the southeast of central Europe, Romania was a communist country until the revolution of December 1989, when it started a long and challenging transition toward a democratic political system and a market economy. The country is a member of the North Atlantic Treaty Organization (NATO), the World Trade Organization (WTO), the Council of Europe, and the United Nations (UN). While it has also acquired full membership in the European Union (EU), since January 2007, and has undertaken substantial socioeconomic transformations, Romania has, however, an inferior life expectancy and general health status when compared to EU and regional averages (average life expectancy is six years shorter in comparison with EU average). Cancer is among the three leading causes of death in terms of noncommunicable diseases (17.6 percent of all deaths in 2006), surpassed by cardiovascular diseases (62.1 percent) and followed by digestive diseases (5.5 percent). The country needs to further advance the health and social protection system, including cancer control and prevention programs, in order to align its performances with the mandatory EU levels.

Data on cancer mortality from the last 20 to 40 years (1969–2004) in Romania show an increasing trend in cancer mortality rates among men, and an unchanged pattern among women. Standardized cancer incidence rates for all types of cancer increased almost two times from 1990 to 2005 (from 120.10 per 100,000 in 1990 to 240.66 in 2005). Fifty-two thousand new cancer cases are estimated to be diagnosed annually, and the number of deaths from the disease is expected to be almost the same.

With 240.66 cancer cases per 100,000 population, Romania currently ranks below the cancer average rate in Europe (460.12 cases per 100,000 inhabitants). In contrast with this relatively lower cancer incidence, cancer mortality shows a rising trend (179.8 per 100,000) equal to the European average (182.79 per 100,000).

The most common leading types of cancer in Romania with regard to new cancer cases in 2012 among men of all ages were lung cancer, colorectal cancer, and prostate cancer, while among women breast cancer incidence was first, followed by colorectal cancer and cervix cancer. In terms of cancer deaths, lung cancer was first, colorectal cancer second, and stomach cancer third among men, while, among women, breast cancer was first, colorectal cancer second, and lung cancer third.

In terms of cancer incidence in women of all ages in Romania in 2013, breast cancer ranked first, with an annual crude prevalence rate of 81.5 per 100,000, colorectal cancer ranked second (40.8 per 100,000), and cervical cancer ranked third (39.4 per 100,000). Also, while 4,343 cervical cancer cases are identified every year, cervical cancer
represents the second most common cancer in women 15 to 44 years old. High cervical cancer rates among Romanian women can be explained by both lack of information about the need for periodical testing as well as hesitancy to be tested. (The incidence of women who have never been tested for cervical cancer is expectedly higher in rural areas and among women with a lower socio-economic status).

The occurrence of colorectal cancer also shows a rapid rise as its incidence and mortality have increased two times over the last 20 years (for instance, 4,150 patients died of colorectal cancer in 2010, and 4,860 in 2012). Although colorectal cancer is considered a disease more frequent among the elderly, the average age of newly diagnosed patients has dropped during recent years.

Similar to other former communist countries in southeastern Europe, Romania still has incomplete and unreliable national or regional cancer registration coverage, and limited cancer control programs. Because of poor access to cancer education, prevention, and screening programs, the diagnosis for more than two-thirds of cancer patients occurs during the advanced stages of the disease, which leads to more complex and traumatic treatment. This current situation calls for intensive prevention and screening programs in view of early diagnosis.

Another issue within the Romanian health care system is that psychosocial support and cancer rehabilitation services are not included in the cancer control programs, mainly because of a poor cooperation between the health and social care sectors. Also, there is a general public reluctance for psychosocial oncology services that may be explained by both stigma of cancer and the Romanian culture of care.

Lara Lengel
Anca Nicoleta Birzescu
Bowling Green State University

See Also: Breast Cancer; Breast Cancer, Sociocultural Differences and; Cervical Cancer; Colon Cancer; European Association for Cancer Research; European Cancer Prevention (organization); Future of Cancer; Global Health Issues and Cancer; International Agency for Research on Cancer; International Association of Cancer Registries; Lung Cancer, Non–Small Cell; Lung Cancer, Small Cell; Prostate Cancer; World Health Organization.

Further Readings

Rosenberg, Barnett

When President Richard Nixon famously declared a national war on cancer in 1973, much research focused on prevention through minimizing
behaviors that created the greatest risks for cancer and its growth, as well as establishing keys to maintaining a healthy lifestyle that would make the diagnosis of cancer rarer. However, in the same era, groundbreaking work was done in heavily funded cancer research facilities that tested new methodologies for treatment as a way, if not to cure the cancer, then to put the often aggressive disease into remission and, in turn, guarantee a quality of life unimaginable for patients just 75 years earlier. It is one of the ironies of the era of cancer research that a physicist working at a state university lab, and with no background in oncology or even chemistry, would be responsible for isolating a chemical compound that actually stopped tumor growth, a revolutionary, even landmark drug patented as cisplatin. The story of Dr. Barnett Rosenberg and the discovery of cisplatin is a story of remarkably diligent observation, persistent research in the face of skepticism within the cancer research field, and ultimately of the kind of serendipitous luck that has always been a part of groundbreaking scientific research.

Barnett Rosenberg was born November 16, 1926, in the working-class environs of Brooklyn. Remarkably gifted early on in science and math, he attended Brooklyn College and graduated in 1948 with a Bachelor’s in Science. He completed his doctoral work in physics at nearby New York University (NYU) in 1956. After two years in the public sector (working in the research department of Westinghouse Electric), Rosenberg returned to academia; after a brief stint back at NYU, he accepted a position at Michigan State University (MSU) to establish a biophysics department, a daunting task as Rosenberg had no background in biology. But Rosenberg thrived in the research freedom his directorship provided as well as the resources and the lab teams available at a major state university. He would remain in East Lansing for the rest of his career. Rosenberg decided as an initial project to examine the implications of work he had completed during his doctoral term when he had noticed that bacteria exposed to an electrical field grew exponentially but did not, indeed could not, divide. How might electricity introduced through the controlled agency of an inert heavy metal, such as platinum, impact cells? Using a bacterial soup of E. coli, he exposed it to electromagnetic pulses. When he disengaged the electromagnetic impulses, what he noticed was odd: the bacteria had indeed grown, far beyond normal parameters, but had not divided.

Once the electric impulse was removed, however, the bacteria resumed its normative division processes. Rosenberg inferred that some element of the process had actually stopped cell splitting; he also realized the potential implications to cancer and specifically the often rapid cell division responsible for the growth of inoperable tumors. Rosenberg, with his background in physics, knew electrical impulses could not be responsible for prohibiting cell division. He focused on the platinum compound, although decades of cancer research to that point had dismissed such heavy metals in treatment regimens.

Meticulously, the research team led by Rosenberg, certain they were onto something potentially groundbreaking, devised numerous research protocols to isolate the actual causal process that, in turn,
resulted in the effects they had observed. Each table of results eliminated some possibilities and created new avenues to research, a classic application of the rigorous protocols of the scientific method. Unlike so many cancer research facilities and drug companies at the time that sought quick results and the resulting headlines, Rosenberg worked quietly, carefully, and under the radar of far more well-known cancer research programs. What he found through the careful process of elimination was that the cis form of platinum had the observed effect. In 1968, the research team tested cis-platinum on laboratory mice and found a stunning result: in a simple eight-day trial, a nearly 100 percent success rate. Tumors could actually be stopped, in essence cured. Certain now of cisplatin's potential, Rosenberg immediately sent the results and his conclusions to the National Cancer Institute.

Given Rosenblatt's comparative lack of specific oncological expertise, the NCI was dubious over such extraordinary claims. However, Rosenberg invited the Institute's researchers to replicate his research. When his results were confirmed and later duplicated in laboratory animals both in the United States and in Britain, Rosenberg understood the full implications. He went public—publishing his findings in the prestigious journal *Nature*, and news of cisplatin electrified the oncology research field.

In 1972, as part of the application for FDA approval, cisplatin was introduced initially to cancer patients who had exhausted all other treatment protocols. Then in numerous research projects, cisplatin was introduced to set appropriate dosage levels and to evaluate side effects. The side effects were harsh—nausea and vomiting, disorientation, hearing diminishment, brain dysfunction, and, most alarming, significant damage to the kidneys. However, the results were undeniable. Pharmaceutical giant Bristol-Myers Squibb acquired the patent, and the FDA moved quickly to approve the drug in 1978.

Over the next decade, in conjunction with research teams internationally, new drugs were introduced to help minimize the side effects. Cisplatin had its greatest effect on testicular cancer (more than 95 percent success rate), but it has been introduced to treat other cancers, including ovarian, bladder, neck, and stomach. Millions of cancer patients benefited from Rosenberg's discovery, and cisplatin became a standard in cancer treatment regimens.

Rosenberg himself was recognized for his landmark achievement and awarded the Charles F. Kettering Prize in 1984 presented by General Motors for the outstanding achievement in cancer research. A year later, he was recognized with the $75,000 Harvey Prize, awarded annually by the Israeli Institute of Technology in a variety of medical, scientific, and technology fields to acknowledge major contributions.

Rosenberg remained modest, quietly working in the research laboratories of MSU—the royalties from the drug patent were used to establish cutting-edge biomedical research facilities on the campus. Rosenberg died August 8, 2009, in East Lansing, Michigan.

Joseph Dewey
Broward College

See Also: Cancer Drugs, Costs and Benefits of; Drugs; Testicular Cancer.

Further Readings

---

**Roswell Park Cancer Institute**

Roswell Park Cancer Institute (RPCI) is America’s first cancer center. It was founded in 1898 by Dr. Roswell Park. Dr. Park created a multidisciplinary approach to the treatment of cancer that required scientists and clinicians to work and consult together. This approach has become the standard used by many modern-day comprehensive cancer centers across the country.

RPCI holds the National Cancer Institute (NCI) designation of “comprehensive cancer center” and serves as a member of the National Comprehensive
Cancer Network (NCCN). A large number of the faculty members at RPCI are also members of NCCN panels that create the Clinical Practice Guidelines in Oncology, which creates internationally recognized standards for clinical policy in oncology. These guidelines also provide comprehensive clinical practice guidelines that are updated on a continuous basis. The patient satisfaction rating at RPCI is in the 97th percentile nationwide, with overall nursing and physician's ratings both in the 99th percentile nationwide.

Throughout its history, RPCI has been instrumental in reducing the cancer burden and has successfully maintained an exemplary leadership role in setting the national standards for cancer care, research, and education. Recently, RPCI has gone through a period of expansion, adding jobs and creating new and innovative programs, including a hospital facility dedicated to Phase I cancer research studies. RPCI has been a proponent of surgical robotics, vitamin D research, immunotherapy, and vaccine therapy, and has conducted studies targeting tumor microenvironment and cancer prevention.

The RPCI campus is comprised of 28 acres in downtown Buffalo and consists of 15 buildings with about 2 million square feet of space. Buildings on the campus include a comprehensive diagnostic and treatment center and a new medical research complex, in addition to educational facilities, with plans for continued growth and development.

The RPCI mission is to understand, prevent, and cure cancer. RPCI would like to be among the top 10 of the nation's leading cancer centers. The values associated with this organization are innovation, integrity, teamwork, commitment, and compassion and respect. RPCI seeks to develop research that helps inform current and future generations about cancer. They are committed to making each decision, whether related to patient care, research, education, or administration, based on standards that are thoughtful, informed, honest, transparent when appropriate, and always respectful of privacy. The members of RPCI work as a team, encouraging the input and constructive feedback of all people within the organization. The RPCI organization is devoted to creating progress for patients and families, scientists and clinicians, and students who seek knowledge about cancer. RPCI prides itself on diversity, and appreciates differences as staff members establish research goals, develop care plans, and interact with one another.

RPCI is a founding member of the Blue Distinction Center for Complex and Rare Cancers created by the BlueCross BlueShield Association. This program provides information to patients who have complex, aggressive, or rare cancers to help support their decision making. Complex and rare cancers comprise approximately 15 percent of new cancer cases each year, and these patients have difficulty finding research facilities with oncology teams experienced in treating these specific types of cancers. This designation lets patients and family members know that the specific range of cancers identified as rare and complex are handled at RPCI using the best care and research available.

RPCI is one of the oldest National Cancer Institute–designated Comprehensive Cancer Centers in the United States. It was founded as an offshoot of the University of Buffalo School of Medicine. In the early 1900s, RPCI engaged in important research on immunological reactions with malignancies, and in 1946 was home to the first-ever studies on the effects of atomic radiation on humans. Research, development, and treatment progressed throughout the 20th century.

In 2006, RPCI opened the University at Buffalo's New York State Center of Excellence in Bioinformatics and Life Science and Roswell Park's Center for Genetics and Pharmacology. This was the first facility in Buffalo, and one of the first facilities in the country, to utilize robotic-assisted surgery for patients with bladder cancer. The pioneering technique offers these patients a less invasive treatment option that has several potential advantages over traditional open surgery. By this time in 2006, more than 1,000 patients had undergone blood and marrow transplantations for treatment of cancer and blood disorders at RPCI since its inception in 1991.

RPCI has also expanded service locations by signing a regional affiliation network agreement with Bradford Regional Medical Center, a rural hospital in Pennsylvania, to enhance oncology and hematology programs through research, education, and patient care in the northwestern Pennsylvania and southern tier of New York regions. RPCI continued to expand and reach more patients by launching an international effort to develop new and innovative programs in the prevention, detection, and treatment of lung cancer by establishing
the Stacey Scott Lung Cancer Registry. Joining lung cancer experts representing 11 leading research institutions around the world, this program is organized and stored at Roswell Park and draws from other member institutions’ research data to help scientists understand how lung cancer develops and evolves. Additionally, RPCI recently opened the Amherst Center in Williamsville, New York, to help meet the increasing demand for chemotherapy and infusion services and to help meet the needs of cancer patients in upstate New York.

In 2007, RPCI received the best Cancer Center Support Grant score in its history, and enjoyed the renewal of a five-year grant. New technology was added, including a Trilogy System installed in the Department of Radiation Medicine, which has significantly increased the treatment options available to cancer patients in the Buffalo-Niagara region. This fully integrated powerful image-guided radiation therapy technology delivers precise high-dose radiation therapy to tumors.

Recently, the Minimally Invasive Surgical Center at Roswell Park performed its 100th robot-assisted radical cystectomy for advanced bladder cancer using the da Vinci Surgical Robotic System. This event distinguished RPCI as one of the world’s premier academic institutions for the procedure. RPCI has also created programs that would involve younger generations in the pursuit of a cancer cure by launching an awareness campaign and supportive Web site, http://www.yroswell.com. This site uses a social networking approach by introducing videos, blogs, and other interactive media elements in an attempt to encourage youth to pursue careers in science and medicine.

RPCI continues to aggressively work to help patients and families. They are continuously engaged in research and development of state-of-the-art technology and treatment methods. The care and concern provided by staff members continued to provide them with high-ranking reviews by patients and governing medical agencies. RPCI is committed to continuing the fight to treat and cure all forms of cancer.

Constance M. Dolecki
Independent Scholar

See Also: American Association for Cancer Education; American Association for Cancer Research; Cancer Communication.

Further Readings

Russia

The northeastern Eurasian nation officially termed the Russian Federation became a modern state in 1992. Contemporary Russian historians usually consider the beginning of Russian history to have started in 862 C.E., when a Slavic leader by the name of Rurik created the country of Gardariki. Gardariki eventually dissolved over time, but in the ensuing centuries, the territories that make up modern Russia became important hubs of trade and culture. Tsars ruled the Russian Empire from 1712 until 1922, when the Communist party came to power and created the Union of Soviet Socialist Republics. Since the collapse of the Soviet Union in 1991, the modern Russian Federation has been a republic.

Recently, incidences of cancer account for over 15 percent of all mortalities in Russia, which is much higher than in certain other parts of the world such as Europe and North America; based on cancer statistics in the country, if you are diagnosed with cancer in Russia you have only a 40 percent chance of surviving, whereas in the United States you would have a 67 percent chance of surviving and in the United Kingdom you would have a 60 percent chance. Furthermore, over 25 percent of all Russian cancer patients will pass away in less than 12 months after their diagnoses. Cancer is currently a large problem for the nation for various reasons. For instance, many in the Russian population simply cannot afford the cancer care that comes along with a diagnosis.

Additionally, nearly all of the nation’s advanced treatment facilities are amassed within the largest cities of the country, like St. Petersburg or Moscow.
If a patient does not live close to these areas, then their chances of being adequately treated drastically decrease. After the collapse of the Soviet Union in the early 1990s, it has become much harder for patients to receive even basic radiation treatment. It is now estimated that only about 30 percent of all cancer patients in Russia can garner access to such treatment.

Moreover, Russia is only one of two nations in the entire world with a negative population rate. This negative population rate has largely been attributed to the popularity of alcohol and tobacco usage in the country, which consequently is believed to have a drastic effect on the rate of cancer incidences there. With regard to Russia’s high levels of alcohol and tobacco consumption, the World Health Organization declared the nation one of the most precarious places to live in the entire world. In countless studies conducted by numerous institutions around the world, alcohol and tobacco usage have been strongly correlated with high levels of cancers, such as lung cancers, esophageal cancers, and stomach cancers. As of 2014, there are almost 50 million Russian smokers. Since lung cancer is the most common form of cancer in Russian men, domestic health advocates are calling for much more intensive public campaigns against the use of tobacco. And since cancers linked to high amounts of alcohol use like esophageal and liver cancer are quickly increasing in the country, health activists are striving for more public awareness regarding reducing such behavior.

Diagnosing and screening practices are an aspect of cancer treatment in Russia that can be greatly improved. There are no national screening initiatives in the country for bowel or uterine cancers, though these types of cancers are extremely prevalent in the country. Domestic data seems to suggest that the average Russian cancer patient is diagnosed with the disease when it is already at a very advanced stage, which also indicates that much more can be done in the nation to identify the disease earlier and more effectively within the Russian population. If steps are taken at the regional and federal level to improve and increase diagnosing efforts, then many Russian cancer patients can be given a much better opportunity to survive the disease.

Currently, the most prevalent forms of cancer incidences in Russia are bowel cancer, breast cancer, cervical cancer, lung cancer, and prostate cancer. Lung cancer accounts for the most common incidences in Russian males, followed by cases of prostate cancer and bowel cancers. And while breast cancer rates in Russian females are significantly lower than those of many other modern nations, it is still the leading cancer incidence in women here, followed by cases of cervical cancer and bowel cancer.

Conversely, within the past 10 years certain cancers such as bladder cancer, kidney cancer, and ovarian cancer have seen a nationwide increase in prevalence, while incidences of skin cancer have steadily but consistently been declining. Industrial and manufacturing portions of the nation experience much higher rates of cancer than other parts of the country, and this is believed to be because of the large amounts of radioactive and chemical pollutants that are produced by industrial operations in those regions.

Unfortunately, many citizens of the Russian Federation have had cancer throughout its history. The popular and acclaimed Russian actor Yevgeny Zharikov passed away from an undisclosed cancer in 2012. Mstislav Rostropovich, a Russian cellist who many critics claim was perhaps the best cellist to have ever lived, died in 2007 after a brief battle with intestinal cancer. Elena Donaldson Akhmilovskaya, a female Russian grandmaster of chess who was once one of the great technicians of the game, succumbed to her bout with brain cancer in 2012.

While it is difficult for many Russians to receive cancer treatment for financial and geographic reasons, there is still a good amount of advanced cancer treatment centers in the country, especially in the larger cities of the nation. There is a lot of promising cancer research being conducted in facilities countrywide, such as at the Russian Institute of Experimental Diagnostics and Cancer Treatment. There, scientists are studying various methods of using chemicals extracted from plants to fight the disease. For example, the Australian tobacco plant has been shown to produce a particular kind of antibodies that seem to display anti-cancerous properties. Russian researchers are hoping to find a breakthrough in the global fight against the disease in the midst of such promising research.

William M. Peaster
Independent Scholar
See Also: Breast Cancer; Cervical Cancer; Lung Cancer, Non–Small Cell; Lung Cancer, Small Cell; Prostate Cancer.

Further Readings

Rwanda

The Republic of Rwanda is a central-eastern African country situated in the Great Lakes region. Rwandan culture is divided into three different ethnic groups: the Hutu, Tutsi, and Twa (pygmy people). Until the late 1800s, the Kingdom of Rwanda was ruled by Tutsi people, who kept their power after German and Belgian colonization in 1884 and 1916 respectively. The Hutu population revolted in 1959, causing a vast massacre of Tutsi people and establishing a new independent Hutu state. In 1990, Tutsi revolted, launching a civil war that culminated in the 1994 Rwandan Genocide. During this 100-day genocide, 500,000 to 1 million Tutsi were brutally massacred by Hutu extremists. The Tutsi eventually won the civil war, but the Rwandan economy suffered a tremendous blow. In addition to deaths from the war, more than 2 million Hutu fled the country for fear of reprisal.

Most of the Rwandan population is comprised of very young people: almost half of its inhabitants are under the age of 15, and less than 3 percent are more than 65 years old. The population is predominantly rural, with more than 85 percent of Rwandans living off subsistence agriculture. Kigali is the largest city, with 1 million citizens, followed by Gitarama, Butare, and Gisenyi, all with less than 100,000 inhabitants. Health care in Rwanda is decentralized and has four referral hospitals which are Centre Hospitalier Universitaire de Kigali (CHUK), Centre Hospitalier Universitaire de Butare (CHUB), King Faisal Hospital (KFH), and the Kanombe Military Hospital. The Bamako Initiative, a joint World Health Organization/United Nations Children’s Fund (WHO/UNICEF) initiative aimed at providing African populations with health care services and essential drugs, gave support to the Rwandan health care system in the pre-genocide era, but much of the progress was lost after the massacre. For example, the national cancer registry, established in the Department of Pathology at the University Hospital of Butare in 1991, stopped functioning.

Before the 1994 massacre, the most commonly diagnosed cancers were liver cancer (12 percent), cervical cancer (12 percent), stomach cancer (9 percent), and HIV-related cancers such as Kaposi’s sarcoma (6 percent). A retrospective study of children admitted to the Butare Teaching Hospital
between 1999 and 2005 found that the most common pediatric cancers were Burkitt’s lymphoma, non-Hodgkin’s lymphoma, and Hodgkin’s lymphoma. In 2008, the International Agency for Research on Cancer (IARC) and the WHO estimated that Rwanda had 34.5 cases of cervical cancer and 25.4 deaths attributable to cervical cancer per 100,000 inhabitants. Significant cancer risk factors in Rwanda are HIV, HPV (human papillomavirus), malaria (a possible risk factor for Burkitt’s lymphoma), and high alcohol consumption. Tobacco use was assessed as rare by demographic surveys.

Today Rwanda’s government focuses significant attention on improving its health care system, considerably increasing the funds for the Ministry of Health, leading to considerable improvements in life expectancy in just 10 years. Rwanda’s economic and health development has been so rapid, that actually it’s the only country in sub-Saharan Africa on track to meet most of the United Nations’ Millennium Development Goals. A community-based health insurance program called Mutuelles de Santé was launched in 1999, allowing the government to grant universal health insurance and to provide for the poorest and most vulnerable individuals. In 2010, thanks to the funding provided by the National Cancer Institute (NCI) at the United States National Institute of Health (NIH), a new cancer registry was developed to assess Rwandan cancer burden.

In 2012 Rwanda’s Ministry of Health, together with charity organizations such as Partners in Health (PIH), opened the first comprehensive cancer referral facility in rural east Africa, the Butaro Cancer Center of Excellence. This Cancer Center has delivered high-quality cancer care to many
patients from Rwanda and its neighboring countries, endorsed national protocols for cancer care, expanded Butaro’s pathology lab into a national referral facility, and implemented an electronic medical record system to support national registry inputs.

Since 2009 a national strategic plan for cervical cancer prevention, care, and control was developed and implemented. In 2010 Merck & Co. donated two million doses of the HPV vaccine Gardasil, which were distributed over a period of three years covering 93.2 percent of the eligible girls in the first year, and 96.6 percent in the subsequent year. Vaccines were delivered through a series of designated “health days” each year, which have also been used for a nationwide health and hygiene education campaign aimed at adolescents, and programs designed to deliver iron and folic acid to pregnant women and vitamin supplements to children. Nurses and physicians received intensive training on how to perform screening tests such as the Papanicolaou (Pap) test, visual inspection with acetic acid (VIA), colposcopy, and biopsy on precancerous lesions.

Options for cancer treatment in Rwanda are still somewhat limited: there are currently just a small number of oncologists in the country, and radiotherapy is not yet available.

However, the Faculty of Medicine of the National University of Rwanda is training many new pathologists, and in March 2012 the First National Baseline Cancer Training was held at the Rwinkwavu Training Center. Rwanda became a member of the International Atomic Energy Agency in 2012, a first step toward the construction of a radiation facility, and National Palliative Care Policy was launched in April 2011 to ensure palliative care to terminally ill patients. All health centers can also provide antiretroviral therapy to prevent HIV-related cancers, and cryotherapy and loop electrosurgical excision procedures (LEEP) are available to surgically remove cancerous lesions.

Claudio Butticè
Independent Scholar

See Also: AIDS-Related Cancers; Cervical Cancer; Liver Cancer, Adult (Primary); Lymphoma, AIDS-Related; Stomach (Gastric) Cancer.

Further Readings
SAGE was founded in 1965 by Sara Miller McCune to support the dissemination of usable knowledge by publishing innovative and high-quality research and teaching content. Today, we publish more than 850 journals, including those of more than 300 learned societies, more than 800 new books per year, and a growing range of library products including archives, data, case studies, reports, and video. SAGE remains majority-owned by our founder, and after Sara's lifetime will become owned by a charitable trust that secures our continued independence.
Contents

Volume 3
List of Articles  vi
Reader’s Guide  xiv

Articles

<table>
<thead>
<tr>
<th>Article</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>S</td>
<td>1013</td>
</tr>
<tr>
<td>T</td>
<td>1135</td>
</tr>
<tr>
<td>U</td>
<td>1203</td>
</tr>
<tr>
<td>V</td>
<td>1271</td>
</tr>
<tr>
<td>W</td>
<td>1297</td>
</tr>
<tr>
<td>X</td>
<td>1329</td>
</tr>
<tr>
<td>Y</td>
<td>1333</td>
</tr>
<tr>
<td>Z</td>
<td>1341</td>
</tr>
</tbody>
</table>

Glossary  1345
Resource Guide  1373
Index  1483
List of Articles

A
Abbott Laboratories (United States)
Acrylic Rubber and Fibers
Adrenocortical Carcinoma
Adrenocortical Carcinoma, Childhood
Advertising
Aerospace Industry
Afghanistan
Age
AIDS-Related Cancers
Albert Einstein Cancer Center
Alcohol
Algeria
Allergan (United States)
Alternative Therapy: Diet and Nutrition
Alternative Therapy: Herbs, Vitamins, and Minerals
Alternative Therapy: Manual Healing and Physical Touch
Alternative Therapy: Mind, Body, and Spirit
Alternative Therapy: Pharmacological and Biological Treatment
American Academy of Pediatrics, Section on Hematology/Oncology
American Association for Cancer Education
American Association for Cancer Research
American Brain Tumor Association
American Cancer Society
American College of Gastroenterology

American College of Radiation Oncology
American Joint Committee on Cancer
American Lung Association
American Psychosocial Oncology Society
American Society for Radiation Oncology
American Society of Clinical Oncology
American Society of Hematology
American Society of Pediatric Hematology/Oncology
Amgen (United States)
Anal Cancer
Angola
Antibiotics
Anticancer Drugs
Argentina
Asbestos
Asian Diet
Aspirin
Assisted Suicide
Association for the Cure of Cancer of the Prostate
Association of Cancer Online Resources
Association of Community Cancer Centers
Association of Freestanding Radiation Oncology Centers
Association of Oncology Social Work
Association of Pediatric Hematology/Oncology Nurses
Astellas Pharma (Japan)
AstraZeneca (United Kingdom)
Australia
Austria
Automobiles
Azerbaijan

B
Bangladesh
Barbara Ann Karmanos Cancer Institute
Battery Acid
Belarus
Belgium
Benin
Bereavement Issues
Beta-Carotene
Bicycles
Bile Duct Cancer, Extrahepatic
Biologic Therapy
Bladder Cancer
Bladder Cancer, Childhood
Bolivia
Bonadonna, Gianni
Bone Cancer, Osteosarcoma/Malignant Fibrous Histiocytoma
Bone Marrow Transplants
Brain Stem Glioma, Childhood
Brain Tumor, Adult
Brain Tumor, Cerebellar Astrocytoma, Childhood
Brain Tumor, Cerebral Astrocytoma/Malignant Glioma, Childhood
Brain Tumor, Childhood
Brain Tumor, Medulloblastoma, Childhood
Brain Tumor, Supratentorial Primitive Neuroectodermal, Childhood
Brain Tumor, Visual Pathway and Hypothalamic Glioma, Childhood
Brazil
Breast Cancer
Breast Cancer, Male
Breast Cancer, Sociocultural Differences and Breast Cancer and Pregnancy
Bristol-Myers Squibb (United States)
Broad-Spectrum Ultraviolet (UV) Radiation
Bronchial Adenomas/Carcinoids, Childhood
Bulgaria
Burkina Faso
Burma (Myanmar)
Burundi

C
Calcium
California Blood Bank Society
Cambodia
Cameroon
Canada
Canadian Association of Medical Oncologists
Canadian Association of Pharmacy in Oncology
Canadian Cancer Society
Canadian Red Cross
Canadian Society of Surgical Oncology
Canadian Urologic Oncology Group
Cancer Association of South Africa
Cancer Communication
Cancer Council Australia
Cancer Drugs, Cost and Benefits of Cancer Therapy Evaluation Program
Candlelighters Childhood Cancer Foundation
Carcinoid Cancer Foundation
Carcinoid Tumor, Childhood
Carcinoid Tumor, Gastrointestinal
Carcinoma of Unknown Primary
Careers
Caregivers
Celebrities and Cancer
Celgene (United States)
Cell Phones
Central African Republic
Central Nervous System Lymphoma, Primary
Cervical Cancer
Chad
Chao Family Comprehensive Cancer Center
Chemical Industry
Chemoprevention
Chemotherapy
Childcare and Cancer Risk
Childhood Brain Tumor Foundation
Childhood Cancers
Chile
China
Chlorine
Chloroform
City of Hope
Clinical Trials
Clothing
Coal Industry
Cold Spring Harbor Laboratory
Colombia
Colon Cancer
Colorectal Cancer, Childhood
Comprehensive Cancer Center of Wake Forest University
Congo, Democratic Republic of
Cosmetics
Cost of Therapy
Costa Rica
Côte d'Ivoire
COX-2 Inhibitors
Croatia
Cuba
Czech Republic

D
Daiichi Sankyo (Japan)
Daily Life
Dana-Farber Cancer Institute
Danish Cancer Society
DDT
Denmark
Deodorizers
Detergents
Developing Countries
Diesel Exhaust
Diet and Nutrition
Disability
Disinfectants and Antiseptics
Disparities Within Nations (Elimination of Cancer)
Dominican Republic
Drugs
Duke Cancer Institute
Dyes and Pigments

E
Ecuador
Education
Egypt
Eisai (Japan)
El Salvador
Electrical Industry
Electronics
Eli Lilly and Company (United States)
Embalming Fluids
Endometrial Cancer
Environmental Justice and Cancer
Environmental Tobacco Smoke
Ependymoma, Childhood
Eritrea
Esophageal Cancer
Esophageal Cancer, Childhood
Estrogen, Steroidal
Ethiopia
Europa Donna, the European Breast Cancer Coalition
European Association for Cancer Research
European CanCer Organisation
European Cancer Prevention
European School of Oncology
European Society for Therapeutic Radiology and Oncology
European Society of Mastology
European Society of Surgical Oncology
Ewing's Family of Tumors
Exercise
Experimental Cancer Drugs
Explosives
Extracranial Germ Cell Tumor, Childhood
Extragonadal Germ Cell Tumor

F
Family Size
Finland
Flame Retardant
Flavoring Agents
Food Additives
Food and Drug Administration
Forest Labs (United States)
Fox Chase Cancer Center
France
Fred & Pamela Buffett Cancer Center
Fred Hutchinson Cancer Research Center
Freon
Future of Cancer

G
Gallbladder Cancer
Gasoline
Gene Therapy
Genentech
Genetics
Genzyme (United States)
Georgia
Germany
Gestational Trophoblastic Tumor
Ghana
Glass Industry
GlaxoSmithKline (United Kingdom)
Global Health Issues and Cancer
Government
Greece
Green, Adele
Gregoire, Christine
Guatemala
Guinea

H
H. Lundbeck (Denmark)
Haemophilia Society (United Kingdom)
Hair Dye
Haiti
Head and Neck Cancer
Health Advocacy
Healthy People
Hepatitis B
Hepatitis C
Hepatocellular (Liver) Cancer, Adult (Primary)
Hepatocellular (Liver) Cancer, Childhood (Primary)
Herbert Irving Comprehensive Cancer Center
Herbicide
History of Cancer
Holden Comprehensive Cancer Center at the University of Iowa
Honduras
Hong Kong Anti-Cancer Society
Hospice Care
Hospitals
HPV Vaccination
Hungary
Huntsman Cancer Institute
Hypopharyngeal Cancer
Hypothalamic and Visual Pathway Glioma, Childhood

I
Immigrant Populations
India
Indonesia
Infection
Insecticides
Insurance
International Agency for Research on Cancer
International Association for the Study of Lung Cancer
International Association of Cancer Registries
International Cancer Alliance for Research and Education
International Committee of the Red Cross
International Myeloma Foundation
International Psycho-Oncology Society
International Society for Cutaneous Lymphomas
International Society for Experimental Hematology
International Society for Preventive Oncology
International Society of Nurses in Cancer Care
International Society of Paediatric Oncology
International Society on Thrombosis and Haemostasis
Intraocular Melanoma
Iran
Iraq
Ireland, Republic of
Ireland (Ohio) Cancer Center
Irish Cancer Society
Islet Cell Carcinoma (Endocrine Pancreas)
Israel
Italy

J
Japan
Japan Lung Cancer Society
Japanese Cancer Association
Japanese Gastric Cancer Association
Japanese Society for Therapeutic Radiology and Oncology
Jet and Rocket Fuels
Jimmy Fund
Johnson & Johnson (United States)
Jordan

K
Kaposi’s Sarcoma
Kazakhstan
Kenya
Kidney (Renal Cell) Cancer
Kidney Cancer, Childhood
Kidney Cancer Association
Kimmel Cancer Center
Kyrgyzstan

L
Laos
Laryngeal Cancer
Laryngeal Cancer, Childhood
Latitude
Lead
Leukemia, Acute Lymphoblastic, Adult
Leukemia, Acute Lymphoblastic, Childhood
Leukemia, Acute Myeloid, Adult
Leukemia, Acute Myeloid, Childhood
Leukemia, Chronic Lymphocytic
Leukemia, Chronic Myelogenous
Leukemia, Hairy Cell
Leukemia & Lymphoma Society
Libya
Liver Cancer, Adult (Primary)
Liver Cancer, Childhood (Primary)
Lombardi Comprehensive Cancer Center
Lung Cancer, Non–Small Cell
Lung Cancer, Small Cell
Lymphoma, AIDS-Related
Lymphoma, Burkitt’s
Lymphoma, Hodgkin’s, Adult
Lymphoma, Hodgkin’s, Childhood
Lymphoma, Hodgkin’s, During Pregnancy
Lymphoma, Non-Hodgkin’s, Adult
Lymphoma, Non-Hodgkin’s, Childhood
Lymphoma, Non-Hodgkin’s, During Pregnancy
Lymphoma, Primary Central Nervous System
Lymphoma Research Foundation of America

M
Madagascar
Malawi
Malaysia
Mali
Malignant Fibrous Histiocytoma of Bone/ Osteosarcoma
Marketing, Drug
Marketing, Hospitals and Clinics
Massachusetts Medical Society
Massey Cancer Center
Mayo Clinic Cancer Center
Mayo Clinic Cancer Center, Jacksonville
Mayo Clinic Cancer Center, Scottsdale
Meat, Cooking
Meat Processing
Media
Medicare and Medicaid
MedImmune (United States)
Melanoma
Melanoma, Intraocular (Eye)

Memorial Sloan Kettering Cancer Center
Menarche, Early
Merck (Germany)
Merck & Co. (United States)
Merkel Cell Carcinoma
Mesothelioma, Adult Malignant
Mesothelioma, Childhood
Mexico
MIT Center for Cancer Research
Moldova
Morocco
Mozambique
Multiple Endocrine Neoplasia Syndrome, Childhood
Multiple Myeloma/Plasma Cell Neoplasm
Mycosis Fungoides
Myelodysplastic Syndromes
Myelodysplastic/Myeloproliferative Diseases
Myeloma, Multiple
Myeloproliferative Disorders, Chronic

N
Nasopharyngeal Cancer
Nasopharyngeal Cancer, Childhood
National Alliance of Breast Cancer Organizations
National Cancer Institute
National Cancer Policy Board
National Cancer Registrars Association
National Childhood Cancer Foundation
National Marrow Donor Program
Natural Causes of Cancer
Nepal
Netherlands
Netherlands Cancer Institute
Netherlands Hemophilia Patients Society
Neuroblastoma
Neutrons
New Zealand
Nicaragua
Nickel Compounds
Niger
Nigeria
Nixon, Richard (War on Cancer)
North American Association of Central Cancer Registries
North Korea
Norway
Novartis Group (Switzerland)
Novo Nordisk (Denmark)
Nuclear Industry

O
Obesity
Occupational Therapy
Ohio State University Comprehensive Cancer Center
OHSU Knight Cancer Institute
Oncology Nursing Society
Ono Pharmaceutical (Japan)
Oral Cancer, Childhood
Oral Cavity Cancer, Lip and
Organisation of European Cancer Institutes
Oropharyngeal Cancer
Ovarian Cancer, Childhood
Ovarian Epithelial Cancer
Ovarian Germ Cell Tumor
Ovarian Low Malignant Potential Tumor

P
Pain and Pain Management
Paint
Pakistan
Pancreatic Cancer
Pancreatic Cancer, Childhood
Pancreatic Cancer, Islet Cell
Paper Industry
Papua New Guinea
Paraguay
Paranasal Sinus and Nasal Cavity Cancer
Parathyroid Cancer
Passive Smoking
Penile Cancer
Perfume
Perlmutter Cancer Center
Peru
Pesticides
Pfizer (United States)
Pharmaceutical Industry
Pheochromocytoma
Philippines
Photodynamic Therapy
Physical Therapy
Pineoblastoma and Supratentorial Primitive Neuroectodermal, Childhood
Pinkel, Donald
Pituitary Tumor
Plasma Cell Neoplasm/Multiple Myeloma
Plastics Industry
Pleuropulmonary Blastoma
Poland
Polishes
Pollution, Air
Pollution, Water
Portugal
Poverty
Prostate Cancer
Proton Therapy
Psychosocial Care/Support
Purdue University Center for Cancer Research

R
Radiation
Radiation, Gamma
Radiation, Ionizing
Radiation Therapy
Raloxifene
Rectal Cancer
Religion
Religion: Jewish Women and Cancer Risk
Religion: Meditation and Risk
Religion: Preventability Versus Preordained
Religion: Use of Interventions
Retinoblastoma
Rhabdomyosarcoma, Childhood
Roche Group (Switzerland)
Romania
Rosenberg, Barnett
Roswell Park Cancer Institute
Russia
Rwanda

S
Salivary Gland Cancer
Salivary Gland Cancer, Childhood
Salk Institute for Biological Studies
Sanford-Burnham Medical Research Institute
Sarcoma, Ewing’s Family of Tumors
Sarcoma, Soft Tissue, Adult
Sarcoma, Soft Tissue, Childhood
Sarcoma, Uterine
Sarcoma Foundation of America
Saudi Arabia
Screening
Screening, Access to
Sedentary Occupations
Selenium
Senegal
Serbia
Sex
Sézary Syndrome
Shire UK
Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins
Sierra Leone
Singapore
Singapore Cancer Society
Siteman Cancer Center
Skin Cancer, Childhood
Skin Cancer, Melanoma
Skin Cancer, Non-Melanoma
Skin Carcinoma, Merkel Cell
Skipper, Howard E.
Slovakia
Small Intestine Cancer
Smokeless Tobacco
Smoking and Society
Smoking Cessation
Society of Gynecologic Oncology
Society of Surgical Oncology
Solar Radiation
Solvents
Somalia
South Africa
South Korea
Spain
Squamous Neck Cancer With Occult Primary, Metastatic
Sri Lanka
St. Jude Children’s Research Hospital
Stainless Steel
Statistics
Stomach (Gastric) Cancer
Stomach (Gastric) Cancer, Childhood
Stress
Sudan
Sun Exposure (Australia)
Sunlamps or Sunbeds, Exposure to Sunscreen
Surgery
Survivors of Cancer
Survivors of Cancer, Families of Sweden
Switzerland
Syria

T
Taisho Pharmaceutical (Japan)
Taiwan

Tajikistan
Takeda Pharmaceutical (Japan)
Tamoxifen
Tanzania
Taxation
Technology, Imaging
Technology, New Therapies
Terry, Luther
Testicular Cancer
Textile Dyes
Thailand
Thymoma, Childhood
Thymoma and Thymic Carcinoma
Thyroid Cancer
Thyroid Cancer, Childhood
Tobacco in History
Tobacco Smoking
Tobacco-Related Exposures
Togo
Town Plans
Toxic Mold
Transportation
Trichopoulos, Dimitrios
Trophoblastic Tumor, Gestational
Tunisia
Turkey
Turkish Society of Haematology
Turkmenistan

U
Uganda
Ukraine
Ultraviolet A Radiation
Ultraviolet B Radiation
Ultraviolet C Radiation
Ultraviolet Radiation Related Exposures
Union for International Cancer Control
United Arab Emirates
United Kingdom
United States
University of Alabama at Birmingham Comprehensive Cancer Center
University of California, Davis, Comprehensive Cancer Center
University of California, Los Angeles, Jonsson Comprehensive Cancer Center
University of California, San Francisco, Helen Diller Family Comprehensive Cancer Center
University of Chicago Medicine Comprehensive Cancer Center
University of Colorado Cancer Center
University of Hawai‘i Cancer Center
University of Michigan Comprehensive Cancer Center
University of Minnesota Masonic Cancer Center
University of New Mexico Cancer Research and Treatment Center
University of North Carolina Lineberger Comprehensive Cancer Center
University of Pittsburgh Cancer Institute
University of Southern California Norris Comprehensive Cancer Center
University of Texas MD Anderson Cancer Center
University of Virginia Cancer Center
University of Wisconsin Carbone Cancer Center
Unknown Primary Site, Cancer of, Childhood
Unknown Primary Site, Carcinoma of, Adult
Unusual Cancers of Childhood
Ureter and Renal Pelvis, Transitional Cell Cancer
Urethral Cancer
Uterine Cancer, Endometrial
Uterine Sarcoma
Uzbekistan

V
Vaccine Workers, HPV and HCV
Vaccines
Vaginal Cancer
Vanderbilt-Ingram Cancer Center
Venezuela
Vermont Cancer Center
Vietnam
Vinyl

Visual Pathway and Hypothalamic Glioma,
    Childhood
Vitamins
Vulvar Cancer

W
Waldenström’s Macroglobulinemia
War Gases and Chemicals
Water Treatment
Western Diet
Wilms’ Tumor
Wistar Institute
Women’s Cancers
Wood Dust
Wood Preserver
Workplace Wellness Programs
World Health Organization
World Health Organization Framework
    Convention on Tobacco Control
Wynder, Ernst

X
X-Rays

Y
Yale Cancer Center
Yemen
Young Adult Cancer Prevention
Yul Brynner Head and Neck Cancer Foundation
    (Head and Neck Cancer Alliance)

Z
Zambia
Zimbabwe
Reader’s Guide

Alternative Treatments and Therapies
Alternative Therapy: Diet and Nutrition
Alternative Therapy: Herbs, Vitamins, and Minerals
Alternative Therapy: Manual Healing and Physical Touch
Alternative Therapy: Mind, Body, and Spirit
Alternative Therapy: Pharmacological and Biological Treatment

Associations by Cancer Type
American Brain Tumor Association
American College of Gastroenterology
American Lung Association
Association for the Cure of Cancer of the Prostate
Candlelighters Childhood Cancer Foundation
Carcinoid Cancer Foundation
Childhood Brain Tumor Foundation
International Myeloma Foundation
Kidney Cancer Association
Lymphoma Research Foundation of America
National Alliance of Breast Cancer Organization
National Childhood Cancer Foundation
National Marrow Donor Program
Sarcoma Foundation of America
Yul Brynner Head and Neck Cancer Foundation (Head and Neck Cancer Alliance)

Associations: Others
American Academy of Pediatrics, Section on Hematology/Oncology
American Association for Cancer Education
American Association for Cancer Research
American Brain Tumor Association
American College of Radiation Oncology
American Joint Committee on Cancer
American Psychosocial Oncology Society
American Society for Radiation Oncology
American Society of Hematology
American Society of Pediatric Hematology/Oncology
Association of Community Cancer Centers
Association of Freestanding Radiation Oncology Centers
Association of Oncology Social Work
Association of Pediatric Hematology/Oncology Nurses
California Blood Bank Society
Canadian Association of Medical Oncologists
Canadian Association of Pharmacy and Oncology
Canadian Cancer Society
Canadian Red Cross
Canadian Society of Surgical Oncology
Canadian Urologic Oncology Group
Cancer Association of South Africa
Danish Cancer Society
<table>
<thead>
<tr>
<th>Country</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burundi</td>
<td>Mali</td>
</tr>
<tr>
<td>Cambodia</td>
<td>Mexico</td>
</tr>
<tr>
<td>Cameroon</td>
<td>Moldova</td>
</tr>
<tr>
<td>Canada</td>
<td>Morocco</td>
</tr>
<tr>
<td>Central African Republic</td>
<td>Mozambique</td>
</tr>
<tr>
<td>Chad</td>
<td>Nepal</td>
</tr>
<tr>
<td>Chile</td>
<td>Netherlands</td>
</tr>
<tr>
<td>China</td>
<td>New Zealand</td>
</tr>
<tr>
<td>Colombia</td>
<td>Nicaragua</td>
</tr>
<tr>
<td>Congo, Democratic Republic</td>
<td>Niger</td>
</tr>
<tr>
<td>Costa Rica</td>
<td>Nigeria</td>
</tr>
<tr>
<td>Côte d’Ivoire</td>
<td>North Korea</td>
</tr>
<tr>
<td>Croatia</td>
<td>Norway</td>
</tr>
<tr>
<td>Cuba</td>
<td>Pakistan</td>
</tr>
<tr>
<td>Czech Republic</td>
<td>Papua New Guinea</td>
</tr>
<tr>
<td>Denmark</td>
<td>Paraguay</td>
</tr>
<tr>
<td>Dominican Republic</td>
<td>Peru</td>
</tr>
<tr>
<td>Ecuador</td>
<td>Philippines</td>
</tr>
<tr>
<td>Egypt</td>
<td>Poland</td>
</tr>
<tr>
<td>El Salvador</td>
<td>Portugal</td>
</tr>
<tr>
<td>Eritrea</td>
<td>Romania</td>
</tr>
<tr>
<td>Ethiopia</td>
<td>Russia</td>
</tr>
<tr>
<td>Finland</td>
<td>Rwanda</td>
</tr>
<tr>
<td>France</td>
<td>Saudi Arabia</td>
</tr>
<tr>
<td>Georgia</td>
<td>Senegal</td>
</tr>
<tr>
<td>Germany</td>
<td>Serbia</td>
</tr>
<tr>
<td>Ghana</td>
<td>Sierra Leone</td>
</tr>
<tr>
<td>Greece</td>
<td>Singapore</td>
</tr>
<tr>
<td>Guatemala</td>
<td>Slovakia</td>
</tr>
<tr>
<td>Guinea</td>
<td>Somalia</td>
</tr>
<tr>
<td>Haiti</td>
<td>South Africa</td>
</tr>
<tr>
<td>Honduras</td>
<td>South Korea</td>
</tr>
<tr>
<td>Hungary</td>
<td>Spain</td>
</tr>
<tr>
<td>India</td>
<td>Sri Lanka</td>
</tr>
<tr>
<td>Indonesia</td>
<td>Sudan</td>
</tr>
<tr>
<td>Iran</td>
<td>Sweden</td>
</tr>
<tr>
<td>Iraq</td>
<td>Switzerland</td>
</tr>
<tr>
<td>Ireland, Republic of</td>
<td>Syria</td>
</tr>
<tr>
<td>Israel</td>
<td>Taiwan</td>
</tr>
<tr>
<td>Italy</td>
<td>Tajikistan</td>
</tr>
<tr>
<td>Japan</td>
<td>Tanzania</td>
</tr>
<tr>
<td>Jordan</td>
<td>Thailand</td>
</tr>
<tr>
<td>Kazakhstan</td>
<td>Togo</td>
</tr>
<tr>
<td>Kenya</td>
<td>Tunisia</td>
</tr>
<tr>
<td>Kyrgyzstan</td>
<td>Turkey</td>
</tr>
<tr>
<td>Laos</td>
<td>Turkmenistan</td>
</tr>
<tr>
<td>Libya</td>
<td>Uganda</td>
</tr>
<tr>
<td>Madagascar</td>
<td>Ukraine</td>
</tr>
<tr>
<td>Malawi</td>
<td>United Arab Emirates</td>
</tr>
<tr>
<td>Malaysia</td>
<td>United Kingdom</td>
</tr>
</tbody>
</table>
United States
Uzbekistan
Venezuela
Vietnam
Yemen
Zambia
Zimbabwe

**Cancer in Society**
Advertising
Asbestos
Asian Diet
Assisted Suicide
Automobiles
Bicycles
Breast Cancer, Sociocultural Differences and Careers
Cell Phones
Childcare and Cancer Risk
Chlorine
Clothing
Cosmetics
Daily Life
Developing Countries
Diet and Nutrition
Disparities Within Nations (Elimination of Cancer)
Drugs
Education
Electronics
Exercise
Family Size
Food Additives
Food and Drug Administration
Future of Cancer
Global Health Issues and Cancer
Government
History of Cancer
Hospitals
Insurance
Lead
Meat Processing
Media
Medicare and Medicaid
Menarche, Early
Obesity
Paint
Pollution, Air
Pollution, Water
Poverty
Radiation

Religion
Religion, Jewish Women and Cancer Risk
Religion, Meditation and Risk
Religion, Preventability Versus Preordained
Religion, Use of Interventions
Sedentary Occupations
Sex
Smoking and Society
Statistics
Stress
Sun Exposure (Australia)
Sunscreen
Survivors of Cancer
Survivors of Cancer Families
Technology, Imaging
Technology, New Therapies
Tobacco in History
Town Plans
Transportation
Western Diet
WHO Framework Convention on Tobacco Control
X-Rays

**Known or Suspected Carcinogens/Causes of Cancer**
Acrylic Rubber and Fibers
Aerospace Industry
Age
Alcohol
Antibiotics
Anticancer Drugs
Battery Acid
Broad-Spectrum Ultraviolet (UV) Radiation
Chemical Industry
Chemotherapy
Chloroform
Coal Industry
DDT
Deodorizers
Detergents
Diesel Exhaust
Disinfectants and Antiseptics
Dyes and Pigments
Electrical Industry
Embalming Fluids
Environmental Tobacco Smoke
Estrogen, Steroidal
Experimental Cancer Drugs
Explosives
Family Size
<table>
<thead>
<tr>
<th>Flame Retardant</th>
<th>Wood Preserver</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flavoring Agents</td>
<td>X-Rays</td>
</tr>
<tr>
<td>Freon</td>
<td></td>
</tr>
<tr>
<td>Gasoline</td>
<td></td>
</tr>
<tr>
<td>Genetics</td>
<td></td>
</tr>
<tr>
<td>Glass Industry</td>
<td></td>
</tr>
<tr>
<td>Hair Dye</td>
<td></td>
</tr>
<tr>
<td>Hepatitis B</td>
<td></td>
</tr>
<tr>
<td>Hepatitis C</td>
<td></td>
</tr>
<tr>
<td>Herbicide</td>
<td></td>
</tr>
<tr>
<td>Immigrant Populations</td>
<td></td>
</tr>
<tr>
<td>Infection</td>
<td></td>
</tr>
<tr>
<td>Insecticides</td>
<td></td>
</tr>
<tr>
<td>Jet and Rocket Fuels</td>
<td></td>
</tr>
<tr>
<td>Latitude</td>
<td></td>
</tr>
<tr>
<td>Lead</td>
<td></td>
</tr>
<tr>
<td>Meat, Cooking</td>
<td></td>
</tr>
<tr>
<td>Natural Causes of Cancer</td>
<td></td>
</tr>
<tr>
<td>Neutrons</td>
<td></td>
</tr>
<tr>
<td>Nickel Compounds</td>
<td></td>
</tr>
<tr>
<td>Nuclear Industry</td>
<td></td>
</tr>
<tr>
<td>Obesity</td>
<td></td>
</tr>
<tr>
<td>Paint</td>
<td></td>
</tr>
<tr>
<td>Paper Industry</td>
<td></td>
</tr>
<tr>
<td>Passive Smoking</td>
<td></td>
</tr>
<tr>
<td>Perfume</td>
<td></td>
</tr>
<tr>
<td>Pesticides</td>
<td></td>
</tr>
<tr>
<td>Pharmaceutical Industry</td>
<td></td>
</tr>
<tr>
<td>Plastics Industry</td>
<td></td>
</tr>
<tr>
<td>Polishes</td>
<td></td>
</tr>
<tr>
<td>Radiation, Gamma</td>
<td></td>
</tr>
<tr>
<td>Radiation, Ionizing</td>
<td></td>
</tr>
<tr>
<td>Smokeless Tobacco</td>
<td></td>
</tr>
<tr>
<td>Solar Radiation</td>
<td></td>
</tr>
<tr>
<td>Solvents</td>
<td></td>
</tr>
<tr>
<td>Stainless Steel</td>
<td></td>
</tr>
<tr>
<td>Sunlamps or Sunbeds, Exposure to</td>
<td></td>
</tr>
<tr>
<td>Textile Dyes</td>
<td></td>
</tr>
<tr>
<td>Tobacco-Related Exposures</td>
<td></td>
</tr>
<tr>
<td>Tobacco Smoking</td>
<td></td>
</tr>
<tr>
<td>Toxic Mold</td>
<td></td>
</tr>
<tr>
<td>Ultraviolet A Radiation</td>
<td></td>
</tr>
<tr>
<td>Ultraviolet B Radiation</td>
<td></td>
</tr>
<tr>
<td>Ultraviolet C Radiation</td>
<td></td>
</tr>
<tr>
<td>Ultraviolet Radiation Related Exposures</td>
<td></td>
</tr>
<tr>
<td>Vinyl</td>
<td></td>
</tr>
<tr>
<td>War Gases and Chemicals</td>
<td></td>
</tr>
<tr>
<td>Water Treatment</td>
<td></td>
</tr>
<tr>
<td>Wax and Soap</td>
<td></td>
</tr>
<tr>
<td>Wood Dust</td>
<td></td>
</tr>
</tbody>
</table>

**Major Cancer Associations**
- American Association for Cancer Research
- American Cancer Society
- American Society of Clinical Oncology
- Association of Cancer Online Resources
- Association of Community Cancer Centers
- Cancer Therapy Evaluation Program
- International Cancer Alliance for Research and Education
- Massachusetts Medical Society
- National Cancer Institute
- National Cancer Registrars Association
- Union for International Cancer Control
- World Health Organization

**Major Hospitals and Treatment Centers**
- Albert Einstein Cancer Center
- Barbara Ann Karmanos Cancer Institute
- Chao Family Comprehensive Cancer Center
- City of Hope
- Cold Spring Harbor Laboratory
- Comprehensive Cancer Center of Wake Forest University
- Dana-Farber Cancer Institute
- Duke Cancer Institute
- Fox Chase Cancer Center
- Fred & Pamela Buffett Cancer Center
- Fred Hutchinson Cancer Research Center
- Herbert Irving Comprehensive Cancer Center
- Holden Comprehensive Cancer Center at the University of Iowa
- Huntsman Cancer Institute
- Ireland (Ohio) Cancer Center
- Jimmy Fund (DFCI)
- Kimmel Cancer Center
- Lombardi Comprehensive Cancer Center
- Massey Cancer Center
- Mayo Clinic Cancer Center
- Mayo Clinic Cancer Center, Jacksonville
- Mayo Clinic Cancer Center, Scottsdale
- Memorial Sloan-Kettering Cancer Center
- MIT Center for Cancer Research
- National Cancer Institute
- Ohio State University Comprehensive Cancer Center
- OHSU Knight Cancer Institute
- Purdue University Center for Cancer Research
Roswell Park Cancer Institute
Salk Institute for Biological Studies
Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins
Siteman Cancer Center
St. Jude Children’s Research Hospital
University of Alabama at Birmingham Comprehensive Cancer Center
University of California, Davis, Comprehensive Cancer Center
University of California, Los Angeles, Jonsson Comprehensive Cancer Center
University of California, San Francisco, Helen Diller Family Comprehensive Cancer Center
University of Chicago Medicine Comprehensive Cancer Center
University of Colorado Cancer Center
University of Hawai'i Cancer Center
University of Michigan Comprehensive Cancer Center
University of Minnesota Masonic Cancer Center
University of New Mexico Cancer Research and Treatment Center
University of North Carolina Lineberger Comprehensive Cancer Center
University of Pittsburgh Cancer Institute
University of Southern California Norris Comprehensive Cancer Center
University of Texas MD Anderson Cancer Center
University of Virginia Cancer Center
University of Wisconsin Carbone Cancer Center
Vanderbilt-Ingram Cancer Center
Vermont Cancer Center
Wistar Institute
Yale Cancer Center

Prevention
Aspirin
Beta-Carotene
Calcium
Chemoprevention
COX-2 Inhibitors
Raloxifene
Screening
Screening, Access to
Selenium
Smoking Cessation
Tamoxifen
Taxation
Vaccines
Vitamins

Treatments and Therapies
Biologic Therapy
Bone Marrow Transplants
Cancer Drugs, Cost and Benefits of
Chemotherapy
Clinical Trials
Gene Therapy
Hospice Care
Pain and Pain Management
Photodynamic Therapy
Proton Therapy
Radiation Therapy
Surgery

Types of Cancer
Adrenocortical Carcinoma
Adrenocortical Carcinoma, Childhood
AIDS-Related Cancers
Anal Cancer
Bile Duct Cancer, Extrahepatic
Bladder Cancer
Bladder Cancer, Childhood
Bone Cancer, Osteosarcoma/Malignant Fibrous Histiocytoma
Brain Stem Glioma, Childhood
Brain Tumor, Adult
Brain Tumor, Cerebellar Astrocytoma, Childhood
Brain Tumor, Cerebral Astrocytoma/Malignant Glioma, Childhood
Brain Tumor, Medulloblastoma, Childhood
Brain Tumor, Supratentorial Primitive Neuroectodermal, Childhood
Brain Tumor, Visual Pathway and Hypothalamic Glioma, Childhood
Breast Cancer
Breast Cancer, Male
Breast Cancer and Pregnancy
Bronchial Adenomas/Carcinoids, Childhood
Carcinoid Tumor, Childhood
Carcinoid Tumor, Gastrointestinal
Carcinoma of Unknown Primary
Central Nervous System Lymphoma, Primary
Cervical Cancer
Childhood Cancers
Colon Cancer
Colorectal Cancer, Childhood
Endometrial Cancer
Ependymoma, Childhood
Esophageal Cancer
Ependymoma, Childhood
Ewing’s Family of Tumors
Extracranial Germ Cell Tumor, Childhood
Extragonadal Germ Cell Tumor
Gallbladder Cancer
Gestational Trophoblastic Tumor
Head and Neck Cancer
Hepatocellular (Liver) Cancer, Adult (Primary)
Hepatocellular (Liver) Cancer, Childhood (Primary)
Hypopharyngeal Cancer
Hypothalamic and Visual Pathway
Glioma, Childhood
Intraocular Melanoma
Islet Cell Carcinoma (Endocrine Pancreas)
Kaposi’s Sarcoma
Kidney Cancer, Childhood
Kidney (Renal Cell) Cancer
Laryngeal Cancer
Laryngeal Cancer, Childhood
Leukemia, Acute Lymphoblastic, Adult
Leukemia, Acute Lymphoblastic, Childhood
Leukemia, Acute Myeloid, Adult
Leukemia, Acute Myeloid, Childhood
Leukemia, Chronic Lymphocytic
Leukemia, Chronic Myelogenous
Leukemia, Hairy Cell
Liver Cancer, Adult (Primary)
Liver Cancer, Childhood (Primary)
Lung Cancer, Non–Small Cell
Lung Cancer, Small Cell
Lymphoma, AIDS-Related
Lymphoma, Burkitts
Lymphoma, Hodgkin’s, Adult
Lymphoma, Hodgkin’s, Childhood
Lymphoma, Hodgkin’s, During Pregnancy
Lymphoma, Non-Hodgkin’s, Adult
Lymphoma, Non-Hodgkin’s, Childhood
Lymphoma, Non-Hodgkin’s, During Pregnancy
Lymphoma, Primary Central Nervous System
Malignant Fibrous Histiocytoma of
Bone/Osteosarcoma
Melanoma
Melanoma, Intraocular (Eye)
Merkel Cell Carcinoma
Mesothelioma, Adult Malignant
Mesothelioma, Childhood
Multiple Endocrine Neoplasia Syndrome,
Childhood
Multiple Myeloma/Plasma Cell Neoplasm
Mycosis Fungoides
Myelodysplastic Syndromes
Myelodysplastic/Myeloproliferative Diseases
Myeloma, Multiple
Myeloproliferative Disorders, Chronic
Nasopharyngeal Cancer
Nasopharyngeal Cancer, Childhood
Neuroblastoma
Oral Cancer, Childhood
Oral Cavity Cancer, Lip and
Oropharyngeal Cancer
Ovarian Cancer, Childhood
Ovarian Epithelial Cancer
Ovarian Germ Cell Tumor
Ovarian Low Malignant Potential Tumor
Pancreatic Cancer
Pancreatic Cancer, Childhood
Pancreatic Cancer, Islet Cell
Paranasal Sinus and Nasal Cavity Cancer
Parathyroid Cancer
Penile Cancer
Pheochromocytoma
Pineoblastoma and Supratentorial Primitive
Neuroectodermal, Childhood
Pituitary Tumor
Plasma Cell Neoplasm/Multiple Myeloma
Pleuropulmonary Blastoma
Prostate Cancer
Rectal Cancer
Retinoblastoma
Rhabdomyosarcoma, Childhood
Salivary Gland Cancer
Salivary Gland Cancer, Childhood
Sarcoma, Ewing’s Family of Tumors
Sarcoma, Soft Tissue, Adult
Sarcoma, Soft Tissue, Childhood
Sarcoma, Uterine
Sézary Syndrome
Skin Cancer, Childhood
Skin Cancer, Melanoma
Skin Cancer, Non-Melanoma
Skin Carcinoma, Merkel Cell
Small Intestine Cancer
Squamous Neck Cancer With Occult Primary,
Metastatic
Stomach (Gastric) Cancer
Stomach (Gastric) Cancer, Childhood
Testicular Cancer  Urethral Cancer
Thymoma, Childhood  Uterine Cancer, Endometrial
Thymoma and Thymic Carcinoma  Uterine Sarcoma
Thyroid Cancer  Vaginal Cancer
Thyroid Cancer, Childhood  Visual Pathway and Hypothalamic Glioma, Childhood
Trophoblastic Tumor, Gestational  Vulvar Cancer
Unknown Primary Site, Cancer of, Childhood  Waldenström’s Macroglobulinemia
Unknown Primary Site, Carcinoma of, Adult  Wilms’ Tumor
Unusual Cancers of Childhood  Women’s Cancers
Ureter and Renal Pelvis, Transitional Cell Cancer
Salivary Gland Cancer

Salivary gland cancer is considered to be one of the rarest forms of cancer that affects the mouth or the respiratory tract. Salivary glands are composed of tissue that can develop into malignant cells that can affect the mucus production in the glands to aid in digestion and protect the mouth from over dryness.

The salivary glands consist of two parts: the major and the minor. The major section of the salivary glands is divided into the following three parts:

- The parotid glands where most of the cancerous cells are detected. These glands are situated in the front of the ears in the human body.
- The sublingual glands are small and are situated near the back of the jaw.
- The submandular glands are near the sublingual glands.

The minor section of the glands is a less-common site for tumors, though tumors that materialize can be cancerous. Minor salivary glands appear in the tongue, sinuses, larynx (or voice box), nose, and inner cheeks.

The World Health Organization (WHO) has broken down the different types of salivary gland tumors into the following five parts:

- Cancerous epithelial skin tumors
- Noncancerous epithelial skin tumors
- Cancerous cells in soft tissues
- Tumors that are not primary cancer sites
- Lymphomas, such as non-Hodgkin’s lymphoma

Risks Associated With Salivary Gland Cancer

Although salivary gland cancer is rare, medical professionals still warn individuals about the associated risks. Exposure to radiation, such as in the treatment of other head and neck cancers causes a greater risk of developing salivary gland cancer. Researcher indicates that exposure to X-rays can increase risk.

Other factors that affect the risk for salivary gland cancer include age, the cancer is more common in older populations, though it can develop at any time; family history; and environmental factors, such as exposure to toxins.

Some researchers have suggested that diet, alcohol or tobacco consumption, and the use of cell phones also increase risk, but these causes have not been definitively proven.

Symptoms and Diagnosis

Symptoms of salivary gland cancer can include being unable to open the mouth fully, or feeling chronic pain or inflammation in the salivary gland.
region. This may cause a lump to form on the jaw mouth, or neck. Patients may also feel numbness on one or both sides of the face, and facial muscles may feel weak and awkward.

In order to diagnosis salivary gland cancer, medical professionals will conduct a thorough examination that includes noting any problems or abnormalities with the head, mouth, neck, and face. The examination will help detect any presence of enlarged lymph nodes or weakness in the muscles of the face.

Medical imaging tests that help detect the cancer include such as X-ray, magnetic resonance imaging (MRI), computed tomography (CT) scan, and positron emission tomography (PET) scan. In addition the medical imaging diagnostic tools, a fine needle aspiration (FNA) biopsy is performed to expel fluid from the tumor in order to test tissue and cells. This test can be done under general anesthetic. Surgery can also be performed to remove malignant cells and tissue from the affected area.

**Treatment**

With less invasive cases of salivary gland cancer, there may be the opportunity to excise the malignant cells out of the infected area. However, there are some side effects to this type of treatment, such as the inability to heal quickly, continual wound invasions, problems with dealing with aftermath of anesthesia, uncontrollable bleeding, pain that needs to be managed with medication, potential damages to the nerves in the mouth and a condition referred to as Gustatory swelling or Frey syndrome. This condition involves the development of swelling over the nerves exposed during surgery.

Radiation therapy is helpful to direct treatment to the affected area. Side effects of radiation include constant dry mouth, extremely sore throat and trouble swallowing, nausea and vomiting, feeling tired and withdrawn, possible loss of taste, pain and damage to the bone in the face and thyroid gland pain.

Salivary gland cancer can also be treated with a biopsy that involves making a small cut while the patient is under anesthesia so the doctor is able to take the tumor away.

Depending on the location of the cancer—whether it is located within the parotid, submandibular, or sublingual glands—there are special treatments for each of the cancers.

Parotid gland, the gland that is closest to the face, is where most tumors occur. Surgery is performed on the gland remove the tumors, though this it is a tricky procedure as they can be hard to reach. However, if the tumors spread from the parotid gland to the superficial lobe they can be even harder for the surgeon to remove.

Submandibular gland surgery, otherwise referred to as the sublingual gland surgery, is done when the tumor is located in one or both of these areas. Unfortunately, the whole gland is usually removed. There is a risk of having to take pieces of bone and tissue, and there is a strong possibility that nerves of the tongue may also be removed.

Minor salivary gland surgery involves the removal of the cancers from areas in the mouth such as the tongue, lips, and throat.

Chemotherapy is a treatment that is used for any type of cancer. There are medications that are used in addition to chemotherapy such as methotrexate, paclitaxel, cisplatin, carboplatin, 5-fluorouracil, and doxorubicin.
Reconstructive surgery will replace and repair any tissue or nerves damaged from surgery to excise cancer from the salivary gland.

Cindy Ferraino
Independent Scholar

See Also: Chemotherapy; Lymphoma, Hodgkin’s, Adult; Lymphoma, Non-Hodgkin’s, Adult; Salivary Gland Cancer, Childhood; Surgery.

Further Readings

Salivary Gland Cancer, Childhood

The salivary gland is an exocrine gland that produces saliva and amylase, an enzyme the body uses to turn starch into maltose sugar. Each gland includes salivons, consisting of an intercalated duct, striated duct, and excretory duct, and termini acini (berry-shaped cell clusters where the secretion of saliva is released). There are about 1,000 salivary glands in the oral cavity, both major and minor.

Major salivary glands include a pair of parotid glands, the largest salivary glands, wrapped around the mandibular ramus (part of the lower jawbone). These glands secrete serous saliva to begin digesting starch and make swallowing easier. Lesions here can have an impact on the patient’s facial expressions, because of the proximity to the relevant facial muscles and nerve branches. Beneath the lower jaws is a pair of submandibular glands, about two inches above the Adam’s apple and two inches below the chin, which produce most of the saliva, about 70 percent. Under the tongue are the two sublingual glands, which produce mucous saliva. The salivons of the sublingual glands are simpler, lacking intercalated and striated ducts. Though we are often more aware of salivating from near the tongue, these glands are actually responsible for only 5 percent of saliva.

The remaining salivary glands are minor glands located throughout the oral cavity, in the submucosa of the labial, lingual, and buccal tissue, the soft palate, the hard palate, the muscle fibers of the tongue, and the floor of the mouth. Their ducts are also simpler, and they sometimes share an excretory duct among several minor glands. Each is only about a millimeter or two in diameter.

Saliva production is important to oral health (dry mouth can lead to tooth loss and significant gum problems in the long term, and increases incidence of cavities and especially gum disease in the short term). Saliva production is sometimes jeopardized by chemotherapy treatments and radiation therapy.

Salivary gland cancer is rare, and most salivary gland tumors in children are benign. Very young children, though, have a greater chance of developing malignant salivary gland tumors. In other cases, salivary gland cancer is a known side-effect of radiation treatment for other cancers, and so may be a side effect of childhood leukemia, for instance. Cumulative incidence of salivary gland cancer is low even among children with other cancers, but childhood cancer survivors treated with radiation face an elevated risk (positively associated with the dose of radiation) for two decades after exposure.

Salivary gland cancers include acinic cell carcinoma, found in the parotid gland and accounting for most childhood salivary gland cancers in first-time cancer patients; mucoepidermoid carcinoma, characterized by mucus-secreting and squamous cells, occurring more often in adults but sometimes striking late adolescents; adenoid cystic carcinoma, the most common form of submandibular gland cancer; and salivary duct carcinoma, which is very aggressive and usually painful, and found mainly in adult men. There are a variety of benign tumors that can develop, including the soft-tissue tumor hemangioma, a swelling of endothelial cells that
line blood vessels and usually occurs in young children; sebaceous lymphadenoma; Warthin’s tumor, a benign cyst that is more often found in heavy smokers; myoepithelioma, found in the parotid gland or palate; and pleomorphic adenoma, the most common tumor found in the parotid gland.

Symptoms of salivary gland cancer usually begin with a painless lump inside the mouth or near the cheek, jaw, lip, or even ear. Fluid may drain from the ear, or parts of the face may feel numb or weak, or experience pain that does not go away. Mouth trouble may be experienced, from difficulty swallowing to difficulty chewing or opening the mouth wide. Of course, all of these symptoms may be caused by other conditions, and salivary gland cancer’s rarity—accounting for only 2 percent of head and neck cancers—can lead to it escaping initial diagnosis, if it is not a side effect of cancer treatment. Diagnosis is usually performed with imaging.

The prognosis for salivary gland cancer in children is good, and the tumor(s) can usually be removed surgically. Sometimes radiation therapy or chemotherapy follows in order to eliminate surviving cancer cells and prevent recurrence. Acinic cell carcinoma has a 20-year survival rate of more than 50 percent.

Bill Kte’pi
Independent Scholar

See Also: Chemotherapy; Lymphoma, Hodgkin’s, Childhood; Lymphoma, Non-Hodgkin’s, Childhood; Salivary Gland Cancer; Surgery.

Further Readings
Research
From the beginning, the Salk Institute envisioned creating a research environment where scientists and researchers could interact and exchange ideas, studies, and projects. The institute was especially interested in developing expertise in the then-new fields of molecular and cellular biology, as these fields promised to reveal better understanding of human life processes. Although arranged into specific research units, the Salk Institute encourages collaboration between groups. Specific research units at the Salk Institute include:

- Cancer research
- Cellular neurobiology
- Chemical biology and proteomics
- Computational neurobiology
- Gene expression
- Genetics
- Immunobiology and microbial pathogenesis
- Molecular and cell biology
- Molecular neurobiology
- Peptide biology
- Regulatory biology
- Structural biology
- Systems neurobiology

These groups work in independent laboratories, although Kahn’s design of the institute consists of a minimum of walls so that members of different groups can easily communicate with each other.

Salk Institute scientists have examined a range of critical issues related to the underlying causes of cancers. Their discoveries have led to new therapies and directions of research. In 1971, the National Cancer Act dramatically increased funding for cancer research. Since that time, Salk Institute scientists have been leaders of the “war on cancer” initiated by President Nixon. Researchers at the institute have studied the diverse genetic mutations that drive the development of individual cancers. These studies have resulted in important contributions that have increased understanding and helped change cancer treatments offered to patients facing the disease. A series of important discoveries have been made at the Salk Institute that continue to shape new treatments and pave the way for future research.

Nobel Prize–winner Renato Dulbecco, who was a member of the Salk Institute from 1962 until shortly before his death in 2012, conducted studies involving the identification and characterization of mammary gland cancer stem cells. Also involved in the human genome project, Dulbecco believed cancer represents a disease of acquired mutations, and that epigenetic modification of a cell might contribute to the development or progression of cancer. The Cancer Center was established at the Salk Institute in 1970, and originally focused on studying tumor virology. As the center grew, it began to explore other areas, including identifying nuclear hormone receptors and determining their role in physiology and development; characterizing transcription factors that control gene expression and cell growth, differentiation, and patterning; and developing viral vectors for gene therapy.

The Cancer Center currently makes up about half of the research at the Salk Institute, and includes 30 members, about 200 postdoctoral researchers, 40 graduate students, and 100 research assistants. A grant from the National Cancer Institute helps support many shared resources at the Salk Institute, including shared equipment, bioinformatics, functional genomics/quantitative PCR, proteomics, cytometry, imaging, peptide synthesis, transgenic facilities, and viral vector production.

Training
Although not a degree-granting institution, the Salk Institute uses the titles of assistant professor, associate professor, and professor for its members. Through an affiliation agreement with the nearby University of California, San Diego (UCSD), the Salk Institute runs a graduate program that permits students to work toward a Ph.D. or M.D./Ph.D. degree. The Salk Institute also runs a well-regarded postdoctoral program, where graduates from other institutions of higher learning receive training in research skills, grant writing, and leadership. In several areas of biology, the Salk Institute is regarded as one of the globe’s premier organizations of its type, as its research output is among the highest in the world.

The Salk Institute has received support annually through monies awarded to its members in the form of research grants. Most of these research grants have been awarded from the National Institutes of Health (NIH), as well as from private foundations, organizations, and individuals. The March of Dimes has continued to provide funds to the Salk Institute
for every year of its existence, in addition to the monies given for the original structure. The organization of the Salk Institute consists of a board of trustees, a president and CEO, an academic council, and a chairman of the faculty. Together, these individuals help to guide the direction of future research endeavors at the Salk Institute.

Stephen T. Schroth
Towson University

See Also: American Cancer Society; National Cancer Institute; Nixon, Richard (War on Cancer); University of California, San Francisco, Helen Diller Comprehensive Cancer Center.

Further Readings

Sanford-Burnham Medical Research Institute

Sanford-Burnham Medical Research Institute is a nonprofit medical research institute with operations in La Jolla, California; Orlando, Florida; and Santa Barbara, California. The institute has over 850 scientists who work on the fundamental molecular causes of various diseases, with research including topics such as cancer, neuroscience, stem cell research, diabetes, and obesity. Being a nonprofit institution, research is supported by funding from National Institutes of Health (NIH), National Cancer Institute (NCI), and Juvenile Diabetes Research Foundation among others. In addition, the institution is in partnership with pharmaceutical companies such as Johnson & Johnson Pharmaceutical Research and Development. In 2008 Sanford-Burnham was awarded a $97.9 million grant by NIH to establish a high-throughput screening center.

The Institute was founded in 1976 as the La Jolla Cancer Research Foundation. It was founded by William H. Fishman and his wife, Lillian Waterman Fishman. The cancer center first received its NCI-designation in 1981. In 1996, the Foundation was renamed The Burnham Institute following a substantial donation from Malin Burnham. A decade later, it was renamed the Burnham Institute for Medical Research. After receiving a $20 million donation from Sanford Health in 2007, followed by an additional $50 million a few years later, “Sanford” was added to the name.

The Sanford Burnham Institute is known for paradigm-shifting research in prevention, treatment, and causes of diseases. The Institute’s collaborative, multidisciplinary research on cancer has led to new cancer therapies. In addition, the center remains active in educating and training the next generation of cancer scientists.

The primary objective of the Sanford-Burnham since its inception has been to focus on cancer research. To reach this objective, the institution has more than 1,000 employees among them about 850 scientists. These scientists include biophysicists, chemists, engineers, computer scientists, and biologists. The center currently houses five research centers and is able to conduct research in a wide array of medical areas. The five centers housed in the institution are the Infectious and Inflammatory Disease Center, the Sanford Children’s Health Research Center, the Del E. Webb Center for Neurosciences, Aging and Stem Cell Research, the Diabetes and Obesity Research Center, and the NCI-designated Cancer Center. The Cancer Center has a variety of specific research programs, including the following:

- **Tumor Initiation and Maintenance** seeks to identify the cells that cause tumors and the signals that allow these cells to expand uncontrollably.
- **Cell Death and Survival Networks** focuses on the study of how cancer cells reprogram their metabolism and protein homeostasis to survive nutrient stress conditions associated with tumor progression, and how they might use autophagy
The Ewing family of tumors (EFT) is a group of cancers that occur in bones or adjacent soft tissues. EFT includes Ewing sarcoma of bone, extrasosseous Ewing tumors, peripheral primitive neuroectodermal tumors (pPNET or peripheral neuroepithelioma), and Askin's tumors (pPNET of the chest wall). EFT is characterized by morphologically similar round-cell neoplasms and the presence of common chromosomal translocation that is unique to this group.
First described in 1918, pPNET is a rare tumor with undifferentiated round cells that form rosettes. It occurs in children and young adults under 25 years of age and has a five-year survival rate of about 53 percent. In 1921, James Ewing reported the first case of Ewing sarcoma as a “diffuse endothelioma of the bone.” In 1975, Angervall and Enzinger identified the first case of Ewing sarcoma arising from soft tissue. Ewing sarcoma can occur in all age groups, but is most commonly seen in people in their 20s. Five-year survival for localized disease is 70 percent, while metastatic disease is about 20 percent. Askin's tumor, initially described in 1984, is a malignant small-cell tumor of the thoracopulmonary region with histologic features similar to pPNET. These tumors have a poor prognosis.

Ewing sarcoma is the third most frequent primary sarcoma of the bone, after osteosarcoma and chondrosarcoma. In children, it is the second most common bone tumor after osteosarcoma accounting for 3 percent of pediatric malignancies and approximately 10 percent of primary malignant bone tumors. In the European Intergroup Cooperative Ewing’s Sarcoma Study 86 trial, only 10 percent of cases were diagnosed in patients over 20 years old. Overall annual incidence is about one case per million but this increases at pubertal age group to about five cases per million. It is slightly more common in males than females (1.6:1).

**Clinical Features**

**Tumor Site.** While almost any bone can be involved, Ewing sarcoma occurs more commonly in both flat and long bones followed by pelvic bone involvement (25 percent of cases). Older patients have more aggressive disease with pelvic and generally large-sized tumors. Fifteen percent of patients may have pathological fractures.

**Signs and Symptoms.** Pain, swelling, and a mass (mostly in extremities) are the most common presenting symptoms. Patients with large pelvic tumors may present with bowel/bladder disturbances in addition to pain. Paraspinal tumors may be associated with neurological impairments. Patients with Askin's tumors may present with shortness of breath, chest pain, cough, and pleural effusion. They may have systemic signs and in some cases, fever. Laboratory studies are nonspecific but may reveal anemia, leukocytosis, or increased erythrocyte sedimentation rate. It is common to have a delay between onset of symptoms and diagnosis. This may be because the mass has to become large enough to be palpable.

**Imaging Features.** Ewing sarcoma of the long bones arises from diaphysis or metadiaphysis. It appears as an ill-defined, focally mottled, destructive lesion on X-rays. Periosteal reaction with a multilayered “onion skin” appearance is commonly seen. Other features that may be present are sunburst or spiculated pattern, as well as Codman’s triangle due to periosteal lifting from the bone at the site of detachment. The major radiological differential diagnoses include osteosarcoma, osteomyelitis, and eosinophilic granuloma.

**Pathological Features.** EFT grossly presents as gray-white tumors with variable amount of necrosis, hemorrhage, or cyst formation. The tumors are composed of small round cells with high nuclear-cytoplasmic ratio. Cells have glycogen in their scant cytoplasm that stains positively with periodic acid-Schiff stain, and round nuclei with little mitotic activity. Tumor histology varies from undifferentiated cells in Ewing sarcoma to more differentiated cells in pPNET. Neural differentiation pattern in the form of Homer Wright rosettes may be visible under light microscopy in pPNET. Electron microscopy may detect neurosecretory granules. CD99 expression is detected at high levels in EFT but is not pathognomonic of this disease. Depending on the extent of differentiation, neuron-specific enolase, S-100 protein, and neurofilaments may be expressed. EFT is reactive to anti-Vimentin antibodies. These immunohistochemical stains help distinguish EFT from other small blue round cell tumors.
**Molecular Features:** EFT is characterized by a \( EWS-ETS \) fusion gene arrangement. Ninety percent of cases harbor a \( EWS-FLI1 \) translocation; \( t(11;22) \) (q24;q12). Other ETS members involved in genetic rearrangements with \( EWSR1 \) are \( ETV1 \) and \( EIAF \). These molecular features can be identified by techniques such as fluorescent \textit{in situ} hybridization and polymerase chain reaction.

**Risk Factors and Staging**

Studies have identified gender, age, tumor size, site, fever, serum lactate dehydrogenase levels, anemia, histological response to chemotherapy, and treatment variables as prognostic factors. Children's Oncology Group studies classify patients into three risk groups: those with localized tumors, with lung metastasis only, and with other or multiple metastases. Pretreatment staging allows for determining the limits of tumor involvement and ruling out metastatic disease. Tissue biopsy with cytogenetic and immunohistochemical studies is paramount in diagnosing EFT. Magnetic resonance imaging (MRI) can be used to detect primary lesions and computed tomography (CT) scans are better at diagnosing metastatic disease. Positron emission tomography (PET) imaging highlights metastatic spread to lymph nodes, bone, and bone marrow.

**Treatment**

Most patients have subclinical micrometastatic disease when they present with apparently localized disease at diagnosis. Chemotherapy and radiation are necessary adjuncts to surgery for EFT treatment. Chemotherapy regimens have significantly improved outcomes in patients with pPNET. Current recommendations suggest surgical resection whenever possible, adjuvant or neoadjuvant chemotherapy, and radiotherapy. Recommended chemotherapeutic regimen includes vincristine, doxorubicin, and cyclophosphamide with ifosfamide and etoposide. Outcomes in metastatic disease have not improved with current therapy. Radiotherapy, though sensitive, has a high risk of second malignancy. Ongoing clinical trials in EFT are designed to use targeted therapy against molecular pathways that are essential to EFT pathogenesis. These trials may help identify drugs that have the most treatment response with the least toxicity such that outcomes can be improved for patients with metastatic disease.

**Research**

While basic research studies help identify crucial survival and growth pathways for EFT, translational research is investing efforts into developing tools that can be used for targeted EFT therapy. Antibodies, peptides, and nucleic acid molecules that block critical molecules in EFT are being currently studied. Drug-delivery vehicles such as nanoparticles are being designed to incorporate chemotherapeutic agents so that maximum delivery occurs to the tumors rather than adjoining normal cells.

Sheetal A. Mitra  
*Children’s Hospital Los Angeles*

**See Also:** Childhood Cancers; Ewing’s Family of Tumors; Sarcoma, Soft Tissue, Childhood.

**Further Readings**

- American Cancer Society. “Ewing Family of Tumors.”  

---

**Sarcoma, Soft Tissue, Adult**

Adult soft tissue sarcoma is a sarcoma that develops in connective tissue. Cancers are classed according to the type of cell from which they develop: carcinomas develop from epithelial cells, lymphomas and leukemias from hematopoietic cells, and sarcomas from non-hematopoietic mesenchymal cells. In humans, sarcomas are far less common than carcinomas, and the major cancers are all carcinoma type cancers. Mesenchymal cells are cells that make up tissue lacking polarity, such as the tissues of the circulatory and lymphatic systems, bones, cartilage, and connective tissues.
Connective tissue is often fibrous, though adipose tissue is non-fibrous and often considered connective tissue. Connective tissue typically includes type I collagen—which constitutes about a quarter of the protein content of the body—as well as ground substance, a clear viscous fluid composed of glycosaminoglycans and proteoglycans, which fix collagen fibers in intercellular spaces. Connective tissue literally connects parts of the body to one another: collagenous fibers bind bones and tissues to each other, elastic fibers provide the elasticity of certain organs (like lungs), and reticular fibers create a scaffolding for other cells, made up of type III collagen and found in the liver, marrow, and lymphatic organs. Connective tissue functions to protect organs, help to provide a framework for the body, supply hormones, repair tissues, and provide defense reactions.

Soft tissue sarcomas are uncommon, accounting for less than one in 100 new cancer cases, in part because soft tissue cells are not continuously dividing, and so the opportunity for mutation is less frequent. Not all soft tissue sarcomas are associated with known risk factors, and their etiology remains little understood. There are a handful of exceptions, like the link between exposure to high doses of radiation and the development of soft tissue sarcoma (which was discovered in the early history of radiation therapy, when it was used to treat non-cancerous conditions like tonsillitis). The hereditary disease Li-Fraumeni syndrome predisposes the individual toward soft tissue sarcomas, among other cancers.

Most soft tissue sarcomas occur in the upper body, but there are exceptions. One case study detailed a 21-year-old man who came to the emergency room with a swollen foot that he believed had been caused by a drunken slip on the walk home weeks earlier, but an X-ray of the foot showed a distinct mass to the side of one of the metatarsals. A subsequent biopsy showed tumor cells in nests surrounded by fibrous stroma and small areas of necrosis.

Soft tissue sarcomas are asymptomatic in their early stages. Because of the physical characteristics of soft tissue, tumors are usually able to form and grow large before they cause any symptoms or become noticeable through swelling. When soreness does finally occur, it is the result of the tumor growing large enough to press against

*Soft tissue sarcoma photographed through an electron microscope. Soft tissue sarcomas are uncommon, accounting for less than one in 100 new cancer cases, in part because soft tissue cells are not continuously dividing and so the opportunity for mutation is less frequent. Not all soft tissue sarcomas are associated with known risk factors. (National Cancer Institute/Timothy Triche)*
adjacent muscles or pinch nerves. Abdominal soft tissue sarcomas can be mistaken for constipation, digestive problems, or menstrual cramps. In such cases, only the failure of the discomfort to respond to treatment or a worsening of symptoms as the tumor grows will lead to the discovery of the tumor.

Whether the tumor is cancerous (malignant) is determined through a biopsy, either surgically, in which case a surgeon removes the tumor and a pathologist diagnoses it under the microscope, or through fine-needle aspiration, in which a hollow needle is inserted in order to obtain a tissue sample. If malignant, a sarcoma is classified as either low-grade or high-grade, depending on whether it is likely to metastasize. If it does, the lungs are the most common site to which soft tissue sarcomas spread.

Soft tissue sarcoma is usually treated with surgery, preferably with a large margin of healthy tissue in order to decrease the odds of local recurrence. In some cases this can result in the need for amputating part of a limb, depending on where the tumor is located and how big it is. Radiation therapy and chemotherapy are both means of reducing the size of the tumor before surgery, and can be used to eradicate surviving cells after surgery. Radiation therapy can also treat tumors that cannot be safely removed by surgery; chemotherapy is not effective in this regard, but can be used to shrink tumors in patients that are not eligible for surgery.

Soft tissue sarcomas are more common in adults than in children, and adults tend to develop different types of soft tissue sarcomas than children do. In the arms, legs, and trunk, sarcomas may develop as fibrosarcoma, malignant fibrous hystiocytoma, or dermatofibrosarcoma, all of which are sarcomas of fibrous tissue; liposarcoma, developing in the fat; rhabdomyosarcoma, developing in the muscle; hemangiosarcoma, developing in blood vessels; and malignant peripheral nerve sheath tumor, developing from peripheral nerves. In the uterus or digestive tract, leiomyosarcoma can develop from smooth muscle tissue. Lymph vessels can develop into lymphangiosarcoma. Additionally, in the legs, synovial tissue (lining joint cavities) can develop into synovial sarcoma or cartilage can form into extraskeletal chondrosarcoma.

See Also: Kaposi’s Sarcoma; Sarcoma, Soft Tissue, Childhood.

Further Readings

Sarcoma, Soft Tissue, Childhood

Soft tissues are composed of connecting and supporting structures that surround organs and the skeletal system. This includes fat, muscles, nerves, tendons, synovial tissues around joints, tissues with admixture of bone and cartilage, blood vessels, and lymph nodes. Malignant tumors arising in these structures in adults or children are called soft tissue sarcomas (STSs). Childhood soft tissue sarcomas (STSs) account for 7 percent percent of all pediatric tumors.
Types of Pediatric STSs

Rhabdomyosarcoma is the most common STS in children aged 0 to 14 years and accounts for 50 percent of tumors in this age group. The remaining STSs are commonly referred to as nonrhabdomyosarcomatous STS and account for about 3 percent of all childhood tumors.

**Skeletal Muscle STS.** Rhabdomyosarcoma is the most common malignant childhood STS and has various subtypes depending on histology and genetic features. Prognosis is associated with tumor stage and grade.

**Connective Tissue STS.** Liposarcomas are rare tumors that arise from fat cells deep in regions such as the thigh or retroperitoneum. Most pediatric liposarcomas are low-grade, spread very slowly, and respond well to treatment. Pleomorphic high-grade liposarcomas, however, have poor treatment response and an unfavorable prognosis.

Desmoid tumors (aggressive fibromatosis) are low-grade fibrous tissue tumors that recur near primary site but rarely metastasize. Most occur sporadically, however 10 percent may occur in individuals with Gardner’s syndrome, a type of familial adenomatous polyposis.

Fibrosarcoma originates in bony fibrous tissue and invades long or flat bones, and may involve the periosteum and overlying muscle. Congenital or infantile fibrosarcoma occurs in children under 4 years of age and may be detected by perinatal ultrasound. Most of these tumors have a chromosomal translocation, t(12;15), and the associated fusion gene ETV-NTRK3 is useful for its diagnosis. Fibrosarcoma in older children and adolescents do not have this genetic change.

Dermatofibrosarcoma protuberans is a skin dermis tumor, 90 percent of which harbor a genetic translocation, t(17;22). The fusion gene COL1A1-PDGFB produces a self-stimulatory growth signal that allows tumor growth. Less than 5 percent of tumors metastasize.

Inflammatory myofibroblastic tumors are characterized by a mix of inflammatory cells localized to a soft tissue area, and may have genetic rearrangements involving the ALK gene. Tumors have random areas of cell growth and death, calcification, and bleeding. They can recur after treatment but rarely metastasize.

**Low-grade fibromyxoid sarcomas** are associated genetic rearrangements, t(7;16) or t(11;16). They have a long clinical course with potential local recurrence or distant metastasis to the lung, sometimes decades after primary diagnosis.

**Peripheral Nervous System STS.** Malignant peripheral nerve sheath tumors affect the covering of nerves that are not part of the brain or spinal cord. About half the cases are seen in patients with a genetic condition termed neurofibromatosis type I.

**Smooth Muscle STS.** Leimyosarcomas are tumors associated with smooth muscles lining blood vessels and hollow internal organs such as stomach, intestines, bladder, and uterus. They are commonly associated with Epstein-Barr virus in HIV-positive children. Children with inherited retinoblastoma are at secondary risk for this disease.

**Vascular STS.** Angiosarcomas grow very rapidly from cells lining the inside of blood vessels and have a tendency to metastasize.

Epithelioid hemangioendotheliomas occur most often in livers of infants although they can be seen elsewhere. In infants, the tumors may go away without treatment and are generally benign. Benign tumors can be treated with liver transplants but may become malignant and spread to lungs, lymph nodes, bones, abdomen, and pelvis in some cases.

Hemangiopericytomas occur in lining of the blood capillaries. It can be very aggressive if found within the nervous tissue. Patients under one year of age have favorable prognosis when compared to older children where the tumor is more likely to metastasize to lymph nodes and lungs.

**Extraskeletal Bone and Cartilage STS.** Extraskelatal chondrosarcoma and osteosarcoma are cartilage and bone tumors that can grow quickly and metastasize.

**Fibrohistiocytic STS.** Plexiform fibrohistiocytic tumors appear as a painless nodule in skin of arm, wrist, or hand and rarely spread.

Undifferentiated pleomorphic sarcoma may be seen in children if they have received radiation previously or have retinoblastoma. They are usually found on extremities and can metastasize.
**Other STS.** Alveolar soft part sarcomas are rare tumors that can spread to other organs. Prognosis is favorable if the tumor is completely resected or is 5 cm in size or smaller. Histologically, the cells are arranged in a similar fashion as lung alveoli.

Desmoplastic small round cell tumors predominantly occur in boys and young adults, and can be aggressive. They occur as an abdominal or pelvic mass and can spread to lungs and other organs.

Perivascular epithelioid cell tumors such as renal angiomyolipomas and pulmonary lymphangioleiomyomatosis commonly occur in children affected with tuberous sclerosis.

Extrarenal (extracranial) rhabdoid tumors are rare, fast-growing cancers that usually occur in young children. They are frequently associated with 22q11.1 chromosomal deletions resulting in loss of SMARCB1 tumor suppressor gene.

Extraskeletal myxoid chondrosarcoma is a rare tumor often characterized by a translocation resulting in the fusion gene EWSR1-CHN. This generally indolent tumor may relapse after treatment with a 40 percent chance to metastasize.

Primitive neuroectodermal tumors are derived from neuroectodermal cells that have not completed differentiation. These rare tumors belong to the Ewing family of tumors and are seen in children and adults under 25 years of age.

Synovial sarcomas occur in soft tissues near joints in extremities, but may also form in the trunk, head or neck. Most cases are associated with a translocation t(x;18) resulting in the SS18-SSX fusion gene that promotes tumor development. Age under 10 years and tumors 5 cm or smaller have good prognosis. Large tumors can spread to other organs.

**Presentation**
Children usually present with painless lumps under the skin over the arm, leg, or trunk. There may be no more symptoms until the tumor grows large enough to press on other surrounding structures or organs.

**Diagnosis**
Imaging can help identify bone involvement and calcification seen in extraskeletal bone tumors, and can detect metastasis. Tumor biopsy can be used for conventional histology, immunocytochemical analysis, cytogenetics, fluorescence in situ hybridization, and molecular pathology given the diagnostic importance of translocations in almost all STSs.

**Treatment**
Treatment is based on age, tumor type, stage, and grade. Childhood STSs have better outcomes with multimodal therapy including surgery, with pre- or post-surgery chemotherapy and radiation therapy that is only reserved for unfavorable cases. Most STSs do not respond to chemotherapetry alone. Radiotherapy is associated with long-term morbidity in children as most organs can be damaged during their development years.

Sheetal A. Mitra
*Children’s Hospital Los Angeles*

**See Also:** Childhood Cancers; Rhabdomyosarcoma, Childhood; Sarcoma, Soft Tissue, Adult.

**Further Readings**
Children's Oncology Group. “Rhabdomyosarcoma.”

*Journal of the National Comprehensive Cancer Network*, v.8/6 (2010).

Medscape. “Nonrhabdomyosarcoma Soft Tissue Sarcomas.”

---

**Sarcoma, Uterine**

Uterine sarcoma is a cancer that forms from the smooth muscle or connective tissue of the uterus. Sarcomas form from mesenchymal cells rather than epithelial cells as carcinomas do, and are the rarer form of cancer in humans. All sarcomas combined comprise only about 1 percent of American cancer diagnoses each year. Uterine sarcomas are largely found in postmenopausal women, especially those who have taken tamoxifen over a long-term period. Pelvic radiation is another risk factor—and so uterine sarcoma is very often the second cancer the patient has developed in her life—and African American women are twice as likely to develop a uterine sarcoma than white or Asian women.
Beyond these risk factors, causes of the disease are not yet understood.

There are several kinds of uterine sarcomas depending on where they originate. Tumors originating in uterine muscle cells are uterine leiomyosarcoma (LMS), accounting for 5 percent to 10 percent of soft tissue sarcomas. Resistant to both chemotherapy and radiation treatment, leiomyosarcomas are also unpredictable in their recurrence, sometimes recurring years later. The best prognoses are for patients who discover the tumor early and in whom surgery with wide margins can be performed. The widest possible margins are preferred when excising uterine sarcomas, in order to ensure that the whole tumor is removed—partly because of the cancer’s tendency to recur and partly because of any surviving cancer cells’ high odds of surviving both chemotherapy and radiation. Hormone treatments have had some success.

LMS are staged using the 2009 FIGO staging system, in which stage I is a tumor limited to the uterus; stage II, extending beyond the uterus but within the pelvis; stage III, infiltrating the abdominal tissue; stage IVA, infiltrating the bladder or rectum; and stage IVB, distant metastasis.

Uterine sarcomas originating in the stroma (connective tissue) of the uterine lining are endometrial stromal sarcomas. Low-grade endometrial stromal sarcomas resemble phase endometrium, but behave more aggressively, and express estrogen and progesterone receptors. Undifferentiated high-grade endometrial stromal sarcoma does not resemble normal endometrial tissue, and is even more aggressive. Either type can metastasize, though undifferentiated sarcoma is more likely to. The sarcoma is visible under a microscope as a tongue-like infiltration of tissue between muscle bundles, with prominent arterioles and 10 to 15 mitotic figures per 10 HPF. Foam cells may be visible in the stroma.

Uterine carcinosarcomas are one of a few types of tumors that are a combination of carcinoma and sarcoma, consisting of both epithelial and mesenchymal cells. Similarly, uterine adenosarcoma combines both uterine cancer of the mesenchymal tissue and a benign glandular component. Uterine adenosarcomas and endometrial stromal sarcomas are staged the same as LMS.

A mixed Mullerian tumor is a type of carcinosarcoma that is found in the uterus, ovaries, or fallopian tubes, and may be either homologous or heterologous. A heterologous tumor includes sarcomatous tissue from outside the uterus, including skeletal muscle, bone, or cartilage. About 2 percent to 5 percent of uterine cancers are mixed Mullerian tumors, found mainly in postmenopausal women.

Uterine sarcoma symptoms may include unusual or postmenopausal vaginal bleeding, pelvic pain or pressure, discharge, or an enlargement of the uterus. There is no specific screening test, and diagnostic tools include computed tomography (CT) or magnetic resonance imaging (MRI) scans, biopsy, and hysteroscopy. Surgery usually involves a total abdominal hysterectomy. Radiation therapy, chemotherapy, and hormonal therapy are all options either following surgery or in lieu thereof. Prognosis is poor for leiomyosarcoma and undifferentiated sarcomas, except in patients who are diagnosed early (in which case the five-year relative survival rate is over 60 percent), but the relative survival rate for endometrial stromal sarcoma is very high.

The uterus can also develop noncancerous tumors in the connective tissue, including leiomyomas, adenofibromas, and adenomyomas, known collectively as fibroid tumors. Most require no treatment, but some may need to be removed because their presence is causing bleeding, pain, or constipation. In such cases, surgery (either a myomectomy or a hysterectomy) is common, but killing the tumor with electricity, freezing it with liquid nitrogen, or blocking the blood vessels until it withers and dies, are all options.

Bill Kte’pi
Independent Scholar

See Also: Sarcoma, Soft Tissue, Adult; Uterine Cancer, Endometrial; Uterine Sarcoma.

Further Readings


Sarcoma Foundation of America

The Sarcoma Foundation of America (SFA) advocates for sarcoma patients by funding research and increasing awareness. The foundation funds research for new sarcoma therapies, advocates for government funding, and encourages alliances with the pharmaceutical and biotechnology industries. In addition the SFA advocates for early detection, optimal patient care, and early access to newly developed treatments.

Incorporated in 2000, the SFA was founded by Dr. Mark Thornton and Mrs. Patricia Thornton. It is a nonprofit organization. SFA has thousands of members in all 50 states. Since 2003, SFA has funded 57 sarcoma research grants. SFA started the Sarcoma Patient Registry, which gathers data that can be used as a resource for oncologists and researchers. Anyone diagnosed with any sarcoma subtype can join the registry for free.

Cancerous tumors found in connective tissues—such as cartilage, muscles, bones, fat, blood vessels, nerves, and deep skin tissues—are sarcomas; they are typed by either bone sarcomas or soft tissue sarcomas. Pediatric patients account for about 15 percent of all sarcomas. Approximately 14,000 new cases are diagnosed per year in the United States. Soft tissue sarcomas, a rare form of cancer, occurs about one percent of the time among all cancer diagnoses. About 3,900 people die each year from this disease. Common causes associated with soft tissue sarcomas include: exposure to phenoxyacetic acid (in herbicides), exposure to clorphenols (in wood preservatives), exposure to high doses of radiation, genetic abnormalities, and chromosome mutations.

Soft tissue sarcomas rarely cause any symptoms in the early stages because soft tissue is very elastic. Tumors tend to grow quite large before any lumps are noticed. It is when the tumor presses on nearby muscles and nerves when pain or soreness occurs. A surgical biopsy is the only form of diagnosis. The following are subtypes of soft tissue sarcomas:

- **Liposarcoma:** Usually develop in deep fatty tissue in the thigh, the gluteal area, the groin, behind the knee, or behind the abdominal cavity.
- **Fibrosarcoma:** Usually found in the arms, trunk, or legs.
- **Dermatofibrosarcoma Protuberans:** A lesion that protrudes out of the skin usually on the back or abdomen;
- **Synovial Cell Sarcoma:** Most often found in the arms or legs next to a joint in young adults.
- **Epithelioid Sarcomas:** Usually found in the hand or foot of young adults.
- **Rhabdomyosarcomas:** Found in the striated or skeletal muscle and most often found in children.
- **Leimyosarcoma and Uterine Sarcoma:** Found in smooth muscle of the uterus and GI tract.
- **Mycomas:** Most often found in the arms and legs of men and women about 50 years of age.
- **Mesenchymomas:** Found throughout the body.
- **Vascular Sarcomas:** Contain many blood vessels.
- **Neurilemmomas:** Found in peripheral nerves and are most common in young to middle aged male adults.
- **Alveolar Soft-Parts Sarcoma:** Found in the extremities and usually occurs in female adolescents and young adults.
- **Kaposi's Sarcoma:** Usually found in the tissues under the skin or the mucous membranes of the mouth, nose, and anus.

Several of these subtypes of soft tissue sarcomas also have their own subtypes.

Surgery, radiation, and chemotherapy are the typical treatment methods used in soft tissue sarcomas. Any of these methods can be used singularly or in combination depending upon the location, growth rate, and size of the tumor. Biological
therapy and targeted therapy continue to be methods available with improvements in prognosis as science advances.

Bone cancer sarcomas have three subtypes: chondrosarcoma (found in the cartilage), Ewing’s sarcoma (found in bone or soft tissue), and osteosarcoma (found in bone). Approximately 2,890 people are diagnosed with bone cancer sarcomas in the United States each year; of those there are approximately 1,410 deaths. Bone sarcomas are much more likely to be diagnosed in children. Symptoms vary depending on size and location of the tumor, but pain is the most common symptom. Other symptoms can be anemia, fatigue, bone fractures, and weight loss.

Surgery and chemotherapy are the most common treatment methods. Amputation is sometimes necessary but limb-saving treatments are available with the use of chemotherapy before surgery to remove the tumor. In this case, chemotherapy or other anti-cancer drugs will also follow surgery.

SFA supports the American Society of Clinical Oncology’s (ASCO) mission to improve cancer care and prevention and that all patients receive the best possible care. The ASCO’s research and education goals includes the Conquer Cancer Foundation. The SFA has helped to fund nine Conquer Cancer Foundation grants, two Advanced Clinical Research Awards in Sarcoma, and four Young Investigator Awards. The Career Development Award supports clinical investigators in their first to third year of a faculty appointment whose goal is to establish an independent cancer research program. The Advanced Clinical Research Award supports researchers who have designed original research that does not yet have funding. The Young Investigator Award is designed to promote research in clinical oncology for researchers during their transition from a fellowship program to a faculty appointment.

Advocating for persons impacted by sarcoma is a core principal of SFA. Active engagement with public policy is a high priority for SFA, especially with regard to access to quality patient care, drug development, and cancer research. The SFA has urged Congress to fully fund the FDA and National Institutes of Health (NIH) since drastic cuts have had a significant impact on the budgets of science and health programs. A bill introduced by Representatives Cliff Stearns (R-FL) and Ed Towns (D-NY) called the Unlocking Lifesaving Treatments for Rare-diseases (ULTRA) Act has been supported by the SFA. The Act would allow the FDA more flexibility to approve drugs for rare diseases. The Creating Hope Act, also supported by SFA, proposed in the U.S. Senate, creates incentives in the development of treatments for rare diseases that have a disproportionate impact on children.

Jessica Hammer
Independent Scholar

See Also: Carcinoid Cancer Foundation; European Association for Cancer Research; Japanese Cancer Association; Leukemia & Lymphoma Society; Lymphoma Research Foundation of America.

Further Readings

Saudi Arabia

Saudi Arabia is an absolute monarchy founded upon the tenets of Islam. The King of Saudi Arabia is the head of the government but his decisions are made after consultation among the senior princes of the royal family and the religious establishment. All references noted herein are government agencies.

Saudi Arabia has kept careful records of incidences of cancer in the country. Per the Cancer Incidence and Survival Report 2007 by the Saudi Cancer Registry, 12,309 cases of cancer were diagnosed in Saudi Arabia in 2007. Saudi Arabia’s population at the time was approximately 17 million. Breast cancer ranked first (13.8 percent), then colorectal (9.9 percent), non-Hodgkin lymphoma (7.7 percent), thyroid (6.4 percent), leukemia (6.2 percent), liver (4.8 percent), and lung cancer (4.5 percent). Most common cancers in women were breast, thyroid, colorectal, non-Hodgkin lymphoma, and leukemia; in men non-Hodgkin...
lymphoma, leukemia, lung, and liver. Female age-standardized incidence rate (ASR) was 84.7 per 100,000 compared to 282.8 per 100,000 for the United States. The ASR for males was 80 per 100,000 compared to 353.4 per 100,000 for the United States.

While the cancer rate is now projected to be lower than the rate in the United States for the next two to three decades, it is still likely to increase. A main reason for this is an aging population, which will bring more people into the “cancer zone.” Another reason is the recent introduction to the country of the Western (U.S.) lifestyle. This is characterized by both a more sedentary lifestyle and an increase in the consumption of Western junk food. In Saudi Arabia, fast-food restaurants are now as popular as they are in the U.S. The number of smokers in the country is also increasing; therefore the prevalence of lung and other smoking-related cancers is projected to increase in the next 20 to 30 years.

The Kingdom of Saudi Arabia is fighting this expected increase in cancer with many facilities where treatment of stages of disease can be given equal care with the highest international standards. Previously, modern cancer treatment could only be found in three major cities: Riyadh, Jeddah, and Dammam. Recently, however, cancer centers have appeared in smaller cities, including Makkah, Madina, and Qaseem, with several more on the way.

Saudi Arabia has also made training physicians a top priority. Most of the practicing oncologists in Saudi Arabia were educated in North America. Ambitious health sciences universities in Saudi Arabia now educate medical, nursing, and other related health science staff to be prepared for the expected increase in cancer diagnoses.

Another unique part of Saudi cancer care is that Saudi law guarantees that all patients with cancer receive free care. There are multiple governmental and nongovernmental organizations dedicated to cancer control, such as reducing tobacco use and screening and early detection programs.

Cancer Organizations
The Saudi Cancer Registry (SCR) is responsible for the collection, maintenance, and dissemination of population-based cancer data. There are over 170,000 cancer cases that were reported from 1994 to 2010 from over 500 governmental and private hospitals, physician’s offices, cancer treatment centers, and pathology laboratories. The SCR collects information on cancer cases such as the types of cancers, the infection sites and extent of cancer at the time of diagnosis. Patient characteristics and predications of cancer are also studied.

The SCR began reporting cancer cases beginning in January 1994. In 2013 the SCR became part of the council of health services. The foremost goal of the SCR is to continue to define population-based rates of cancer occurrence in Saudi Arabia. Additional objectives include programs for early detection and cancer screening, as well as cancer research projects.

A later report from the SCR tracks the incidence of cancers for one year 2010. The total number of cancers reported to the SCR was 13,706. Overall cancer was more prevalent among women than men. Cancers affected 6,579 (48 percent) males and 7,127 (52 percent) females, with a male to female ratio of 92:100.

Childhood Cancers
As part of the SCR 2010 study, childhood cancers were evaluated. The total cancer cases reported among children (0 to 14 years) in 2010 was 796. This figure represents 5.8 percent of the total cancers reported. The incidents show that cancer was more prevalent among boys than girls—482 (60.6 percent) cases reported were boys and 314 (39.4 percent) among girls, with a male to female ratio of 154:100. Childhood cancer is most important because 41.7 percent of the Saudi population is under 15 years of age. In addition to this, there has been a major breakthrough in the cure of childhood cancers. The leading cancer among Saudi children was leukemia, which accounted for 33.3 percent, followed by brain, 12.9 percent, Hodgkin’s disease, 9.2 percent, non-Hodgkin lymphoma, 8.1 percent, and kidney, 6.1 percent. This report has many charts and tables illustrating the above findings.

Cancer Incidence for Most Common Sites, 2010
According to the data collected from January through December 2010, statistics for the top four cancer diagnosed are as follows:

Breast Cancer. There were 1,473 female breast cancer cases. Breast cancer ranked No.1 among females, accounting for 27.4 percent of all newly diagnosed
female cancers (5,378) in 2010. The ASR was 24.9 per 100,000 population for female population.

**Colorectal.** There were 1,033 cases of colorectal cancer equaling 10.4 percent of all newly diagnosed cases. This cancer ranked first among males and third among females. It affected 541 (52.4 percent) males and 492 (47.6 percent) females with a male to female ratio of 110:100. The overall ASR was 9.6/100,000. ASR for males was 9.9/100,000 and for females 9.2/100,000.

**Non-Hodgkin Lymphoma.** Non-Hodgkin lymphoma is any of a large group of cancers of lymphocytes (white blood cells). Non-Hodgkin lymphomas can occur at any age and often present with enlarged lymph nodes as well as fever and weight loss. There are many types of non-Hodgkin lymphoma. There were 703 cases of non-Hodgkin lymphoma, 7.1 percent of all newly diagnosed cancers. This cancer ranked second among male population and fourth among female population. It affected 407 (57.9 percent) males and 296 (42.1 percent) females with a male to female ratio of 138:100. The overall ASR was 5.7/100,000. ASR for males was 6.2/100,000 and 5.2/100,000 for females.

**Thyroid.** There were 697 reported cases of thyroid cancer or 7.0 percent of all newly diagnosed cases. This cancer ranked second among the female population and 12th among the male population. It affected 149 (21.4 percent) males and 548 (78.6 percent) females with a male to female ratio of 27:100. The overall ASR was 4.9/100,000. ASR was 2.3/100,000 for males.

The remaining reported cases of cancers was as follows: leukemia, liver, lung, Hodgkin disease, skin (nonmelanoma), stomach, kidney, prostate, bladder, and ovarian cancer.

**Conclusion**
Saudi Arabia will likely become a giant in the care and cure of cancer. They have the money to invest in facilities and top physicians. However, as noted, they may need all they can get. The forecast is for the cancer rate to rise significantly in the next 20 to 30 years.

Kenneth B. Alexander
Independent Scholar

See Also: Breast Cancer; Childhood Cancers; United Arab Emirates.

**Further Readings**

**Screening**

Early detection is key to preventing and treating many cancers as it provides doctors a better chance to outline effective treat and ensure better survival rates. Promoting awareness of these screening tests is an important part of improving outcomes for patients.

**Evidence-Based Recommendations and Implications for Care**

The U.S. Preventive Services Task Force (USPSTF) is responsible for many of the cancer screening recommendations in existence today. Made up of 16 volunteer members who are experts from a variety of medical backgrounds, this task force continually reviews scientific evidence on preventative health care services and develops recommendations for clinicians. The USPSTF not only evaluates the research on services in terms of preventing or detecting a disease, but also evaluates the benefit/harm ratio of the service. The preventive services recommended by the USPSTF cover many diseases and conditions, and generally fall into four categories: screening tests, immunizations, counseling, and preventive medications.

The USPSTF recommendations are important for a number of reasons. The recommendations are based on a continual, systematic review of many studies over a long period of time, meaning no single study will influence their recommendations.
The task force does not simply approve or reject a preventative service; instead, each recommendation is given a letter grade based on the evidence and the benefit/harm ratio of the preventative service, and the recommendations provide specific information regarding age, gender, medical history, and health behaviors. Fourth, the USPSTF recommendations have implications for health care delivery. Because the task force has the support of the Federal government (and is convened by the Agency for Healthcare Research and Quality), the recommendations often affect which preventative clinical services are covered by Medicaid, Medicare, and even private health insurance plans. In fact, one important component of the Affordable Care Act requires that most preventative clinical services recommended by the USPSTF be covered by the health insurance plan at no additional cost to the patient (i.e., no cost-sharing for the patient).

Cervical Cancer Screening
Cervical cancer is one of the easiest cancers to prevent. There are two cervical cancer screening tests that women can receive, and each comes with different recommendations depending on a patient’s age, medical history, and frequency of test.

The first is the Pap test (sometimes called a Pap smear). The Pap test is one of the most widely used cancer screenings in the world. Developed by an American Obstetrician/Gynecologist around 1930, the Pap test is extremely successful in detecting precancerous cells on a woman’s cervix. The test is performed by a doctor, usually in conjunction with a pelvic exam. A speculum is used to widen the vagina, then a small brush is inserted to collect a sample of cells and mucus from the lining of the cervix in order to determine if any abnormal cells are present. An unclear or abnormal result typically means that there are cell changes or abnormalities on the cervix and that the patient may need further follow-up tests to see if those abnormalities are cancer-related.

For many years the recommendation for cervical cancer screening was once a year. In 2012, however, the USPSTF changed the recommendation for screening (via a Pap test) to once every three years for women aged 21 to 65, or once every five years for women ages 30 to 65 if the Pap test is done in combination with the test for human papillomavirus (HPV). Additionally, women were previously advised to begin screening within three years of onset of sexual activity, or no later than 21 years of age. However, the new recommendations advise women to begin screening at age 21 and not any earlier, essentially eliminated the consideration of sexual activity as a risk factor in determining the necessity for the test. One recommendation that did not change is that healthy women without a history of negative test results should stop screening at age 65. While these changes to the recommendations for cervical cancer screening initially caused concern among doctors and patients, the USPSTF has determined that risks of more frequent screening (or screening at younger ages) outweigh the benefits. In any case, women with a history of repeated negative test results should continue to receive annual screening for 20 years from the date of the last negative result, even if this means going past age 65. The second screening test is the human papillomavirus (HPV) test.

Persistent infections of several high-risk strands of HPV are known to cause more than 90 percent of cervical cancers. Because of this, detecting a high-risk HPV infection early can alert doctors and patients to the need for more frequent testing and monitoring, in case cervical cancer does develop (although most HPV infections do clear up on their own). The HPV test is usually, but not always, performed in conjunction with a Pap test. Both tests use a similar technique in which cells are collected from the cervix using a small brush, the sample is sent to a lab, and then for this specific test, a computerized system assesses the cells for the presence of high-risk HPV. Even though the HPV can be present in both men and women, the test is only available to women because it is designed to assess cells taken from the cervix.

Prior to 2012 the USPSTF did not have any recommendations for regular HPV testing because the task force did not have enough evidence to create guidelines for this test. However, in 2012, the task force recommended that women under 30 need not have an HPV test, because most HPV infections clear on their own in young, healthy women. Additionally, as previously mentioned, the USPSTF designated that women over the age of 30 can reduce the frequency of Pap tests they receive, from every three years to every five years, if they also have an HPV test every five years.
Breast Cancer Screening

There are three general types of breast cancer screenings that can be done. The first two are very similar and can be completed without any medical equipment; they are the clinical breast exam (CBE) and the breast self-exam (BSE). The main difference between the CBE and the BSE is that a doctor performs the BSE. This is important to note for two reasons.

First, the doctor may detect something that the patient misses, as they are highly trained to detect symptoms. Second, the CBE provides an excellent opportunity for the doctor to teach the patient how to perform a correct BSE. In either case, the individual performing the test first checks for a change in breast appearance, such as color, shape, and size. Next, using various levels of pressure, the breast tissue is felt for any lumps or abnormalities. If one is discovered, the doctor may discuss further screenings or procedures with the patient, such as a biopsy. However, the doctor may also be able to decide if a suspicious lump is merely a cyst or, by knowing a patient’s history, that this particular patient has fibrocystic breasts (which often have small bumps throughout them). Because both of these screening procedures are non-specific and have much room for error, and no literature exists supporting their efficacy in comparison to no screening activity, the USPSTF actually recommends against teaching BSE to patients, and concludes there is insufficient evidence to support CBE. However, anecdotal evidence abounds in support of the value of these screening tests. Hence, many health organizations recommended monthly BSEs and regular CBEs with a doctor.

The main tool used by health care professionals for breast cancer screening and diagnosis is the mammogram. A mammogram is performed by taking an X-ray (using very low levels of radiation) of each breast, making it possible to see small tumors or lumps that cannot be felt. During a mammogram, the breast is compressed between two metal plates in order to spread out the breast tissue for a better X-ray view. If the doctor determines that the X-ray shows abnormalities, a follow-up biopsy of any lumps may be performed. It is important that the doctor have access to previous patient mammograms for comparison, as this will allow him or her to see if any changes have occurred in the breast tissue.

At the time of this writing, the USPSTF was in the process of reviewing the scientific evidence on breast cancer screening practices. The recommendations from 2009 state that healthy women begin receiving biennial mammograms (every 2 years) starting at age 50; after age 75, the recommendation is that women receive no benefit from continued screening. In addition, because breast cancer is linked to genetics and family history, the USPSTF specifically recommends that women at a higher risk for breast cancer speak with their individual doctor about beginning regular mammogram screening earlier in life.

The USPSTF’s 2009 guidelines differ widely from the recommendations for early detection from the American Cancer Society which recommends CBEs and mammograms once a year for all women over the age of 40, and CBEs alone every three years for women in their 20s and 30s. Additionally, counter to the USPSTFs discouraging BSE, the American Cancer Society encourages all women to perform self-exams starting in their 20s, as a way to familiarize themselves with the normal look and feel of their breasts as a way to better identify any changes that may occur. For women considered high-risk,
due to genetic or other factors, magnetic resonance imaging (MRI) may also be recommended.

**Colon Cancer Screening**

There are several types of colon cancer screenings recommended by the USPSTF; these screenings vary in terms how the test is done and how often a person needs to get screened.

The colonoscopy is the most comprehensive and invasive colon cancer screening test. The colonoscopy is performed in a doctor’s office. The doctor uses a long, lighted tube with a small camera, called a colonoscope to see inside the rectum and the entire colon for polyps, tumors, or inflamed areas. The image is transmitted to a large screen in the examining room, which allows the doctor a clear view of the area. The tube may also be equipped with a small device for taking tissue samples of the colon, in order to further examine the tissue for cancerous markers; this is known as a biopsy. Polyps may also be removed during the colonoscopy.

Though the colonoscopy is an in-office procedure, patients do undergo mild sedation and generally need some time to recover before going home. While the colonoscopy itself only takes about 30 to 45 minutes, a patient does have to engage in several pre-colonoscopy tasks that ensure his or her bowel is empty (which is necessary for a clear view of the colon). This includes, but is not limited to: limiting solid food intake for a day before the test, drinking a bowel preparation solution that helps to clean out the bowel, and receiving one or two enemas before the procedure. Many patients report the preparation for the colonoscopy is more uncomfortable than the procedure itself.

The USPSTF recommends that healthy people begin regular colonoscopy screening at 50 years of age and receive follow-up screenings every 10 years. The task force also recommends that routine colonoscopy screening is unnecessary for healthy patients age 76 and older, and no screening is recommended for patients over 85. However, high-risk patients of any age with certain gastrointestinal conditions, a family history of colon cancer, or other high-risk factors are advised to talk with their doctor about more frequent screening.

The flexible sigmoidoscopy is similar to the colonoscopy and is also performed in a doctor’s office. After the patient participates in the same bowel cleaning tasks described above, the doctor uses a lighted tube called sigmoidoscope (which is significantly shorter than the colonoscope) to see into the rectum and the lower third of the colon. The doctor will look for polyps, tumors, and other inflamed areas, and may take a biopsy. There are two main differences between the colonoscopy and the sigmoidoscopy. First, the sigmoidoscopy is considered slightly less invasive than the colonoscopy. Many patients do not need the mild sedation during this test and therefore have quicker recovery time; they can drive themselves home. Second, the sigmoidoscopy is not as comprehensive a test as the colonoscopy, because it only examines the lower third of the colon. This portion of the colon may appear healthy, but there could be problems in the upper two-thirds of the colon.

The USPSTF recommends that healthy people should begin regular flexible sigmoidoscopy screening at 50 years of age and should have the test once every five years. Because it is a less thorough test than the colonoscopy, the task force recommends that those relying on the sigmoidoscopy screening every five years should complement their care with a fecal occult blood test every three years (described below). The sigmoidoscopy is not recommended for patients over 76 years of age (and especially those over 85 years of age), though high-risk patients should discuss more frequent screenings with their doctor as necessary.

The fecal occult blood test (usually just called FOBT) can be done at home. Patients are given a test kit by their doctor and are instructed to use the provided stick or brush to take one or more samples of their stool; they then return the test kit containing the obtained sample to their doctor. The stool sample is sent to a lab and is tested for traces of blood, which may be a symptom of colon cancer. If the test gives a positive or inconclusive result, a follow-up procedure such as a colonoscopy is usually recommended. Some newer tests, such as the fecal immunochemical test (FIT) or immunochemical fecal occult blood test (iFOBT) even allow the patient to perform the blood test at home by adding certain chemicals to the sample to detect if blood is present. However, these tests are more expensive than the regular FOBT. The USPSTF recommends that healthy people should begin regular FOBT screening at 50 years of age and should be screened every year.
Promoting Use of these Screening Tests

One of the biggest challenges to successful cancer control is underutilization of these screening procedures. Each of the screening tests described in this entry comes with its own unique challenges. In addition, different patient population characteristics, such as education, race/ethnicity, and geographic location, can affect whether these screening procedures are used.

The Pap test, and to a lesser extent, the HPV test, have been extremely useful tools in the early detection of cervical cancer. These tests alert doctors and patients to early symptoms of the disease, which allows for earlier diagnosis, treatment, and monitoring.

While cervical cancer rates are still relatively high, the U.S. Department of Health & Human Services reports that between 1955—soon after the introduction of the Pap test—and 1992, cervical cancer rates fell more than 60 percent. In 2010 (before the new USPSTF recommendation for starting Pap tests at age 21), the CDC reported that only 73.2 percent of women aged 18 years and over had received a Pap test in the last three years. This means that more than a quarter of American women were not following recommended Pap test screening guidelines, putting themselves at risk of not detecting the early signs of cervical cancer. Extant literature cites lack of knowledge, lack of health care coverage, uncomfortableness, and embarrassment as some of the main reasons women forego regular Pap testing. However, with the recent USPSTF recommendation for regular HPV testing combined with recent advances in cervical cancer prevention through the use of a vaccine that targets high-risk strains of HPV, cervical cancer rates are expected to continue to fall in the United States.

Despite frequent media coverage and popular awareness campaigns (i.e., pink ribbons) of breast cancer, the rates for mammography screening are still relatively low: the CDC reports only 67.1 percent of women 40 years and older had a mammogram in the past two years. Breast cancer incidence rates have remained stable from 2001 to 2010, though there was a small but significant decrease in the number of breast cancer deaths in the same time period. Research reveals that lack of health care coverage, uncomfortableness, pain from the test, and fear are all reasons women forego regular mammograms. Less research has focused on breast self-exams and clinical breast exams, though many believe these are important screening procedures in the early detection of breast cancer.

According to the CDC, the combination of the colon cancer screening tests described above have resulted in a significant decline in colon cancer incidence and mortality rates from 2001 to 2010 in the United States. Despite this, colon cancer remains the second leading cause of cancer-related death in this country, and it is estimated that 60 percent of those deaths could have been avoided if the individuals had participated in regular colon cancer screenings.

In fact, as recently as 2008, only about 10 percent of adults 50 years and older had received a FOBT in the past year and only 50.2 percent had received either a sigmoidoscopy (in the past five years) or a colonoscopy (in the past 10 years). There are many barriers to colon cancer screening including lack of health care coverage (cost), inadequate education from primary care providers about the importance of these screening procedures, discomfort, inconvenience, and fear. Improved awareness of these screening procedures, especially through community outreach programs that encourage at-home FOBT tests and improved patient-provider communication about the importance of these screenings, will help to improve the adoption of these screening procedures.

Conclusion

Patients have access to effective screening tests for cervical, breast, and colon cancers. The USPSTF provides an important service to both doctors and patients by evaluating evidence-based preventive services and providing clear recommendations for those who should receive specific cancer screenings.

For cervical, breast, and colon cancers, a number of cancer screening tests exist that are effective at detecting precancerous symptoms or early cancerous symptoms in the body. The education about these screening tests among the appropriate populations is important for ensuring they are used to promote early detection in order to give those diagnosed with cancer the best possible outcomes. As medical technology continues to develop, newer screening procedures may prove...
to be more effective and perhaps less invasive than what is available to patients today.

Katharine J. Head
Indiana University–Purdue University Indianapolis
Elisia L. Cohen
University of Kentucky

See Also: Breast Cancer; Cervical Cancer; Colon Cancer; Education; HPV Vaccination.

Further Readings

Screening, Access to

Screening, as it relates to cancer, is a strategy employed to identify undiagnosed disease. It is directed toward asymptomatic individuals or those who have symptoms that are not recognized. The goal is to identify disease early in its course when intervention and treatment are likely to be more effective than in later stages when symptoms appear. Access to and awareness of screening programs may be limited among low-income, uninsured, or underinsured patients, and less-educated population groups. In 1968 the World Health Organization established criteria for screening programs. In brief these are, as follows:

1. The condition for which screening is conducted should represent an important health problem.
2. Effective treatment for the condition should exist.
3. Facilities for diagnosis and treatment should be available to the population screened.
4. There should be a latent, asymptomatic stage of the disease.
5. There should be an effective, sensitive, and specific test for the disease.
6. The test procedure should be acceptable to the population.
7. The natural history and progression of the disease should be understood.
8. A policy on patient selection for treatment should exist.
9. The cost of screening and diagnosis should be in balance with the total medical expenditure.
10. Screening should be ongoing rather than a one-time activity.

There are numerous modalities that may be employed in screening for disease. A physical examination may be conducted and patient history taken including health habits, prior illnesses, and disease history of close relatives. Laboratory testing of blood, tissue, urine, and other substances may be done. Imaging as X-rays, computed tomography (CT), or magnetic resonance imaging (MRI) may be employed. In some cases tests for gene mutations may be conducted.

Not all screening tests are beneficial. It is important to identify the risk/benefit ratio of testing. Certain screening procedures can cause trauma or other problems. Colon cancer screening with a sigmoidoscopy or colonoscopy can cause tears in the lining of the colon or rupture. A false positive test result can lead to unnecessary procedures as well as patient anxiety. A false negative result can delay or even prevent treatment even though a cancerous condition is present. The American Cancer Society has published screening guidelines for early cancer detection in average risk and asymptomatic patients. The following is a summary.

Breast. In the population of women ages 20-plus, three modalities are specified. Breast self-examination (BSE) is regarded as optional. Education on the technique to employ, and benefits of, this procedure should be explained by a health care professional.
to women in their early 20s. For women who chose BSE the importance of reporting any symptoms should be stressed. The second modality, clinical breast examination (CBE) for asymptomatic women in their 20s and 30s should be done as a part of a periodic health examination, at minimum every three years. After 40 this should be done annually. The third modality is mammography which should be conducted annually after age 40.

Cervix. Two tests are recommended, the PAP test and the HPV DNA test. Women ages 21 to 29 should be screened with the PAP test every three years. For women ages 30 to 65 both tests should be administered every five years or the PAP alone every three years. Women over 65 with a history of normal test results or a total hysterectomy may discontinue cervical cancer screening. Women with a serious history of abnormal results continue being tested for 20 years, even if that testing continues past the age of 65.

Colorectal. For men and women ages 50 or over, a fecal occult blood test or fecal immunochemical test is recommended annually. Flexible sigmoidoscopy or double contrast barium enema every five years, or colonoscopy every 10 years is recommended. Computed tomography (CT) colonography may be conducted every five years as well.

Endometrial. Women at menopause with average risk should be counseled concerning risks and symptoms and encouraged to report bleeding or spotting to their physicians.

Lung. Current or former smokers ages 55 to 74 who are asymptomatic and apparently healthy, and who have at least a 30 pack-year history, may receive a low-dose helical CT (LDCT). Any current smoker or one who has quit within the last 15 years should be counseled by a clinician on the benefits, limitations, and potential risks associated with LDCT screening. A high priority should be given to smoking cessation counseling for current smokers. They should be informed of their ongoing risk of lung cancer. Screening should not be regarded as an alternative to smoking cessation.

Prostate. Men age 50-plus should receive a periodic digital rectal examination and prostate-specific antigen test (PSA). Men who have at least a 10-year life expectancy should receive information on the benefits, risks, and uncertainties associated with prostate cancer screening.

Cancer-Related Checkup. Men and women ages 20-plus at their periodic health examination should be examined for cancers of the thyroid, testicles, ovaries, lymph nodes, oral cavity, and skin. They should be counseled regarding tobacco use, solar exposure, diet and nutrition, risk factors, sexual practice, and environmental and occupational exposures.

The U.S. Preventive Services Task Force (USPSTF) recommends screening tests for breast, cervical, or colorectal cancer. Data from the 2010 National Health Interview Survey (NHIS) were analyzed to measure use of the recommended tests. The data were categorized by age, race, ethnicity, education, length of U.S. residence, and source of health care financing. The goal was to identify groups not receiving the benefits of screening and to identify possible means to increase screening rates. The breast cancer screening rate of potential patients was 72.4 percent, cervical cancer screening was 83.0 percent, and colorectal cancer screening was 58.6 percent. Screening rates for all three cancers were lower among Asians than among whites and blacks. Hispanics were less likely to be screened for cervical and colorectal cancer.

Asians were categorized as Chinese, Filipino, or other Asian. Hispanics were categorized as Puerto Rican, Mexican, Mexican-American, Central or South American, or other Hispanic. As might be expected, increased rates were observed in population segments with higher education, greater availability and utilization of health care facilities, and length of U.S. residence. For breast cancer, immigrant women who had been in the United States for 10 or more years were almost as likely as U.S.-born women to report having had a mammogram within the past two years whereas a significantly lower percentage of immigrants in the United States for less than 10 years reported being screened in the past two years. For cervical cancer among Asians, Filipinas were more likely to have been screened than other Asians. Those without insured access to health care were less likely to receive testing. In colorectal cancer screening whites were significantly more likely to report being screened than
blacks or Asians. Hispanics were less likely to have been screened than non-Hispanics. Among those who had been in the United States for less than 10 years and did not have a usual, nonemergency department source of care or did not have health insurance, less than a quarter reported having been screened within the recommended interval.

To improve availability of screening, Congress passed the Breast and Cervical Cancer Mortality Prevention Act of 1990, which directed the Centers for Disease Control and Prevention (CDC) to create the National Breast and Cervical Cancer Early Detection Program (NBCCEDP). The NBCCEDP funds all 50 states, the District of Columbia, five U.S. territories, and 11 American Indian/Alaska Native tribes or tribal organizations to provide screening services for breast and cervical cancer. The program is intended to assist low-income, uninsured, and underinsured women gain access to breast and cervical cancer screening and diagnostic services. In addition to other activities this program provides free or low-cost mammograms and PAP tests to low-income women with limited or no health insurance. The services provided include the following:

- Clinical breast examinations
- Mammography
- PAP tests
- Pelvic examinations
- Human papillomavirus (HPV) tests
- Further diagnostic testing based upon abnormal results
- Referrals to appropriate health care facilities for treatment

In 2000, Congress passed an amendment to NBCCEDP which gives the option to offer women who are diagnosed with cancer in the NBCCEDP access to treatment through Medicaid. All 50 states and the District of Columbia have approved this Medicaid option. In 2001, with passage of the Native American Breast and Cervical Cancer Treatment Technical Amendment Act, Congress further decreed that this option also applies to American Indians/Alaska Natives who are eligible for health services provided by the Indian Health Service or by a tribal organization. Federal guidelines establish eligibility for direct services to uninsured and underinsured women below the federal poverty level, ages 21 to 64, for cervical cancer screening, and ages 40 to 64 for breast cancer screening. Approximately 10 percent of U.S. women are eligible for NBCCEDP cervical cancer screening, and about 9 percent are eligible for breast cancer screening. Since 1991, NBCCEDP-funded programs have served more than 4.6 million women, provided more than 11.6 million breast and cervical cancer screening examinations, and diagnosed more than 64,718 breast cancers, 3,576 invasive cervical cancers, and 167,169 premalignant cervical lesions, of which 40 percent were high-grade.

Implementation of health care reform through the Affordable Care Act will increase access to breast and cervical cancer screening services for many low-income and underserved women through expanded insurance coverage. However barriers will continue to exist. Geographic isolation, limited health literacy, lack of provider availability, language barriers, and fear may play a part.

There are numerous examples of local programs that implement the concepts included in the NBCCEDP. In Alaska in 2007, the Breast and Cervical Health Check (BCHC) partnered with the Alaska Aces, a semiprofessional hockey team based in Anchorage, to plan a series of preseason hockey games focused on the importance of finding breast and cervical cancer early. The Aces, BCHC, and other community cancer groups contributed to awareness and fundraising events. The events continued in 2008 and 2009. In 2010, the Aces began having yearly general cancer awareness events, which included breast cancer and comprehensive cancer control.

In 2012, the Aces still had a focus on breast cancer, including ads on local TV. In Oregon the Oregon Breast and Cervical Cancer Program (BCCP) and the Oregon Health and Science University Center for Women's Health began working together in 2009 to increase the number of free breast and cervical cancer screenings for low-income women. Free breast and cervical cancer screenings were offered to women with monetary, logistical, or other barriers. Community donors and other funding paid for the screenings and for treatment if a woman was diagnosed with cervical or breast cancer. Later the program was expanded statewide to include women not eligible for BCCP.

In Mississippi, where African American women are more likely to die from breast cancer than women of other racial and ethnic groups, the Mississippi
Breast and Cervical Cancer Program (MBCCP) worked with faith-based organizations to educate African American women about their breast cancer risk and the importance of early detection. The MBCCP initiated a direct-mail campaign to faith-based organizations across the state, asking them to conduct outreach activities. In West Virginia in 2006, the West Virginia Breast and Cervical Cancer Screening Program (WVBCCSP) noticed fewer women being screened in Webster County, an area with high poverty rates. Because one clinic stopped providing services through the WVBCCSP, only one small clinic was available to screen all 900 eligible women in that area. Women found it hard to be screened because of the clinic’s small size and remote location. Communications between WVBCCSP and a community coalition resulted in a partnership with the Webster County Cancer Education Project, a coalition of more than 30 partners that offers cancer screening clinics, education programs on cancer prevention, and analysis of the benefits of the services. These and many others are examples of local programs to expand access to cancer screening.

Lung cancer will account for more than 224,000 diagnoses and 159,000 deaths in the United States during 2014. This malignancy accounts for more deaths than any other cancer in both men and women. Cigarette smoking is the primary risk factor for this disease. Unfortunately resistance to screening for lung cancer is inextricably intertwined with the tobacco habit. In addition to socioeconomic and educational barriers, resistance to smoking cessation represents an extra burden. Many smokers will avoid available screening partly through fear of discovery of the possible disease that their habit engenders, and partly through avoidance of advice on the ordeal of quitting.

The benefits of screening for lung cancer are demonstrable. In 2014 The International Association for the Study of Lung Cancer (IASLC) published results from an extensive study of the costs of screening and treatment that was conducted prospectively in the Pan-Canadian Early Detection Study. It was determined that the cost to screen patients at high risk with low-dose computed tomography, added to the cost of curative treatment of early stage lung cancer, is less than the cost to treat advanced stages of the disease. In addition treatment of late-stage lung cancer is unlikely to result in a cure.

Screening of high-risk populations offers other benefits. CT scanning can assist in development of drugs for treatment of early disease by tracking progress. Also, the images developed can identify the presence of chronic obstructive pulmonary disease (COPD) and obstructed coronary arteries. These are potential results of smoking as well.

A multitude of opportunities for lung cancer screening are available across the United States. Many hospitals and clinics are equipped to provide this service to high-risk populations. Although screening is not covered by Medicare or Medicaid, an independent government panel, the United States Preventive Services Task Force (USPSTF), has approved and recommended the procedure for those at high risk. Many private group plans and related insurance carriers have declared that such screening is “medically necessary.” Coverage however is not automatic in some instances, and cost sharing may be imposed. This is the case although it has been demonstrated that CT screening for lung cancer in a high-risk population is less costly than screening for breast, cervical, or colorectal cancer and the cost/benefit ratio favors lung cancer screening.

Smoking cessation should be considered essential in the screening and counseling process. Quitting smoking will have a greater effect upon the incidence of lung cancer than any screening program or treatment regimen. Cessation may be undertaken using a number of techniques: counseling from health care professionals, group counseling, medications or nicotine replacements such as patches, or simply through the will of the smoker alone. Studies have shown that the latter is the most common method, although a period of gradual reduction as a cessation strategy was demonstrated in at least one study to be ineffective. Avoidance of external cues to smoking and such factors as workplace and public place restrictions, as well as increasing the price of tobacco products through taxation, have a positive effect in deterring the habit. Self-efficacy to cease smoking and acceptance of the associated cravings and symptoms appear to be important contributors to success.

National surveys have shown that not all smokers receive advice on quitting from health care providers. A review has shown that only half of smokers received such advice from a physician or dentist during a 12-month period. Improvement in health care professional curricula and continuing education
were recommended. Mass media anti-smoking campaigns when evaluated by the U.S. Task Force on Community Preventive Services were deemed effective in combination with other interventions, but a review of effectiveness by Cochrane questioned their stand-alone role and value.

The health benefits of smoking cessation are beyond question. Within hours after quitting blood pressure and heart rate decrease, blood levels of carbon monoxide normalize, and sense of smell and taste begin recovery. In a period of a year circulation and lung function improve, breathing is easier, and the coronary risk is halved. After five years stroke risk is equal to that of a nonsmoker.

In summary, screening of asymptomatic and undiagnosed populations at risk for cancer can be a valuable strategy. Identification of the presence of disease at early stages allows intervention and treatment when most likely to be effective. On the other hand screening is not without some pitfalls. It is important to identify the risk/benefit ratio, since some screening procedures can cause trauma or other problems. A false positive test result can lead to unnecessary tests and procedures as well as patient anxiety. A false negative result can delay or even prevent treatment even though a cancerous condition is present. Access to and awareness of screening programs may be limited among low-income, uninsured, or underinsured patients, and less-educated population groups. Geographic isolation, limited health literacy, lack of provider availability, language barriers, and fear may all present barriers to the total success of screening programs.

Walter Landers  
Independent Scholar

See Also: Breast Cancer; Cervical Cancer; Colon Cancer; International Association for the Study of Lung Cancer; Lung Cancer, Non-Small Cell; Lung Cancer, Small Cell; Smoking Cessation; Tobacco Smoking.

Further Readings


Sedentary Occupations

Sedentary behavior, typically defined by activities requiring little energy expenditure such as sitting or lying down for prolonged periods, is an important risk factor associated with poor health and mortality. According to the U.S. Department of Labor’s Dictionary of Occupational Titles, sedentary occupations are those that involve sitting for most of the duration of work time including, for example, bookkeeping and computing professionals. While often used interchangeably, sedentary behavior is distinguished from physical inactivity, which encompasses both insufficient physical activity during periods of leisure as well as greater sedentary behavior both at home and in occupational settings. One of the first studies to investigate the impact of sedentary behavior in the workplace examined occupational activity and cardiovascular events among bus drivers and postal workers. In this study, researchers found a higher rate of cardiovascular events in sedentary bus drivers and mail sorters than among workers in the same industry whose occupational roles required more activity. Research has since extended to investigate the relationship between sedentary behavior in the workplace and other health-related risk factors.
A number of epidemiologic studies have identified sedentary behavior as being independently linked with chronic disease risk factors including elevated blood sugar, insulin resistance, and central adiposity. Obesity is a known risk factor for cardiovascular disease, and growing research suggests that it may also contribute to the risk for cancer. Research has shown that a body mass index (BMI | kilograms/meters²) ≥ 25 in women and ≥ 30 in men is associated with increased cancer risk, and that this association grows stronger as BMI increases. One well-known study examined the relationship between being overweight or obesity and cancer mortality in over 900,000 men and women in the United States. During a 16-year follow-up period, over 56,000 people died from cancer. Importantly, risk of cancer mortality was 50 percent and 60 percent greater for men and women with the highest BMI compared to individuals who were of normal weight.

Since the 1960s the daily amount of occupation-related energy expenditure (i.e., calories burned as result of work) has declined, which has corresponded with increases in the mean body weight for both men and women in the United States. The National Health and Nutrition Examination Survey (2008) also found that the average American adult spends approximately 55 percent (7.7 hours) of their waking time sedentary. Other studies, assessing employees that work in environments such as offices, customer service, and call centers found that 76 percent of the workday was sedentary. Thus, while sedentary workers may be less likely to be exposed to hazardous work conditions, the trade-off for prolonged periods of sitting and other work tasks with low metabolic demand may be a greater risk for obesity and subsequently cancer.

A number of biological pathways exist which may facilitate this relationship. For example, obesity is associated with elevations in blood sugar or insulin which may promote the development and growth of tumors. Adipose tissue is linked to the production of excess estrogen which at high levels is associated with increased risk of breast and certain gynecological cancers in women. Fat cells also produce hormones called adipokines, including leptin which also promotes cell growth. Obesity is also associated with chronic low-grade inflammation which may further contribute to cancer risk. Vitamin D bioavailability is also a suspected pathway independently linking sedentary behaviors to cancer risk, and recent research has linked a subset of genes related to obesity to lower levels of Vitamin D among individuals carrying these genetic variants.

Interestingly, international guidelines suggest that a reduction or return to normal body weight may reduce cancer risk. Emerging evidence suggests that people who have undergone bariatric surgery exhibit reduced cancer incidence, especially in comparison to severely obese individuals who have not had weight-loss surgery. Notably, improvement of other health-related comorbidities (i.e., hyperinsulemia) is one of the pathways thought to play a role in this post-weight loss risk reduction.

To date, several studies have evaluated the relationship between occupational sitting and cancer at multiple sites. While some studies have reported null or negative findings, others have found a positive association between mostly sedentary or sitting work histories and breast, ovarian, and colorectal cancers. Findings for breast cancer has also been noted to differ by whether women are pre- or postmenopausal, as studies have typically reported an increased risk of cancer due to sedentary work history in the latter, but not the former. More recent research suggests that occupational sitting is related to all-cause cancer mortality in women but not men.
By site, more consistent evidence has come from research investigating sedentary occupations and colorectal cancer. For example, in one study, lifestyle, physical activity, and lifetime job history were assessed in over 900 colorectal cancer patients and 1,000 control cases. In comparison to individuals with non-sedentary work histories, participants who spent 10 or more years in sedentary work had almost twice the risk of distal colon cancer and a 44 percent increased risk of rectal cancer. An important consideration from this study is that the association between sedentary work history and cancer risk remained even after accounting for leisurely physical activity. As others have proposed, this suggests that physical activity and sedentary behaviors may influence cancer risk through different mechanisms.

Despite several meta-analyses and reviews of the literature, additional research would help clarify whether sedentary work is directly linked to heightened cancer risk or merely increases the likelihood of obesity-related cancers.

Christopher L. Edwards  
LaBarron K. Hill  
Duke University Medical Center  
Jaslynn Cuff  
North Carolina Central University

See Also: Breast Cancer; Colon Cancer; Obesity.

Further Readings

Selenium comprises more than two dozen selenoproteins that the human body uses in DNA synthesis, thyroid metabolism, reproduction and to protect the body from oxidative stress and infection. This trace element, required in humans, comes in two forms: inorganic as selenite and selenate and organic as selenomethionine and selenocysteine. The soil contains the inorganic forms, and plants store the selenites and selenates so that it can be converted to organic structures.

Most of the body stores of selenium can be found in skeletal muscle where it consists of 28 percent to 46 percent of the selenium pool in the body. The plasma and serum concentrations of selenium represent the most common measurement of selenium status. Healthy people show normal selenium concentrations of 8 micrograms (mcg)/dL or higher levels.

From a historical perspective, August von Wasserman completed the first animal study that used injections of selenite to stop tumor progression in mice, in Berlin in 1911. By 1920, colloidal selenium treated breast cancer in human patients with significant results. Since the early 1900s, researchers continued to use different preparations of selenium for research treatment of many different cancers. Cancer remains the most common cause of death globally and, therefore, investigating the biology of substances like selenium may generate new possibilities for the prevention and treatment of cancers.

Food Sources of Selenium
For guidelines on the intake of selenium in food, the Institute of Medicine sets the recommended daily allowance (RDA) for adult males and females at 55 mcg per day except for pregnancy states where the selenium RDA increases to 60 to 70 mcg per day. The most abundant food sources of selenium happen to be protein foods that contain effective dietary sources of selenium, such as, egg yolks, seafood, poultry, and kidney, liver and muscle meats.
Some vegetables sources of selenium consist of asparagus, broccoli, garlic, mushrooms, onions, and tomatoes. Even whole grains (e.g., wheat germ and bran), some nuts, and seeds contain this essential mineral. In fact, one ounce of Brazil nuts contains 544 mcg; whereas, the next highest concentration of selenium is in three ounces of tuna (92 mcg).

Vegetables, grains, and seeds contain varying levels of selenium depending on the amount of selenium present in the soil. Soil with volcanic ash contains high levels and so does soil that gets its moisture from seawater. The amount of selenium in plants varies depending on the soil; factors like soil pH, presence of organic matter in the soil, and the form of selenium affect levels. Therefore, the selenium concentration in plant-based foods differs widely by geographic location. One theory indicates that the reason cancer rates remain so high in such places as Linxian, China, relates to the deficiency of selenium in the soil. Geography appears to play a significant role in cancer rates.

**Action of Selenium**

As a trace element, selenium exhibits a prominent position in maintaining a healthy state in humans. As a member of a small collection of selenocysteine-containing selenoproteins, selenium triggers both structural and enzymatic functions. Selenium deficiency amplifies infection exposure and creates alteration in mood conditions. Selenium plays a major role in redox control and antioxidant reactions, and then in membrane integrity, energy consumption, and defense against DNA damage. A group of approximately 50 diverse selenoproteins encoded by 25 separate genes facilitate the function of selenium. Selenoproteins comprise a few forms of the enzymes glutathione peroxidase, thioredoxin reductase and iodothyronine deiodinase.

Selenium exhibits a protective effect against cancer by a number of possible different methods. The mineral triggers the enzyme glutathione peroxidase, and it in turn guards against the creation of free radicals (the molecules causing damage to DNA). In laboratory studies, selenium obstructs cancer growth and helps control the normal life span of cells, guaranteeing that the cell dies when it is supposed to instead of growing wildly into a malignant cell. Selenium as an immune stimulant represents another possible mechanism. A deficiency of selenium constrains the destruction of macrophage-mediated tumor destruction and obstructs tumor necrosis factor-alpha production in animal model studies.

**Selenium and Cancer**

Laboratory and some early trials demonstrated the possibility that selenium might be effective in the prevention of a variety of cancers such as breast, bladder, esophageal, liver, prostate, and stomach. When used in combination with beta-carotene, vitamin C and E, the selenium inhibits chemical reactions that generate free oxygen radicals in the body. Free oxygen radicals damage the body’s DNA and trigger cells to produce cancers. Selenium prevents the damaged DNA particles from replicating so cancer is not produced. Consequently, the cancer is stopped before it even begins. Selenium with vitamin A and E lessens the deleterious side effects of chemotherapy drugs. It appears to augment the efficacy of chemotherapy and radiation while decreasing the damage to the body’s healthy cells. Stephen Fortmann et al. discussed the influential effects of selenium on esophageal, colorectal, lung and prostate cancers. Selenium reduces gastric and lung cancer in populations exhibiting low serum selenium levels, but individuals with normal serum levels showed no change in cancer rates.

Mahsa Jessri and colleagues conducted a case-control study of 143 subjects in Iran on the association of selenium to esophageal squamous cell carcinoma. Selenium showed a protective effect against esophageal squamous cell carcinoma with an odds ratio of 0.12 (CI 0.04-0.69).

Raluca Pais and D. L. Dumitrascu carried out a meta-analysis of clinical trials using antioxidants to prevent colorectal cancer. Many antioxidant supplements underwent review in this analysis, but only selenium appeared to possess anti-carcinogenic actions, although further research is needed.

M. Vinceti, et al., conducted a Cochrane Systematic Review of selenium cancer studies. A total of 55 observation studies found lower cancer incidence (odds ratio [OR] 0.69) and decreased cancer mortality (OR 0.60). Stomach, bladder, and prostate comprised the body sites with the most decrease in cancer occurrence. The results looked promising, but these study designs possess major limitations on quality and heterogeneity preventing accurate interpretation of the statistics.

The Cochrane Systematic Review of selenium analyzed eight randomized clinical trials (RCT).
In the eight RCTs, no clear evidence appeared that selenium supplementation lowered the risk of any of the cancers or the cancer related mortality. In fact, in the nonmelanoma skin cancer study, skin cancer risk increased (relative risk [RR] 1.44). Two other trials, the Nutritional Prevention of Cancer Trial (NPCT) and the Selenium and Vitamin E Cancer Trial (SELECT) found a possible association between type 2 diabetes, alopecia, and dermatitis to the selenium supplementation. A second NPCT found that selenium did not reduce the risk of cancers and specifically did not reduce prostate cancer.

A 2003 retrospective study showed a positive association between an initial serum selenium level and a chemotherapy delivery dose with outcome (tumor growth, disease-free survival) in non-Hodgkin's lymphoma. Earlier studies showed that many cancer patients exhibit selenium deficiency. R. Muecke and colleagues provided evidence for the positive effect of selenium supplements in patients receiving radiotherapy after surgery for cancers of the cervix or endometrium. All 81 subjects exhibited selenium deficiency by blood levels less than 84 micrograms before radiation therapy. The females underwent randomization to either the selenium treatment group (300 to 500 micrograms) or to a placebo group. The treatment group suffered significantly less radiation-induced diarrhea. The selenium produced no effect on disease free cancer survival. R. Kasseroller studied 179 post-mastectomy patients with lymphedema using a randomized controlled study design. This smaller study on selenium supplementation and lymphedema showed promising significant results of a decline in lymphedema volume and in incidence of infection at the lymphedema sites in the group treated with selenium. The action of selenium on the lymphedema remains unknown, though scientists believe selenium reduces free radicals and protects human endothelial cells from oxidative damage by inducing GPx and thioredoxin reductase as a method for reducing lymphedema.

**Selenium Neutriepigenetics**
The new term, epigenetics, describes modifications in gene expression due to heritable, but theoretically reversible, alterations in DNA methylation and chromatin structure. Epigenetic mechanisms represent new areas to investigate for cancer prevention approaches occurring early during carcinogenesis and representing potentially initiating events for cancer development. In recent years, nutriepigenetics (the influence of dietary components on mechanisms influencing the epigenome) has emerged as an exciting new field in current epigenetic research.

Carcinogenesis causes deregulation of many cellular functions and pathways. Recent evidence from in vitro studies reveal that epigenetic alterations add to the cellular defects caused by carcinogenesis, but that natural chemopreventive agents like selenium compounds potentially counteract the cancer-related epigenetic alterations by modifying the activity of DNA methyltransferases and histone transforming enzymes. The evidence so far on the anticancer effects of selenium on epigenetic mechanisms comes from animal and cell culture experiments. Future research in randomized clinical trials is needed to determine the real affect in humans.

Thomas Prates Ong and colleagues describe one study in humans showing that selenium plasma levels showed an inverse relationship with genomic DNA methylation in leukocytes. The subjects in the study comprised individuals exposed to arsenic from ground water in Bangladesh. The unknown mechanisms and significance of this study results are unclear and future research should unravel the meaning of these findings.

Juliana Xavier de Miranda and colleagues studied the use of selenium as an anti-breast cancer trace element. This laboratory study evaluated the effects of two selenium compounds, methylselenic acid (MSA) and selenite, on cell proliferation and demise and the expression of a tumor suppressor gene (RASSF1A) and epigenetic marks in MCF-7 human breast adenocarcinoma cells. Each of the selenium compounds showed diverse responses when interacting with the cancer cell line. This study demonstrated the anti-breast cancer potential of selenium, but highlighted that the response is dependent on the chemical form.

**Interactions With Pharmaceutical Agents**
Selenium possesses the ability to interact with certain medications. One medication encompasses
cisplatin, a chemotherapy agent, used to treat ovarian, bladder, lung and other cancers. Cisplatin reduces selenium levels in hair and serum. Currently, it is unknown whether the decreased levels influence the health status of humans.

Giuseppe Lippi, et al., described the interference of laboratory measurements of selenium when an injection of the contrast agent, gadolinium, transpires within two hours of using the mass spectrometry for selenium assessment. Magnetic resonance imaging (MRI) imaging uses gadolinium as a contrast agent. The contrast agent causes abnormal elevation of the selenium results.

Z. W. Liu and colleagues delineated the ability of selenium to protect against Adriamycin-induced cardiac dysfunction. Selenium supplementation protects the cardiac function with Adriamycin administration by increased expression of the KATP gene. Selenium can potentially be useful in cancer chemotherapy.

Conclusion
Selenium appears to show encouraging results for radiotherapy protection and edema treatment in cancer patients. The function of selenium for cancer prevention in healthy subjects remains controversial; though subjects with selenium deficiencies appear to benefit from supplementation. However, the recent systematic review of research on selenium and different cancers showed undisputable non-protective effects.

The recent innovation of nutriepigenetics holds the promise for novel approaches to cancer prevention and early treatment. Natural chemopreventive agents like selenium compounds can potentially counteract the carcinogenesis process.

Sharon A. Takiguchi
Independent Scholar

See Also: Alternative Therapy: Diet and Nutrition; Alternative Therapy: Herbs, Vitamins, and Minerals; Breast Cancer; Vitamins.

Further Readings


The Republic of Senegal is situated in western Africa. It is bordered on the north by Mauritania, on the east by Mali, on the south by Guinea-Bissau and Guinea, and on the west by the Atlantic Ocean. It is the 24th-most populous country in Africa and 75th in the world, with a population of over 12.9 million. French is the statutory national language and there are 38 living indigenous languages still spoken by respective ethnic groups in Senegal; the most widely spoken ethnic languages include Jola, Malinke, Mandinka, Pulaar, Serer, and Wolof. Senegal has a long tradition of modern medical practice and an even much longer history of traditional healing.

Many essential medications are in short supply in Senegal. For example, morphine is an effective and relatively inexpensive medication used for treating severe pain frequently associated with certain cancers. However, Senegal only imports about one kilogram of morphine each year, only enough to treat about 200 patients suffering from pain due to advanced cancer. Human Rights Watch reports that about 70,000 Senegalese patients annually need palliative care to control symptoms related to chronic, potentially fatal diseases. In fact, morphine is reportedly only available in Dakar, the capital, and even there access is frequently limited due to shortages. In 2013, Senegal used about 0.084 mg of morphine per capita, which is 71 times less than the global average of 5.96 mg per capita.

Alongside of, and very commonly instead of, public or private health care in Senegal is traditional medicine. This includes treatment with herbal preparations and use of plant extracts, as well as use of incantations and spiritual healing ceremonies. Traditional medicine plays a significant role, particularly in rural areas. Traditional medicine is typically less expensive and more readily accessible than the public health system. Further, many Senegalese believe that traditional healers are more powerful and take a more holistic approach than Western practitioners. In Senegal, a traditional healer is called asontena by the Jola, oh pan or koumah by the Serer, and fadjcat by the Wolof.

Traditional healers prescribe an array of medicinal plants to treat ailments, including cancers. For instance, Never-die (Morenga oleifera) leaves, referred to as nebedaye in Wolof, are used for treating over 300 diseases, including cancers. Most of these traditional medicinal preparations incorporate use of myriad local plant materials, many of which have shown medicinal properties in laboratory studies. For example, extracts of Hibiscus sabdariffa have demonstrated antitumor activities. Analysis of extracts of Peristrophe bicalyculata, which the Serer call luben and the Wolof call moto, show it as a potential source of a chemotherapeutic agent. Thus, a rather wide array of traditional medicinal preparations is available for potentially treating cancer and associated problems in Senegal.

There are serious deficiencies of modern pharmaceutical supplies, as opposed to traditional preparations, and in modern medical services for cancer and similar conditions in Senegal. According to the World Health Organization's "Health System Response and Capacity" as of 2010 there was no general availability of either chemotherapy or radiotherapy in the public health system in Senegal.

Senegal is a signatory to the Single Convention on Narcotic Drugs, Convention on Psychotropic Substances, and U.N. Convention against the Illicit Traffic in Narcotic Drugs and Psychotropic Substances. Consequently laws exist to control narcotic and psychotropic substances and precursors. The annual consumption of controlled substances is highly regulated to curtail abuse. Accordingly, the annual consumption of morphine is 0.047 mg per capita, and fentanyl is 0.0007 mg per capita. In 2010, the annual prevalence of use of all opiates as a percentage of the population aged 15 to 64 years in Senegal was 0.08 percent, which ranks it as the 116th highest country. This, as noted, makes the delivery of palliative care problematic, and the experience of living with and dying from cancers is very different in Senegal from parts of the developed world.

The average number of cancer cases annually in Senegal is 103.1 per 100,000 of the population. Cancers account for a substantial amount of disability and suffering among impacted populations. According to the World Health Organization's report "Disease and Injury Country Estimates," the age-standardized disability adjusted life year estimates for 2004, the 10 most prevalent cancers in Senegal were led by liver cancer at 388 per 100,000 population; cervical and uterine cancers at 128 per 100,000 population; breast cancer at 112 per 100,000 population; lymphomas at 89 per
Serbia

The Republic of Serbia is a central-eastern European country located in the Balkans region. The capital, Belgrade, is one of the oldest and largest in eastern Europe. Serbian history is very rich and varied, as it was influenced by many different cultures throughout the ages. The first Kingdom of Serbia was established during in 1217, under Byzantine authority and control, later to be conquered by the Ottoman Empire during the 16th century, until their annexation under the Hasburgic Crown. After World War I Serbia was part of a federation of six republics that founded Yugoslavia in 1918, but numerous ethnic, political and religious tensions arose during the 20th century, causing it to breakup. The Kosovo War, from 1998 to 1999, ended a 10-year period of political isolation that caused economic collapse, the effects of which are still felt today.

During the Republic of Yugoslavia period, healthcare was technically free because of the communist regime politics, but was practically unavailable to most people due to widespread corruption, general abuse of services, and inadequacy of equipment and supplies due to poor funding. Today’s reforms still fail to achieve a basic level of health services for all people, and only those who possess some form of health insurance can access treatment and hospitalization, although the National Health Insurance Fund (NHIF) is responsible for financing the system. Even though health structures such as

See Also: Cancer Association of South Africa; Developing Countries; Guinea; Mali.

Further Readings
hospitals and clinics are relatively well staffed with qualified doctor and nurses, the overall quality of health care is poor because of the absence of proper organization and communication between facilities, bribes and corruption, a lack of equipment, and the poor condition of buildings. Similarly, the health care system in Kosovo is organized in three sectors including primary, secondary, and tertiary health care, and shares the same economic and organizational problems of its Serbian counterpart, albeit to a lesser extent.

After World War II, in Kosovo there were only five hospitals with just nine doctors in total. Living conditions were terrible, and the illiteracy rate reached 98 percent. Today the largest tertiary care institution, the University Clinical Center of Kosovo (UCCK), houses more than 400 doctors and consists of many clinics and institutes. Among these, the National Institute of Public Health (NIPH) is Kosovo’s largest and highest medical and scientific institution, whose duty is to organize and improve public health by defining hygienic-sanitary measures and promoting medical and health education.

In Serbian men, lung cancer showed the highest incidence, followed by colorectal, prostate, and bladder cancer. Breast cancer was the most common form of cancer in women, followed by cervical, colorectal, and lung cancer. After NATO bombings in 1999 with radioactive depleted uranium (DU) ammunitions, cancer incidence and mortality in Serbia saw a progressive increase. Also, incidence and mortality are significantly higher compared to other neighboring European countries, and Serbia has the highest mortality for lung cancer in the world. Although two United Nations Environment Program (UNEP) and World Health Organization (WHO) missions from 2000 to 2001 did not find detectable widespread contamination of the ground surface by DU, a significant increase of all types of cancer was reported by local doctors and internationally recognized medical figures such as Dr. Slobodan Cikaric, president of the Association to Fight Cancer. For example, after the 1999 bombings, the rate of childhood leukemia in Kosovo was found to be 10 times higher than previous reports. Many important Serbian and Kosovar personalities died of cancer, such as the Albanian leader and former president of the Republic of Kosovo Ibrahim Rugova, and the politician Mahmut Bakalli.

Recent studies tried to find a correlation between specific genomic variations among Serbian population, and prostate cancer risk and progression. Meta-analysis studies demonstrated association between single nucleotide polymorphisms (SNPs) at locus 17q12, and at the nitric oxide synthase NOS3 gene locus, suggesting they are both genetically susceptible factors for the progression of prostate cancer and patient outcome.

Because of the generally subpar conditions of the health care system, cancer prevention is often lacking, and patients often refer to hospitals in later stage malignancies, which are difficult to treat. To solve this problem and increase early cancer diagnoses, government authorities issued prevention programs, such as a wide cervical cancer screening project that ran from 2002 to 2007 and a National Day Against Breast Cancer, launched by Fund B92 in March 2013. In 2006, the Ministry of Health of Serbia appointed the Institute for Oncology and Radiology of Serbia to write and implement a set of national guidelines for cancer prevention, designed for primary health care doctors in the country. In 2012, it was established NALOR, the National Association of Cancer Treated Patients, which is comprised of 14 member organizations among nine different cities that help support and improve the quality of life of cancer patients throughout the country.

Claudio Butticè
Independent Scholar

See Also: Breast Cancer; Cervical Cancer; Lung Cancer; Leukemia, Acute Myeloid, Adult; Prostate Cancer; Radiation Therapy.

Further Readings
Thanks to the many advances of modern medicine, there are more and more patients who survive a cancer diagnosis. As a result, there is new focus on the long-term goals of living with and surviving cancer, including healthy sexual functioning after a cancer diagnosis and treatment. There are many, many factors that contribute to healthy sexual functioning for the cancer survivor. These include such things as the physical effects of treatment, the patient’s body image, and the impact on the patient’s partner.

The Effects of Treatment
Much of the literature on sexual health and cancer treatment has focused on breast and gynecologic cancers for women, and prostate cancer for men. Sexual problems can exceed 50 percent in these populations. However, there are some common ailments that affect sexual functioning that occur across all types of cancer. A primary effect of treatment can be overwhelming fatigue. This can be a very disabling factor when discussing sexual functioning. If fatigue prevents one from performing regular day-to-day activities (e.g., showering, eating), sexual arousal may be the furthest thing from one’s mind. There are, however, several things that can be done to mitigate the effects of fatigue on sexual functioning:

Keeping a consistent sleep schedule. Having a structured sleep/wake cycle is one of the best stabilizers of fatigue.

Developing a daily schedule of activities (including sex). Returning to the normal activities of life after dealing with cancer, whether it’s an afternoon of work, or participating in the soccer practice car pool, can take some time. If one is given a finite energy supply each day, it helps to reserve enough energy to enjoy sex.

Adjusting premorbid behavioral patterns. It is important to assess the level of precancer sexual health activities and behavioral patterns. If sex occurred only once a week before the diagnosis, it is certainly not a reasonable expectation that sex will occur more often during and after cancer treatment. Additionally, other adjustments such as extended foreplay,
use of sexual aids ("toys," film, written media) may be needed to jump-start the libido, and so forth.

Decrease the level of performance expectations. Adjusting to a new body, especially if one feels "betrayed" by one's body, takes time. Deconditioning happens quickly. The effects of surgery can limit one's range of motion or sexual sensitivity, bowel and bladder issues may be factors, or negative body image (due to scars) may be a factor. Relaxation and communication can help the survivor ease back into healthy sexual activity. Sometimes "cuddling" is enough to maintain intimate contact with one's partner.

Impact on the Partner
It may be hard for the partner of a cancer survivor to navigate a new sexual relationship. Partners need to be aware that that they may be with a person that does not, in any explainable way, resemble the individual to which they were initially attracted, and there may be concerns over interest in or ability to engage in sexual activity.

Communication with one's sexual partner is the key. Often there are long periods of time for couples dealing with cancer treatment during which sex does not occur. The disease often occupies a central role in the relationship. The physical and emotional needs of the partner are often put on the back burner—perhaps resulting in feelings of resentment and anger. These feelings should be explored, so that the survivor and his/her partner can move forward. Living a new life means taking care of any baggage from one's old life so that misperceptions can begin to be healed. There is often anticipatory anxiety related to resuming one's sex life, post-cancer. It is important to realize that intimacy does not begin and end with intercourse. In time, the survivor's desire for intercourse will resume, but it may not be in the same timeframe as the partner. Stop, listen, and explore are three tips for getting a couple to reinvigorate their intimacy efforts.

Effect on Body Image
The effects of surgery, radiation, and chemotherapy can leave the survivor looking different than before treatment. For some partners, the change will not impact their sexual attraction. For others, the loss of hair, an impaired physical appearance due to surgery, and radiation burns can modify the survivor's physical appearance: sometimes to such a degree that the survivor may not feel attractive to the partner and may feel self-conscious about disrobing—and the partner may have trouble adjusting to the survivor's new body as well. In addition, the stress of having one's body poked and prodded during physical examinations may compromise one feeling like a sexual being.

Conclusion
Sexual health is a multidimensional concept and often very complicated. The health care team, along with the survivor and his/her partner, need to be open and honest all through diagnosis, treatment and post-treatment. If the treatment team addresses the sexual health of the survivor and his/her partner throughout the treatment process—from assessment through to discharge—sex may be less of an obstacle to conquer once treatment has concluded. For a couple dealing with cancer, communication and creativity can go a long way in preserving intimacy.

Barbara A. Barton
Western Michigan State University

See Also: Chemotherapy; Surgery; Survivors of Cancer; Survivors of Cancer, Families of.

Further Readings

Sézary Syndrome
Sézary syndrome is a rare but very aggressive kind of cutaneous lymphoma, or skin cancer, that affects
for the most part those over the age of 60, and as data has shown most often affects men. Because the primary symptom of the early stages involves red rashes in thick itchy patches in different areas of the body, the disease early on is often mistaken for psoriasis or eczema and treated with topical lotions and Benadryl-based or Cortisone-based over-the-counter products. Once the correct diagnosis is made—after a biopsy of the bumps that appear in the rashes (known as erythroderma), patients have a variety of options for treatment. But none actually permits remission—the prognosis for patients with Sézary syndrome is not encouraging. The disease is particularly aggressive and resists most conventional cancers treatments, including chemotherapy. The median survival rate is only two to four years.

Sézary syndrome is a particularly insidious kind of lymphoma as it masquerades as other far more benign conditions (the chemical processes behind the reddening of the skin are also responsible, for instance, for nervous or excited blushing); thus for an extended period of time when the disease is just forming, time critical to effective treatment, its symptoms raise few questions about possible cancerous involvement in patients who most often believe the red patches and the itching are simple treatable run-of-the-mill infections. Indeed, the initial research into SS was begun as part of a larger research study into tracking the signs and symptoms of venereal diseases. Algerian-born physician and dermatology researcher Albert Sézary (1880 to 1956) pioneered groundbreaking investigations into treatments of venereal diseases in the last era before the availability of penicillin.

Living in Paris, Sézary described the spread of venereal diseases, particularly syphilis, as a critical public health crisis, the moral dimension of which often convinced patients not to seek help. In studies completed between 1938 and 1949, even as France struggled within the chaos and brutalities of war and German occupation, Sézary worked with more than 5,000 syphilitics. What Sézary noticed, however, was that in rare cases the generalized erythroderma resisted conventional treatments and in fact when cells of it were put under a microscope revealed what are called transportable cells, that is infected T cells (white blood cells) that can move in turn to other parts of the body's internal systems, most notably the lymph nodes. At that point, Sézary noted, far more specific symptoms were manifested, symptoms not associated with venereal diseases, including rapid hair loss; pronounced enlargement of the lymph nodes; a thickening of the skin on the palms of the hands and the soles of the feet; loss of fingernails and toenails; unusually rapid weight loss; prolonged fevers; loss of appetite and a general malaise; and most peculiarly a tendency of the lower eyelids to flip outward. Sézary also tracked an alarming one- to three-degree drop in average body temperature as if the body were responding to a far more insidious viral invasion. In addition, the mortality rates of these isolated cases, Sézary noted, were nearly triple the mortality rates of patients diagnosed with venereal diseases, and death in these cases occurred far more rapidly. Sézary, although he had no specific medical training in oncology, suspected that this handful of cases pointed less toward the spirochetes associated with syphilis and more to the aggressive cellular self-destruction then associated with the spread of cancers.

Sézary conjectured that the impacted T cells had become cancerous and in turn had caused the massive reddening of the skin and the characteristic lumps. Although the T cells were found in the rashes and bumps, they only became a problem when they moved from the blood to the skin, the skin in a way importing the cancer itself from the T cells in the blood. Decades after Sézary’s groundbreaking theorizing, and following his lead, cancer researchers have still not been able to account for the T cell anomaly—although research in the late 1980s suggested the influence at the genetic level, specifically chromosomal abnormalities consistent with other cancer patients. But even that was conjecture. The reality is that close to a century after Sézary first isolated this type of virulent skin cancer, there is little known of its cause and advice for its prevention is the advice that generally relates to cancer-prevention (monitoring nutrition, visiting the doctor regularly, inspecting the body periodically, maintaining a general healthy lifestyle). SS is rare. It accounts for less than 3 percent of skin cancer diagnoses annually worldwide, often mistaken for the far more prevalent non-Hodgkin cutaneous lymphoma known as mycosis fungoides. World Health Organizations estimate that SS affects one in every 20 cases of mycosis fungoides.

The stages of SS are fairly typical and patterned: from itchy red patches and skin inflammation
(the condition was long known as Red Man’s Disease), the infected blood cells move from the blood to the skin surface and from there to the lymph nodes and from there grow into the ulcerated patches on the skin’s surface (tumors) that characterize the advanced stages of the disease. Although the syndrome can spread to the entire internal organ system, that is rare. It is largely manifested in the skin inflammation and in the major compromising of the lymph system.

At that point, after treating the spread with drugs including psoralen and bexarotene, three primary aggressive treatments can be applied. First, a process known as photopheresis that involves cleaning the blood entirely twice a month by filtering it through a machine as in dialysis and then recycling it back to the patient. The blood itself is shot with UV light before it is returned to the body in an effort to remove the infected T cells early on. In nonresponsive cases, chemotherapy can also be used—not only the traditional soup of chemical poisons regularly injected into cancer patients but also a special kind of chemotherapy skin lotion targeted to specifically attack the inflamed scaly body patches that have the widest and most aggressive range. And as a last stage, radiation can be used to blast the cancer cells; if the T cells have invaded the entire lymph system, doctors use total skin electron treatments, debilitating to the patient but the most effective way to target large areas of tumor growth in the lymph system. Failing that, physicians can recommend more unorthodox medical treatments that are essentially clinical trials, including the use of interferon and retinoid. At this point, however, patients are willing to try these treatments as a way for doctors and researchers to learn more about how best to approach the terminal stages of Sézary syndrome.

Joseph Dewey
Broward College

See Also: Melanoma; Mycosis Fungoides; Skin Cancer, Melanoma; Skin Cancer, Non-Melanoma.

Further Readings


Shire UK

Shire UK in the United Kingdom is an indirect wholly owned subsidiary of Shire Plc. It is a global specialty biopharmaceutical company that works closely with various professionals in the health care system, among them nurses, physicians, and home care givers. This close linking with health care professionals is intended to help develop and market medicines that improve quality of life for patients, their families and care givers. Shire UK was started in 1986, when a team of entrepreneurs began to capitalize on a number of unmet medical needs in the society. Within its first two years of operation the UK-based specialty pharmaceutical company had launched a range of supplemental calcium products for patients seeking to treat or prevent osteoporosis. Following the successful marketing of these initial products and positive consumer feedback, the company undertook innovative drug development programs. These programs saw the development of drugs on behalf of patients facing such challenging conditions as Alzheimer’s and end-stage renal failure.

The company’s operations in the UK currently comprise the original range of products, additional specialty pharma products, and therapies for genetic disorders. The operations by Shire UK are primary to the United Kingdom, especially in Basingstoke. Currently operations by the company are focused in a number of therapeutic areas which are: ulcerative colitis, seizures and epilepsy, chronic kidney disease, Alzheimer’s disease, chronic constipation, essential thrombocythaemia, Gaucher’s disease, Fabry disease, Hunter syndrome, attention-deficit/hyperactivity disorder (ADHD), and hereditary angioedema. The company has also managed
to successfully establish itself as a market leader in providing adjunctive therapies for patients with osteoporosis through a range of calcium-based supplements available. The company has a focus and dedication to gastrointestinal and renal (kidney) diseases, with products for the treatment of mild to moderate ulcerative colitis, a type of inflammatory bowel disease, and a phosphate binder for use in some patients with chronic kidney disease. Currently, Shire UK has a number of products in the UK pharma market.

Shire UK has a reputation for having a strong commitment of its employees, who aim to make a difference in the lives of patients, their families, and caregivers, as well as to the medical community. In addition to the products available in the market, Shire UK has an active community initiative that provides support to a variety of charitable events held each year. The company employees are an active part of Shire’s global Volunteer Day program whereby the company allows employees to use a day of work in a voluntary capacity. Through these, several events have been launched.

The Basingstoke Alzheimer’s Society Christmas lunch is a key event in which Shire participates. During the event, Shire UK volunteers service residents in the Alzheimer’s wing with a Christmas meal and will celebrate the day with patients.

Shire’s donation of Christmas gifts for the elderly has been running for some years and is very successful. During the event, Shire UK employees have the opportunity to accompany the organizers and hand out gifts personally.

Volunteer days that benefit local schools and charities include accompanying disabled children from a designated school with the local Rotary Club for a day of outdoor learning where students can, for example, create garden space where they can learn to grow their own vegetables.

The company supports additional charity events such as Wear it Pink Cancer Relief, Comic Relief, Macmillan’s Big Coffee Morning appeal, and the annual Jeans for Genes fundraising day where the company matches employees’ donations.

Shire’s environmental conservation activities include encouraging company employees to actively “Think Recycling” at home and at work. In the company facilities, recycling facilities are used in the office to ensure all paper, cardboard, some plastics, and office waste such as printer cartridges are recycled. In addition, all the Shire UK offices in Basingstoke have energy efficient heating and lighting that automatically switches off.

Through a partnership with a local volunteer service called “The Link,” unwanted materials such as books, CDs, clothing, household equipment, and small items of furniture are passed on to worthy causes such as children’s home, scout groups, and the local archaeological society.

Other initiatives include allowing employees to donate to their chosen charities each month directly from their paychecks, opportunities for employees to donate blood to the National Blood Service that visits the Basingstoke area twice a year, and a matching-funds program for employee fundraising activities.

In early 2014, Shire UK acquired ViroPharma, a high growth, rare disease biopharmaceutical company.

Michael Fox
Independent Scholar

See Also: Cancer Drugs, Costs and Benefits of; Drugs; Pharmaceutical Industry.

Further Readings

Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins

The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins began in 1973. Formerly the Hopkins Cancer Center, it was renamed in honor Sidney Kimmel, the founder and chairman of Jones Apparel Group, to acknowledge his $150 million donation to Johns Hopkins University. The Johns Hopkins Kimmel Cancer Center is a pioneer in deciphering
the mechanisms of cancer and new ways to treat it. It was recognized early on as a “Center of Excellence” by the National Cancer Institute (NCI), and was one of the first to earn Comprehensive Cancer Center status.

The Center is currently headed by Director William Nelson, M.D., Ph.D., recognized nationally as an expert in the translational research of prostate cancer. The Johns Hopkins Kimmel Cancer Center is one of the 41 cancer centers in the United States designated as the Comprehensive Cancer Center by the NCI. Its mission is to be a leader in scientific and medical research, and translate the discoveries into the very best cancer therapies. It has active programs in clinical research, laboratory research, education, community outreach, and prevention and control. It has 33 different specialty centers and clinics for consultancy.

The main clinical building at the Sidney Kimmel Cancer Center is the Harry and Jeannette Weinberg Building, a 350,000-square-foot facility housing the ambulatory services, an inpatient and outpatient surgical center, 16 operating suites, 62 medical oncology beds, 72 surgical beds, and 20 intensive and intermediate care beds. The Weinberg Building offers a specialized inpatient-outpatient clinic for stem cell and bone marrow transplant patients, as well as outpatient chemotherapy and inpatient units for solid tumors and hematologic malignancies.

Sidney Kimmel Comprehensive Cancer Center is internationally recognized for excellent programs in molecular genetics of cancer; brain tumor research and treatment; bone marrow transplantation; new drug development; pediatric oncology; radiation oncology; and esophageal cancer research, treatment, and prevention. The center is also known for its research in gene therapy and development of novel therapeutic approaches for the treatment of breast cancer. It provides comprehensive information and genetic counseling for patients at a high risk for the development of breast, colon, and ovarian cancers.

Patients are treated by multidisciplinary teams at specialty clinics for individualized treatment plans. The center pioneered research on cancer as a genetic disease, resulting in the development of genetic tests for hereditary cancers and the development of a stool test for colon cancer. The center was also the first to develop therapeutic cancer vaccines, especially the pancreatic cancer vaccine, and those for cervical cancer, prostate cancer, and leukemia. Research at the Sidney Kimmel Cancer Center linked DNA methylation to the leukemia precursor myelodysplastic syndrome and resulted in the approval of the first DNA demethylating agent. This work also earned recognition from the NCI for most outstanding research in the Specialized Programs of Research Excellence (SPORE), an honor that has been granted to the center multiple times. Currently, the Kimmel Cancer Center runs specialized research programs on lung cancer, gastrointestinal cancer, head and neck cancer, prostate cancer, breast cancer, cervical cancer and lymphoma.

The Kimmel Cancer Center offers fellowship programs in Hematology/Medical Oncology, Neuro-Oncology, and Pediatric Hematology/Oncology. It also offers several additional fellowship and training opportunities in Anti-Cancer Drug Development (ACDD), Training Program in the Pathobiology of Cancer, Cancer Training Fellowships in Epidemiology, and Molecular Biology & Genetics for health professionals. The center also operates several communication channels to inform the general public as well as specialists about the latest advancements in cancer research.

The Sidney Kimmel Cancer Center has a unique fellowship program called CUPID (Cancer in the Under-Privileged Indigent or Disadvantaged) with the mission to promote the discipline of Oncology to medical students interested in caring for the underserved. It is a seven-week summer fellowship and includes laboratory-based research and lectures on topics ranging from basic oncology to health care disparities. The program also includes clinician shadowing in the medical, surgical, and radiation oncology clinics. The fellows visit the NCI and interact with the researchers addressing the issues of health care disparities at a national level.

In addition, the Martin D. Abeloff Scholars Program at the Sidney Kimmel Cancer Center is a mentoring program that offers training and support to the next generation of cancer specialists.

The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins has initiated a partnership program with the Howard University Cancer Center, working toward a strong national cancer program addressing the disparity in cancer rates and outcomes in minority populations. The current
studies include translational research on the genetics of cancer in African Americans in order to identify the factors that would help eliminate cancer health disparities. It also aims to conduct research on cancer prevention and control research, and to develop novel therapeutics which could reduce the existing disparities associated with cancer treatment in African Americans.

The center is also recognized as having a highly professional nursing environment. The cancer center has an elite designation as a Magnet hospital, the highest nursing honor in the world. Over the last decade, attempts have been made to reduce hospital stays and treatment-related complications at the Sidney Kimmel Cancer Center. This move has led to a reduction of costs, even for the most intensive treatment modalities.

The Sidney Kimmel Comprehensive Cancer Center is committed to its mission of teaching, research, and patient care. The nurses working at the Kimmel Cancer Center work on the cutting-edge of clinical care and are also responsible for conducting research and developing models for patient care. The nursing teams are trained not only to work in the inpatient units, they also participate in diagnosis and therapy at outpatient clinics, and carry out detailed monitoring of the clinical trial research. The center regularly offers new courses, mentorships, seminars, and classes to the nurses.

The center provides exhaustive information on the clinical trials offering new drugs, new surgery approaches, and new treatments to patients.

Poonam Balani
Independent Scholar

See Also: Education; Poverty; Screening, Access to.

Further Readings

Sierra Leone

The Republic of Sierra Leone is a western African country rich in natural resources such as diamonds, gold, and titanium. Despite its vast natural wealth, most of Sierra Leone’s population—around 70 percent—still lives in poverty conditions. With an estimated population of 1.2 million, Sierra Leone’s largest city is Freetown, its capital. Freetown was founded in 1787, when the British Crown attempted to resettle freed black slaves after the American Revolutionary War. Through the 19th century, Freetown was the major port for liberated Africans (the so-called “Recaptives”) and African Americans and West Indians freed from slavery, giving birth to a new mixed-blood ethnicity called Creoles or Krio people.

Following the end of British Colonialism, in 1961, Sierra Leone declared its independence. After a brief period of democracy, a series of armed military coups in 1967 led to the reign of Siaka Stevens as prime minister (and later president). Stevens’ remained in power despite multiple coups attempts, and amid accusations of mismanagement and corruption, until he stepped down in 1985. Authoritarian rule survived in various forms in Sierra Leone until 1991, when Civil War erupted. The war lasted 11 years, leaving over 50,000 dead and hundreds of thousands of refugees. In 2002, United Nation military forces intervened and the rebels were disarmed. In 2007, Sierra Leone held presidential and parliamentary elections.

Today Sierra Leone is one of the least developed countries in Africa; more than two-thirds of the population is illiterate and the health care system is severely lacking in resources. In 2010 Sierra Leone Government launched a “Free Health Care Medical Insurance” system to cover all medical expenses for women who are pregnant and breastfeeding and children under five. However, in spite of the program, medical services are often charged a fee or are simply unavailable to those living in rural areas. Over 100 nongovernmental organizations (NGOs) operate in the health care sector in Sierra Leone, and funds from the United Kingdom and United Nations helped rebuild many hospitals destroyed during civil war. Among these, the most important national hospitals in Sierra Leone are Connaught Hospital, Masanga Hospital, Princess Christian Maternity Hospital, and St John of God Hospital.
In Sierra Leone cancer services are still very primitive, with almost no forms of screening or prevention, and a widespread absence of modern equipment to treat cancer patients. In 2012, a National Cancer Registry program was launched in Connaught Hospital, Freetown, with the help of World Health Organization (WHO) funds, to assess local cancer burden and major risk factors. Also a 24-bed palliative care center for patients with terminal conditions including cancer was created. Because of the absence of a national cancer registry up until very recent times, there is little statistical information about cancer incidence in the region. However, in surrounding countries in western Africa, the highest rates of cancer are of the cervix and breast cancer in women; liver and prostate cancers, and Kaposi’s sarcoma in men; and Burkitt’s lymphoma in children. Known risk factors are Human Papillomavirus (HPV) and Human Immunodeficiency Virus (HIV), alcohol consumption, smoking, and malaria. About 23.3 percent of women in the general population are estimated to harbor the HPV infection at a given time.

Getting cancer treatment in Sierra Leone is often very hard if not impossible for families that struggle even to obtain water and other basic needs. The few who can afford the trip, travel to Ghana to seek out much higher quality treatment. Cancer is often considered a taboo due to the widespread belief that it is a transmittable diseases like HIV, and radiation therapy is not available. Plans to build a radiotherapy center in 2014 and 2015 were made through various partnerships between the government, NGOs, and the International Atomic Energy Agency (IARC), however a massive Ebola outbreak in 2014 placed an enormous burden on the country’s already fragile health care system.

Public awareness projects such as “Breast Week,” which took place in 2006, provided free screenings, and education on breast cancer and importance of breast health for 1,200 women. In addition, starting in 2013, the government of Sierra Leone joined in with cancer groups around the world to commemorate “World Cancer Day,” which takes place every year on February 4.

In addition to provided education through health-awareness campaigns, many NGOs collect data about cancer patients who seek treatment inside their clinics. For example, the Thinking Pink Breast Cancer Foundation, in Freetown, built a Well Woman Clinic that provides clinical breast screenings and cancer prevention programs, and cancer support and treatment. Another important cancer center is the Lady Deborah Berewa Hospital in Lakka, a free outpatient clinic, built in 2012 by Greatest Goal Ministries, that also conducts health education and training for local health care providers.

Traditional African medicine is still a part of the primary health care system in Sierra Leone, and the Ministry of Health and Sanitation founded the construction of training schools and healing centers in Makeni and Kono. While most of the traditional African medicine consist of religious and spiritual rituals that aim to heal both the soul and the body, many practitioners claim they can assist in the treatment of cancer through herbal remedies, such as Sutherlandia frutescens (cancer bush) which is often used as a cancer tonic. Some plants used in traditional African medicine were actually found to contain alkaloids that showed antiblastic and antitumor effects, for example vincristine and vinblastine in Catharanthus roseus (Madagascar periwinkle).

Others possess a significant antioxidant power which may be used as complementary cancer therapy, such as Sorghum Bicolor (sorghum) and Moringa Oleifera (drumstick tree). Moringa leaves contain nutritional properties that have also been very useful in combatting malnutrition, especially among infants and nursing mothers, as well as for patients under cancer treatment when malnutrition is an issue.

Claudio Butticè
Independent Scholar

See Also: AIDS-Related Cancers; Breast Cancer; Cervical Cancer; Liver Cancer Adult (Primary); Lymphoma, AIDS-Related.

Further Readings
Singapore

Singapore is a city-state and island country in Southeast Asia which is on the southern end of the Malay Peninsula near the equator. The country's territory consists of a main island called Singapore Island plus about 60 small islets. The country is mostly urban with minimal vegetation. Singapore is known worldwide for its strong business and shipping functions. Manufacturing is a particularly important industry in Singapore. The population of Singapore is approximately 5.4 million based on 2013 June estimates and approximately 2 million of these are foreign-born. Seventy-five percent of the population is Chinese.

The health care system of Singapore is generally efficient, but health expenditures are relatively low for a developed country. According to the World Health Organization's (WHO) World Health Report, Singapore health care system is ranked sixth overall in the world. Singapore has had the lowest infant mortality rate in the world for the past two decades. Life expectancy is 80 and 85 for males and females respectively, placing the country fourth in the world for life expectancy. The government's health care system includes a program called Medifund for those who need help with paying for health services, Medisave to help people save for their health expenses and the government-backed Medisheld helps patients with insurance navigate the system.

With the efficient health care system, cancer is the number one cause of death in Singapore, constituting 29.3 percent of total deaths in 2009. The number of deaths caused by cancer increased from 78.2/100,000 (78.2 deaths for every 100,000 deaths) in 1970 to 111.9/100,000 in 1995. This reached a peak in 1997 with 122/100,000 rate and over the past 10 years has shown a slow decline with a rate of 94.9/100,000 in the period of 2006 to 2010. The country has the highest age-standardized rate (ASR) of cancer in southeast Asia. The incidence rates in males and females has increased for the period 2006 to 2010, compared with that reported for the period 2005 to 2009 and currently stands at 229.6 and 208.0 per 100,000 person-years in males and females, respectively. This translates into a total number of 51,657 cancer cases diagnosed in the resident population during the period 2006 to 2010. Of these cases, 48.6 percent were reported in males.

For specific cancer types, lung cancer and breast cancer had the highest mortality rates in males and females respectively. In the country, lung cancer accounted for 27.6 percent of cancer deaths among males and breast cancer accounted for 17.9 percent of cancer deaths among females. Given the high number of Chinese among the country's population, the incidence of cancer was highest among the Chinese for ethnic groups, with 23,164 males and 23,925 females suffering from the disease. For the resident population, prostate cancer lung, and colorectal were the top ranked cancers among males while lung cancer, colorectal, and breast were the top-ranked cancers among females.

Singapore Society of Oncology (SSO), founded in 1981, is a professional medical organization for all Singapore health care professionals who treat and manage cancer patients. The objectives of the SSO is providing an active platform to promote the practice of oncology through education, research, collaborations, and partnerships with allied local, regional, and international organizations. To ensure practitioners in the field of cancer are skilled for effective care, the SSO provides continued medical education and other opportunities for the cancer medical specialist community to further enhance their knowledge, skills and expertise in the rapidly changing practice of oncology.

As Singapore transitioned from a developing country to a developed country, the pattern of illnesses in the country changed within a space of a few decades. This was due to advancement in the economic status of the country and the creation of a more effective health care. However, given the complexity of cancer, it soon overtook cardiovascular...
diseases as the number one cause of deaths in the country. As a result of this, in 1992, the Review Committee on National Health Policies suggested the overall development of a national cancer center that can focus on many critical aspects of care. The national cancer center is also responsible for training oncologists and other allied health workers, facilitating and conducting cancer research, and developing cancer databases.

Currently, the country has five public and 12 private hospitals that are equipped to diagnose and initiate the treatment of newly diagnosed cancers. There also are two public institutional centers that specialize in cancer care in Singapore: the National Cancer Centre Singapore (NCCS) and the National University Cancer Institute. In addition to public institutions and facilities, the private sector has several small cancer centers. The objective of these institutions is to function as a comprehensive cancer center, providing multidisciplinary services, within their organizations. The NCCS is located at the same location as the general hospital, the largest in Singapore, with 1,600 beds. The NCCS began its operations in the country in 1996. And to effectively deliver on its operational objectives of clinical service, research and education, the center has five clinical departments: medical, surgical, oncology, radiation oncologic imaging, and palliative medicine. It also has three research divisions: clinical trials and epidemiological sciences, medical sciences, and cellular and molecular research. In its education program, the NCCS has students from the two medical schools in Singapore, local and overseas fellows, as well as pre- and postdoctoral graduate students. Through the years, the NCCS has grown in strength and numbers, and currently treats 60 percent to 70 percent of all subsidized patients and 50 percent of all cancer patients in Singapore.

The effort toward fighting cancer has seen more entrants. In Singapore, there are many charitable and welfare organizations that provide support for patients and their families. One of these is the Singapore Cancer Society (SCS) established in 1964 and endorsed by the Ministry of Health. The society plays a prominent role in the support of patients with cancer by, for example, organizing public education forums and screening clinics.

Michael Fox
Independent Scholar
See Also: China; Developing Countries; Singapore Cancer Society.

Further Readings

Singapore Cancer Society

The Singapore Cancer Society (SCS) is a cancer advocacy organization established in 1964 that addresses cancer-related issues through multiple platforms across diverse population groups in Singapore. Its vision is to become the leading charitable cancer organization in Singapore, and in the Asia-Pacific region. To target the problem of cancer in a holistic manner, SCS’s strategy is to involve both cancer patients and the general public in its outreach efforts. Specifically, SCS has seven core programs that drive its vision to become effective in combating cancer. The seven core programs are (1) community partnerships, (2) cancer screening, (3) cancer research, (4) hospice care, (5) public education, (6) cancer support service, and (7) welfare services.

Community Partnerships
SCS recognizes the important role of the community in the fight against cancer as they help raise awareness and provide financial support for its programs. An annual “Flag Day” dispatches students to different locations in Singapore to raise funds for SCS. SCS also organizes an annual “Race against Cancer” run that is a highly publicized event and “Tee for Cancer” (a charity golf event) with many participating sponsors. These community networks increase the visibility of SCS’s works.

Cancer Screening and Research
SCS offers a spectrum of affordable cancer screenings to the population. In line with its objective of minimizing the impact of cancer on health, it encourages the public to go for early screening. To increase the screening uptake, SCS offers free clinical breast examinations, Faecal Immunochemical Tests (FIT) for colorectal cancer, and Pap smears for cervical cancer throughout the year.

SCS is an active supporter of cancer research in Singapore. Since 1973, SCS gives awards and grants to cancer research in both science and social science to improve cancer treatment and patient care to enhance the quality of life for cancer patients. Some of the research areas it supports include: tumor biology, genetics, and clinical (e.g., clinical pharmacology) studies. SCS also supports social science research such as statistical analyses on factors associated with cancer patients’ psychosocial needs and well-being, as well as factors related to employers’ intent to hire and retain cancer survivors.

Hospice Care
SCS has a Hospice Care department that provides care for terminal cancer patients through a team of doctors, nurses, occupational therapists, and case workers. One of the goals of the hospice is to provide quality care to cancer patients at the last stages of their illness to ensure that they live comfortably. Since its inception in 1987, SCS Hospice Care has grown from providing basic clinical care and pain relief to include support services that target the psychosocial well-being of cancer patients. It has a structured home rehabilitation program to provide outpatient support in helping cancer patients...
gain confidence and control over aspects of their lives that were temporarily hindered because of the illness.

Public Education
SCS is active in raising public awareness of various forms of cancer in Singapore through campaigns, dialogue sessions, symposiums, and talks. SCS conducts regular talks at community centers, schools, and business corporations. To raise public awareness of risk factors as well as availability of screening and treatment options, SCS has dedicated certain months for a specific form of cancer. For example, annually the month of May is dedicated to raising awareness for cervical cancer while the month of October is for breast cancer. These campaigns are often reported in the mainstream media because of the creative and catchy campaign theme. The theme for colorectal cancer awareness month in February 2013 was “Don't Flush Away Early Detection,” while the cervical cancer awareness month in July 2013 was themed “Lift your skirt, save your life.” Some of the other cancers that are featured in the monthly awareness publicity are ovarian, prostate, gastric, and lung cancers.

Cancer Support and Welfare Services
As the process of cancer treatment can be traumatic, SCS offers rehabilitation support to help cancer patients. Cancer patients are placed in support groups. Members often meet regularly (monthly or weekly) and share coping strategies and discuss the challenges faced—professional health care providers and therapists are often present to give patients additional insights and to correct any misconceptions. These support groups also engage in activities such as workshops and recreational activities.

The welfare services arm of SCS seeks to provide financial aid to help needy cancer patients buffer treatment and living costs through various funding schemes. The SCS Cancer Treatment Fund helps cancer patients offset part of the cost of chemotherapy drugs while the SCS Welfare Aid Fund provides support for necessary medical products such as colostomy bags. SCS Hospital Transportation Services provides free transportation for low-income patients from their homes to the hospitals. The SCS Help the Children and Youth Program helps reduce the cost of education by providing children and adolescent patients with free tuition, school allowance, and awards for academic achievement.

Conclusion
SCS has grown to become one of the largest cancer advocacy groups in Singapore. To achieve its vision of becoming a stellar resource for the cancer community, it has expanded beyond raising public awareness and education to include wide-ranging patient care and welfare services, as well as contributing to cancer research locally.

Shirley S. Ho
Edmund W. J. Lee
Nanyang Technological University

See Also: China; Developing Countries; Singapore.

Further Readings

Siteman Cancer Center
The Siteman Cancer Center is a cancer treatment and research facility located in St. Louis, Missouri. It is affiliated with Barnes-Jewish Hospital and Washington University School of Medicine. The center specializes in imaging, genomics, and prevention strategies that have contributed significant advances to cancer research and treatment. Through its partnership with the Washington University School of Medicine, researchers at the center have developed an interdisciplinary approach to cancer care. Patients and survivors are treated by multidisciplinary teams of doctors. Significant fields of research include breast cancer research,
cancer and developmental biology, oncologic imaging, tumor immunology, as well as cancer prevention and control. The center is a leader in gene therapy, clinical trials, vaccines, chemoprevention, and nanotechnology.

The Siteman Cancer Center opened in 1995 and serves over 40,000 patients annually. The center has operated under the direction of Timothy Eberlein, M.D., since it was founded. In 2004 it was designated a Comprehensive Cancer Center (CCC) by the National Cancer Institute (NCI). In 2006 it became one of the 25 members of the National Comprehensive Cancer Network (NCCN), a non-profit group of cancer centers committed to the improvement of cancer care and treatment.

A collaboration between the Siteman Cancer Center and the Genome Institute at Washington University has led to groundbreaking research on cancer and genetics. The center has identified genetic mutations that can reduce the efficacy of conventional cancer therapies and lead to increased mortalities. By sequencing the complete genome of patients with acute myeloid leukemia (AML), scientists at the center discovered that a single gene mutation can inhibit the efficacy of treatment. AML patients with a mutation of the gene DNA methyltransferase 3A (DNMT3A) lived on average just over a year, while patients in the study without the mutation lived for an average of 3.5 years. The identification of the DNMT3A mutation could lead to new drug research and therapies for the AML patients for whom current treatments are less effective.

Partnering with the Mallinckrodt Institute of Radiology at Washington University, researchers at the center developed new methods for diagnosing cancer and for monitoring cancer treatments. The Mallinckrodt Institute of Radiology’s Cancer Center for Clinical Imaging Research (CCIR) is dedicated to the advancement of research in clinical imaging. Located within Barnes-Jewish Hospital, the CCIR serves the combined goals of imaging research and patient care. The CCIR employs a state-of-the-art scanner that combines positron emission tomography (PET) and magnetic resonance imaging (MRI) scanning capabilities. The scanner simultaneously performs both PET and MRI scans, and produces finely detailed images. The PET/MRI reduces the radiation exposure risk to patients by emitting about half of the radiation of combined PET/computed tomography (CT) scanning. The CCIR builds upon a long history of PET scanner research at Washington University where Michel Ter-Pogossian developed the first PET scanner in the 1970s.

The Siteman Cancer Center’s Program for the Elimination of Cancer Disparities (PECaD) was established in 2003. PECaD works to remove social barriers from cancer education, prevention, diagnosis, and treatment. Through community outreach in the St. Louis region, PECaD is developing a national model for reducing and eliminating the uneven distribution of cancer resources among minority populations and the medically underserved. Studies show that demographic factors such as income, age, race/ethnicity, and access to health insurance have an effect on rates of cancer prevention and treatment resources among patients. Medically underserved women, for example, cited variables including fear of cost, lack of transportation, and lack of childcare as obstacles to mammogram screening. Siteman Cancer Center’s Mamography Outreach Registry was developed in 2006 to determine the effectiveness of mobile mammography among underserved urban and rural women of Missouri.

PECaD has developed a network of cancer community partnerships that bring together cancer survivors, advocates, community representatives, and academic faculty to create program strategies to eliminate cancer disparities. These cancer community partnerships include the Breast Cancer Community Partnership (BCaP) in North St. Louis County, the Prostate Cancer Community Partnership (PCCP), and the Colorectal Cancer Community Partnership (CCCP). These community partnerships help connect cancer patients to existing services and educate the community about cancer prevention. PECaD engages in public service messaging campaigns through local newspapers, billboards, radio stations, and public libraries in the St. Louis area. The center has been instrumental in the development of interactive technologies such as a free mobile app for mobile devices that evaluates risk factors for cancer, diabetes, and other diseases.

The institution is named for Alvin J. Siteman, former president of Flash Oil Corporation and former director of Barnes-Jewish Hospital. In 1999, Alvin J. and Ruth Siteman donated $35 million to Barnes-Jewish Hospital and Washington University School of Medicine for cancer patient care, research, and community education. In 2001 Alvin J. Siteman committed a further $1 million per year to fund prevention and diagnostic programs. Along
with the CCC designation, the center receives yearly research grants from the NCI.

Jessica A. Hutchins
Independent Scholar

See Also: Breast Cancer; Disparities Within Nations (Elimination of Cancer); Experimental Cancer Drugs; Gene Therapy; Genetics; Leukemia, Acute Myeloid, Adult; National Cancer Institute; Technology, Imaging.

Further Readings

Skin Cancer, Childhood

Childhood skin cancers are exceedingly rare, accounting for 1 percent to 3 percent of all cancers diagnosed in the pediatric population. In order of incidence, malignant melanoma, basal cell carcinoma (BCC), and squamous cell carcinoma (SCC) account for the overwhelming majority of cutaneous pediatric malignancies. In most cases, children with skin cancer possess an underlying risk factor such as a precursor lesion or other predisposing condition. Given that the prognosis of skin cancer is highly dependent on early detection, it is crucial that clinicians have adequate familiarity and index of suspicion for skin cancer in children.

Malignant Melanoma
Malignant melanoma is a tumor of melanocytes, the cells responsible for the production of the dark pigment that accounts for the color of skin. Malignant melanoma is the most common skin cancer in the patients under the age of 20, with approximately 400 new cases diagnosed in the United States each year. Though malignant melanoma may arise de novo, it is estimated that up to 65 percent of cases in children arise from a preexisting nevus. Malignant melanoma most commonly affects children with fair skin, blonde or red hair, and blue eyes, though cases of pubescent malignant melanoma are more frequently observed in non-Caucasian patients.

Pediatric malignant melanoma is frequently found on the head and trunk region in boys, but is more common on the arm and leg region in girls. It typically presents as an enlarging, raised papule that is brown or black. However, pediatric cases of malignant melanoma are frequently amelanotic, signifying a lesion that is red, pink, or white in color. In contrast to benign lesions, malignant melanomas tend to be asymmetric with irregular borders, heterogeneous in color, and larger than 10mm in diameter. It is common for patients to report associated itching, ulceration, bleeding, crusting, or pain. On diagnosis, examination of regional lymph nodes is critical, as palpable lymph nodes suggest metastatic spread and are an indication for more extensive workup.

Several conditions are associated with a significantly increased risk for the development of malignant melanoma in the pediatric population. The most common among these conditions are xeroderma pigmentosum, giant melanocytic nevi, and Werner syndrome. Additionally, increased numbers of melanocytic nevi, dysplastic nevi, or freckles portend heightened risk for malignant melanoma. Other risk factors include immune system deficiency or suppression, fair complexion, red hair, blue eyes, freckles, inability to tan, high levels of ultraviolet (UV) light exposure, and blistering sunburns. Finally, a family or personal history of melanoma or retinoblastoma is indicative of higher risk for malignant melanoma among children.

With suspicion of malignant melanoma, full thickness excision is required to assess depth of the lesion, which then guides all further treatment. The treatment of choice for localized melanoma is surgical resection, with margins that range from 0.5 centimeter (cm) to 2 cm, based on the thickness of the lesion. Sentinel node biopsies are offered to patients at increased risk of spread, with complete lymph node dissection indicated with a positive initial test. Patients who are found to have regional lymph node involvement are offered treatment with adjuvant interferon alfa-2b.
For patients with metastatic disease, prognosis is poor, but potential treatment options include dacarbazine, temozolomide, sorafenib, or interleukin-2. Newer therapies that have specifically shown promise in pediatric trials include ipilimumab and vemurafenib. As in adults, the prognosis of malignant melanoma is based on thickness, depth of invasion, and presence of ulceration. Over 75 percent of pediatric cases are localized with excellent prognosis. Overall, five-year survival in individuals under 20 years old with malignant melanoma approaches 90 percent.

**Basal Cell Carcinoma**

BCC is a tumor of the basal cells of the epidermis. Lesions typically present as raised growths that are lumped or ulcerated. Pediatric BCC is most common on the upper, central portion of the face, as well as other uncovered regions that have high predilection for sun exposure. In general, BCCs are locally invasive tumors with slow growth that are highly unlikely to exhibit metastasis.

Risk factors for pediatric BCC include prolonged UV sunlight exposure, and exposure to radiation therapy for the treatment of other malignancies. The diagnosis of BCC should prompt further workup for common underlying conditions, such as xeroderma pigmentosum, albinism, BCC nevus syndrome, Gorlin syndrome, Bazex syndrome, or Rombo syndrome. As in malignant melanoma, diagnosis of pediatric BCC is often delayed due to a low index of suspicion in children. Regional lymph nodes should be inspected extensively with diagnosis, in order to rule out local invasion. The treatment of choice is complete excision, but curettage and electrodessication may be considered in smaller lesions. The prognosis of SCC is variable. Smaller lesions stemming from normal skin are highly unlikely to metastasize. On the other hand, lesions secondary to radiation exposure, scars, or chronic wounds tend to be more aggressive.

**Squamous Cell Carcinomas**

SCC is a malignant tumor of squamous epithelial cells within the epidermis. SCC is very rare in children, with only a handful of cases reported each year. Lesions are characteristically red, scaly, and raised, with variable induration. They may be associated with telangiectasias, crusting, ulceration, or necrosis. The most common location of SCC in the pediatric population is the lower face, including the lower lip and pinna of the ear, as well as the dorsal aspects of the hand and forearm. In the pediatric population, lesions are frequently mistaken for sites of eczema, infection, or trauma.

SCC may arise in normal skin, but is frequently observed on skin with prolonged sun exposure, or with damage due to trauma, burns, or chronic inflammation. As with malignant melanoma and BCC, SCC is associated with a number of underlying conditions that include xeroderma pigmentosum, immune system deficiency or suppression, chemotherapy, radiation therapy, and HPV infection, particularly in the context of immunosuppression.

Histological evaluation of SCC is based on lesion depth and the cytological features of malignant cells. As in BCC, the treatment of choice is complete excision, but curettage and electrocautery may be considered in smaller lesions. The prognosis of SCC is variable. Smaller lesions stemming from normal skin are highly unlikely to metastasize. On the other hand, lesions secondary to radiation exposure, scars, or chronic wounds tend to be more aggressive.

Kourosh Beroukhim  
*David Geffen School of Medicine at UCLA*  
Navid Ezra  
*Indiana University School of Medicine*

**See Also:** Childhood Cancers; Skin Cancer, Melanoma; Skin Cancer, Non-Melanoma; Ultraviolet Radiation Related Exposures.

**Further Readings**


**Skin Cancer, Melanoma**

Melanoma is a tumor produced by malignant transformation of pigment-producing cells (melanocytes)
found primarily in the skin, but also located in the eyes, gastrointestinal tract, mucous membranes, brain, and meninges. The epidemiology, risk factors, and clinical presentation of skin lesions suspicious for melanoma are important determinants in diagnosis and prognosis, and help dictate appropriate management.

**Epidemiology**

Melanoma is the sixth most common form of cancer in the United States, and its incidence has nearly tripled in the Caucasian population in the last 20 years. Incidence in Caucasian men and women has increased significantly by approximately 1.6 percent in the last decade, but remained level among other races. Caucasian individuals are at significantly greater risk for disease development; however, mortality rates are higher for African Americans and Hispanics due to the subtype of melanoma that affects these races, as well as more advanced disease at presentation. Although melanoma accounts for only 4 percent of all skin cancers, it is the leading cause of skin-cancer related deaths, accounting for over 75 percent.

The current lifetime risk for developing melanoma in the United States is one case per 33 Americans. Outside of the United States, the highest incidence is reported in Australia and New Zealand, owing to high ultraviolet light exposure in a predominately white population. Invasive melanoma has a higher predilection for females in patients under 39 years of age, whereas in patients aged 40 and older, there is a higher incidence in males. Yet, the median age at diagnosis is 59 years, and mortality risk increases significantly in persons older than 50.

**Risk Factors**

Certain personal characteristics place individuals at higher risk for the development of melanoma. These include blue eyes, fair/red hair, pale complexion, skin that is easily sunburned, high number of melanocytic nevi (colloquially referred to as moles), and various immunosuppressive states, such as solid organ transplant patients. Furthermore, lifetime exposure to UVB and UVA radiation, number of blistering sunburns, use of tanning beds, positive family history, the presence of an evolving skin lesion (the most important clinical warning sign), and older age, all confer greater risk for the development of melanoma.

Prevention of melanoma centers on sun protection: specifically, avoiding the sun during mid-day, wearing sunscreen year-round, wearing protective clothing, avoiding tanning beds, and becoming familiar with one’s own skin in order to notice changes that may require attention. Nevertheless, these prevention strategies have yielded only modest results as the incidence continues to increase in Caucasians and has remained stable among other races.

**Presentation**

The most common warning sign for the development of melanoma is a new or evolving skin lesion. Characteristics that are suggestive of malignancy are summarized by the acronym “ABCDE,” which include the following:

- A: Asymmetry
- B: Border irregularity
- C: Color variations (especially blue, red, or white tones in a black or brown lesion)
- D: Diameter greater than 6mm
- E: Evolving over time or an elevated surface

Lesions demonstrating these characteristics are suspicious for melanoma, and diagnostic accuracy increases when these criteria are found in combination. Although symptoms such as bleeding, ulceration, itching, and pain are less common, a pigmented lesion with such characteristics warrants evaluation as well.

In Caucasian patients, lesions are typically found on the trunk and lower legs, while in African Americans, Hispanics, and Asians, lesions are typically located on the palm, plantar surface of the foot, subungal, and mucosal sites. There are four major subtypes of cutaneous melanoma, with each subtype portending a different race predilection and prognosis. These subtypes include superficial spreading melanoma, nodular melanoma, acral lentiginous melanoma, and lentigo maligna melanoma; differentiation between these subtypes depends primarily upon histologic growth pattern.

**Workup**

A careful history, review of systems, and physical exam are important factors in accurate clinical diagnosis of melanoma, and all lesions suggestive of melanoma should be biopsied to confirm the diagnosis. The approach to skin biopsy varies depending on the size of the lesion and the anatomic site, but a general guiding principle is that the thickest part of the lesion should be sampled and a low threshold for biopsy should be maintained.
Histologic classification of the biopsy specimen facilitates diagnosis of the particular subtype of melanoma and allows for staging of the malignancy. Various classification schemes for disease staging have been proposed, including the Breslow classification, Clark classification, and TNM (tumor, node, metastasis) staging system; each of these classification schemes stage the tumor based on the thickness of the lesion or the anatomic level of invasion into the skin layers. The TNM system further stages the disease based on the presence of lymph node metastasis and metastasis into distant organs. Lesions greater than 1mm in thickness, and the presence of metastasis are poor prognostic factors.

Management: Medical and Surgical
Following biopsy-confirmed diagnosis of melanoma, a wider excision of the tumor is employed, although further surgery is usually required to reduce the risk of recurrence. Indeed, surgical excision is the standard of care for localized cutaneous melanoma, and surgical margins vary depending on the stage of the tumor. Current recommendations suggest surgical margins of 5mm for melanoma in situ, 1cm for melanomas ≤ 2mm in depth, and 2cm margins for melanomas greater than 2mm thick.

Adjuvant therapy may be required for patients with high-risk melanomas, including high-dose interferon, various chemotherapy agents, immunotherapy, and radiation therapy following resected advanced-stage melanoma. Although adjuvant medical therapies may prolong the time until relapse, a survival benefit has not been consistently demonstrated. Clinical trials are currently underway exploring the benefits of interferon alfa, melanoma vaccines, and biologic response modifiers. Basic and translational research has generated multiple novel therapeutic modalities that have demonstrated promising early results, such as the BRAF inhibitor Vemurafenib.

Patients are monitored regularly after a diagnosis of cutaneous melanoma, because most metastases occur within the first three years after treatment of the primary lesion. Regular skin examinations are recommended for the rest of the patient’s life to detect recurrent/metastatic disease and to evaluate for new primary melanoma.

Prognosis
Prognosis after diagnosis depends on several factors, including the thickness of the tumor, presence or absence of histologic ulceration, and, most importantly, lymph node involvement and distant metastasis. Survival is quantified by the five-year survival rate, which is the percentage of patients who live at five years after cancer diagnosis, excluding those that died of other causes.

Cutaneous melanomas (stage I and II) with thin primary lesions (≤1mm) have a five-year survival of 94 percent to 97 percent, intermediate thickness (1.01mm to 4mm) have a five-year survival rate of 68 percent to 91 percent, and high-risk tumors (>4mm) have a 71 percent five-year survival rate without ulceration and a 53 percent survival rate with ulceration of the primary tumor. Indeed, ulceration confers a significantly reduced five-year survival at every tumor stage, regardless of lymph node involvement. Regional lymph node involvement (stage III) is associated with a five-year survival of 38 percent to 78 percent depending on the number of nodes involved. Patients with distant metastasis (stage IV) have a grim prognosis, with median survival of seven to eight months and a five-year survival of <20 percent.

Saami Khalilian
Natanel Jourabchi
Johns Hopkins University School of Medicine

See Also: Skin Cancer, Childhood; Skin Cancer (Nonmelanoma); Sun Exposure (Australia).

Further Readings

Skin Cancer, Non-Melanoma

Nonmelanoma skin cancer is the most prevalent type of cancer in the United States and can be
diagnosed by a physician through clinical examination of the skin, with biopsy of suspicious lesions for histological confirmation. Among this subset of cancers, up to 80 percent occur as basal cell carcinomas while nearly 20 percent occur as squamous cell carcinomas. The development of both cancer types is highly associated with ultraviolet (UV) sun exposure and therefore proper sun protection is the most effective risk reduction strategy. Treatment options are dependent on the location and severity of the lesion in question. Overall, prognosis is typically favorable, especially when the lesion is discovered and treated early.

**Epidemiology**
Basal cell carcinoma (BCC) is the most common type of nonmelanoma skin cancer, responsible for up to 80 percent of cases. Its prevalence is largely dependent on geographic location. Populations closer to the geographical equator are at higher risk of BCC and Australia has the highest reported incidence rates of BCC, between 1 percent and 2 percent per year, followed by the United States and Europe. In particular, individuals with fair skin, history of sun-damaged skin, and high exposure to UV radiation are more commonly affected. The lack of organized cancer registries in many countries makes it difficult to approximate the number of patients worldwide suffering from BCC.

Squamous cell carcinoma (SCC) is the second most common type of nonmelanoma skin cancer in the United States after BCC, responsible for nearly 20 percent of cases. The incidence of SCC has increased during the past 20 years due to an aging population, increased sun exposure, and improved detection. Similar to BCC, SCC is more prevalent in areas closer to the equator with more UV exposure, and in the older population, and less common in darker skinned individuals. Studies suggest that people with intermittent sun exposure are at higher risk for BCC, while individuals with chronic sunlight exposure have an increased risk of developing SCC.

**Etiology and Prevention**
The development of BCC is associated with genetic factors, such as individual skin phototype, and exposure to ultraviolet radiation in the UVA and UVB spectrum. It is postulated that mutations in the p53 tumor suppressor gene in the basal cell layer of the epidermis play a role in BCC development. Tumorigenesis of BCC is also linked to constitutive activation of the sonic Hedgehog cellular signaling pathway, though the exact mechanism is not yet well understood. Similar to BCC, SCC is believed to primarily develop from UV-induced mutations in epidermal keratinocytes. Mutations in the p53 tumor suppressor gene, as well as inhibition of the Raf kinase, have also been demonstrated in cases of SCC. These mutations are believed to prevent apoptosis and allow for proliferation of genetically mutated keratinocytes.

Measures for preventing BCC and SCC include reducing exposure to ultraviolet radiation from the sun. This can be accomplished by avoiding sunlight during peak hours of the day, wearing sunscreen that protects against both UVA and UVB radiation with a sun protection factor (SPF) of 40 or greater, routine self-skin examinations for early detection of potentially malignant lesions, and regular visits to a dermatologist for professional skin examinations. In addition, wearing sunglasses, a brimmed hat, and avoiding tanning salons can also help reduce the risk of these skin cancers.

**Diagnosis**
Patients who are fair-skinned, have had a history of considerable sun exposure or skin burns,
and anyone with concerning skin lesions, should undergo a regular whole body skin examination by a dermatologist to check for skin cancers. The dermatologist checks for skin findings such as pink pearly papules, nonhealing scabs or ulcers, nodules with rolled borders, and other lesions that may be suggestive of skin cancer. A skin biopsy is typically performed to provide histological confirmation of the diagnosis. The histological findings can further provide information about the tumor grade, prognostic factors such as tumor differentiation, depth, presence of perineural invasion, and risk of recurrence. Even though skin cancers can develop on any region of the skin, physicians can expect to find most lesions in sun-exposed parts of the body such as the head, face, and extremities.

**Treatment**

Once diagnosed, treatment of nonmelanoma skin cancer depends on multiple factors, including the location, size, and histological grading of the lesion, in association with findings such as poorly defined lesion borders, rapid growth, and tendency of the tumor to recur.

Surgical excision is typically the treatment of choice, in patients who are an appropriate surgical candidate. Other treatment options such as electrotherapy, cryotherapy, topical medicines, and radiation therapy may also be used in certain patient populations. Mohs surgery may be utilized, especially when the lesion is on a cosmetically sensitive area such as the face. This surgery consists of complete examination of the surgical margin using intraoperative sectioning and histological staining to confirm tumor removal. Complete circumferential peripheral and deep margin assessment is another surgical option, especially for SCC. For unresectable or metastatic SCC, chemotherapeutic agents can be utilized, and if the cancer has infiltrated the lymph nodes, aggressive surgical resection may be necessary with potential adjuvant radiation therapy.

**Prognosis**

The prognosis for patients with BCC is excellent if proper treatment is carried through in the early stages of the lesion. BCC rarely metastasizes and is a very slow growing tumor. Studies indicate that the metastasis rate of BCC is as low as 0.05 percent. If a non-metastasized lesion is left untreated it may ulcerate and pose wound-healing issues. When metastasis occurs, the lesions are usually deeply invasive or large in area, and can spread to regional lymph nodes, lungs, and bones. If metastasis occurs the prognosis is tends to be poor, with a median survival time of approximately 10 months after diagnosis of metastatic BCC. Approximately 20 percent of treated patients may develop a new BCC within one year, and 40 percent within five years, of the initial diagnosis. Frequent follow-up is recommended to check for recurrences or new malignancies.

The prognosis for SCC is also favorable. SCC generally has a low recurrence rate with appropriate treatment and management. Approximately 75 percent of recurrences occur within one year of the initial treatment, and metastasis occurs in 2 percent to 5 percent of cases. If the tumor metastasizes, it commonly infiltrates local lymph nodes or spreads to distant sites, with 10-year survival rates of 20 percent and 10 percent, respectively. Furthermore, patients treated for SCC are at an increased risk of a second skin cancer, as well as cancers elsewhere in the body, thereby making regular visits to the physician very important for surveillance of their condition.

Daniel Yazdi
David Geffen School of Medicine at UCLA
Natanel Jourabchi
Johns Hopkins University School of Medicine

**See Also:** Skin Cancer (Melanoma); Skin Cancer, Childhood; Sun Exposure (Australia).

**Further Readings**


**Skin Carcinoma, Merkel Cell**

Merkel cell carcinoma is an aggressive form of skin cancer and neuroendocrine tumor, also known as primary small cell carcinoma of the skin, primary neuroendocrine carcinoma of the skin, or trabecular carcinoma of the skin. Most—about 80 percent—of Merkel cell carcinomas are caused by the Merkel cell polyomavirus (MCV). MCV was discovered in 2008 at the University of Pittsburgh, and is one of seven viruses that have been discovered to cause cancer in humans. Polyomaviruses are small double-stranded DNA viruses, and only five have been discovered that infect humans—MCV is closely related to a polyomavirus that infects African green monkeys, supporting the hypothesis that MCV has coevolved with primates. The discovery of the virus may lead in turn to a vaccine which, like the human papillomavirus vaccine, could prevent the development of Merkel cell carcinoma, or could assist the immune system in fighting existing tumor cells. The cause of MVC-negative Merkel cell carcinomas is unknown.

Merkel cells are oval receptor cells found in the skin, and are involved in the sense of touch, especially our ability to distinguish shapes and textures through touch. They’re clear cells found at the bottom of sweat duct ridges, and can especially be found in association with sensory nerve endings. Much about Merkel cells remains unknown, from the mechanisms of their involvement with the sense of touch to their possible neuroendocrine function to whether their origin is in the epidermis or the neural crest.

MCC is twice as common in men as in women, and is more common in whites than non-whites. Advanced HIV, chronic lymphocytic leukemia, and other immune disorders greatly increase the odds of developing it. It typically presents in white men ages 60 to 80. Because it’s so rare, accounting for about one in 1,000 skin cancer cases, it is often initially mistaken for another skin cancer like basal cell carcinoma or malignant melanoma, or for a benign cyst. The first symptom of MCC is usually a visible dome-shaped tumor on the surface of the skin that is red, blue, or flesh-colored. Firm and painless, they can appear anywhere on the body, about half of them appearing on sun-exposed parts of the head and neck. Usually starting small—the size of a pimple or insect bite—they expand quickly. This often leads to rapid metastasis as the cancer infiltrates subcutaneous fat, muscle, or fascia, and expands beyond the skin to the lymph nodes, or through the blood vessels to the liver, lung, bone, or brain.

MCC is similar enough to other skin cancers that frequently it is not until the pathological examination after it has been removed surgically that it is identified, because so little differentiates it from other skin cancers. Usually a margin or “cuff” of healthy tissue is removed from the surrounding area in order to help prevent local recurrence; if the lesion has developed beyond one centimeter in diameter, lymph nodes may be removed as well. Sentinel lymph node biopsy is important because it has detected the spread of MCC in one-third of patients whose cancer had been underestimated.

Radiation therapy is a common treatment for MCC, usually with a very large field of exposure, because of the cancer’s aggressive metastasis. Radiotherapy has been shown to significantly reduce the rate of recurrence, and a patient with a negative sentinel lymph node biopsy and no distant metastases has a 90 percent five-year survival rate with postsurgical radiotherapy.

MCC risk factors probably include sun exposure and exposure to UV light through artificial sources like tanning beds, though this isn’t known for certain. Merkel cell carcinomas have a 60 percent five-year survival rate overall.

Bill Kte’pi
Independent Scholar

**See Also:** Radiation Therapy; Skin Cancer, Melanoma; Skin Cancer (Nonmelanoma).

**Further Readings**


Johannessen, J. V. and V. E. Gould. “Neuroendocrine Skin Carcinoma Associated With Calcitonin
Skipper, Howard E.

When Dr. Howard Earle Skipper was born in Avon Park, Florida, at the height of World War I (on November 21, 1915), the idea of treating cancer by injecting toxic chemical compounds directly into the blood stream in an attempt to stop the furious cell division and uncontrollable tumor construction typical of the disease was dismissed by the most respected cancer specialists as crude medicine that often caused the patient more agony than the cancer, and seldom stopped the cancer’s spread. Ironically, it was during World War I that Allied doctors first noticed the particular killing strength of chemical compounds, specifically nitrogen mustard, that went into producing that war’s most controversial weapon responsible for massive civilian casualties—mustard gas. Nitrogen mustard worked by simply killing all the cells it contaminated with a nearly 100 percent rate. More than 40 years later, after his own stint in the biochemical division of the Army during World War II, Skipper would be among the first and certainly the most prominent research oncologists to glimpse the potential and to test the viability of nitrogen mustard not as a weapon but rather as a potent, potentially lifesaving anticancer medicine.

Little in Skipper’s early years would have predicted a nearly 40-year career in the quiet of a research laboratory—he grew up in Sebring, in central Florida’s rich farmlands, working on his father’s cattle ranch and earning extra money performing daring diving exhibitions for tourists in the summer. At the University of Florida, he earned a full athletic scholarship, a commanding presence on both the football team and the swim team. But science was his passion. He completed his B.S. in 1938, his master’s the following year, and his doctorate in biochemistry and nutrition in 1941, all in Gainesville. After completing his doctorate, he immediately enlisted in the army and served in the toxicology section of the army’s medical division in Bethesda, Maryland. He had a keen interest in chemical weapons, particularly the strength of nitrogen mustard. He was convinced that the compound could be used in the chemical treatment of certain cancers. There was at the time no specific research to back up his intuition. Much later he would credit that spark of informed guessing, which he called inductive reasoning, as the cornerstone of his revolutionary reconceptualization of chemotherapy.

However, he needed a laboratory. He was offered a position to help start and then direct a biochemistry department at the Southern Research Institute in Birmingham, Alabama. When Skipper made it clear he would take the position only if he could follow his hypothesis about nitrogen mustard, the Institute agreed. Skipper quietly, methodically went about recruiting a staff of researchers, including virologists, organic chemists, biologists, and oncologists. It was a revolutionary idea, to secure different fields of research to work together, but Skipper, with his unassuming demeanor and his general disdain of the egoism of leadership, preferring the camaraderie of teamwork, was in many ways the perfect choice for director.

Skipper began by having the team gather hard data that his intuitive leap lacked. The research team at Southern Research earned a national reputation for its groundbreaking use of animal models, in this case mice, to trace the effects of different combinations of nitrogen compounds on cells. They studied the cells that survived the chemical doses and those that did not. They measured different levels of dosage and kept meticulous records on the progress of the cancers and the tumors and most importantly, measured the necessary intervals between dosages. Using mice models, Skipper led his team to creating what became among the first protocols for the contemporary conception of chemotherapy. He directed his team to evaluate the impact of chemical treatment on mice artificially injected to create leukemia, lymphomas, and a variety of solid tumors. He was certain that nitrogen compounds, because of their high toxicity, would be effective in halting the growth and spread of cancerous cells. Conventional wisdom at the time held that chemical treatments were most effective if they killed a
percentage of the cancerous cells and then left the body’s natural immune system to get the idea and in turn kill the rest of the cancerous cells, as if cancer were some bacterial presence, a dicey proposition as the malignant cancer cells could divide so rapidly. Further, Skipper found out that hospitals seldom measured the dosages and that most of the data was therefore inconclusive.

Skipper devised a protocol for measuring exact amounts of chemicals necessary to completely kill the cancer cells. Although he often modestly dismissed his pioneering research work by dismissively referring to himself as the “mouse doctor,” he understood that he was onto a major revision of long-held notions about the chemical treatments of cancers. If traditional chemotherapy held that cancer was a kind of generally benign bacteria that the body, if assisted, could ultimately overcome, like some uninvited guest, Skipper redefined the cancer itself, using his background in warfare, to view it as a massive invasive agency, like some menacing foreign military occupation, that could not be controlled by partial resistance. Rather the body, the cells themselves, had to fight off the cancerous invasion with no goal less than total annihilation. The body had to be helped through chemical infusions to destroy the cancerous invasion entirely. His conception, indeed his research data, redefined the import of chemotherapy—by using compounds derived from mustard gas, Skipper introduced the idea of chemotherapy as a kind of all-out war against the cancer—a far more militant conception of treatment than any before him. For his efforts he was awarded the 1974 Albert Lasker Award, which annually recognizes significant advances in the treatment of diseases, and the 1982 Kettering Prize for outstanding contribution to cancer research.

Although his introduction of nitrogen compounds into chemotherapy regimens was not without controversy within the field of oncology treatment (patients would often experience heightened side effects from the treatments, including intense nausea and a debilitating fatigue), there was little doubt as to the success of Skipper’s tested
protocols. Even when he was named director of the Southern Research Institute in 1974, Skipper never left the research division, determined to track and measure the impact of aggressive chemotherapy. He wanted only to reassure cancer patients that treatment was available and offered authentic hope, and although he authored more than 200 research documents in refereed journals, he also produced a line of booklets designed to inform and reassure cancer patients of the promise of chemotherapy. After he retired in 1989, he continued his own research protocols. He died, January 2, 2006, at the age of 90, in Mountain Brook, Alabama.

Joseph Dewey
Broward College

See Also: Chemotherapy; Clinical Trials; Experimental Cancer Drugs.

Further Readings

Slovakia

The Slovak Republic is one of the landlocked countries at the heart of the European continent with the boundaries covering about 49,000 km². More than 85 percent of the population in the country is Slovaks. The country has been a signatory to the United Nations and the other associated agencies; it is also a member nation in the European Union and NATO, the Council of Europe, and the Organization for Security and Co-operation in Europe (OSCE). One of the most interesting things about this country is that when compared with other Organisation for Economic Co-operation and Development (OECD) states, in 2006 they reached the highest growth rate in the economy, though the global economic crisis in 2008 slowed this growth.

As far as health and development are concerned the Slovak constitution institutes the right to every citizen to receive health care a fundamental right. In the Slovak Republic cancer in the society is as much of a concern as in other countries.

Comparative studies between the United Kingdom and countries such as Slovakia and Turkey indicate that the Slovak Republic has made significant strides toward the ability to detect and handle cancer. Of special note is the fact that in Slovakia there is equipment at hand to scan patients for cancer early. The availability of high-tech equipment is a signal of just how far the republic has come in the battle against cancer.

Osteoporosis
This metabolic skeletal disease has been a significant challenge to the health care industry in Slovakia for a very long time. Over the past few years the epidemiologic data that is available in the industry has shown that there is a steady increase in the number of people that are continually being diagnosed with the condition. As a matter of fact, reports suggest that by the year 2050, it is expected that there will be more than 6 million reported bone fractures as a result of osteoporosis in the country, which marks a significant growth from the figures in 1990 of 1.5 million.

Cancer patients in the country, especially those that are dependent on hormone therapy, such as those suffering from breast cancer and prostate cancer, or even those that are getting treatment in hormonal metabolism, ovarian cancer, thyroid cancer, germ cell tumor, and other associated conditions, are at a higher risk of suffering from osteoporosis.

Breast Cancer
According to 2011 reports, breast cancer accounted for 1.8 percent of the overall deaths in the country. According to the statistics, this puts the figure at 823 individuals who died of breast cancer alone, ranking Slovakia 64th in the whole world for deaths from the disease.

Industry experts have reported that those suffering from breast cancer are also at a very high risk for osteoporosis as a side-effect of anticancer therapy. Postmenopausal women are at an even higher risk.
In order to deal with the cancer situation in the country that is fast getting out of hand, the government, in partnership with the other organizations, has been working on bone mineral density measurement for postmenopausal women. Such patients are commonly treated with tamoxifen or aromatase inhibitors at the St. Elisabeth Cancer Institute. The procedure often takes more than one year because the density of the bones is measured at the beginning of the treatment, in the course of the therapy, and as soon as the therapy is completed.

One of the most important features of this study in the industry was to lay an emphasis on the fact that it is important to consider the evaluation and the relation between osteoporosis and cancer in the Slovak Republic.

Testicular Cancer
Testicular cancer is not just a problem in the Slovak Republic, but it is a problem all over the world. However it is worth noting that when detected early enough, it is possible to treat testicular cancer, and as a matter of fact the healing rate currently stands at 90 percent. The catch however is in making sure that the diagnosis is done at a very early stage, and most importantly done correctly.

In the Slovak Republic, more than 1 percent of the male population is currently suffering from malignant testicular cancer. The worst thing about this is that the number of those who are suffering from testicular cancer is on the rise, with reports indicating that the increase has multiplied more than five times.

Most of those who are affected are men between the ages of 20 and 40 years. A good number of those in this category have their testicular cancer as a result of germ cell tumors, which have been further classified as under seminoma and nonseminoma germ cell tumors. More than half of those who have testicular cancer in the Slovak Republic have it as a result of nonseminomatous germ cell tumor.

The Cancer Research Institute SAS has been around since 1946, and is at the moment the oldest research institute in the country devoted to cancer research. The institution is tasked primarily with studying and understanding molecular mechanisms of the cancerous cells, and with this in mind they have also focused on running the inquiries under a multidisciplinary approach. There are a lot of scientists that work under this institute to further the objectives, including a number of high-profile molecular biologists, chemists, and geneticists.

In as much as this is primarily a research facility, the institute has also been working together with the oncology unit at the Bratislava St. Elisabeth Institute. They also actively published Neoplasm, an oncology-based journal.

Michael Fox
Independent Scholar

See Also: Breast Cancer; Extragonadal Germ Cell Tumor; Testicular Cancer.

Further Readings


Small Intestine Cancer
There are five types of small intestine cancer, with the most common type being adenocarcinomas. All forms of small intestine cancer are fairly rare, affecting only a small percentage of the population. This disease tends to be prevalent in those who have Cohn's or celiac disease, cystic fibrosis, and those with a history of adenomatous polyps.

The following are types of small intestine cancer:

- Adenocarcinomas: This form of small intestine cancer is the most common
Small Intestine Cancer

type, and it usually forms in the cells that live in the walls of the small intestine. Much of the time, adenocarcinomas will develop from noncancerous polyps, which are small growths on the intestinal walls.

- **Carcinoid**: When suffering from this type of cancer, a person will endure slow-growing cancerous tumors within his or her small intestine.
- **Sarcoma**: Cancer that forms within the connective tissue found in the small intestine is known as sarcoma.
- **Lymphomas**: Although this form of cancer is known as an immune system disease, it often begins its development in the small intestine.
- **Gastrointestinal Stromal Tumors**: Much like sarcoma, this form of cancer starts out by attacking the soft tissue in the intestines.

**What Does the Small Intestine Do?**

To understand small intestine cancer, it’s first important to understand the function of the small intestine in the human body. The small intestine is part of a major system within the body, which is most commonly referred to the digestive system; this system is composed of the mouth, throat, esophagus, stomach, small intestine, large intestine (colon), rectum, and anus.

It is the digestive system’s purpose to remove and process foods. It separates nutrients from waste, allowing the “good” material to stay in the body, and the “bad” material to be excreted. The small intestine itself lies between the large intestine and stomach, connecting the two organs.

**Factors That Influence Development of Small Intestine Cancer**

Though cancer of the small intestine is rare, there are certain factors that increase risk. Those with a history of Crohn's or celiac disease, those with cystic fibrosis, and those with a family history of adenomatous polyps are considered at a higher risk. In addition, there are certain behavioral and environmental factors that can increase the risk of small intestine cancer, such as eating foods high in fat, tobacco and alcohol use, and exposure to certain chemicals, including vinyl chloride.

**Signs and Symptoms**

Being aware of the symptoms of small intestine cancer increases the likelihood that person will seek medical attention at the first signs of the disease. As with other cancers, early detection and treatment increases the changes for a positive outcome. Signs and symptoms of small intestine cancer include the following:

- Weight loss for an unknown reason
- One or more lumps in the abdomen
- Blood in the stool
- Abdominal pain and/or cramps

If a person notices any of these signs or symptoms, it is highly recommended that he or she visit a physician as soon as possible.

**Methods for Detection and Diagnosis**

If a physician believes that a patient may be suffering from small intestine cancer, certain tests will be administered. It is through these tests that the exact form of small intestine cancer can be identified, which then makes it possible to carry out the proper treatment methods. The processes that are used to identify cancerous cells within and around this area of the body are most commonly referred to as staging. The following is a list of tests that are often administered to identify and diagnose small intestine cancer:

- **Physical Exams**: A simple yet very effective way to see if there are signs of small intestine cancer is a physical exam. A physician will assess a patient’s past medical history and risk factors, as well as check for any lumps are present in the abdomen.

- **Liver Function Tests**: This type of test is carried out by collecting a blood sample. The sample is then checked to see how much of certain substances are being released into the human body by the liver. If higher than normal amounts of certain substances are noticed, this is a good indication that small intestine cancer is present.

- **Blood Samples**: A blood test checks for a wide array of substances in the blood. If higher or lower than normal amounts of certain substances are noticed, this is a good indicator of the presence of small intestine cancer.
Endoscopies. This type of test allows a physician to look at the small intestine and identify whether there are any abnormalities. There are three types of endoscopy that can be performed, which include an upper endoscopy, capsule endoscopy, and a double balloon endoscopy.

Other tests used to identify the presence of small intestine cancer include laparotomy, biopsies, upper GE series with small bowel follow-through, computed tomography (CT) scans, or magnetic resonance imaging (MRI).

Treatment for Small Intestine Cancer
There are three primary ways that physicians treat small intestine cancer, which are surgical removal of the cancerous lump or polyp, chemotherapy, or radiation therapy if the cancer has spread to other parts of the body.

Survival Rates of Small Intestine Cancer
The survival rates for small intestine cancer are largely dependent on the stage of cancer that a person suffers from. According to the American Cancer Society, the following rates apply:

- Stage I: 55 percent
- Stage IIA: 49 percent
- Stage IIB: 35 percent
- Stage IIIA: 31 percent
- Stage IIIB: 18 percent
- Stage IV: 5 percent

Whitney Cann
Independent Scholar

See Also: Alcohol; Chemotherapy; Esophageal Cancer; Radiation Therapy; Sarcoma, Soft Tissue, Adult.

Further Readings


Smokeless Tobacco
Smokeless tobacco includes a variety of tobacco products that are consumed (or otherwise used) recreationally in some way other than smoking. It generally excludes electronic cigarettes, which simulate the experience of smoking and include nicotine. All forms of tobacco consumption pose carcinogenic risk, and in some cases the additives used in various forms of tobacco increase the risk of cancer and other health-related problems.

Chewing Tobacco
Chewing tobacco is perhaps the best known form of smokeless tobacco. For a long period in the 19th century, chewing tobacco was made with cigar clippings, but today it uses loose leaf or scrap tobacco, pellets of tobacco, or loose leaf tobacco bundled into a plug with an added sweetener. Chewing tobacco is one of the original forms of tobacco consumption, dating to the pre-Columbian period, and it was developed commercially by the tobacco plantations in the Southern colonies of North America. In the antebellum south and much of the frontier, chewing tobacco was an almost universal habit among men over 10 years of age, and practiced by over half the women as well. In contrast, daily smoking never enjoyed such widespread use. Chewing tobacco continues to be popular in the south, midwest, and mountain states, and is common in certain professions such as commercial trucking. Long associated with baseball, it has been displaced in that sport by dipping tobacco.

Chewing tobacco is known to be linked to oral cancers. Several well-known ball players developed cancer associated with chewing tobacco, including notably Babe Ruth, who died of nasopharyngeal cancer, and Tony Gwinn, who died of salivary cancer. After Babe Ruth’s death, cigarettes gained popularity among ballplayers, but the federal push
Smokeless Tobacco

Smokeless tobacco to warn the public of the dangers of smoking in the 1970s brought back chewing tobacco. Dipping tobacco or moist snuff is finely ground tobacco that is moistened, known by a variety of names in different parts of the country, including dip, rub, chew (though it is not chewing tobacco), snuff (though dry snuff is different), chaw, and daps. Skoal and Copenhagen are popular brands. Dipping tobacco was introduced by Copenhagen in 1822, and is primarily popular in the south and rural Canada, as well as in professions where smoking is banned. Dip is consumed by placing a pinch of tobacco between the lower lip and the gum, and letting it sit there for 10 to 30 minutes. Nicotine and other substances are absorbed through the inferior and superior labial arteries, as well as under the tongue. Both chewing tobacco and dipping tobacco cause excess saliva that needs to be spat out, since swallowing saliva infused with tobacco can cause nausea and vomiting. Dipping tobacco is associated with tongue, lip, cheek, gum, throat, and salivary gland cancer, as well as tooth loss and gum disease, and probable cardiovascular problems.

In parts of Alaska, Blackbull is a form of dipping tobacco mixed with the ash of Phellinus igniarius, a fungus that infects black walnut trees. It’s consumed by some Alaska Natives and sold in general stores.

In central Asia and the Indian subcontinent, and among immigrants from that region, naswar is a moist powdered tobacco similar to dipping tobacco. It is stuffed under the lower lip or inside the cheek, and requires periodic spitting. It is processed with lime (which helps make the nicotine bioavailable), air-cured and dried, sometimes flavored with juniper, and dyed with indigo. The National Institutes of Health have established a positive link between naswar and mouth and throat cancers.

**Snuff**
Snuff or dry snuff is also made from ground tobacco, which is inhaled through the nose for a quick nicotine buzz and accompanying scent, if the snuff is flavored. The tobacco is absorbed through the mucus membranes of the nose, so does not need to be inhaled deeply enough to reach the sinuses. Not surprisingly, snuff is associated with nasal and throat cancers.

Dry snuff originated with Native Americans and became popular in Europe after the colonization of North America, remaining popular there long after chewing tobacco and cigarettes had overtaken snuff’s popularity in the United States. “Medicated” snuff is made with menthol to clear the sinuses. Numerous flavors of snuff are offered, from traditional spice, fruit, and floral flavors to modern whiskey- and cola-flavored snuff. Snuff boxes became popular in Europe when snuff was in its heyday, designed to fit in a pocket and protect snuff from drying out. Members of the British House of Commons continue to be provided with rose-scented snuff because of the centuries-long ban on smoking in the building.

**Snus**
A similar product to dipping tobacco is snus, a finely ground moist tobacco powder developed in Sweden in the early 1700s. Unlike most American tobacco products, Swedish snus is not fermented during the curing process, and it is not sweetened. Placed under the upper lip rather than the lower, it does not stimulate the production of excess saliva, and does not require spitting. It is linked to oral, pharyngeal, and pancreatic cancers, as well as hypertension and tachycardia. The European Union banned snus in 1992, except in Sweden and Norway. Recently, American companies like Camel have started selling snus as an alternative to other smokeless tobaccos, though it is prepared slightly differently and contains less bioavailable nicotine. Swedish snus often comes in smoked, juniper, bergamot, or citrus flavors, while American snus comes in various mint and fruit flavors.

**Creamy Snuff**
One of the more unusual smokeless tobacco products in the United States is creamy snuff, a blend of tobacco, clove oil, spearmint, menthol, camphor, and glycerin, with a texture like that of toothpaste (and sold in a similar tube). The paste is rubbed on the inside of the mouth or gums and allowed to linger before rinsing. This too is linked to oral cancers and hypotension.

**Conclusion**
Health professionals do not agree on the relative merits or dangers of smokeless tobacco. There is no doubt that compared to avoiding all tobacco use, smokeless tobacco is dangerous. However, many health professionals, citing the doctrine of harm reduction, credit smokeless tobaccos with being
significantly less dangerous than cigarette smoking. While the carcinogenicity is undeniable, research is fairly compelling that smoking, especially smoking cigarettes, is far more carcinogenic, and more likely to lead to death by cancer, than smokeless tobacco usage. Furthermore, even if risks to the user were completely equal, smokeless tobacco poses a lesser public health concern since there is no analogue to secondhand smoke, the dangers and carcinogenic contributions of which many researchers believe are still understated. In Sweden, snus is widely used in smoking cessation programs, and tobacco-related mortality among men is lower in Sweden than in any other European country. However, the use of smokeless tobacco in smoking cessation programs has a noncarcinogenic alternative as well, in the form of nicotine gum or nicotine replacement therapy. Such treatments are considerably more expensive, though.

Bill Kte’pi
Independent Scholar

See Also: Lung cancer; Oral cancer; Smoking and Society; Smoking Cessation; Tobacco Smoking.

Further Readings

Smoking and Society

The World Health Organization (WHO) forecasts that up to 1 billion people could die this century from smoking or from being exposed to tobacco, if current smoking rates continue. Around 6 million people die every year due to smoking or exposure to secondhand smoke. In spite of these rates, consciousness about the health risks associated with smoking is on the rise in many countries thanks to widespread antismoking campaigns. However, in developing countries such as India, tobacco accounts for about 40 percent of all cancers.

Smoking increases the risk of acute hypertension, tuberculosis, heart diseases, lung cancer, oral cancer, and diabetes. Passive smokers (those exposed to secondhand smoke) are also at risk. Prolonged cigarette-smoking can rob a decade of life, on an average. Smoking during pregnancy can lead to everything from low birth weight and birth defects to stillborn births. The cost of cigarettes can have an economic impact on smokers, and the litter from smoking can contaminate the waterways and the soil. Smoking can create clashes among smokers and nonsmokers, as the general public may oppose smoking in public places. There are more than 50 countries that have banned indoor smoking in workplaces, hotels, restaurants, etc.

The World Health Organization has opposed passive smoking, which also affects the health of pets. Children of smoking parents are at greater risk of becoming smokers themselves. The social learning
theory supports that conceptions of behaviors among children guide their future actions. Children learn that smoking is a normative behavior, which can impact their willingness to smoke in the future. Even if parents make it a point not to smoke in the sight of children, the ill-effects of smoking still affect families.

There are several myths which are prevalent in developing societies which may prevent people from seeking treatment for cancer. For example, according to a *Lancet* report, around 80 percent of cancer patients in India seek treatment from unqualified medical professionals before going to reputable doctors, in part because many of people prefer cheaper methods of care. Even today, many people believe that cancer is incurable and that a diagnosis an automatic death sentence. But, this fear still does not deter people from smoking.

There has been a rise in smoking among women. Researchers state that excessive smoking among women may lead to a rise in infertility and cancer. Research conducted by the *British Medical Journal*, from 1980 and 2012 among smokers in 187 countries, confirmed this trend. Women in China and India are increasingly turning to cigarettes as a form of socialization. Moreover, cigarette manufacturers have realized that India and China are good markets which need to be targeted. That will lead to less dependence on Western markets for cigarettes where antismoking laws are becoming more stringent. The tobacco companies have diverted their targets to middle- and low-income countries. In a paper published by the Mumbai-based Tata Memorial Centre, it has been observed that the cost of tobacco consumption in 2002–2003 exceeded the total combined government revenue and capital expenditure on medical and public health, water supply, and sanitation.

To curb smoking, France is considering the option to support unbranded packaging. France is also considering instituting one of the toughest antismoking policies in the world. Plain packaging has been successful in reducing smoking rates in France. Less than one-third of the population is now engaged in smoking in France. Australia has pioneered plain packaging for cigarettes since 2012. Britain, New Zealand, and Ireland have also planned similar bans. Nicotine-replacement therapy has proven to be a success in Europe and the United States in the drive for antismoking. But, to date, poverty-stricken, developing societies have failed to understand the benefits of the therapy.

Strong antismoking laws are a starting point to creating a smoking-free society. Taking stern action against tobacco companies may affect local economies, but it is necessary for the greater good of the community.

Advertisement of cigarette brands plays a significant role in influencing smokers to continue with the addiction and has been proven to encourage young people to start smoking. Aggressive anti-smoking ad campaigns can have just as much influence in preventing people from starting smoking in the first place. In India, for example, where smoking and tobacco use are the leading causes of cancer, movie halls show short public service announcements that encourage smokers to quit.

Many societies have started engaging in aggressive campaigns against smoking, although it is worth noting that these campaigns have been less successful, as measured by the rate of smokers quitting, in developing countries as compared to industrialized countries. Public awareness on exposing children to secondhand smoke is growing. Bans on household smoking will have favorable effects on children. Long before children start smoking, prevention programs for adolescents are required.

Quitting smoking can take an enormous amount of one’s determination and will. Family members may play an important role by becoming the
Smoking Cessation

Nicotine replacement therapy (NRT) is used to aid in the transition from cigarette smoking to smoking cessation. NRT is a temporary means of replacing the nicotine from cigarettes in an attempt to reduce an individual’s motivation to smoke, and to ease nicotine withdrawal symptoms. The nicotine in cigarettes is the active ingredient that often leads to physical dependence on smoking. If someone tries to quit smoking, the physical dependence can result in withdrawal symptoms. Nicotine dependence occurs early and easily as people begin to smoke cigarettes. It does not take much use before withdrawal symptoms and cravings occur. Nicotine is a substance that increases the levels of the brain chemicals dopamine and norepinephrine. When people stop smoking, the chemical levels drop, causing the body to experience withdrawal symptoms, including anxiety, irritability, and hunger.

NRT supplies the body with a lower dose of nicotine to help reduce nicotine withdrawal and resulting cravings. NRT uses about one-third to one-half as much nicotine as cigarettes. Nicotine from NRT also increases dopamine and norepinephrine levels, like cigarettes, which reduces withdrawal symptoms while reducing the level of nicotine ingested. The NRT process helps as a temporary replacement for the nicotine received from smoking cigarettes, and can be adjusted so that the smoker can decrease the amount of the medicine they use in a steady decline until it is no longer needed and they have been weaned from nicotine. Inhalation of tobacco smoke moves quickly into the lungs and bloodstream. The nicotine replacement products take longer to enter into the lungs and bloodstream, and are much less likely to cause dependence on nicotine. NRT is safe when properly used, and is not as harmful as smoking because NRT does not provide the tars, carbon dioxide, and other harmful chemicals present in tobacco. NRT delivers nicotine in the form of gums, patches, sprays, inhalers, or lozenges, but does not contain the other harmful chemicals in tobacco. NRT can help relieve some of the physical withdrawal symptoms so that an individual can focus on the psychological aspects of quitting.

Nicotine replacement therapy has been an effective means of helping people try to quit smoking, but there are some limitations. According to the U.S. Agency for Healthcare Research and Quality Clinical Practice Guideline on Smoking Cessation in 2000, this medicine should not be used when someone is pregnant or suffers from heart disease. This was revised in 2008, as the agency stated that the nicotine patch could be safely used with a doctor monitoring the process. NRT products have been linked to low birth weight in children born to...
mothers who use it during pregnancy. While this risk is present, smoking during pregnancy is also an important risk to consider. Although NRTs expose the fetus to nicotine, smoking exposes the fetus to nicotine and additional harmful chemicals. The effects of smoking while pregnant could also have long-term effects on subsequent child development. It is best to quit smoking, or at least reduce the amount smoked, before becoming pregnant. If an individual becomes pregnant, or plans on becoming pregnant, they should contact their physician and discuss possible safe options. They will likely need to try other methods during the pregnancy.

A physician should also be consulted if an individual has heart disease, has had a recent heart attack, or has serious heart problems like irregular or rapid heartbeat or chest pain. Studies indicate that the benefits of quitting smoking outweigh the risks for individuals with cardiovascular disease. Risks are still present, but the greater risks seem to be with smoking cigarettes. When looking at NRT use, the benefits of quitting smoking must outweigh the potential health risks of NRT for each person. NRT products are not recommended for people under the age of 18 because they have not been tested on younger populations. The side effects of nicotine replacement therapy for young people are unknown. It is always better to consult with a physician before beginning any type of NRT, healthy or otherwise. This allows the physician to recommend products that would be most useful and monitor the effects. NRTs have not yet been proven to help people who are lighter smokers. Individuals who smoke fewer than 10 cigarettes a day might not see the effects of NRTs as easily as heavier smokers. Light smokers might want to talk with a doctor about a lower dose of NRT if they smoke less than that, but feel that they need nicotine replacement.

In many cases, research indicates that using some form of nicotine replacement therapy increases an individual’s chances of quitting smoking. NRT can help with the withdrawal symptoms and cravings that the majority of smokers indicate as the reason they have either not tried to quit smoking, or have been unsuccessful in efforts to quit smoking. All forms of nicotine replacement products appear to be about equally effective, when properly used. In some cases, combining the use of products, such as the nicotine patch and another form of NRT, can increase efficacy. As with any other medication, this option should be discussed with a physician before beginning, and should be monitored by the doctor throughout. It is believed that NRT treatments work best for quitting smoking when combined with a behavioral program of smoking cessation. These programs often include setting goals for quitting, creating plans for dealing with triggers to smoking, and working with a doctor, counselor, or other support system.

It is often possible to quit smoking without resorting to NRT treatments, but there are usually multiple attempts because most people do not succeed on the first attempt. In most cases, smokers need many tries before they are able to permanently quit smoking. Most smokers who try to quit end up smoking again within the first three months without nicotine. This lack of success can usually be attributed to the accompanying withdrawal symptoms. The reduction of withdrawal symptoms with NRT can reduce the negative physical effects. Smokers seem to have the best chance of quitting and remaining smoke free if they have the help of a professional and personal support network.

NRT treatments only work on the physical dependence, and do not address psychological feelings of dependence and reliance. It only works on one part of the smoking problem, and often cannot be successful without addressing the other elements of the issue. Smokers will need to utilize other treatment methods to address the psychological (emotional and mental) part of smoking, such as a stop-smoking program or support group. People seeking to quit should use these resources during treatment with NRT, and stick with them for at least a few months after quitting to help them remain smoke free. Studies have shown that pairing NRT with a program that helps to change behavior can improve the likelihood of successfully quitting and staying quit compared to approaches that only use one method. The best time to start NRT is when an individual first stops smoking. Smokers often try to quit without the aid of NRT therapy first, and then find that they need extra help, which leads them to try NRT shortly after the initial attempt to quit. This does not give the process the greatest likelihood of success.

**Side Effects**
The different NRTs work equally well. As a result, smokers can choose a treatment based on how it
fits with the individual’s lifestyle and comfort zone. Each person needs to create a program that works best for them, including taking into account the potential side effects. All NRTs have side effects, but the types of side effects differ across NRTs, and are based on each individual. Very few people (less than 5 percent) have to stop using a nicotine replacement product altogether because of side effects, but a smoker should contact their doctor to make sure which therapy would work best based on their overall health and ability to deal with the possible side effects. As with cigarette use, the sudden cessation of nicotine replacement therapy may cause some of the same withdrawal symptoms that occur when an individual stops smoking cigarettes. Individuals are less likely to have withdrawal symptoms with a gradual reduction of the dose or number of uses of the specific NRT each day. Although rare, it is possible for an individual to become dependent on a nicotine replacement product.

The U.S. Food and Drug Administration (FDA) has approved five forms of nicotine replacement therapy, including gums, patches, nasal sprays, inhalers, and lozenges. Nicotine gum and lozenges release nicotine through the mouth. Nicotine patches stick to the skin and release nicotine through the skin into the bloodstream. A nicotine inhaler delivers a puff of nicotine vapor into the mouth and throat. No prescription is necessary for nicotine gum, patches, and lozenges, but a prescription is necessary to buy nicotine inhalers. Non-prescription NRTs cannot be sold to individuals under 18 years of age, although a doctor can prescribe an NRT for an underage nicotine user.

**Gum**

Nicotine gum is a fast-acting form of replacement in which nicotine is taken in through the mucous membrane of the mouth. Individuals can buy it over the counter without a prescription, and it comes in 2 milligram (mg) and 4 mg strengths. The gum should be chewed slowly until the individual experiences a peppery taste or tingle. The gum should then be held against the inside of the cheek until this taste fades. The gum is chewed again until the taste or tingle returns, it is held against the side of the mouth until it fades, and the process continues to repeat for about 20 to 30 minutes. Users should not eat or drink anything from about 15 minutes before gum use through 15 minutes after gum use so that the nicotine can be absorbed in the proper proportion.

The gum dose that an individual uses will be based on how many cigarettes he or she is currently smoking per day, whether or not they smoke within 30 minutes of waking up in the morning, and how much trouble they have when they are in a position where they cannot smoke for a period of time. If any of these symptoms are present, the individual should start with the higher 4 milligram gum dose. Individuals cannot chew more than 24 pieces of gum in one day, and the process is normally recommended for six to 12 weeks, up to a period of six months. Users are advised to begin tapering down the amount of gum used at about three months. The gum has some advantages. The gum allows individuals to control the doses of nicotine that are ingested, and it can be used as needed or on a convenient fixed schedule during the day. This flexibility allows users to determine when they need it the most, and to use it accordingly. Additionally, if an individual has sensitive skin, they might prefer the gum to the patch.

Some possible side effects of nicotine gum include a residual bad taste, throat irritation, mouth sores, hiccups, nausea, jaw discomfort, and racing heartbeat. The gum also has a tendency to stick to dentures or dental work, potentially causing damage. Symptoms related to the stomach and jaw are usually caused by improper use of the gum, such as swallowing the nicotine or chewing too fast. No one has all of the side effects, and some people have none. If an individual experiences a racing heart or irregularity in the beat, they should stop using the gum and talk to their doctor. If the NRT dose is too low, it is also possible to experience withdrawal symptoms. Long-term dependence is one possible drawback of nicotine gum. Some research indicates that a few gum users who are able to quit smoking keep using the gum beyond 6 months. Nicotine is addictive, and people can transfer their dependence from cigarettes to the gum.

**Patch**

Patches give a measured dose of nicotine through the skin. Individuals move from higher to lower dose patches over the course of a few weeks. Patches can be bought with or without a prescription, and come in different types and strengths. Packages contain instructions on how to use them, and list special
considerations and possible side effects. Directions should be carefully followed. Light-to-average smokers can use the 16-hour patch, which is less likely to cause adverse side effects. It does not deliver nicotine overnight, which means that individuals with early morning withdrawal symptoms might have trouble and need a different patch. The 24-hour patch provides a steady dose of nicotine, and helps reduce the withdrawal symptoms in the morning. Users tend to experience additional side effects, like disrupted sleep patterns and skin irritation.

Most smokers should start using a full-strength patch daily for four weeks, and then use a weaker patch for another four weeks to begin to wean off of it. Quitters would put a new patch on in the morning after cleaning and drying the area thoroughly. A good place to put the patch is an area without much hair, below the neck and above the waist—for example, on the upper arm or chest. The FDA has determined that it is safe to use the patch for a total of three to five months. Side effects of nicotine patches may include skin rashes from the sticky backing of the patch or the ingredients in the patch. Other side effects could include redness and itching, dizziness, racing heartbeat, headaches, nausea, or muscle aches and stiffness. Individuals might also experience problems sleeping when they use the 24-hour patch. These side effects could be influenced by the strength of the dose of nicotine, the brand of the patch, presence of skin allergies, length of time the patch was used, and how the patch was applied.

No one has reported having all of the side effects, and some people have none. Some side effects, such as racing heart, may occur because the dose of nicotine is too high. It is also possible to experience nicotine withdrawal symptoms during this time, if the NRT dose is too low. Quitters can reduce side effects by keeping from smoking while using the patch. They can also try a different brand if the skin becomes irritated, try a patch with a lower dose, switch to a patch with a shorter time length, or move to a different NRT.

**Nicotine Nasal Spray**

The nasal spray is easy to use, and delivers nicotine to the bloodstream quickly because it is absorbed through the nose. This type of NRT is prescribed by a physician. The nasal spray provides quick relief of withdrawal symptoms and control of nicotine cravings. One negative to this is that the quick-fix approach of the nasal spray can increase the risk of developing dependence issues. As a result, nasal sprays should only be used as long as needed, and should be taken by the direction and prescription of a physician. The FDA recommends that the spray be prescribed for three-month periods, and that it not be used for longer than six months. Side effects can include nasal issues, watery eyes, sneezing and runny nose, sore throat, and coughing. These side effects normally only last about one or two weeks, but people who have respiratory issues such as asthma or allergies, along with sinus problems, might not be appropriate for this method and should look into other forms of NRT. It is also possible to use too much of the nasal spray.

This form of NRT should be carefully handled and securely stored because it poses a more serious risk to small children and pets. Even empty bottles of the spray can contain enough nicotine to harm them, if ingested or absorbed. Nicotine absorbs through the skin as well as mucous membranes like the mouth or eyes, and can cause serious harm. If there is any skin contact, the user should rinse thoroughly with plain water right away. If a bottle breaks or liquid leaks out, put on plastic or rubber gloves.
to clean it up. Call Poison Control and get emergency help if there is any question of an overdose.

**Nicotine Inhalers**
Inhalers are controlled and only available by prescription. Inhalers consist of a thin plastic tube with a nicotine cartridge inside. When an individual takes a puff from the inhaler, the cartridge puts out a pure nicotine vapor. Most types of inhalers deliver medicine to the lungs. Nicotine inhalers, however, send most of the nicotine vapor to the mouth, where it is absorbed into the bloodstream. Nicotine inhalers are the FDA-approved nicotine replacement method that is most like smoking a cigarette, which some smokers find helpful. The recommended dose is between four and 20 cartridges a day, which are slowly tapered off over six months. The most common side effects, especially when first using the inhaler, include coughing, mouth and throat irritation, and upset stomach. Nicotine inhalers pose a significant risk to small children and pets because the used cartridges still have enough nicotine in them to cause harm if it gets on skin or mucous membranes. It is not a good choice if an individual has asthma, allergies, a sinus condition, or any other respiratory problems. Inhalers are also the most expensive form of NRT on the market. They are not electronic cigarettes, which are not approved by the FDA.

**Nicotine Lozenges**
Nicotine-containing lozenges are not controlled substances, and can be purchased over the counter without a prescription. The lozenges are somewhat similar to nicotine gum. They come in two strengths: 2 and 4 milligrams. Smokers choose their dose based on how long after waking up they normally have their first cigarette. Lozenges should be used as part of a 12-week program, with the recommended dose of one lozenge every one to two hours for six weeks, then one lozenge every two to four hours for weeks seven to nine, and finally one lozenge every four to eight hours for weeks 10 to 12. It is helpful to follow a few guidelines in the use of lozenges. Individuals should stop smoking when using the lozenges. Users should not eat or drink for 15 minutes before using a lozenge. The lozenge should be sucked for the full time until it is dissolved. It should not be bitten, chewed, or swallowed because the nicotine should be absorbed through the mucous membranes of the mouth. No more than five lozenges should be used in any six-hour period, with no more than 20 lozenges total for a 24-hour period. The lozenges should only be used for 12 weeks, with additional use approved by a doctor. Possible side effects of the nicotine lozenge could include trouble sleeping, nausea, hiccups, coughing, heartburn, headaches, and excessive gas.

**Information to Consider**
It is normal to begin coughing within the first week after quitting smoking, regardless of the method used. It is the body’s means of trying to clear the lungs. Acidic beverages ingested at the same time as use of NRT can prevent the absorption of the nicotine. They should be avoided for 15 minutes before use through 15 minutes after use. Choice of NRT is a matter of personal choice, and if one form is not desirable because of side effects, switch to another and see if it works better. Nicotine overdose is rare, but possible. NRT products are labeled to provide a dose of nicotine fairly close to what an individual has been receiving from cigarettes. Higher doses of nicotine can cause harm. To avoid this, dosing instructions must be carefully followed, and keep the NRT product away from children and pets.

Most NRT product dosages are recommended on the basis of how much an individual smokes. A light smoker would be someone who smokes fewer than 10 cigarettes per day, whereas a heavy smoker would smoke a pack or more a day. The average smoker would fall somewhere in between. A pack year would be calculated by multiplying the number of years that an individual has smoked by the number of cigarettes smoked per day. An individual who smokes 20 cigarettes, or the number of cigarettes in a pack, per day for one year would smoke one pack year. This figure is used to determine the risk of smoking-related disease. For heavier smokers, it is possible to combine the patch with other shorter-acting nicotine replacement products. The idea is to receive a steady dose of nicotine with the patch, and then use one of the shorter-acting products when they have strong cravings. Combining NRTs is thought to be relatively safe, and might work better. This type of use has not yet been approved by the FDA, and additional research will provide a better picture of this process. For now, it would be best to consult a physician before doing so. Heavy smokers might also use higher doses of NRTs, but should be monitored by a physician.
NRT use can begin as soon as an individual stops smoking. There is no waiting period before beginning use of the patch, gum, lozenges, nasal spray, or inhalers. NRT products should not be used while an individual is still smoking. They are also used for limited periods of time, during which the individuals taper down and eventually cease their tobacco use. For example, the patch is used for 3 to 5 months, so use should begin to be reduced by the second or third month, and continually reduced from there to avoid withdrawal symptoms and reduce risk of relapse. Continued research will pinpoint more specific time periods, and the most important suggestion is to keep in contact with a physician and consult before creating any changes.

Constance M. Dolecki
Independent Scholar

See Also: Drugs; Smokeless Tobacco; Smoking and Society; Tobacco in History; Tobacco Smoking.

Further Readings

Society of Gynecologic Oncology

The Society of Gynecologic Oncology (SGO) is a medical specialty society for health care professionals trained in gynecologic cancers. The SGO encourages research, education, raising standards of practice, advocating for patients, and collaboration with national and international organizations. There are five main types of gynecologic cancer: cervical, ovarian, endometrial, vulvar, and vaginal. Cervical cancer is one of the most common cases of cancer deaths in women. Approximately 12,360 women are diagnosed with cervical cancer each year, and 4,020 will die from the disease. Cervical cancer is most common among Hispanic women, then African American women, followed by Asians, Pacific Islanders, and whites. If caught early, women diagnosed with cervical cancer have an excellent survival rate of 92 percent (first five years following diagnosis). Most cases are diagnosed in women aged 30 to 60, but about 20 percent will be over the age of 65.

The two main types of cervical cancer are squamous cell carcinoma and adenocarcinoma. Cancer found in the outer surface of the cervix is called squamous cell carcinoma. Adenocarcinoma cancer occurs in the glandular cells, usually located higher in the cervical canal. Ovarian cancer forms in the ovaries. Approximately 21,980 cases of ovarian cancer will be diagnosed each year in the United States, and 14,270 deaths will result. Ovarian cancer is 9th of the top 10 cancers among women, and is the most lethal of gynecologic cancers. Cancer that occurs in the inner lining of the uterus (that sheds with monthly menstrual cycles) is called endometrial. This is the most common cancer in the female reproductive system. Approximately 52,630 cases are diagnosed annually, and 8,590 deaths will occur in the United States.

Vulvar cancer originates in the outer portions of the female reproductive system (i.e., the clitoris, vaginal lips, and opening of the vagina). Less than 1 percent of all female cancers are vulvar. Approximately 4,850 new cases occur annually, and 1,030 will die from the disease. Cancer of the vagina occurs in 1 out of every 100 cancers of the female reproductive organs. Malignant cells are found in the tissue of the vagina in about 3,170 cases annually, and about 880 women will die from this form of cancer. Most of the time, vaginal cancer occurs when cancer in another part of the body invades the vagina.

SGO members provide a variety of cancer treatments, including chemotherapy, surgery, supportive care, and radiation therapy. There are more than 1,700 members nationally and internationally.
Members are allied health care professionals, hematologists, surgical oncologists, obstetrician/gynecologists, physician assistants, radiation oncologists, pathologists, nurses, and medical oncologists. Members are present in a variety of settings, including academia, cancer centers, hospitals, and private practice.

The SGO was founded by doctors Averette and Mikuta with likeminded fellows of the American College of Obstetricians and Gynecologists in 1968. The SGO was formalized in 1969. In 1970, the first annual meeting was held. That same year, the SGO was incorporated, and its first committees were formed. In 1974, the first written and oral examinations for certification for Special Competence in Gynecologic Oncology were given. In 2012, the SGO became a nonprofit organization, and the Foundation for Gynecologic Oncology was created. The foundation is responsible for education, fundraising, research, and development. The SGO assumed responsibility for membership activities, government relations, and clinical practice at that time.

The mission of the SGO is to promote the highest quality of comprehensive care through research and education in the treatment and prevention of gynecologic cancers. Its vision is to eradicate gynecologic cancers. The strategic goals of the SGO include education, research, advocacy, communication, collaboration, and leadership. The SGO plans to be the authoritative source of gynecologic oncology education. It identifies the educational needs of members and other audiences while enhancing the program quality and content during educational activities. The SGO provides e-learning opportunities and explores and develops continuing medical educational topics and credits. The SGO also explores credentialing and delivery of public education internationally. The SGO promotes research in gynecologic oncology. It fosters quality research and database development to advance care. The foundation supports increased funding for basic, clinical, and translational research through public and private partnerships, including a research summit. It represents the interests of patients and members through a leadership role that defines quality of care and facilitates reporting of findings. The SGO explores and promotes practice models that are new and methods to secure adequate funding and reimbursement for gynecologic cancer care. It advocates for all facets of research and raises awareness by developing and operationalizing effective and user-friendly strategies that include social media. The SGO seeks to collaborate with organizations that advance similar missions and visions by building, leading, and joining together in advocacy. The SGO also aligns and joins organizations that support and promote gynecologic cancer prevention and treatment. Finally, the SGO leads through identification and response to the needs of members and to continue to increase and diversify revenue. A plan for outreach to allied health professionals and international organizations is aligned with and supports the SGO’s philanthropic, communicative, research, and educational strategies.

The SGO’s purpose is defined by its bylaws, to (1) promote and further common goals among cancer clinicians and scientists, (2) develop and promote high practice standards and ethical practice, (3) cooperate and interact with other allied health professional organizations, (4) develop educational programs and professional materials to enhance allied health professionals’ ability to meet the needs of gynecologic cancer patients, (5) communicate with the public about gynecologic cancer both directly and through allied health professionals, (6) work independently with groups to influence state and federal agencies to further the interests of patients and families that cope with gynecologic cancer, and (7) operate as a professional association.

Jessica Hammer
Independent Scholar

See Also: AIDS-Related Cancers; European Society of Mastology; International Association for the Study of Lung Cancer; Japanese Breast Cancer Society; Leukemia and Lymphoma Society of America.

Further Readings


Society of Surgical Oncology

The Society of Surgical Oncology (SSO) was founded in 1940 by the James Ewing Society. It is a premier organization for surgeons and allied health professionals who are dedicated to advancing and promoting the science and treatment of cancer. The society participates in the Annual Cancer Symposium, promotes educational initiatives, and produces a monthly scientific journal, the Annals of Surgical Oncology. James Stephen Ewing M.D. is widely regarded as the father of oncology. The primary focus of his nonprofit foundation is to support education and research in surgical oncology. The foundation relies on contributions from SSO members, patients, other individuals, and organizations to sponsor lectureship and awards, including the James Ewing Lecture, the Harvey Baker Traveling Fellow Award, the Clinical Investigator Awards, and the James Ewing Layman's Award.

The mission of the SSO is to improve multidisciplinary patient care by advancing the education, science, and practice of surgical oncology worldwide. Key values include professionalism (advocacy for the cancer patient with integrity and ethical conduct), quality (improved understanding of the biology of cancer, compassionate communication, and optimization of outcomes across the continuum of care), lifelong learning (ongoing multidisciplinary education), leadership (developing disciplines and providers for the future and leading the public and health professional on the importance of surgery in multidisciplinary care), and discovery (innovative patient care). Along with the mission of the SSO in clarifying the role of the surgical oncologist, the SSO also recognizes that managing a surgical oncology practice is complex. With that in mind, the SSO assists the practicing surgeon with evidence-based clinical guidelines in breast cancer, gastrointestinal cancers, melanoma, biliary cancer, endocrine cancer, and sarcoma.

In 2007, the SSO began the Clinical Investigator Award Program (CIA) with a goal of encouraging patient-oriented research by training surgical oncologists in clinical and translational sciences. The award is $50,000 annually for two years. Beginning in 2013, the administration and management of the program was moved to the James Ewing Foundation. The foundation also assumed solicitation of grant funding and support. Applicants must be surgical oncologists within 10 years of the completion of training and SSO members for at least six months prior to application.

The SSO strongly encourages its member surgeons to recruit patients for appropriate trials. The Alliance for Clinical Trials in Oncology, consisting of the American College of Surgeons Oncology Group, Cancer and Leukemia Group B, and the North Central Cancer Treatment Group, is a center for information regarding surgical oncology trials. Also, the Annals of Surgical Oncology promotes high-quality surgical oncology management by disseminating advances in research that are relevant in the provision of multidisciplinary care of patients with cancer. The Annals of Surgical Oncology is the official journal not only for the SSO, but also for the American Society of Breast Surgeons.

As a leading provider of continuing education, the SSO was awarded the designation of Accreditation with Commendation by the Accreditation Council for Continuing Medical Education (ACCME). This is the highest accreditation, extending the reaccreditation period from four to six years. Only 15 percent of the 2,000 accredited providers receive this distinction. The SSO was found to exhibit compliance in all 19 of ACCME’s criteria.

The SSO’s accomplishments include a comprehensive consensus guideline on margins for conserving breast tissue during surgery, an international exchange program, and assistance with the development of the first qualifying exam in complex general surgical oncology. In 2013, the SSO approved the short-term International Career Development Exchange Program. In its first year, participants were from the Indian Association of Surgical Oncology, Japanese Society of Gastrointestinal Surgery, and Sociedad Mexicana de Oncologia.

In February of that year, the SSO released the comprehensive consensus guideline on margins for conserving breast tissue during surgery with the American Society of Radiation Oncology. The guidelines were developed, in part, from a grant from the Susan G. Komen foundation. It is endorsed by the American Society of Clinical Oncology and the American Society of Breast Surgeons. Supporting documentation for the guideline is available in the SSO’s Annals of Surgical Oncology with complimentary access to increase...
the impact of the research. The guidelines are available on the SSO’s Web site. Collaborating with the American Board of Surgery, the Accreditation Council for Graduate Medical Education, and the American Board of Medical Specialties resulted in the Complex General Surgical Oncology Exam, which first was offered in September 2014.

The SSO is currently promoting two fellowships. The Breast Oncology Fellowship Match matches qualified applicants with positions in breast oncology fellowship training programs approved by the SSO. The Surgical Oncology Fellowship Match is coordinated by the National Resident Matching Program, and SSO members are encouraged to apply.

The SSO is also promoting an opportunity to experience the United Kingdom as a visiting professor. The Royal Society of Medicine and the Royal Society of Medicine Foundation also promote this opportunity. The successful candidate receives $10,000 to cover travel and living costs, with support from the trustees of the L.W. Froehlich Charitable Trust. The opportunity enables the candidate to spend two weeks in the United Kingdom and visit three to four prearranged centers to deliver lectures.

Jessica Anne Hammer
Independent Scholar

See Also: American College of Radiation Oncology; Canadian Society of Surgical Oncology; European Society of Surgical Oncology; Hong Kong Cancer Chemotherapy Society; Japanese Association for Molecular Target Therapy of Cancer.

Further Readings

Solar Radiation

The sun accounts for cutaneous synthesis of vitamin D in humans; however, the sun’s light also carries dangers. Sunlight at the top of the Earth’s atmosphere is 50 percent in the infrared spectrum, 40 percent in the visible spectrum, and 10 percent ultraviolet (UV). Although the atmosphere filters out more than 70 percent of the UV, enough reaches the surface to form the primary cause of skin cancer. More than 90 percent of skin cancer incidence is caused by exposure to UV radiation from the sun. Solar UV is composed of two components, 95 percent UVA and 5 percent UVB. UVB exposure carries greater danger of producing sunburn and cancer in humans through deoxyribonucleic acid (DNA) damage. Such solar exposure, and incidental other exposures such as tanning beds, are recognized as increasing the risk of all three primary types of skin cancer, basal cell, squamous cell, and melanoma. Skin cancer is the most common form of cancer in the United States, with approximately 3.5 million diagnoses in over 2 million patients annually. Basal cell and squamous cell cancers, often termed nonmelanoma skin cancers, are unlikely to spread beyond the skin to other areas of the body, in contrast to the more aggressive melanomas.

Types of Skin Cancer
Basal cell cancers account for approximately 80 percent of nonmelanoma skin cancers. This is the most common form of skin cancer, with an estimated 2.8 million annual diagnoses in the United States. This lesion is slow growing, and may damage the surrounding tissues, which can present a small inflamed area around the margin. The lesion usually appears as a shiny raised area of the skin, sometimes with an associated ulcer. Treatment can usually be performed on an outpatient basis in the office of the physician or clinic. The first step after visual examination is a biopsy. Under local anesthesia, a small sample of tissue is removed and microscopically examined. If basal cell cancer is confirmed, the tumor is usually removed surgically, again under local anesthesia. The extent of the surgery is determined by the size, location and depth of penetration of the tumor. Pain or discomfort during and following the procedure is rare, and the outcome is normally positive.

Squamous cell cancer is the second most common type of skin cancer, with an estimated 700,000 annual diagnoses in the United States. Squamous cell cancers are more likely to spread, but like basal cell cancers, they are unlikely to result in death.
In the United States, these two nonmelanoma cancers cause less than 0.1 percent of all cancer deaths. Squamous cell cancer usually presents as a raised lesion with a scaly top, again possibly with an ulcer. A margin of inflamed tissue surrounding the lesion may also be present. As with basal cell cancer, treatment is usually by surgical removal. One of several surgical techniques may be employed. With ordinary excisional surgery, a scalpel is used to remove the growth, along with a surrounding margin of apparently healthy tissue. If the wound is extensive, it may be closed with sutures, otherwise it is simply bandaged. The tissue is sent to a laboratory for microscopic examination to insure that all cancer cells have been removed. In some cases, additional surgery may be required, although this is uncommon.

In Mohs micrographic surgery, a scalpel or curette is used to remove the lesion along with a thin layer of surrounding tissue under local anesthesia. The layer of tissue is microscopically viewed to determine if tumor cells are present. If so, succeeding layers are viewed until the final layer is free of tumor cells. Electrosurgery, or electrocautery, may be used. Here, the lesion is excised with a curette, and then the burning heat of an electrocautery needle is used to eradicate any additional tumor cells and to control bleeding. The procedure is repeated on a layer-by-layer basis to eliminate any residual tumor cells. This procedure is primarily used in basal cell cancers, and may not be as effective in squamous cell tumors. Two less-employed surgical techniques are cryosurgery and laser surgery. In cryosurgery, the tumor is frozen with liquid nitrogen. No anesthesia is required. The application is repeated several times to destroy malignant cells. The area develops a scab that usually sloughs off in a matter of days or weeks. In laser surgery, a laser is used to remove the outer epidermal layer and some deeper tissue. Since the laser seals blood vessels as it cuts, the procedure is bloodless. Currently, this technique is primarily limited to patients with basal cell cancer and comorbid bleeding disorders.

Cutaneous melanoma is becoming a more common disease. An estimated 76,000 new cases representing 4.6 percent of all new cancer cases were diagnosed in the United States during 2014, with 9,700 estimated deaths. The increasing incidence may be attributed to increased recreational exposure to sunlight, an increasing amount of UVB making the descent through Earth's atmosphere to the surface, or more alert early detection of the disease. About 2.1 percent of men and women will be diagnosed with cutaneous melanoma at some point in their lifetime. The male to female ratio of diagnoses is roughly 3:2, and is most frequently diagnosed in patients between 55 and 64 years old. Typically, the melanoma patient is fair in complexion and light eyed, with red or blond hair and a tendency to sunburn, rather than tanning.

Identification and Treatment
The most common site for cutaneous melanoma lesions in men is the back; in women, the legs. The first step in diagnosis is visual, using the acronym ABCDE to identify signs and symptoms: the cancerous lesion is Asymmetrical in shape; the Border of the lesion is irregular, ragged, or notched, rather than smooth; Color—melanomas usually have multiple shades of black, brown, or tan;
Solar Radiation

Diameter—moles greater than 6mm are more suspicious than smaller lesions; and Enlarging—the lesion is enlarging or growing. The initial diagnosis is confirmed with a biopsy. Metastatic melanomas may be detected by X-rays, computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET), or ultrasound scans. Treatment options, depending on the stage of the disease, may include surgery, chemotherapy, immunotherapy, or radiation therapy. Evaluating the stage of the disease is important in order to determine the treatment modality or modalities to be employed. Melanoma stages are determined based on the size or thickness of the tumor, whether it has spread to the lymph nodes or other organs, and the rate at which the lesion is growing. The stages and potential treatments are:

Stage 0. The cancer cells are confined within the epidermis and have not spread or penetrated. Treatment is usually by surgical excision alone, with adequate margins to reduce the possibility of recurrence at the original site.

Stage I. Cancer cells have penetrated deeper into the skin, but have not spread to the lymph nodes or other organs. Subcategories involve penetration less than 1mm without ulceration, or ulceration and rapid division, or one to two millimeter penetration without ulceration. Treatment is usually by wide surgical excision. In some cases involving the subcategories that make the possibility of spread to nearby lymph nodes more likely, a sentinel node biopsy is recommended. If positive, surgical removal of all nearby lymph nodes may be recommended.

Stage II. Cancer cells have penetrated more deeply into the skin, but have not spread to the lymph nodes or beyond. Subcategories involve depth of penetration, one to two millimeters, two to four millimeters, or deeper than four millimeters with or without ulceration. The treatment is wide surgical excision, and may include sentinel node biopsy and lymph node dissection. Adjuvant therapy with interferon may also be employed.

Stage III. Cancer cells have spread to nearby lymph nodes, but not distant organs. Subcategories include spread to one to three nearby lymph nodes, or nearby areas of skin or lymphatic channels, but not to lymph nodes, or the above and four or more nearby lymph nodes. Wide surgical excision, lymph node excision, and adjuvant therapy may be employed, as well as radiation therapy to the area of lymph node removal. Other possibilities for treatment may include targeted therapy, immunotherapy, chemotherapy, or a combination of these.

Stage IV. The cancer cells have spread beyond the epidermal layers and regional lymph nodes to distant organs such as the liver, lungs, or brain, or distant lymph nodes and areas of the skin. Curative therapy at this stage is unlikely, but many modalities have been sought to prolong survival. Chemotherapy may include administration of drugs like dacarbazine or temozolomide. A combination of chemotherapy with interleukin-2 or interferon may be used. Clinical trials with new targeted drugs, immunotherapy, and combination chemotherapy are ongoing. In a few short years, the approved drug armamentarium has been expanded to include newer agents such as vemurafenib, ipilimumab, dabrafenib, and trametinib. These and other agents currently in trials offer hope at least for prolonged survival and improved quality of life for late stage melanoma patients.

Even with improvements in therapy, a primary weapon against the scourge of skin cancer is prevention. Measures to minimize the exposure of the skin to ultraviolet radiation should be taken, although with a sense of balance toward the necessity for outdoor occupations and the pleasures of recreational activities. When practical, protective clothing should be worn, including such wardrobe items as long sleeves, long trousers, sunglasses, and wide-brimmed hats. If possible, exposure to sunlight at peak radiation hours between 9 A.M. and 3 P.M. should be avoided or minimized. A guideline can be to avoid exposure when an individual's shadow is shorter than their height. A broad spectrum sunscreen with a sun protection factor (SPF) rating of at least 30 should be applied to exposed areas. Beyond 30, the incremental protection achieved is minimal. Some clinicians question the value of sunscreens in long-term exposure, but definitive studies have not been conducted.

Walter Landers
Independent Scholar
Solvents

A solvent is a substance used to dissolve another chemically or physically different one, called a solute, such as a gas dissolved into a liquid, to form a solution. Commonly used solvents are found in nail polish and hair extension removers (acetone, acetonitrile), paint and lacquer thinners (turpentine, naphtha), spray and aerosol pressurized liquids (propane, isobutane), perfumes (ethylic alcohol), and detergents (various terpenes). Solvents are roughly classified into polar and nonpolar, depending on their dielectric constant and their ability to dissolve ionic compounds. Other important physical properties of solvents are boiling point, which defines the temperature and speed at which a given substance will evaporate, and density. Whereas the first is helpful to predict if that solvent will instantly transform into a gas at room temperature (e.g., in sprays), the second will define its partitioning when mixed with other liquids such as water (i.e., if it will form a separate layer on top, or if it will sink to the bottom of the container).

Direct or chronic exposure to organic solvents constitutes a well-known health hazard in many industrial facilities, shipyards, and workplaces, such as in painting, printing, dry cleaning, and rubber manufacturing. To address this problem, various standards to ensure worker safety have been defined through the years. Direct exposure to large amounts of organic solvents may cause severe acute reactions including toxicity to the nervous system, liver, or kidneys; dermatitis; respiratory impairment; sudden loss of consciousness; and even death. Chronic exposure to even small quantities of solvents may cause long-term adverse effects such as neuropsychiatric effects, eye cataracts, and an increased risk of cancer.

Many studies provide detailed information about the correlation between casual or occupational exposure to organic solvents and cancer outcomes. For example, in Canada, 40 percent of male cancer patients in Montreal experienced exposure to solvents, and occupation as a painter has consistently been associated with a 40 percent increased risk of lung cancer, and a 20 percent increased risk of all cancers. Scientific literature has primarily focused on exposure to specific compounds, including benzene, trichloroethylene, tetrachloroethylene, and methylene chloride, but many studies on mixtures of unspecified organic solvents have also been made.

Benzene

Benzene is probably the most thoroughly investigated solvent because it is commonly found in the environment, coming from industrial discharge, motor vehicle exhaust, burning oil and coal emissions, and even indoor tobacco smoking. Many organic solvents used in industrial manufacture contain benzene, or are broken into byproducts that form it. Benzene is nonpolar, colorless, and very volatile, yet is able to dissolve in water, and thus can pass through the soil into underground water, further contaminating the environment. Everyone is exposed to a small amount of benzene every day, mainly through breathing air containing small percentages of it. Benzene has been determined as a known carcinogen by many sources such as International Agency for Cancer Research (IARC), U.S. Environmental Protection Agency (EPA), and U.S. Department of Health and Human Services (DHHS). It has repeatedly been shown to induce hematopoietic cancers such as acute myeloid leukemia (AML) and cancers of the ovaries, mammary glands, pancreas, and liver. A vast retrospective
cohort study conducted in China during the early 1980s among 28,460 benzene-exposed workers showed a relative risk for leukemia of 5.74, and for lung cancer of 2.31. Also, mortality for malignant neoplasms was more than doubled among the exposed subjects. Benzene exposure has also been directly linked to birth defects, and it is a known teratogen.

**Chloroform**
Chloroform (trichloromethane) is a colorless dense liquid with a pleasant odor and sweet taste. It was one of the first inhaled anesthetics used through the 19th and 20th centuries during surgery practices, but was later abandoned in favor of ether. Today, it is mostly used in the chemical industry as a precursor to refrigerants and Teflon, and its only medical use is as a solvent in nuclear magnetic resonance (NMR) spectroscopy. Chloroform may be found in small amounts in chlorinated drinking or swimming pool water, and may pose a risk for people who work with it, especially if inhaled. Acute inhalation exposure to chloroform in humans causes central nervous system depression and possible liver and kidney damage. Chloroform is suspected of causing cancer because liver and kidney tumors have been reported in laboratory animals exposed to this substance. Even if epidemiologic studies on human subjects suggest an association between cancer of the large intestine, rectum, and bladder and chlorinated water, data is still incomplete and not yet consistent enough to confirm these claims. Nonetheless, the DHHS determined that chloroform may reasonably be anticipated to be a carcinogen, while the EPA determined that chloroform is likely to be carcinogenic to humans by all routes of exposure, but only under high-exposure conditions.

**Formaldehyde**
Formaldehyde is a colorless flammable gas with a characteristic pungent smell. It has a broad range of uses, ranging from the production of fertilizers, glues, paper, pressed-wood household furniture, and insulating materials to a wide variety of other industrial uses such as fungicide, germicide, preservative, embalming fluid, and as an important precursor to many other materials and chemical compounds. Formaldehyde is normally present in both indoor and outdoor air at low levels (ranging from 0.02 to 0.04 parts per million), but various materials containing formaldehyde (such as plywood, furniture, and carpets) can release formaldehyde gas or vapor into the air. Other sources of this substance include cigarette smoke, automobile exhaust, gas and wood stoves, heaters, and glues/resins. Exposure primarily occurs by inhalation of formaldehyde gas and vapor, and by absorbing liquids containing it (such as formalin) through the skin. Effects of acute exposure to formaldehyde usually include eye and mucous membrane irritation, coughing, asthma, and headaches. Formaldehyde has been classified by both the IARC and EPA as a known human carcinogen, confirmed by various epidemiological studies. Professionals exposed to formaldehyde in their occupation, such as funeral industry workers and embalmers, showed an increased risk of leukemia and brain cancer compared with the general population. Other cohort and case-control studies found an association between formaldehyde exposure and nasopharyngeal and nasal sinus cancer.

**Methylene Chloride**
Methylene chloride (dichloromethane, or DCM) is an organic colorless liquid compound used in degreasing metal parts, as a paint stripper, industrial solvent, aerosol and pesticides propellant, and in the manufacture of photographic film, textiles, and plastics. DMC is highly volatile, constituting a potential acute inhalation hazard that may lead to a carbon monoxide poisoning, hepatitis, and chemical skin burns. In many laboratory animal studies, methylene chloride showed various degrees of carcinogenicity, inducing liver, lung, and pancreas tumors in various rodents. Several cohort studies of potential occupational hazards examined many workers daily or occasionally exposed to dichloromethane for up to 20 years, showing mixed results. However, the World Health Organization (WHO), EPA, and DHHS classified methylene chloride as a probable cancer-causing agent in humans.

**Styrene**
Styrene is an organic compound that appears as a colorless, somewhat volatile liquid, with a sweet pungent smell. Its main use comes from its ability to polymerize, a chemical property that allows styrene to act as a precursor for many other substances such as polystyrene and other copolymers (acrylonitrile butadiene styrene, or ABS; styrene-butadiene rubber, or SBR; and styrene-acrylonitrile, or SAN). These polymers and styrene are used to
manufacture rubber, plastic, carpet backing, synthetic foams, fiberglass, automobile and boat parts, pipes, and shoes. Effects of acute exposure to styrene usually manifest with nervous system toxicity symptoms like concentration problems, hearing loss, or change of color vision. Both the IARC and DHHS classify styrene as reasonably anticipated to be a human carcinogen, an assessment that has recently been backed up by the U.S. National Toxicology Program's findings.

**Tetrachloroethylene**
Tetrachloroethylene (perchloroethylene, or PCE) is a volatile nonflammable liquid with a distinctively sweet odor. It is widely known worldwide for its use as dry-cleaning fluid. Tetrachloroethylene exposure may cause skin irritation through direct contact because it dissolves epidermal fats, and can act as a central nervous system depressant if inhaled in large doses. Many studies that assessed the effects of chronic tetrachloroethylene exposure on dry-cleaning workers suggested that this compound may increase the risk factor for cancer in humans. Also, tetrachloroethylene has been shown to cause liver tumors in mice and kidney tumors in male rats. For these reasons, the IARC and DHHS classified it as probably a carcinogen.

**Trichloroethylene**
Trichloroethylene is a clear nonflammable liquid used as an industrial solvent to remove grease from metal parts, and as dry-cleaning spot remover. In the past, it was also used to extract vegetable oils (e.g., soy, palm, and coconut oil), for coffee decaffeination, and as a volatile anesthetic together with nitrous oxide. Although Europe and North America replaced its pharmaceutical and food industry uses because of its acute and chronic toxicity, it still saw some use as a potent inhaled obstetrical analgesic in less-developed African countries. It enters the body mainly through inhalation of its vapors or direct skin contact, but it can also be ingested by drinking contaminated water in areas near factories or waste disposal sites. Other than the acute toxic effects reported after ingestion or inhalation of high levels this substance, such as kidney and liver damage and arrhythmias, trichloroethylene is considered probably carcinogenic to humans. Epidemiologic meta-analysis showed a relative risk (RR) of 1.7 for kidney cancer, 1.9 for liver cancer, and 1.5 for non-Hodgkin's lymphoma. Recent molecular epidemiology studies confirmed its supposed carcinogenicity by showing specific renal cell mutations primarily found in renal cell carcinoma patients exposed to trichloroethylene.

Claudio Butticè
Independent Scholar

**See Also:** Breast Cancer; Kidney Cancer; Leukemia, Acute Myeloid, Adult; Leukemia, Acute Myeloid, Childhood; Liver Cancer; Nasopharyngeal Cancer.

**Further Readings**

**Somalia**

The Somali Democratic Republic is situated in eastern Africa. It is bordered on the north, east, and south by the Indian Ocean, and on the west by Djibouti, Ethiopia, and Kenya. It is the 27th most populous country in Africa, and 89th in the world, with a population of over 8.3 million. The two statutory national languages are Arabic and Somali, while English and Italian are statutory working languages, and there are 14 living indigenous languages still spoken by respective ethnic groups in Somalia. The most widely spoken include Kiswahili, Maay, and Oromo.

Somalis have depended upon traditional medicine, particularly medicinal plants, for a long time, and they still largely depend on this practice, augmented by medieval Arabic medical practices. Each ethnic group has a rich tradition of ethnomedicine. For example, a traditional healer who uses...
medicinal plants for treating ailments is known as wadaad in Arabic, mganga in Kiswahili, and dofa in Oromo.

There are many traditional medicinal preparations used in Somalia for treating cancers and other conditions. Most of these traditional medicines incorporate the use of local plant materials, many of which have shown medicinal properties in laboratory studies. For example, myrrh or Commiphora myrrha, which is used in Somali traditional medicine as a panacea for many ailments, including cancers, has demonstrated antitumor, antibacterial, and anti-diarrheal efficacy. Research suggests that use of certain plants may help protect against cancer by reducing oxidative stress and stimulating enzymes and other processes that help the body fight carcinogens. For example, an extract from Boswellia serrata, referred to as yagar or yigaar in Somali, demonstrated antioxidant properties.

Medicinal plants are prescribed by traditional healers to treat respective ailments, including cancers. For instance, juice from Commelina forskoolii is used by traditional healers in Somalia for treating uterine cancer. A root decoction of Adenium obesum, which in Arabic is called sim-es-samak and in Somali is called warrab-karon, dun-durwa, or habaarticaa, is traditionally used to treat rhinitis. Commiphore guidottii is traditionally used to treat stomach problems, including diarrhea. The leaves of Sansevieria bagamoyensis are pounded, squeezed, and then filtered; the resulting liquid is drunk, and the residue is topically applied for treating convulsive fevers.

Somalia is a signatory to the Single Convention on Narcotic Drugs, Convention on Psychotropic Substances, and U.N. Convention Against the Illicit Traffic in Narcotic Drugs and Psychotropic Substances; consequently, laws exist to control narcotic and psychotropic substances and precursors. The annual consumption of controlled substances is highly regulated to curtail abuse. Accordingly, the annual consumption of morphine in 2009 was 0.000285 milligrams per capita, and pethidine was 0.16131 milligrams per capita. In 2010, the annual prevalence of use of all opiates as a percentage of the population aged 15 to 64 years in Somalia was 0.16 percent, which ranks it as the 19th-highest country. These factors make the provision of palliative care for cancers and other ailments problematic. Further, there are serious deficiencies of modern pharmaceutical supplies, as opposed to traditional preparations, and in modern medical services for cancer and similar conditions in Somalia. According to the World Health Organization (WHO), in 2010, there was no general availability of either chemotherapy or radiotherapy in the public health system in Somalia.

Partly because of the shortage of medical services and supplies, health problems are endemic in Somalia. The five leading causes of morbidity, in rank order, are malaria, respiratory infections, dyspepsia, parasitic diseases and infections, and pneumonia. The average number of cancer cases annually are 113.5 per 100,000 of the population. Cancers account for a substantial amount of disability and suffering among impacted populations. According to the WHO, in 2004, the 10 most prevalent cancers per 100,000 population in Somalia were led by liver cancer at 258; lymphomas at 242; cervical and uterine cancers at 234; esophageal cancer at 233; breast cancer at 135; mouth and oropharynx cancers at 120; stomach cancer at 119; leukemia at 92; colon and rectal cancers at 80; and trachea, bronchial, and lung cancers at 77.

Modern medical supplies and services are in short supply in Somalia. Both prescription and over-the-counter products are often unavailable. Consequently, health problems are endemic and limit development. For example, an estimated 43,000 people live with human immunodeficiency virus (HIV) in Somalia, which ranks the country 38th highest in Africa, and 65th highest in the world. The mortality rate for HIV/acquired immunodeficiency syndrome (AIDS) is 81 per 100,000 population. Debate continues on the relative risks in Africa for respective cancer types for those infected with HIV. The mortality rate for tuberculosis is 64 per 100,000 population, and that for malaria is 51 per 100,000 population.

Skin cancers are the 11th most-common cause of age-standardized cancer deaths in Somalia, and occur at a rate of 3.57 per 100,000 population, which ranks 13th highest in the world. Furthermore, according to the WHO, in 2008, the age-standardized estimates of deaths from all cancers was 105 per 100,000 population for males and 97 per 100,000 population for females. As a consequence, life expectancy is only 47.71 years, which ranks Somalia 32nd in Africa and 203rd in the
With this ethnic diversity come a variety of languages (official and other home languages), cultures, and religious beliefs, all of which challenge cancer control in the country. Cancer treatment and education were not available to most South Africans until the end of apartheid in 1994. Most quality health care and cancer treatment was only available to whites; however, that continues to change over time with the work of the Cancer Association of South Africa (Cansa). Another major challenge is the availability of health care workers; World Development Indicators report that there are 80 physicians (generalists and specialists) for every 100,000 people, and 490 nurses per 100,000 people, for a population approaching 53 million and a growing cancer burden.

Approximately one in four South Africans are affected by cancer in their lifetime, with more than 100,000 South Africans diagnosed with cancer yearly, and more than 60,000 dying from cancer each year. About one in six South African men and one in seven South African women will have cancer during their lives. In South Africa age, race, gender and socioeconomic status play an important role in determining the prevalence of certain cancers. The prevalence of behavioral and environmental factors related to smoking, alcohol consumption, and diet are also salient. For example, the grinding process of homegrown maize has been linked to esophageal cancer. It is believed that the silica produced from the grinding process injures the esophagus and prolonged inflammation increases the risk of cancer. This phenomenon has resulted in the former Transkei region on the eastern Cape being identified as an esophageal cancer hotspot. The rate of this cancer type is six times the national average when compared to the rest of the country.

The cancers affecting all South African men, in order of prevalence, are prostate, lung, esophageal, bladder, and colorectal cancer. The cancers that are more prevalent among black South African men are esophageal, lung, liver, and larynx cancer. The cancers affecting all South African women, in order of prevalence, are breast, cervical, colorectal, lung, and esophageal cancer. Cancers that are more prevalent among black South African women, in order of prevalence, are cervical, breast, esophageal, uterine, and lung cancer. The cancers most prevalent among South African children, in order of prevalence, are leukemia, brain tumors,
South Korea

The east Asian nation officially called the Republic of Korea is one of the newer nations in the world, authoritatively established in 1948 after Japan's withdrawal from the country in 1945. An agreement at the United Nations led to Korea's split in half along the 38th parallel north, with the top portion of the territory turned into the Democratic People’s Republic of Korea, and the bottom portion becoming the modern Republic of Korea. Presently, the nation has one of the top 25 most bustling economies in the world, and it is composed of a population of over 50 million citizens.

In recent times, South Korea has been the site of extremely promising research in the battle against cancer. In January 2014, researchers at Chonnam National University in Gwangju, South Korea, claimed to have created the first nanobots capable of fighting cancer. More specifically, the researchers genetically altered salmonella bacterium to train the bacteria to seek out cancer cells to destroy them. The bacteria are able to locate a patient’s cancer cells as a result of the bacteria searching for a particular secretion that only cancer cells emit. Although the technique is still in development, and the bacteria can only seek out certain kinds of cancers, the discovery is potentially a huge breakthrough in cancer research. Recently, South Korean scientists have also conducted research regarding the possibility of using magnets to eradicate cancer cells. Magnetic fields might be a viable way to combat the disease.

Annette Madlock Gatison
Southern Connecticut State University

See Also: AIDS-Related Cancers; Cancer Association of South Africa; Tobacco.

Further Readings


Every year, cancer is estimated to cause over 50,000 deaths in South Korea, and information collected from regional cancer registries within the nation suggests that mortality incidences related to cancer will continue to increase in coming years. In 1980, the Korean Ministry of Health and Welfare established the nation’s first nationwide cancer registry, the Korea Central Cancer Registry. In 1995, with the Ten Year Plan for Cancer Control, the Korean government mounted a concerted national effort to combat the rise of the disease, which has now become the leading cause of death in the country. Fortunately, the vast majority of the Korean population has health insurance, which has allowed Korean physicians to effectively and quickly diagnose cancer cases in the nation.

Currently, the most prevalent forms of cancer in South Korea are bowel, breast, lung, stomach, and thyroid cancer. Bowel, liver, lung, and stomach cancers account for over two-thirds of all cancer incidences in males in South Korea, whereas breast, bowel, stomach, and thyroid cancers make up over one-half of all cancer incidences in females there. The Republic of Korea has the highest rate of stomach cancer incidences in the entire world, with over 40 Koreans diagnosed annually with the disease per every 100,000 Korean citizens; scientists believe that the reason for such high stomach cancer rates within the Korean population is a result of certain nutrition factors, such as high levels of sodium in the average Korean’s diet. Incidences of uterus cancer in females are increasing within the nation, whereas incidences of lung cancer in both genders is declining.

Many famous South Korean citizens have been diagnosed with cancer during the nation’s history. For instance, Jang Jin-Young, an actress and former winner of the Miss Korea beauty contest, died in 2009 at the age of 35 after losing her brief battle with stomach cancer. John Tae-Suk Lee, a prominent South Korean Catholic missionary who spent many years providing medical services in Africa, passed away in 2010 as a result of bowel cancer. Moreover, South Korean Myung Jae Nam, who created the famous martial arts styles of Hankumdo and Hankido, died in 1999 after succumbing to stomach cancer.

South Korea has an excellent health care system, highly trained specialists, and numerous world-class medical facilities. For example, Dr. Kang Hyun Lee became the sixth president of the Korean National Cancer Center on July 18, 2014. Dr. Lee has long contributed his expertise to the Republic of Korea’s battle against cancer, and he even worked at the Seoul National University Hospital in the nation’s capital. The Seoul National University Hospital is one of the most advanced medical facilities in the world, and is home to 26 separate cancer treatment centers. This allows patients at the hospital access to incredibly personalized and specialized treatment regimens.

William M. Peaster
Independent Scholar

See Also: Bowel Cancer; Breast Cancer; Lung Cancer; Stomach Cancer; Thyroid Cancer.

Further Readings
Spain

Spain has a population of 47 million inhabitants, with one of the lowest birth rates in Europe. As a country from the southwestern area, Spain has specific features related to cancer, its registries, control, and incidence. In that Mediterranean region, the number of cases and deaths is lower than in western Europe, and much lower than in eastern Europe. In general, the population from Sweden, Spain, Switzerland, and France has a lower mortality rate compared to southeastern countries in Europe. However, cancer is still a big killer in the old continent—the incidence of cancer in men in Spain is one of the highest in the world.

According to data from the International Agency for Research on Cancer, in 2012 the most common cancer among men was prostate cancer (as in the rest of Europe), but with a very low mortality rate. The second-most common among men is lung and trachea cancer, with a high mortality rate. The most common among women is breast cancer, with a high incidence and low number of deaths for that cause. The second-most common among women is large bowel cancer, also with a low mortality rate. Also in 2012, about 215,534 cases were diagnosed, and there was an estimated risk of 21 percent suffering cancer before 75 years old. The expected number of cases for 2015 is 227,076, a higher rate because of the aging of the population. In absolute figures, the incidence of cancer is higher among the male population (135,954) than among females (91,122). According to the Spanish Institute of Statistics, malignant tumors are the first cause of death among men, and the second among women. In men, the five-year relative survival was 44 percent for all kind of cancers, and for women 59 percent. The mortality rate remains low thanks to early diagnosis and the efficacy of treatments, although it is still far from other countries like the United States.

With the conviction that prevention is the first step to fight cancer, priority to prevention programs was given in the last decades. Those programs are organized according to two categories: primary prevention (actions meant to prevent disease occurrence, such as informing people about good health habits) and secondary prevention (activities mean to reduce the impact of a disease through early detection and treatment, such as screening programs to facilitate early detection of the disease). The benefits of screening are successful when a high participation of the population is involved—and for that purpose everyone has to be properly informed, even about the negative effects of Control of Smoking was created in 2003 with the purpose of reducing the prevalence of tobacco consumption and protecting the population against the dangers of smoke. The mortality rate from lung cancer has decreased compared to 20 years ago, but it has increased for women, especially those between 46 and 64 years old. From the point of view of exposure to carcinogen agents, about 25 percent of the working population in Spain is susceptible of suffering from cancer because of external (occupational or environmental) elements.

Spain is a member of the European Network of Cancer Registries, established in 1990 by the European Commission within its program Europe Against Cancer. It organizes activities and coordinates projects of collaboration between different European national registries. Spain is one of the first European countries to have created a registry of cancer patients between 1902 and 1908, following the German attempt to register all cancer patients under treatment. However, the first modern registry was created in 1960 in Zaragoza, and 1976 the National Population-based Cancer Registration Plan was launched. Current registries meet the quality indicators established by the Agency for Research on Cancer. Progressively, all registries became involved in collecting detailed data on patients’ treatments, diagnosis, or disease stage. Currently, there are a total of 23 regional cancer registries and 63 hospital cancer registers in the country. Other reliable sources of data are provided by the White Paper of Spanish Oncology that offers a general vision of the situation in Spain, or the Directory of Resources for Palliative Care, edited by the Spanish Society for Palliative Care. The National Catalogue of Hospitals is an inventory of what kind of equipment and treatments are offered at each hospital.
Squamous Neck Cancer With Occult Primary, Metastatic

Metastatic squamous neck cancer with occult primary is a form of cancer where cancerous squamous cells spread to lymph nodes in the neck. (Lymph nodes are small bean-shaped structures that are found throughout the body and are responsible for the production and storage of immune cells in the body.) Squamous cells cover the skin surface and the lining of body cavities and hollow organs like the uterus and blood vessels, as well as the lining of the respiratory (breathing) and digestive tracts. The mouth, esophagus, lungs, kidneys, and uterus all have a lining of squamous cells. Once the cancer has spread (metastasized), it is not possible to know the site of cancer initiation in the body. Metastasis in the upper and middle neck regions is generally attributed to head and neck cancers, whereas metastasis in the lower regions of the neck is believed to have a primary tumor site below the clavicle.

Squamous cell cancer of the neck, whose site of origin cannot be diagnosed, is referred to as the occult (hidden) primary tumor. Such cancers constitute about 5 to 10 percent of all patients with cancers of unknown primary site. Squamous cell cancer of the head and neck is one of the most common cancers worldwide. It constitutes about 4 percent of all cancers in the United States, and 5 percent in the United Kingdom. In cases where the primary tumor is occult, the primary tumor generally regresses either because of a slower growth rate or an impaired neovascularization. In such events, the result is the formation of a biologically adapted tumor with a metastatic phenotype. Metastatic tumors are extremely aggressive and resistant to systemic therapies. A known primary site of the carcinoma enables administration of focused therapy to the primary site. However, in case of an occult primary carcinoma, the treatment is targeted at all secondary sites, resulting in a significantly higher morbidity, predominantly from radiation and chemotherapy.

Head and neck squamous cell carcinomas are differentiated depending on the histological appearance, as well differentiated, moderately differentiated, or poorly differentiated, depending on the difference in appearance from a normal squamous epithelium. Poorly differentiated squamous carcinomas are more aggressive, and have been associated with poor prognosis. The incidence of squamous cell carcinoma has risen, although there has been a fall in the number of cases with head and neck cancer because of public health efforts against the use of tobacco. Alcohol consumption is also associated with an increased risk. High-risk human papillomavirus (HPV) subtypes have been identified in a number of squamous cell cancers, and include HPV strains 16, 18, 31, and 33. Higher risk has also been associated with having multiple sexual partners, and engaging in high-risk sexual behavior.
Typical presentation of an occult primary squamous cell carcinoma of the neck is the presence of a painless neck mass. According to the patient, the neck mass has usually been present for weeks to months. Other associated symptoms may be the feeling of a lump in the throat or throat pain. Sometimes, the condition may remain asymptomatic during the early stages of the disease. Analysis of fine needle aspirate may reveal metastatic squamous cell carcinoma of the neck. After a metastatic squamous neck cancer with occult primary has been diagnosed, further evaluation is performed to check the spread of cancer to other sites in the body. The tumor is classified either as untreated or recurrent because there is no standardized staging protocol for metastatic tumors. Several clinical tests such as chest X-ray, computerized tomography (CT) scan and magnetic resonance imaging (MRI) are used to evaluate secondary tumors in other parts of the body.

Surgery alone can be used for patients with early-stage neck disease, followed by post-operative radiation therapy in cases involving multiple lymph node and connective tissue invasion. However, curative surgical removal of an occult primary is limited to the removal of the affected lymph nodes, followed by radiation therapy of the head and neck. Advanced stages may also require a combination with systemic chemotherapy as a palliative measure. As large areas of tissue are radiated, the treatment can have severe side effects, and may result in debilitating morbidity in the long term. Untreated metastatic squamous neck cancer with occult primary may be treated by surgery where the affected lymph nodes are resected.

Depending on the individual case, a physician may decide to give radiation therapy in combination with surgery. Chemotherapy is another option to treat metastatic squamous neck cancers with primary occult. Several clinical trials also offer options for treatments that are novel and may involve a combination of chemotherapy and radiotherapy with new drugs or a cocktail of drugs. Some trials also test the efficacy of novel drugs that block specific cellular pathways in cancer cells.

Poonam Balani

Independent Scholar

See Also: Head and Neck Cancer; Yul Brynner Head and Neck Cancer Foundation.

Further Readings

Sri Lanka

The Democratic Socialist Republic of Sri Lanka, formerly known as Ceylon, is an island country south of the Indian subcontinent, home of many different cultures and religions. Moors, Kaffirs, Sinhalese, Tamils, Burghers, and many other ethnic groups live together in its capital, Colombo, which has more than 4.5 million inhabitants. Sri Lanka was colonized by Portuguese and Dutch explorers from the 17th century until the early 1800s, when Great Britain occupied and then conquered the country. The British started cultivating vast plantations of coffee, tea, cinnamon, and rubber, changing the country’s economy into a major commodities exporter. Following the end of colonialism and the fall of the British Empire, in 1972, Sri Lanka repudiated its dominion status and declared independence, becoming a republic.

Tensions between the ruling Sinhalese culture and the Tamil community started to rise in 1983, with a series of insurgencies against the government by the Liberation Tigers of Tamil Eelam (LTTE). The Sri Lankan Civil War erupted, lasting until 2009, when the LTTE front was finally defeated with the help of the Indian Peace Keeping Force (IPKF). These 26 years of war caused over 150,000 refugees, almost 300,000 displaced people, and 60,000 to 100,000 deaths.
Sri Lanka provides free universal health care and education to all its citizens. Government hospitals and other health care facilities such as laboratories are very well equipped, and all doctors and nurses are properly qualified and trained. There are 555 government hospitals in Sri Lanka, together with many private luxury clinics and Ayurvedic system facilities. The National Cancer Institute (NCI) in Maharagama is the most important cancer treatment facility in the country with a 742-patient capacity, more than 40,000 patients admitted every year, and many modern facilities providing cancer screening and diagnostic services, chemotherapy, surgery, and radiotherapy. The NCI is also the major training center for medical students of the Postgraduate Institute of Medicine (PGIM), a training program of the University of Colombo's Faculty of Medicine.

A national cancer registry, called the National Cancer Control Programme, was established in 1980, but it is partly incomplete because cancer cases from the Jaffna District between 1985 and 1995 were missed because of the civil war. The data collected was registered with all modern methodologies, and comes from the NCI, the teaching hospitals in Kandy, Karapitiya, and Jaffna, and the General Hospitals in Badulla and Anuradapura. Cancer is the second-leading cause for death in Sri Lanka, followed by ischemic heart diseases, and its incidence per 100,000 population showed an increase in 10 years, from 31.8 to 37.3 in the male population, and from 31.5 to 43.5 in the female population. A female preponderance is also shown in the crude incidence rate of cancers: 63.8 in males, and 72.2 in females in 2007.

The five leading cancer sites among males were oropharyngeal cancer; trachea, bronchus, and lungs cancer; esophagus cancer; colorectal cancer; and lymphoma. Among females, the top five cancer sites were breast cancer, cervical cancer, thyroid gland cancer, esophagus cancer, and ovary cancer. The pattern of cancer incidence in Sri Lanka is thus very different than that of Western countries. The preferred treatment routes for cancer were chemotherapy (52 percent), radiotherapy (50 percent), surgery (40 percent) and hormone therapy (14 percent).

Together with other common risk factors for cancer such as smoking, high animal fat consumption, alcohol abuse, and a sedentary lifestyle, in Sri Lanka some peculiar regional habits could represent additional sources of cancer. For example, betel leaves and areca nuts are chewed as mild stimulants and for their breath-freshening effects, even if they pose a serious risk of developing oral submucosal fibrosis (OSF), cancers of the mouth and esophagus, and many other systemic diseases such as type 2 diabetes and hypertension. High habitual consumption and chewing of betel liquid may account for the higher percentage of oropharyngeal malignancies diagnosed in south and southeast Asia regions: of the 390,000 cancers of this type estimated to occur in the world every year, 228,000 (58 percent) occur in these regions alone.

To improve cancer prevention and early detection, the Sri Lankan government issued a series of screening projects. Among these, many screenings of the oral cavity for oral cancer were issued among tea estate workers, identified as a high-oral-cancer-risk group. Also, sensitization and awareness campaigns against breast cancer were organized, and October was designated as breast cancer awareness month. Many volunteer national and international organizations also help by increasing public awareness about cancer prevention, and by providing psychological support for adults and children fighting cancer.

Some specialist clinics in Sri Lanka also offer Ayurvedic and traditional herbal immune therapies as complementary cancer therapies. Ayurveda medicine tries to maintain or reestablish harmony between the mind, body, and forces of nature, and while its effectiveness has not been proven by scientific literature, some of the herbs used may possess therapeutic value. Also, Ayurvedic treatment promotes body detoxification through cleansing, massage, exercise, and meditation, which in turn may improve immune response among cancer patients and reduce the side effects of chemotherapy. Ayurveda therapy may nonetheless pose a danger to health because potentially poisonous heavy metals such as arsenic, lead, and mercury are often used in excess in Ayurvedic medicines.

Claudio Butticè
Independent Scholar

See Also: Breast Cancer; Cervical Cancer; Oropharyngeal Cancer; Oral Cavity Cancer, Lip and; Tobacco-Related Exposures.
Further Readings

St. Jude Children’s Research Hospital

Research hospitals have a significant influence on the treatment, control, and prevention of cancer. Located in Memphis, Tennessee, St. Jude Children’s Research Hospital opened its doors on February 4, 1962. Upon entering the hospital, a warm atmosphere greets families, their littlest patients, and visitors. Vibrant colors adorn the walls, and a variety of small red wagons are available to transport patients through the corridors. A bright blue telephone perches atop a counter, allowing visitors who do not speak English to access support for language translation. A bust of founder Danny Thomas reveals a nose that has been worn down over the years by all the people who have rubbed the nose for good luck. Patient artwork decorates many of the walls, including a corridor of the ABCs of cancer, with entries that depict topics such as “C is for cure,” “J is for joy is everywhere,” and “N is for needles.”

According to the late founder, Danny Thomas, the hospital stands as a shrine to St. Jude Thaddeus, the patron saint of hopeless causes. Thomas was at a turning point in his life, not yet a star and with a growing family, when he contemplated giving up his dream of show business success to pursue a more stable job. He prayed to St. Jude for guidance, with the promise to build a shrine in gratitude. Shortly thereafter, Thomas was discovered and went on to become a successful entertainer and producer, best known for the television sitcom Make Room for Daddy. Thomas kept good on his word and traveled extensively to raise money to build the hospital, even going door to door in apartment complexes to ask for donations. The dedication and combined efforts of Thomas, Memphis resident Ed Barry, Dr. Lemuel Diggs, Michael F. Tamer, and the American Lebanese Syrian Associated Charities (ALSAC), and others led to fulfillment of the promise and the opening of the hospital.

Based upon a suggestion from Dr. Lemuel Diggs, the hospital was targeted toward childhood catastrophic diseases, rather than general care. Two of founder Thomas’s core beliefs guide the mission and vision of the hospital, that “no child should die in the dawn of life,” and that no child should be denied treatment based on race, religion, or a family’s ability to pay. Families do not receive a bill from the hospital for treatment, travel, housing, or food. In June 2012, the daily operating cost of the hospital was $1.9 million, predominantly covered by individual contributions.

In 1957, Danny Thomas founded ALSAC, a non-profit organization that is the fundraising partner of the hospital. Additionally, many high schools, colleges, and universities around the country actively participate in fundraising efforts for the hospital. Fraternities such as Tau Kappa Alpha and Kappa Alpha Sigma, and sororities such as Delta Delta Delta and Lambda Theta Alpha are also fundraising partners for the hospital. The campus includes housing for short-term care, Grizzly House for up to one week; medium-term care, Ronald McDonald House for one week to three months; and long-term care, Target House for more than three months. Since its inception, the hospital has treated patients from every state in the United States, as well many countries from around the world, and on average has more than 67,000 patient visits each year.

St. Jude Children’s Research Hospital has become a leader in the research, treatment, and care of pediatric patients facing catastrophic illnesses. Through the work of its dedicated staff, survival rates for acute lymphoblastic leukemia (ALL), which in 1962 were 4 percent, are now 94 percent. It is the only...
comprehensive cancer center specifically devoted to children, as designated by the National Cancer Institute. In addition to its leading role in cancer treatment, the hospital also helps pediatric human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS) patients, and has created one of the largest programs to treat pediatric sickle cell disease patients. It was the first pediatric cancer research center in the United States housing a good manufacturing practice (GMP) facility onsite, which creates biopharmaceuticals for use in clinical trials.

Ranked as one of the top pediatric cancer hospitals in the country, St. Jude Children's Research Hospital has also been ranked as one of the top 10 places to work in academia by the Scientist, and as one of the 100 best companies to work for by Fortune magazine. The hospital is partnered with Washington University School of Medicine in St. Louis for the Pediatric Cancer Genome Project. This project is geared toward understanding the genetic origins of childhood cancers, and thus far has completed whole genome sequencing of over 700 pediatric cancers. The faculty includes Nobel Prize winners, members of the National Academy of Sciences, members of the Institute of Medicine of the National Academy of Sciences, and Howard Hughes Medical Institute investigators. Founder Danny Thomas died on February 6, 1991, two days after he celebrated the 29th anniversary of the hospital with caregivers, patients, and families at the hospital. He is buried near his wife, Rose Marie, on the grounds of the hospital where a memorial garden and pavilion are located. The hospital that originally was built as a shrine to honor the patron saint of hopeless causes continues to provide hope to pediatric patients from around the world.

Kelly Morrison
Michigan State University

See Also: Leukemia, Acute Lymphoblastic, Childhood; National Cancer Institute.

Further Readings


Stainless Steel

The term stainless with respect to steel came about early in the development stages of steel that was in use for cutlery applications. This was a generic term that has since come to be associated with different types of steel, in particular the grades that are resistant to oxidation or corrosion. Stainless steel is available in three main categories: austenitic, ferritic, and martensitic. Stainless steel is an alloy made up of at least 10.5 percent chromium. There are other alloy elements that may have been added into the metal structure to help in supporting the supposed properties, and in particular properties such as strength, formability, and the cryogenic toughness that is associated with the metals. Some of the common alloys include nickel, copper, titanium, and molybdenum. Besides metallic additives, there are also some nonmetallic additives that are included into the metal structure of stainless steel, such as carbon and nitrogen. One of the main elements of stainless steel is that it is supposed to be resistant to corrosion within a given environment, or for a particular application. There are different grades of stainless steel, based on different corrosion resistance requirements.

In metallurgical terms, stainless steel is known as inox, or inox steel, which comes from the French term inoxydable, meaning the inability of the metal to be affected by oxidation, or corrosion. Stainless steel does not readily stain with water, rust, or corrode like other types of steel. However, when in an environment where there is high salinity, low oxygen, and poor circulation, even the highest grade of stainless steel will corrode. Therefore, there are different grades and surface finishes that are applied to stainless steel to suit particular environments.

Numerous studies, as summarized by Sørensen and colleagues, have found that welders are at increased risk for lung cancer. Some studies have also found that welders are at increased risk of other types of cancer, including nasal and larynx cancer.

A cohort study by Sørensen and colleagues found increased risk for lung cancer for Danish men
working as welders in the stainless steel and mild industries, even after controlling for tobacco use and exposure to asbestos. They studied 4,539 men who worked in the stainless steel or mild steel industries in Denmark for at least one year between 1964 and 1984, using information drawn from questionnaires (work history and smoking status) and from the Danish Cancer Registry (through December 2003). Lifetime exposure to welding fumes was estimated for each worker, using information about the occupational history of each worker and measurements of fume particulates in different welding processes. They found an increased risk of lung cancer among the welders (standardized incidence ratio 1.35, 95 percent CI 1.06–1.70) and, for stainless steel welders, an increasing risk of lung cancer associated with increased exposure to welding particulates. The increased risk with exposure may be due to the fact that stainless steel welders are exposed to water-soluble nickel and hexavalent chromium during their work, with the latter being a known lung carcinogen.

Michael Fox  
Independent Scholar

See Also: Aerospace Industry; Battery Acid; Electrical Industry; Lead.

Further Readings

Statistics
There are many different cancer statistics, but only a few basic ones are needed to understand a nation’s or other collectivity’s general cancer experience. The first population statistics were measures of population size and identification of citizens for government purposes through a census. Citizens were not especially happy to be counted and identified, because they would then be taxed, and for men, be subject to induction for military service and/or forced labor in public works projects. Suspicion about the intentions and use of statistics continue to this day in some quarters, which makes the gathering of valid statistics problematic in some countries.

Vital statistics, literally measures of life and death, are a later development and the basis of many government programs involving planning and provision of services according to age cohorts, such as schooling for the young and services for the elderly. Vital statistics at first were simply measures of each person’s date of birth and date of death. Spread into columns of the years of birth on one axis, and the years of death on the other axis, a life table reveals such statistics as life expectancy, or the average of the intervals from life to death along the birth columns. In its simplest form, this merely involved gathering the dates of birth and death inscribed on tombstones or church records of christenings and funerals. Practical applications, such as life insurance premiums, are calculated from these numbers. These vital statistics form the basis of the sociological field of demography, the study of human populations. Vital statistics provide basic information for public health and government planning. Calculation of birth rates and death rates led to the theory of demographic transition from the traditional society with high birth rates and high death rates, to the modern society with low birth rates and low death rates.

Mortality
When the cause of death is included, mainly from the physician’s filling out of a death certificate, then the vital statistics include mortality from the various causes given across a population. This is simply the number of deaths from such causes as heart attack, cancer, stroke, or pneumonia. However, this very common procedure suffers from a number of problems. Different physicians may disagree about the cause of death, the cause may not be clear to the observer without an autopsy, and in the absence of a clear diagnosis, the physician or other official may simply characterize the death as from “natural causes.” This is particularly the case for a deceased elderly person, the group most likely to suffer from cancer. The problem of agreement has been resolved
by the development and use of standard categories in the International Statistical Classification of Diseases (ICD), which is regularly evaluated and updated. The next updating is scheduled for 2017. However, the problem of classification when the cause is not apparent is more difficult to manage.

Some causes of death are hidden (occult), whereas others appear directly on observation. Also, causes of death vary along such axes as proximate to ultimate. Decades ago, the vital statistics of Australia were used to investigate the cause of prostate cancer, mainly a condition of very elderly men. The study compared the cause of death (a prostate cancer diagnosis) with the number children of the deceased in the medical records. It was found that men without children were less likely to be diagnosed with prostate cancer. This finding led to speculation that prostate cancer was caused by male virility, high levels of testosterone, or an active sex life. More likely, considering that the prostate is an occult organ, autopsies were more frequently performed on elderly males when there were interested offspring present who were attending their deceased parents’ affairs. The conclusion is that even carefully recorded causes of death may have hidden biases that reduce the validity of the resulting statistics.

Cancer mortality “ultimate causes” that are not directly physiological, such as smoking, sedentary life style, obesity, and alcohol abuse are not included on death certificates. However, it is just as important to know the risks of cancer from these causes as the more proximate causes described on death certificates. So, mortality statistics on these ultimate causes are calculated, but through an elaborate process of estimation from the more directly observable proximate causes. For example, lung cancer can be attributed to smoking in general and exposure to irritants such as asbestos for certain occupations, and stomach cancer to ingestion of carcinogens in the diet of specific ethnic groups. To a certain extent, these estimates are more controversial and subject to debate than other statistics. Yet, all statistics are a product of human activity, and may contain hidden biases.

Incidence

Compared with the mortality statistic, there are more complex statistics of incidence and prevalence. Incidence is defined as a cancer diagnosis on a patient during a specific time period. Each diagnosis is a count, and the total count is the incidence of the population or cohort for that time, such as a year. A related static, prevalence, is the total count of all patients alive at a specific time who are afflicted with that type of cancer. For nations with a modern health system, the ICD is very useful in practice because it equalizes counts among different physicians and hospital records. With a national cancer registry to record these counts, each form of cancer can be calculated, compared, and monitored over time. One of the most interesting of these specialized registries has been the linkage of the medical records of the mother during pregnancy to the health condition of her offspring in later life. Through those registries, a daughter’s likelihood of contracting clear cell adenocarcinoma (CCA) of the vagina and cervix was linked to the mother’s ingestion of the synthetic estrogen drug diethylstilbestrol (DES). Now, there is a DES Cancer Registry to carry on this work.

Cancer incidence and prevalence statistics are different from mortality statistics. The medical technology used for the discovery of cancer in normal healthy people changes over time. There is no IDC for modern screening and technology, so earlier detection and more extensive screening will alter incidence and prevalence statistics by continually expanding their findings. Cases will increasingly be found where the cancer is small, not growing, or growing so slowly that it will not be a threat to the individual’s life or health. Autopsy studies of elderly men, for example, have found that most men over 80 years of age have some form of prostate cancer, but they do not die from it, or even experience symptoms. A smaller but significant proportion of women from 40 to 80 years of age have been discovered to have breast cancer on autopsy after dying from other causes. Studies of these women found up to 15 percent with undiagnosed breast cancer. There is no statistical baseline for defining small and slowly growing, non-life-threatening cancers. As a result, the meaning of incidence and prevalence will change through an inflation of cases as medical diagnosis and screening continues to advance.

Calculated together, mortality and incidence provide another vital statistic, the life expectancy of the patient, not from birth to death, but from diagnosis to death. This particular life expectancy is called survival. While life expectancy is calculated as the
number of years of expected life, as from the time of the purchase of a life insurance policy, survival is calculated somewhat differently. It is the proportion (expressed in percentages usually) of patients still living within a period of time after diagnosis, such as five years. While useful at present, this statistic will lose its meaning as inflation of incidence continues. Lifetime risk is calculated from mortality and prevalence statistics. Two versions of lifetime risk are calculated. Risk of contracting cancer in one’s lifetime comes from prevalence life tables for each type of cancer. The risk of dying from cancer is calculated from cancer mortality tables. Individuals can calculate their risks in great detail from the National Cancer Institute Web site. While extraordinarily useful in monitoring the forms of cancer and their treatment, statistics can be misleading. They must be interpreted with care and with a certain degree of skepticism.

Keith R. Johnson
Oakton Community College

See Also: National Cancer Institute; Screening.

Further Readings


Stomach (Gastric) Cancer

Gastric (stomach) cancer is a disease in which malignant (cancer) cells form in the tissue lining the stomach. Stomach malignancy is linked to Helicobacter pylori (H. pylori) bacterium infection, or Epstein-Barr virus (EBV) infection. H. pylori is a pathogen responsible for the development of chronic gastritis, peptic ulcer disease, and gastric cancer. It seems to be neither genotoxic or mutagenic. H. pylori infection tends to be correlated with poor socioeconomic conditions. EBV (also called human herpes virus 4, HHV-4) belongs to the herpes family, and is one of the most common viruses in humans, causing various types of diseases.

Gastric cancer was the most common neoplasm in 1975, and was the second cause of cancer deaths worldwide in 1985 and 1990. According to GLOBOCAN 2012, gastric cancer is now the fifth most common type of cancer worldwide, after lung, breast, colorectum, and prostate cancers. In cancer-related deaths, gastric cancer is the third-leading cause worldwide (723,000 deaths, or 8.8 percent of the total). High mortality rates occur in eastern Asia (the highest, 24 per 100,000 in men and 9.8 per 100,000 in women), central and eastern Europe, Latin America, and the Caribbean, while Africa and North America have the lowest (2.8 per 100,000 in men, and 1.5 per 100,000 in women in the United States). The eastern Asian region includes China, Japan, Mongolia, North Korea, South Korea, and Taiwan. South Korea had the highest rate of stomach cancer, followed by Mongolia and Japan.

Whereas cases of gastric cancer have increased because of population growth, mortality rates of stomach cancer have rapidly declined, especially in developed countries in recent decades. Some researchers (e.g., M. Amiri and colleagues) have projected that with this consistent trend, stomach cancer is likely to become far less deadly in Europe in the future. Middle-aged or older males residing in eastern Asia are still at high risk of gastric cancer.

Risk Factors
Most gastric cancer cases are associated with H. pylori infection. In 1995, the International Agency for Research on Cancer (IARC) of the World Health Organization classified this organism as a Group 1 human carcinogen for stomach malignancy. Patients with H. pylori infection are significantly more likely to develop stomach cancer than those who do not. However, only about 1 percent of infected individuals will develop gastric cancer. Other factors such as gender (male), socioeconomic condition at the time of birth, age at first H. pylori infection, different strains of H. pylori (genetic structure and virulence), family history of stomach cancer, previous stomach
Surgery, some types of stomach polyps, genetic conditions, diet, dietary supplements, tobacco use, certain occupations (coal, metal, and rubber industries), and exposure to radiation can also affect the risk of stomach cancer.

Demographic Factors
GLOBOCAN 2012 reports that more than 70 percent of stomach cancer cases (677,000 cases) occur in developing countries (456,000 in men, 221,000 in women). Half of stomach cancer cases worldwide take place in China. However, this is because of the sizable Chinese population. Age-standardized incidence rates (per 100,000) indicate that South Korea has the highest (62.3 in men, and 24.7 in women, followed by Mongolia (47.4 and 20.2, respectively), and Japan (45.7 and 16.5, respectively). Asian males are vulnerable to gastric cancer, whereas western Africans have a very low risk of stomach cancer (3.3 in men, and 2.6 in women). In the United States, the National Cancer Institute estimates that there will be 22,220 new cases of stomach cancer, and more than 10,990 Americans will die of the disease, in 2014. Between 2004 and 2010, the five-year survival rate of stomach cancer survivors in the United States was 28.3 percent.

Types
The most common type of stomach cancer is adenocarcinoma, comprising 90 to 95 percent of cases. The cancer starts in the gland cells that form the innermost lining of the stomach, known as the mucosa. Other less common types include lymphoma non-Hodgkin (cancer of the immune system tissue in the wall of stomach, about 4 percent of cases), gastrointestinal stromal tumors (GIST, cancerous tumors that start in the digestive system, and about 60 percent of the tumors are in the stomach), carcinoid tumors (they grow in the hormone-producing tissues in the digestive system, about 3 percent of cases) and others (such as squamous cell carcinoma, small cell carcinoma, and leiomyosarcoma).

Symptoms and Stages
The general signs and symptoms of stomach cancer include stomach pain, loss of appetite, weight loss for unknown reason, nausea, vomiting, a change in bowel movements (constipation or diarrhea), weakness, and anemia. These symptoms could be similar to that of other diseases (such as stomach flu, chronic fatigue, or food allergy) and may go unnoticed until the cancer spreads. In early-stage stomach cancer, symptoms include indigestion and stomach discomfort, a bloated feeling after eating, mild nausea, loss of appetite, and heartburn. The signs and symptoms in advanced stages are blood in the stool, vomiting, weight loss for no known reason, stomach pain, jaundice (yellowing of eyes and skin), ascites (build-up of fluid in the abdomen), and trouble swallowing. To compound the difficulty in detection, many stomach cancer patients are asymptomatic, especially in early stages.

Screening and Diagnosis
In addition to commonly used medical tests (physical exam and medical history, X-ray of the abdomen, blood chemistry studies, computed tomography or CT scan, biopsy, and complete blood count), two procedures are particularly useful for screening stomach cancer. Upper endoscopy is a procedure to check if there are abnormal areas inside the esophagus, stomach, and duodenum (first part of the small intestine). A conventional endoscope is a thin tube-like instrument with a light and a lens that is passed through the patient’s mouth and down the throat into the esophagus. It helps physicians see the inside of the stomach; however, it is invasive to patients.

Advances in imaging technology have invented a new procedure—capsule endoscopy. The capsule is the size of a large vitamin pill that has a camera inside. The patient swallows the capsule; once it is activated, it starts taking thousands of pictures while traveling through the patient’s digestive tract. The pictures are transmitted to sensors attached to the patient’s chest and the recorder on a belt the patient wears around the waist area. Eventually, the capsule is discharged by the patient into the toilet and flushed away. Barium-meal photofluorography (or upper gastrointestinal or GI series) refers to a series of x-ray films of liquid-coated esophagus and stomach. The patient drinks a liquid that contains barium (a silver-white metallic compound) in advance to produce the coating effect. The barium swallow test seems to be less effective than endoscopy.

Treatment and Side Effects
Stomach cancer is strongly linked to H. pylori infection, therefore, a H. pylori screen-and-treat strategy is one solution. Treatment with antibiotics to
eradicate *H. pylori* infection may prevent gastric cancer. However, because many factors contribute to a person’s risk of stomach cancer, elimination of the infection alone may not produce expected results. Another example is anti-*Helicobacter* therapy; it has shown potential in the treatment of low-grade gastric mucosa-associated lymphoid tissue (MALT) lymphomas, yet its long-term effect is unclear.

Once stomach cancer (mostly adenocarcinoma, or in some cases squamous cell cancers) is diagnosed, the most common treatment method is surgery. In the early stage of stomach cancer, when it has not spread, endoscopic resection is an effective procedure by using an endoscope to cut out a tumor or cancerous cells. Subtotal or partial gastrectomy is used to remove the affected areas of the stomach, and some lymph nodes and tissue near the stomach. In some cases, total gastrectomy is needed to remove the whole stomach. If the cancer is advanced, and cannot be removed, palliative surgery is the option. The purpose of palliative surgery is to help control the cancer or relieve symptoms or problems (such as bleeding); it rarely cures the disease. Palliative surgery includes several options, such as subtotal gastrectomy, gastric bypass (gastrojejunostomy), endoscopic tumor ablation, stent placement (a hollow metal tube is placed by using an endoscope), and feeding tube placement.

Side effects of surgery include bleeding from the surgery, blood clots, and damage to the nearby organs. Post-op recovery also includes side effects such as risk of infections during the healing process, pain, nausea, heartburn, abdominal pain, and diarrhea (especially after eating), and shortages of some vitamins. If part of the stomach is removed, dietary habits have to be changed in terms of portion and frequency (smaller portions eaten frequently) to manage upset stomach. A feeding tube placement may also be needed. If the whole stomach is removed, it leads to a lifestyle change, in addition to a change of diet. Individuals without a stomach will not be able to absorb B12; they will need regular shots (of B12) to maintain healthy blood and nerves. Total gastrectomy presents a special challenge to pediatric cancer patients and their life expectancy. Side effects of radiation and chemotherapy are nausea, vomiting, diarrhea, skin reactions, and tiredness.

Side effects of radiation and chemotherapy are similar to those of treating other types of cancer. They include nausea, vomiting, diarrhea, skin reactions, and tiredness. Because chemotherapy kills the fastest-growing cells in the body (e.g., the stomach lining, hair, and blood cells), its side effects also include hair and weight loss.

All these side effects can be managed with medication and diet, and they phase out after treatment is completed. A new targeted drug for treating advanced stomach cancer recently received approval from the U.S. Food and Drug Administration in April 2014. Cyramza (ramucirumab) was developed to treat patients with advanced stomach cancer that cannot be surgically removed (unresectable) or has spread. The new drug is an angiogenesis inhibitor that blocks the blood supply to tumors. In a clinical trial of 355 participants (median age was 60) with unresectable or metastatic stomach or gastroesophageal junction cancer, Cyramza showed evidence of slowing the tumor growth and extending survival (participants’ lives). Common side effects of using Cyramza during clinical testing were diarrhea and high blood pressure.

**Prognosis and Five-Year Survival Rate**

Prognosis (chance of recovery) of gastric cancer depends on if it is detected in an early stage, or if it has spread at the time of diagnosis. The five-year survival rate refers to the percentage of cancer survivors who live beyond five years after initial diagnosis. Many factors contribute to the five-year survival rate, including the type and location of the stomach malignancy, the stage of development, the patient’s age, the patient’s general health, and the patient’s response to treatment. For any type of cancer, early detection is vital to the five-year survival rate. In stomach cancer, the early stage five-year rate is as high as 90 percent (Stage 0) and 78 percent (Stage 1A). The survival rate drops to 58 percent (Stage 1B, where stomach malignancy has spread into the lymph nodes or under the main muscle layer), and it further deteriorates to the point of 34 percent (Stage II), 20 percent (Stage IIIA), 8 percent (Stage IIIB, where malignancy has grown through all the stomach layers and wall, infecting between 7 and 15 lymph nodes), and 7 percent (Stage IV, where cancerous cells have spread to other organs and have metastasized). The sad reality is when gastric cancer is diagnosed, it is often in an advanced stage (such as Stage IIIB or later). The prognosis is poor, and long remissions are rare.
Stomach (Gastric) Cancer, Childhood

Conclusion

The stomach is a delicate and complex organ. As a result, screening and treating gastric cancer is challenging. It is difficult to detect early gastric cancer until it is too advanced with a poor prognosis. Screening and detecting stomach cancer in moderate- to high-risk populations via endoscopic screening programs are effective in reducing mortality rates in eastern Asia (China, Japan, and Korea). This type of population screening or targeted screening is also cost effective in regions where incidence rates of stomach cancer are high. However, mortality rates in developed countries (such as Europe) exist without such screening programs. Regional differences are evident in gastric cancer. Innovative approaches (such as imaging technology and endoscope, better diagnostic skills, targeted drugs, clinical considerations for high risk groups, biomarkers of the blood of stomach cancer patients, DNA sequencing, and genetic inheritance factors) are under development. They bring hopes that one day stomach cancer can be detected early, and patients will be able to have a better outlook in life expectancy.

Paige Mayleen True
California State University, Monterey Bay

See Also: Radiation Therapy; Stomach (Gastric) Cancer, Childhood; Surgery; Survivors of Cancer; Survivors of Cancer, Families of.

Further Readings


Stomach (Gastric) Cancer, Childhood

Cancer in children is less common than in adults. According to the National Cancer Institute, approximately 1 in 285 children (0.35 percent) in the United States will develop cancer before the age of 20. Pediatric cancers represent 1 percent of all new cases of cancer in the United States. In 2014, there were an estimated 10,450 new cases of pediatric cancer, and 1,350 children died of the disease. Pediatric cancers are the second-leading cause of deaths in children ages 5 to 14 (accidents are the first cause). The most common types of cancers among children (ages 0 to 14) are acute lymphocytic leukemia (26 percent), brain and central nervous system (CNS) (21 percent), neuroblastoma (7 percent), and non-Hodgkin’s lymphoma (6 percent). Gastric cancer is a rare cancer in children, according to the Physician Data Query (PDQ). The most common type of stomach cancer is adenocarcinoma, comprising 90 to 95 percent of cases. The cancer starts in the gland cells that form the innermost lining of the stomach, known as the mucosa.

The signs and symptoms of stomach cancer are usually difficult to diagnose, especially for children. A child might be diagnosed as having stomach flu if these symptoms (of stomach cancer) are present, such as stomach pain, loss of appetite, diarrhea, and weakness. In early-stage stomach cancer, symptoms may include indigestion and stomach discomfort, a bloated feeling after eating, mild nausea, loss of appetite, and/or heartburn. The signs and symptoms in advanced stages are blood in the stool, vomiting, weight loss for no known reason, stomach pain, jaundice (yellowing of eyes and skin), ascites (build-up of fluid in the abdomen), and trouble swallowing.
Screening and Diagnosis
Many commonly used medical tests may be helpful in screening for and diagnosing lung cancer, including taking a medical history, doing a physical exam, performing blood chemistry studies, and conducting tests such as a biopsy, a complete blood count, a CT (computerized tomography) scan, and an abdominal X-ray. In addition, upper endoscopy and capsule endoscopy exams are particularly useful in screening for pediatric stomach cancer.

Upper endoscopy is performed using a conventional pediatric endoscope, a thin, tube-like instrument including a light and a lens, which is passed through the mouth and down the throat into the patient’s stomach. Upper endoscopy allows the physician to check for abnormal areas within the esophagus, stomach, and duodenum (first part of the small intestine) but carries the disadvantage of being invasive and possibly traumatic to the patient.

Capsule endoscopy is a more recently developed procedure that requires the patient to swallow a capsule (that is about the size of a large vitamin pill) containing a camera. While the capsule is passing through the individual’s digestive tract, the camera records thousands of images that are transmitted to sensors and a record outside the patient’s body. Eventually, the capsule passes out of the patient’s body and is discarded. Because it is experienced as less invasive, capsule endoscopy may be particularly useful with child patients.

An alternative test, barium-meal photofluorography, is less effective than endoscopy. In barium-meal photofluorography, the patient drinks a liquid containing barium, a silver-white metallic compound, and a series of X-ray films are taken of the patient’s liquid-coated esophagus and stomach.

Treatment and Side Effects
The treatment of a childhood cancer brings up physical, psychological, emotional, cognitive, and social challenges to the child and the family. Because children are still growing and developing while having cancer, it is highly recommended that child cancer patients seek treatment at pediatric oncology centers that offer comprehensive cancer care and clinical trial programs. Stomach cancer is linked to Helicobacter pylori (H. pylori) bacterium infection. The infection is often acquired in childhood, and is considered a risk factor for the development of gastric malignancies in adulthood. Early age at first infection may determine a gastric neoplastic outcome in adults (H. pylori infection is most common where socioeconomic conditions are poor). To detect H. pylori infection in children, however, is challenging because they usually show no symptoms of the infection (except peptic ulcers in a very small number of infected children).

The most common treatment method for stomach cancer is surgery. Endoscopic resection, a procedure in which an endoscope is used to remove a tumor or cancerous cells, is commonly used if the cancer is in an early stage and has not spread. In subtotal or partial gastrectomy, the affected areas of the stomach and some lymph nodes and tissue near the stomach are removed. In some cases, total gastrectomy is needed to remove the whole stomach. If the cancer is advanced and cannot be removed, palliative surgery is the option. The purpose of palliative surgery is to help control the cancer or relieve symptoms or problems (such as bleeding); it rarely cures the disease. Palliative surgery includes several options, such as subtotal gastrectomy, gastric bypass (gastrojejunostomy), endoscopic tumor ablation, stent placement (a hollow metal tube is placed by using an endoscope), and feeding tube placement.

Surgery carries the risk for side effects, including damage to nearby organs, blood clots, and bleeding. Side effects may also occur during the post-operative recovery period, including infection, pain, heartburn, diarrhea (especially after first eating), and vitamin deficiencies. If part of the stomach is removed, dietary habits have to be changed in terms of portion and frequency (smaller portions eaten frequently) to manage upset stomach. A feeding tube placement may also be needed. If the whole stomach is removed, it leads to a lifestyle change, in addition to a change of diet. Individuals without a stomach will not be able to absorb B12; they will need regular shots (of B12) to maintain healthy blood and nerves. Total gastrectomy presents a special challenge to pediatric cancer patients and their life expectancy.

Radiation and chemotherapy can also produce side effects, including fatigue, nausea, vomiting, diarrhea, and skin reactions. These side effects taper off after the treatment is completed and can be managed with medication and diet but may still have a substantial impact on a child’s health and development. A new, targeted drug for treating advanced stomach cancer received approval from the U.S. Food
and Drug Administration in April 2014. Cyramza (ramucirumab) was developed to treat patients with advanced stomach cancer that cannot be surgically removed (unresectable) or has spread. The new drug is an angiogenesis inhibitor that blocks the blood supply to tumors. In a clinical trial of 355 adult participants (median age of 60) with unresectable or metastatic stomach or gastroesophageal junction cancer, Cyramza showed evidence of slowing the tumor growth and extending survival (participants’ lives). Common side effects of using Cyramza during clinical testing were diarrhea and high blood pressure. The safety and effectiveness of Cyramza in pediatric patients, however, are unknown.

Prognosis and Five-Year Survival Rate
Prognosis (chance of recovery) of gastric cancer depends on if it is detected in an early stage, or if it has spread at the time of diagnosis. The five-year survival rate refers to the percentage of cancer survivors who live beyond five years after initial diagnosis. Many factors contribute to the five-year survival rate, including the type and location of the stomach malignancy, the stage of development, the patient’s age, the patient’s general health, and the patient’s response to treatment. Early detection is vital to the five-year survival rate. In stomach cancer, the early stage five-year rate is as high as 90 percent (Stage 0) and 78 percent (Stage IA). The survival rate drops to 58 percent (Stage IB, where stomach malignancy has spread into the lymph nodes or under the main muscle layer), and it further deteriorates to the point of 34 percent (Stage II), 20 percent (Stage IIIA), 8 percent (Stage IIIB, where malignancy has grown through all the stomach layers and wall, infecting between 7 and 15 lymph nodes), and 7 percent (Stage IV, where cancerous cells have spread to other organs and have metastasized). Because childhood stomach cancer is rare, the five-year survival rate of the disease has not been established. The most common causes of death in childhood cancer are recurrence of the primary cancer, a second primary cancer, and heart and lung damage.

Late Effects
Late effects are a special condition for child cancer survivors, from a developmental perspective. After
Stress

A review of the literature on stress and cancer reveals that cancer can be seen as a result of environmental stressors and as a cause for further stressors among patients. Results of cancer-related stressors may include anxiety, feelings of depression, cancer worry, and even post-traumatic stress disorder (PTSD). Cancer is a life-threatening disease, with uncertain survival in the near and more distant future. Cancer recurrence looms in one's arena of fears and anxieties. Stigma, based on the reaction of friends and acquaintances, can add to stressors experienced by the patient. PTSD is often discussed as a result of being diagnosed and treated for cancer, but epidemiological evidence is inconclusive. The effects of cancer on personality, self-concept, and world outlook are described in many

Further Readings


Stress

A review of the literature on stress and cancer reveals that cancer can be seen as a result of environmental stressors and as a cause for further stressors among patients. Results of cancer-related stressors may include anxiety, feelings of depression, cancer worry, and even post-traumatic stress disorder (PTSD). Cancer is a life-threatening disease, with uncertain survival in the near and more distant future. Cancer recurrence looms in one's arena of fears and anxieties. Stigma, based on the reaction of friends and acquaintances, can add to stressors experienced by the patient. PTSD is often discussed as a result of being diagnosed and treated for cancer, but epidemiological evidence is inconclusive. The effects of cancer on personality, self-concept, and world outlook are described in many

Further Readings


Stress

A review of the literature on stress and cancer reveals that cancer can be seen as a result of environmental stressors and as a cause for further stressors among patients. Results of cancer-related stressors may include anxiety, feelings of depression, cancer worry, and even post-traumatic stress disorder (PTSD). Cancer is a life-threatening disease, with uncertain survival in the near and more distant future. Cancer recurrence looms in one's arena of fears and anxieties. Stigma, based on the reaction of friends and acquaintances, can add to stressors experienced by the patient. PTSD is often discussed as a result of being diagnosed and treated for cancer, but epidemiological evidence is inconclusive. The effects of cancer on personality, self-concept, and world outlook are described in many

Further Readings


Stress

A review of the literature on stress and cancer reveals that cancer can be seen as a result of environmental stressors and as a cause for further stressors among patients. Results of cancer-related stressors may include anxiety, feelings of depression, cancer worry, and even post-traumatic stress disorder (PTSD). Cancer is a life-threatening disease, with uncertain survival in the near and more distant future. Cancer recurrence looms in one's arena of fears and anxieties. Stigma, based on the reaction of friends and acquaintances, can add to stressors experienced by the patient. PTSD is often discussed as a result of being diagnosed and treated for cancer, but epidemiological evidence is inconclusive. The effects of cancer on personality, self-concept, and world outlook are described in many

Further Readings


Stress

A review of the literature on stress and cancer reveals that cancer can be seen as a result of environmental stressors and as a cause for further stressors among patients. Results of cancer-related stressors may include anxiety, feelings of depression, cancer worry, and even post-traumatic stress disorder (PTSD). Cancer is a life-threatening disease, with uncertain survival in the near and more distant future. Cancer recurrence looms in one's arena of fears and anxieties. Stigma, based on the reaction of friends and acquaintances, can add to stressors experienced by the patient. PTSD is often discussed as a result of being diagnosed and treated for cancer, but epidemiological evidence is inconclusive. The effects of cancer on personality, self-concept, and world outlook are described in many
articles within the journals of psycho-oncology and psychosocial oncology.

Cancer stress is often a function of the nature of symptoms, cancer site, severity of the cancer, type of treatment (e.g., surgery, radiation, or chemotherapy), and its side effects. Stressors may also be posed by the patient’s concerns about the uncertainties of survivorship. Other variables that can influence stress levels include stage of the patient’s life course and their family circumstances. For example, breast cancer has a different meaning for a young mother than for a retired grandmother. A prevalent theme in many psychosocial studies of survivorship is the concept of posttraumatic growth (PTG).

The stress-buffers-outcome model is useful for understanding the effects of stressors on diverse outcome variables. The factors that can buffer cancer-related stress include the patient’s coping styles and strategies. Instrumental and emotional social supports from family and friends offer major survival and psychological benefits to patients facing cancer-related stress. There are also formal resources, such as ties with health care personnel and access to legal and educational resources that can serve valuable buffering functions. Of particular note are mental health professionals who specialize in oncology, including social workers and psychologists.

**Studies on Cancer Stress**

In a national health survey, participants who developed cancer and a cancer-free control group were reinterviewed 10 years later. Cancer survivors demonstrated adverse effects, compared to the control group, in mental health, mood, and other aspects of psychological wellbeing. Nevertheless, the cancer survivors also showed resilience, reflected in social wellbeing, spirituality, and personal growth. Younger survivors demonstrated higher levels of anxiety and depression than their age-matched peers. In contrast, older survivors reported few adverse psychological effects, consistent with others their age.

In another study, comparing eight-year survivors of breast cancer to a suitable control group, small differences were found, favoring controls in positive quality-of-life outcomes. When limited to women who remained disease free over the entire follow-up period, survivors’ quality of life was similar to controls. In contrast, survivors who developed recurrence or a new primary cancer experienced worse quality of life in all domains, except social functioning. A study of quality of life and mental health in cervical and endometrial cancer patients found no significant differences in depressive symptoms between survivors and controls. However, cervical cancer survivors reported significantly higher levels of anxiety than endometrial cancer survivors. Cancer survivors who were unemployed or living alone were found to be at special risk for mood and mental health difficulties.

A large-scale study of quality of life in patients with colorectal cancer one year after diagnosis revealed that in comparison to the general population, the colorectal patients scored only slightly worse on a quality of life (QOL) global-health measure. More severe limitations were observed on the emotional and social functioning scales, including financial difficulties, and on the physical symptom subscales of fatigue, dyspnea, insomnia, constipation, and diarrhea. These differences predominantly affected younger patients. As in other cancer studies, older cancer survivors fared better than younger survivors.

**Focus on Long-Term Survivors**

A study by Boaz Kahana explored life perspectives of older adults who were long-term cancer survivors. Interviews were conducted with 321 survivors, age 60 and over, who were at least 5 years post diagnosis and treatment. The sample included survivors of breast, colorectal, and prostate cancers. The majority looked back upon their past cancer as a traumatic experience (57 percent). Approximately 40 percent worried about their cancer coming back. However, only 15 percent stated that cancer had changed the person that they were, and 13 percent said that they felt that they were not a whole person since they had cancer.

These data underscore that even older long-term cancer survivors recognize the stressful nature of the cancer experience. However, the essential personhood of survivors remains intact. It is also notable that African American survivors in this study found cancer to be less of a stressor than Caucasians. They portrayed lower scores on a depression scale, scored higher on an optimism scale, and had fewer cancer worries. This might relate to more positive appraisals of illness, in the context of lives that are fraught with many social stressors, including economic disadvantage. Also, older adults no longer grapple with the disruption of role obligations.
that face younger survivors. Although older people are always facing the possibility of their cancer reemerging, they nevertheless strive to normalize the world in which they live.

Factors That Exacerbate and Ameliorate Cancer Stress
The stressors posed by cancer can challenge cognitive functioning and information processing that is necessary to understand the course of treatment, to comply with health maintenance regimens, and to engage in health-promoting behaviors. Depression can impair the patient's ability to learn and maintain health behaviors, or to undertake complex tasks that require planning for one's recovery. Poor coping strategies often lead to inability to adhere to treatment regimens and poor management of one's illness. Low motivation to monitor one's illness and feelings of pessimism, based on fears of recurring illness, can delay the adoption of new salutary health practices. Negative coping strategies in responding to the stressors of cancer may be manifested in adverse health habits such as smoking, alcohol consumption, eating foods containing high fats or sugars, poor sleep patterns, and a decline in exercise.

External obstacles to coping with cancer include poor doctor-patient communications that may lead to poor illness management. Doctors and nurses are often pressed for time, and may not be sensitive to the psychological needs of their cancer patients. Patients need to receive general education about cancer and education specific to their type of cancer and different methods of treatment. Health care consumerism and patient advocacy can reduce cancer related stress and improve patient outcomes. Patients also need to learn which medical centers are most knowledgeable and experienced when dealing with the patient's particular cancer. Adverse effects of cancer, including PTSD, are greatly exacerbated among terminally ill cancer patients. Patients with advanced or terminal cancer need the full support of a palliative care setting to minimize the stress for both patient and family.

Economic pressures can also exacerbate cancer-related stress. Financial problems, job loss either before or after cancer diagnosis, and inadequate health insurance all pose added burdens for patients coping with cancer. Low income is a strong risk factor for many negative outcomes, including illness, disability, lack of transportation to visit the doctor, inability to pay for medical visits or to purchase medications, or even to visit support groups or travel to the grocery store and pharmacy. In one study, socially isolated breast cancer patients had a 66 percent higher rate of dying from all causes compared to socially integrated women.

Optimism and self-efficacy are related to emotional resilience and better coping with one's illness. Adaptive and useful coping strategies to deal with cancer-related stress include information seeking, problem solving, and positive reframing, such as seeing the cup as half full rather than half empty. At least 83 percent of breast cancer survivors found at least one benefit following diagnosis and treatment of their illness. Despite the stressful nature of cancer, many patients respond with highly protective coping and survival skills.

Boaz Kahana
Cleveland State University

See Also: Breast Cancer; Coping; Mental Health; Posttraumatic Growth; PTSD; Social Support.

Further Readings

Sudan

For most of its history, the north African country of Sudan was ruled and influenced by Arab and Nubian cultures. In 1821, it was conquered by the Ottoman Empire, which annexed it to Egypt.
In 1890, Sudan was liberated by the British, who treated it as a colony, sowing the seeds for revolution, which erupted after the Egyptian Revolution in 1952. Sudan’s cultural and religious mix generated much internal conflict during its modern history, culminating in the 2011 separation of South Sudan, which claimed independence.

Its numerous civil wars, including the war in the Darfur region, and the authoritarian theocratic government brought about a widespread disrespect for human rights. Thus, even if Sudan is a somewhat modernized nation, with more than 30 million inhabitants, much of the population (46.5 percent, according to United Nations Development Programme) live in poverty, with very little or no access to health care, and a lack of hospital facilities. Except for some free clinics and hospitals managed by international humanitarian organizations such as Emergency and Doctors Without Borders (Médecins Sans Frontières), there are very few doctors available (16 per 100,000 inhabitants), so underdiagnosing of all types of cancer is a major issue. Also, much of the rural population still believe in traditional shamanistic healing and herbal remedies, and they are often reluctant to seek modern medical treatment to properly treat even the most common diseases.

Even though in 1982 a National Cancer Control Programme (NCCP) was initiated, until 2009, data about cancer research and incidence in Sudan was sparse because there was no population-based cancer registry, except for a very incomplete early 1967 register that was discontinued in the early 1980s. All data available came from the patient cases evaluated by the only two existing cancer centers in this country: the Radiation and Isotope Center in Khartoum (RICK), and the Institute of Nuclear Medicine Molecular Biology and Oncology (INMO) in Wadmedani. Nonetheless, according to hospital reports, cancer was the third-leading cause of death after malaria and viral pneumonia, accounting for 5 percent of all deaths. In 2009, the first National Population-based Cancer Registry (NCR) was established in Sudan, collecting all data from cancer patients in Karthoum State.

From 2009 to 2010, 6771 new cancer cases were registered. The data from NCR indicated that prostate and breast cancer were the most commonly diagnosed cancers in men and women in Khartoum, while cancer of the cervix trailed behind, portraying a cancer picture similar to that of the developed world. In children less than 15 years of age, leukemia was the most common cancer, followed by lymphoma. A very recent study suggested a strong association between Epstein-Barr virus (EBV) and breast carcinoma in Sudanese patients, and considerable epigenetic silencing of tumor suppressors that may likely be an outcome or an association with viral oncogenesis.

The data available is incomplete because most of the patients from the South Sudan region seek treatment in cancer facilities in neighboring countries such as Uganda because of the long distance from the only two available centers, lack of road safety, and scarcity of financial means. Only 5 percent (1,135 out of 20,954) of the registered cases in the National Cancer Registry for 2009 to 2010 were found to be from South Sudan. Recent government surveys indicate a high prevalence (10.7–13.1 percent) of human immunodeficiency virus (HIV), and a high hepatitis B surface antigen (HBsAg) endemicity (more than 8 percent) in the South Sudan population. They both constitute a significant regional risk factor for cancer, together with the high prevalence of human papillomavirus (HPV) and high consumption of alcohol among South Sudanese people.

Sudan has initiated a series of educational strategies that aim to dispel many of the misconceptions about cancer among the general population (who are 80 percent either nomadic or rural), such as superstitious beliefs and fears, or the misperception that cancer is transmissible. Booklets and posters have been distributed within schools, hospitals, and work places, together with radio, newspaper, and television educational programs. Some attempts to improve cancer prevention through early detection have also been made, by training some local populations to perform breast cancer screening in Keremet County in 2012.

One of the most prominent figures in cancer treatment and research is Dr. Sulma Mohammed, a native of Sudan and an associate professor of cancer biology at the Department of Comparative Pathobiology, Purdue Center for Cancer Research, Purdue University and Indiana University School of Medicine. Dr. Mohammed is a council member of the African Organization for Research and Training in Cancer (AORTIC), a nongovernmental organization that is dedicated to the promotion of cancer control, increasing public awareness, and reducing
the stigma associated with cancer. Dr. Mohammed has received a number of awards, including the African American Institute award, African women leaders in science award, and many American Association for Cancer Research travel awards.

Claudio Butticè
Independent Scholar

See Also: AIDS-Related Cancers; Breast Cancer; Leukemia, Acute Myeloid, Childhood; Liver Cancer; Lymphoma, AIDS-Related; Prostate Cancer.

Further Readings

Sun Exposure (Australia)

The interaction of human skin and the sun’s rays is complex. While sunlight warms the skin and aids in cooling the body through evaporation, it also contains energetic ultraviolet wavelengths (UVW) that harm the skin’s deoxyribonucleic acid (DNA). They also destroy folate, an essential nutrient in the body. Fortunately for life on Earth, the shortest UVWs below 100 nanometers and the next most energetic, between 100 and 280 nanometers (UVC), are screened out by the oxygen and ozone of the atmosphere, while UVB, between 280 and 315 nanometers, is 90 percent screened out. The rest of UVW (UVA, above 315 to 400 nanometers) passes through, but how much arrives at the planet’s surface depends on a variety of factors, including moisture in the atmosphere, the incidence of the sunlight (latitude), and the height above sea level (thickness of the atmosphere). Each of these factors has been registered on human skin when a people has lived in a place for enough human generations to reflect the evolutionary pressures on the skin, as noted by the biologist Nina G. Jablonski.

Humans require solar radiation in order to produce an essential nutrient, vitamin D. Thus, there is evolutionary pressure to have light skin that allows sunlight to enter. The alternative interaction is that certain ultraviolet rays are carcinogenic, and produce skin cancer, including life-threatening melanoma. The degree of melanin in a person’s skin is a testament to that individual’s ancestry. Extremely light skin that never darkens on sun exposure will only burn, and is most often a demonstration of ancestral origins in the far northern latitudes. However, a condition of albinism can occasionally appear in the tropics of Africa, and the unfortunate inheritor of genetic loss of all skin melanin yields a 1,000 times greater incidence of skin cancer for the albino over the dark-skinned African. Light skin that contains melanocytes that darken on direct sun exposure is one evolutionary adaptation to changing sunlight intensity over the annual cycle of seasons. The original peoples of northern Europe and Asia have this adaptation, as do their descendants across the planet. The peoples of the tropics have varying degrees of brown to black skin tones that let in enough sun to produce vitamin D.

The continent of Australia is exposed to the sun more than most because of modern technology, the use of chemicals that destroy the polar ozone that impedes the transmission of UVB. As displayed in the dark skin tone of Australia’s indigenous people, the aborigines, there has long been enough UVW arriving to cause major harm. The arrival of light-skinned people from Great Britain two centuries ago laid the foundation for an epidemic of skin cancer in Australia. The country is now among the world leaders in skin-cancer incidence, with 400,000 new cases each year in a population of
about 20 million. This is a major expense for the Australian health system, accounting for about 1 million physician visits a year, with a high proportion for skin diagnosis and treatment.

**Responses**

There have been two responses to this situation. The first was a campaign to stop the industrial and consumer use of chlorofluorocarbons. This came about when scientists determined that these chemicals were destroying the ozone layer. The unanticipated discovery of an ozone hole over the South Pole began the process, and when it was monitored and found to migrate northward to cover Australia, the alarm grew. An international agreement to prohibit the use of chlorofluorocarbons was made, and has proved effective. After some years of enforcement of the agreement, the ozone returned to the atmosphere. However, the actual size of the damage from this unanticipated exposure of the Australian people to a carcinogen that they could not see, hear, or feel will not be known for some time. The exposure of young people under age 30 has been found to be a major cause of these skin cancers, with most cases appearing years to decades after this critical exposure. The concern for public health is that the ozone hole years have caused a hidden threat of skin cancer that has yet to fully appear. With the aging of the Australian population that was exposed decades ago, a crisis will be at hand. It is estimated that two out of three Australians will contract skin cancer by the age of 70. The one positive is that there will be time to prepare and educate the public on the need for early detection and treatment. Skin cancers are visible and treatable in most cases. The need is for a many-sided effort to educate the public for prevention and early detection.

The second response includes increasing public awareness of the vulnerability of the white population to skin cancer, about the clear prevention techniques available, and the need for constant monitoring of one's skin. The education campaigns are targeted to specific populations, with emphasis on the protection of young people from exposure, and close monitoring of the skin of older Australians. In 1980, the Australian public health campaigns began. The Sun Smart campaign of 1980 to 1981 was the first national Australian social media campaign for cancer prevention. It featured a simple message, “Slip, Slap, Slop” to children, with a seagull cartoon singing for the audience to “slip on” sun proof clothing, “slap on” sunscreen with application instructions, and “slop on” a broad-brimmed hat. It was also directed to adults. Later campaigns also targeted specific populations who had been identified as at high risk for cancer or for low use of preventive methods. These later campaigns were less about using preventive methods, instead emphasizing the dramatic side of cancer incidence.

The tragic case of a young woman dying of melanoma at age 26 was transformed into a media awareness campaign, featuring the woman before her death. Clare Oliver gave her message in 2008 as a personal appeal to her young viewers: “No tan is worth dying for.” Other messages have been given during the dramatic removal of a skin cancer on screen. These messages have targeted teenagers and young adults who are less concerned about their sun exposure.

**Protection Measures**

Media campaigns are not the only part of the process of social change in a population at risk from a danger that they cannot see. Protection efforts begin by identifying problems of sun exposure and then responding to them. Public places where people gather can be provided with sources of shade. School children can be required to wear suitable hats when playing outside, and shade provided with shade sails. Workplace policies can do the same general monitoring for adults. Behavior (such as wearing appropriate hats and protective clothing) can be observed and counted before and after a campaign. However, behavior has generally been measured by surveys, not observation. Attitudes and awareness of educational messages can be tracked by surveys. Ideally, survey responses can be connected to studies of observed behavior rather than substituted for it. Campaigns can be segmented by people's place in the sun, their age, and other demographics.

Perhaps the most important of the techniques developed in Australia is the establishment of a sun exposure baseline. This statistic can be used to compare exposures at different venues. The baseline of 22 percent of the participants being sunburned was set from surveys, which are less valid than studying people on Australian beaches, but behavior has also been directly observed, as at schools. Then campaigns can be evaluated by how much they reduce reported sunburn at that venue. In a second
use of the baseline, studies of sports venues found an unexpectedly high rate of sunburn there, also 22 percent. So, this became the basis of a campaign directed at sports fans. Finally, the daily monitoring of the level of UVW, with published alerts when the index reaches dangerous levels, helps cue protective behavior while maintaining awareness of the risk.

The success of these efforts has been seen in a number of outcomes. Concerned parents have demanded that their children's schools take responsibility for monitoring children's sun exposure. The government's irregular appropriations for the media campaigns have been tracked, and decreases in media exposure are followed by an increase in reported sunburn, a direct indicator of risk. An economic analysis concluded that 24 cents per capita spending on educational campaigns saves 2.32 health dollars. These campaigns appear to have been successful in more than public awareness. The incidence of skin cancer in Australia in the most recent report demonstrated a decline.

Keith R. Johnson  
Oakton Community College

**See Also:** Skin Cancer, Melanoma; Skin Cancer, Non-Melanoma; Solar Radiation.

**Further Readings**


---

**Sunlamps or Sunbeds, Exposure to**

Sunlamps and sunbeds are a known risk factor for developing basal cell carcinoma, squamous cell carcinoma, and melanoma. Indoor tanning exposes the skin to a spectrum of ultra violet (UV) radiation that creates a cosmetic tanning of the skin. This exposure also induces mutations in the skin cell's deoxyribonucleic acid (DNA) leading to the development of skin cancers. The use of indoor tanning has increased the prevalence of skin cancers at an earlier age. Besides the known risk of skin cancers, individuals using sunlamps or sunbeds are at risk for premature skin aging, developing cataracts, photokeratitis (arc eye), and immunosuppression. Sunlamps and sunbeds are occasionally used in the treatment of psoriasis and vitamin D deficiency. This treatment is not intended for cosmetic self-use and is only used under strict medical supervision. There has been an increase in indoor tanning use since the first sunbed was brought to the United States in 1979. Women between the ages of 18 and 29 years old are most likely to regularly use indoor tanning methods, and are at highest risk for skin cancers at earlier ages. The use of sunbeds and sunlamps can become addictive in nature. The *Diagnostic and Statistical Manual of Mental Disorders* (DSM) outlines how to diagnose dependencies, which are modifiable for the diagnosis of indoor tanning dependence and abuse. Guidelines and regulations on sunbed use, along with education on their dangers, are needed to decrease sunbed use, and thus decrease the risk of skin cancers.

**UV Exposure**

Sunbeds and sunlamps are methods of indoor tanning that individuals use to attain a cosmetic tanning of their skin. The amount of cosmetic tanning depends on the individual's skin phototype, likelihood of sunburn, and melanocyte class. Those who always burn tend not to tan, and those who are melano-compromised will burn in both natural and artificial UV exposure. Sunlamps create a tanning effect in the skin by emitting UV radiation. The bulbs used in indoor tanning are fluorescent lights with phosphor mixtures, or quartz lights that emit a spectrum of UV radiation. UV radiation is a known human carcinogen that increases risks of certain cancers. The most common UV radiation emitted from sunlamps is UVA, with a minor portion of UVB rays. The sunbed industry once claimed that sunlamp use was safer than natural sunlight because of the high degree of UVA rays. However, UVA rays are now known as a Class I carcinogen, with exposure causing an increased incidence of melanoma,
and should also be avoided. Recently, sunlamp manufacturers have started using UVB rays, in addition to UVA rays. These lights are marketed to mimic the natural solar spectrum and speed up tanning. No UVC rays should be emitted from any sunlamp. Certain sunlamps are capable of exposing individuals to UV rays that are up to five times stronger than the UV rays in midday Australia.

**Increased Risk of Skin Cancers**

Sunbed and sunlamp exposure to UV radiation increases an individual's risk of developing skin cancer via DNA mutagenesis. The use of sunlamps and sunbeds before the age of 35 has been shown to have a 75 percent increased risk of developing melanoma. Childhood exposure to UV radiation is a known risk factor for developing melanoma in adulthood. The National Institute of Health found that the incidence of melanoma among women in the United States has almost tripled during the last 30 years, positively correlated with the increased use of sunbeds. The melanomas diagnosed in recent years have become thicker and more lethal, also possibly linked to sunbed usage.

Sunbeds also expose a larger area of skin to UV radiation than sunbathing in natural sunlight. This creates a larger area for skin cancers to develop. Along with the increase in skin cancers, artificial tanning increases the risk of precancerous skin lesions, such as actinic keratosis and Bowen's disease (squamous cell carcinoma in situ). These lesions may develop into cancers, and can be risk factors for developing cancerous lesions elsewhere on the body. Certain medications and cosmetics can increase photosensitivity, causing increased damage to skin and burning with sunlamps and sunbed exposure. These products should be avoided during sunlamp use to prevent accelerated skin damage and cancer risk. Overall, sunlamps and sunbeds emit the same UV rays as the sun, a known carcinogen, thus they should be avoided or used in moderation.

**Methods to Regulate Sunbed and Sunlamp Exposure**

Each state has individual laws regulating the use of sun lamps and sunbeds for minors. The U.S. Food and Drug Administration (FDA) prohibits the indoor tanning industry to use the words “safe” and “safer than” when promoting sunbeds and sunlamps. Sunbed salons are not allowed to claim health benefits from sunbed use. The government also requires all indoor tanning salons to post warnings about the effects of UV radiation, as well as the risk to eyes if individuals do not wear protective goggles. Additional warnings required to be displayed in sunbed establishments include “no one under 18 should use sunbeds” and “sunlamps increase aging of the skin and may cause skin cancers.” Signs in commercial sunbed salons also need to include warnings that “people with skin that does not tan should not use sunbeds,” and “exposure to sunlight or sunlamps should be avoided 48 hours after previous use of a sunbed.” These warnings also need to be printed on a consent form that the client must read, sign, and date, acknowledging the risks of sunbed use.

UV protective eyewear is mandatory during the use of sunbeds and sunlamps to prevent permanent damage to vision. Additional methods to decrease UV exposure include training workers at salons to educate tanners about the risks of sunlamps, and not having unattended sunbeds. The sunbeds should also comply with the regulations set by national standards, and supply exposure recommendations based on sunlamp strength. The International Commission on Non-Ionizing Radiation Protection has developed recommendations for individuals who should avoid sunbed and sunlamps. They include individuals less than 18 years of age, individuals with melano-compromised skin types, individuals with multiple nevi or freckles, individuals with history of frequent childhood sunburns or premalignant skin lesions, and individuals who wear cosmetics or take medications that may cause photosensitivity.

**Increase in Sunlamp/Sunbed Usage**

The first sunbed was brought to the United States in 1979. Since then, indoor tanning has grown into a billion dollar industry. The increase of sunbed use is partly because of the change in culture. Popular culture promotes a tanned skin as desirable, healthy, and attractive. The tanning industry has marketed a tan as a symbol of wealth, beauty, and health. Many young women say that they feel and look better with a tan. These messages have led to an increase in sunbed use. The risk of UV exposure from sunbed and sunlamp use is increased when the bed is unregulated, at home, or if the salon staff is not
trained in educating customers about UV exposure for each type of sunbed and skin type. There is also an increase in sunbed use when salons are competing by having the lowest prices for those who tan more frequently, and offering unlimited tanning for specific amounts of time.

**Indoor Tanning Dependence**

Indoor tanning dependence can develop, with the continued use of sunlamps and sunbeds mirroring substance dependence. Dependence on indoor tanning can be identified in individuals who are frequent tanners and fail to cut back on tanning, along with tolerance, withdrawal, and physical and psychological problems. One can use a tanning-adapted model of *The Structured Clinical Interview for DSM IV Axis I Disorders* to identify individuals who have indoor tanning abuse and addictions. One method of screening for tanning dependence is using the CAGE questionnaire that is frequently used in identifying alcohol dependence. This questionnaire assesses if the tanner has ever tried to Cut back on tanning, if those around them become Annoyed with their tanning habit, if they ever feel Guilty for tanning, and if they ever woke up feeling the urge to tan (an Eye opener). Two or more affirmative answers to these questions identify a tanning dependence. Some psychiatrists consider that tanning dependence is similar to, or a component of other psychiatric disorders, such as body dysmorphic disorder and obsessive-compulsive disorder.

Theories supporting sunbed and sunlamp dependence suggest that the mechanism of dependence could be from the release of endogenous opioids during use. Other researchers have shown that tanning increases cerebral blood flow to the same areas in the brain as a drug reward. The degree of dependence can be seen when individuals risk their health after the diagnosis of a sunbed related cancer. There has been evidence of continued sunlamp use, even after the diagnosis of skin cancers, despite knowledge that this increases risks of future skin cancers. A similar model can be seen in individuals with nicotine dependence continuing to smoke after the diagnosis of lung cancers and other nicotine-related cancers.

**Conclusion**

Sunbeds and sunlamps are currently being used for cosmetic tanning of the skin, but these devices are additionally exposing users to dangerous UV radiation. The increased use of sunlamps over the years mirrors the increase in melanoma diagnosed in the United States.

These melanomas are more lethal in nature, and are occurring at younger ages, especially in women who have known sunlamp exposure. Because most skin cancers are related to UV exposure, regulating sunbed and sunlamp use can decrease the incidence of skin cancers. The need to regulate sunlamp and sunbed use is currently a nationwide issue. The FDA, along with the World Health Organization, is working to educate the population on the risks of sunlamp exposure and to eliminate the use for those under the age of 18. There is also a need to educate the public on tanning dependence.

Samantha Armstrong  
Navid Ezra  
*Indiana University School of Medicine*

**See Also:** Melanoma; Skin Cancer, Melanoma; Skin Cancer, Non-Melanoma; Ultraviolet A Radiation; Ultraviolet B Radiation; Ultraviolet Radiation Related Exposures.

**Further Readings**


**Sunscreen**

Exposure to ultraviolet (UV) radiation in sunlight has both beneficial and harmful effects on human health. Sunlight stimulates the synthesis of Vitamin D, sets biological rhythms, and has favorable effects on mood. On the other hand, exposure to UV radiation is also responsible for photoaging, sunburns,
and skin cancer. Sunscreens are topical agents that reflect or absorb UV radiation, and thereby help mitigate the deleterious effects of UV light. There are a variety of types of sunscreens, with some formulations better suited for a given individual than another; however, sunscreen should be used by all individuals regardless of skin type. The proper use of sunscreen is a critical component in preventing skin cancer and photoaging, and is generally regarded as having an excellent safety profile.

Public health messages have generally focused on the health hazards of excessive sun exposure. Approximately 95 percent of the UV radiation that reaches the Earth is in the form of UVA radiation, which penetrates deeply into the skin and can damage deoxyribonucleic acid (DNA) molecules, thereby promoting the generation of skin cancer and leading to photoaging. The contribution of UVA radiation to the formation of sunburn is thought to be minor, thus some sunscreens do not block UVA radiation. On the other hand, UVB radiation accounts for only 5 percent of the total UV radiation that reaches the Earth, but is the primary cause of sunburns, and includes the most biologically active wavelengths. In addition to causing sunburns, UVB is the primary determinant of hyperpigmentation, photoaging, and skin cancer.

All individuals need sunscreen, regardless of race or skin color. People of all skin types get skin cancer, with 2 to 3 million non-melanoma skin cancers and 132,000 melanoma skin cancers worldwide occurring each year. Many of these skin cancers could have been prevented by the use of sunscreen and other sun-protective measures. However, sunscreens are particularly beneficial for people with lighter skin types and those who are more susceptible to sunburns. Sunscreens should be used daily, especially when performing outdoor activities in sunny weather. Sun tanning is unsafe and is not recommended by the American Academy of Dermatology.

Types
Sunscreens can be classified into two major types: chemical (organic) and physical (inorganic). Chemical sunscreens contain a variety of special ingredients that act as filters to absorb UV radiation and convert it to a negligible amount of heat, thereby reducing the amount of UV radiation that penetrates the skin. These types of sunscreens primarily block UVB radiation; however, newer compounds also block UVA. Physical sunscreens, also referred to as sunblock, are able to reflect and scatter UV radiation from both UVA and UVB wavelengths. They contain mineral compounds such as titanium dioxide or zinc oxide, and are considered more stable and less irritating than chemical sunscreens.

However, older preparations are considered cosmetically unacceptable by many people because they produce a visible white film on the skin and do not easily wash off. Newer nanoparticle preparations produce a transparent film on the skin while maintaining a high level of UVA/UVB protection; however, the use of nanoparticle formulations of titanium dioxide or zinc oxide have raised concerns regarding the systemic absorption and toxicity of these substances.

Sunscreens are labeled using a standardized sun protective factor (SPF), which is a measure of a sunscreen's capacity to protect against UVB radiation and a sunburn. SPF is the ratio of the minimal amount of UV radiation needed to produce skin redness in sunburned and nonsunburned skin. However, SPF does not describe a sunscreen's protection against UVA radiation, which constitutes over 90 percent of the UV radiation that reaches the human skin. The American Academy of Dermatology recommends that all individuals wear sunscreen when they will be engaging in outdoor activities, even on cloudy days because more than 80 percent of the sun's harmful UV rays can still reach the skin. Sunscreens should be applied at least 15 minutes before going outdoors, applied liberally to all sun-exposed areas, and reapplied every 90 to 120 minutes. The amount necessary to cover the entire body is about one ounce, or the size of a shot glass. It is best to use a sunscreen with an SPF of 30 or higher, and because skin cancer can also form on the lips, it is recommended to also use a lip balm with an SPF of 30 or greater. Broad-spectrum sunscreens that offer both UVA and UVB protection should be used because both of these forms of UV radiation are involved in photoaging and carcinogenesis.

Efficacy and Safety
There is strong evidence to suggest that the use of sunscreen protects against various photodermatoses, such as actinic keratoses or “pre-skin cancer,” and squamous cell carcinoma. Additionally, some randomized trials have demonstrated decreased incidence of melanoma with the regular use of sunscreen, and a systematic review by the U.S. Preventive Services Task Force found that regular sunscreen use was associated with decreased squamous cell carcinoma. However, the role of sunscreen in the prevention of basal cell carcinoma (BCC) is less clear.
because some studies have demonstrated a decreased incidence of BCC, but with results that were not statistically significant. Furthermore, the use of broad-spectrum sunscreen can reduce the photodamage and photoaging associated with chronic sun exposure, such as wrinkling and pigment changes.

Most sunscreens are considered to have an excellent safety profile, with many decades of research and use without adverse side effects. Rarely, an individual may develop an allergic reaction to the components of some sunscreens, with a local irritation in the areas to which the sunscreen was applied. There have also been reports of anaphylactic reactions to the use of some sunscreens, but this is rare. Furthermore, while sun exposure is necessary for the formation of biologically active vitamin D, there is no evidence to suggest that the use of sunscreen significantly suppresses the formation of vitamin D in the skin.

Although considered safe, some sunscreens have been shown to have estrogenizing effects in animal models when used in immature rats, but hormonal effects have not been demonstrated in humans. Recently, concern has been generated because of the systemic absorption of sunscreens that contain nanoparticle formulations of zinc oxide and titanium dioxide. Animal studies have shown that these molecules can lead to the generation of reactive oxygen species when absorbed into the blood stream, and therefore lead to potential toxicity. Although studies have shown that these particles remain on the outer surface of the skin and do not undergo cutaneous absorption, it is thought that aerosol formulations that contain these nanoparticles may be inhaled and lead to systemic absorption. Nevertheless, sunscreen is widely agreed to be beneficial and contribute to prevention of skin cancer and photoaging. The U.S. Food and Drug Administration ruled that sunscreen should be exempt from sales tax in an effort to promote the use of sunscreen as a public health measure.

Saami Khalifian
Natanel Jourabchi
Johns Hopkins University School of Medicine

See Also: Skin Cancer, Melanoma; Skin Cancer, Non-Melanoma; Sun Exposure (Australia).

Further Readings


Surgery

Since the earliest days of medicine, surgery has been employed to treat cancer. Medical advances such as the introduction of general anesthesia, antibiotics, and blood transfusions have fostered the development of safe and effective cancer operations. Surgical therapy has evolved as the understanding of the nature of cancer has grown. Today, surgery is often used as part of a multidisciplinary approach with chemotherapy, targeted therapy, and/or radiation. Surgery has a role not just in the first line treatment of cancer, but also in its diagnosis, staging, and palliation. The earliest description of cancer was found in an Egyptian papyrus from approximately 3000 B.C.E. It describes eight patients with breast tumors, one of whom was treated with a “fire drill.” The writings of Hippocrates discuss malignant tumors, which he called karkinos, and caution that removal of even small cancers hastened the death of the patient. Roman physician Galen (2nd century C.E.) named tumors oncos, Greek for “mass” or “swelling,” and recommended widely excising them and cauterizing the base to kill the “roots of the tumor.”

The 18th century saw a number of surgeons rise to prominence while treating cancer. John Hunter, a famed surgeon of the time, believed that surgery could be curative if the cancer was localized. He remarked that “if the tumor is moveable . . . there is no impropriety in removing it.” However, surgery during this time period was risky, and often resulted in the afflicted individual’s demise. The accomplished Scottish surgeon Alexander Monro
reported a case series of 60 patients undergoing surgery for breast cancer, only two of whom survived for two years.

The development of safe anesthesia in the 1840s and the widespread adoption of antiseptic techniques developed by Joseph Lister in 1867 ushered in a new era, where surgery could be more extensive without resulting in the death of the patient. The first major cancer operation under general anesthesia is believed to have taken place in 1846, when John Collins Warren removed a patient’s cancerous salivary glands. The “century of the surgeon” marked a time when improved survival statistics and the paucity of effective systemic treatments made surgical removal the primary treatment for most cancers. During this time, many of the operations still used today were developed and refined.

The surgical philosophy at the time was exemplified in the treatment for breast cancer, perfected and widely taught by William Halstead at Johns Hopkins University in the late 19th century. He noted that patients’ cancers were more likely to recur if the tissues surrounding the breast were not excised as well. In his classic operation, known as the radical mastectomy, not only was the breast removed, but also the muscles and sometimes bones of the chest wall, as well as all the regional lymph nodes. He reported a five-year survival rate of 40 percent, which was considered excellent at the time. The resulting disfigurement, however, was significant, and it became clear that more extensive surgery did not prevent the disease from recurring in the rest of the body.

It is now understood that while many early cancers can be completely cured with surgery, the presence of circulating tumor cells in the blood and lymphatic system may also require the addition of other modalities, such as chemotherapy and radiation therapy to prevent recurrence and spread. In the case of breast cancer, as these other therapies have been developed and refined, the extent of surgery has decreased. Today, it is common for women with breast cancer to be treated with removal of the tumor and preservation of the breast, and the radical mastectomy has largely become an operation of historical interest.

Surgery for Diagnosis

Today, surgery still has a significant role in the management of cancer. Although less invasive methods such as needle biopsy are now favored for tissue diagnosis, surgical biopsy remains an important tool for tumors that are inaccessible by other means, or when needle biopsy is inconclusive. Cancers within the lung, for example, are frequently not amenable to needle biopsy. Surgical biopsy is also useful where larger pieces of tissue are required for analysis. The diagnosis of lymphoma and certain sarcomas can be exceedingly difficult to make histologically if the scaffolding in which the cells live cannot be examined as well. In some circumstances, cancer can only be diagnosed when the entire lesion is removed, and the interface between normal and malignant tissue can be examined for telltale evidence of invasion, as in follicular cancer of the thyroid gland. At times, the diagnosis of cancer requires removal of an entire organ, especially when it is located deep in the abdomen. Investigation of suspicious masses in the adrenal glands and kidneys often necessitates surgical removal of these organs with subsequent pathological examination, and cancers of the ovary and testicle are frequently diagnosed in the same way.

Surgery as First Line Therapy

Surgery remains the first line of treatment for most solid tumors. The goal of surgery is to remove the entire primary tumor with microscopically negative margins, although the amount of normal tissue that needs to be removed to ensure a negative margin varies by the type of cancer and the organ involved. Breast cancer can be considered safely removed if there are no malignant cells seen at the cut edge of the tissue, but sarcomas of the bone require a 2 to 3 centimeter margin of normal tissue, often necessitating the sacrifice of a limb. Sometimes, the involvement with cancer is too extensive, and negative margins are simply not possible. This is seen in certain abdominal malignancies, such as ovarian cancer, sarcomas and carcinoid tumors, and also in brain tumors like anaplastic astrocytomas or glioblastomas. In those situations, debulking of a tumor can help increase the efficacy of other modalities such as chemotherapy, and provide symptom relief for the patient.

Sometimes, surgery targets secondary cancerous growths in addition to the primary tumor. Once a cancer has spread to sites distant from its organ of origin, it is considered Stage 4 (metastatic). In certain types of cancer, it has been found that removal of the metastasis, especially if confined to a single
Surgery site, can produce long-term survival for patients with Stage 4 disease. Metastectomy, as the procedure is called, is most commonly used for colon cancer that has spread to the liver, and can be curative in selected cases. It is also performed for secondary tumors of the lung (most often from osteosarcoma of the bone) and of the brain (from the kidney, melanoma, and sarcomas).

Surgical excision can take the traditional form of cold steel (cutting with a knife), but can also involve other technologies. Radiofrequency ablation kills cancer cells by heating them with high frequency radio waves delivered through a probe inserted into the tumor. Liver and kidney tumors are sometimes treated in this fashion after being exposed with a traditional abdominal incision. Tumors can also be frozen with a cryoprobe, or dissolved with injected ethanol. Lasers are sometimes utilized in surgery for tumors of the brain, and also to burn away lesions in readily accessible sites such as the cervix, larynx, skin, penis, or anus.

As an adjunct to its role as the primary treatment of cancer, surgery can be used to glean information about the stage of the disease, or its extent of spread. Certain types of cancer (carcinomas) spread by traveling first to regional lymph nodes, and so sampling of these tissues has become a part of the surgical management of diseases like breast cancer and melanoma. For other cancers, sampling is not sufficient or feasible, and so removal of all the adjacent lymph nodes is necessary. This is called a lymphadenectomy, and is usually done during the primary surgery. Other types of surgical staging also exist. Abdominal exploration still remains the most reliable way to stage many abdominal malignancies, such as ovarian and pancreatic cancer, even though imaging modalities such as computed tomography (CT) scan and magnetic resonance imaging (MRI) have improved the ability to detect disease outside of the primary organ. Similarly, thoracic surgery is sometimes needed to confirm secondary spread of cancer to the lung and its lining.

**Minimally Invasive Surgery**

Although cancer surgery has traditionally been considered maximally invasive, with large incisions into body cavities, increasingly more is being done with modalities that minimize the insult to the body. Laparoscopic surgery, utilizing ports placed into multiple small incisions through which a camera and a variety of instruments can be introduced, was first pioneered in the 1980s and popularized for the removal of the gallbladder. Laparoscopic techniques have since been applied to many oncologic procedures, and now intestines, kidneys, adrenal glands, and many other organs have been laparoscopically removed for the treatment of cancer. Robotic surgery, in which the instruments and camera are controlled by the surgeon at a bedside console, takes this a step further, and has been embraced in areas of the body where laparoscopy is more technically challenging, such as prostate, rectal, and gynecologic pelvic surgery. Endoscopic surgery, in which a flexible camera is inserted into an orifice, has revolutionized the treatment of small tumors of the urinary, digestive, and respiratory tracts, allowing their removal without external incisions.

*Surgery remains the first line of treatment for solid tumors and can often target secondary cancerous growths in addition to the primary tumor. (National Cancer Institute)*
Surgery and Other Treatment Modalities
In addition to being the primary treatment for many cancers, surgery can be used to aid delivery of other modalities of treatment. The simplest example of this is the placement of indwelling intravenous catheters into the large veins close to the heart in order to allow safe infusion of chemotherapy agents. Sometimes, chemotherapy is not systemically given to the whole body, but rather directed at the affected organ or limb. This requires placement of specialized catheters directly into adjacent arteries or veins. For the treatment of liver tumors, an infusion pump is sometimes implanted into the abdomen to deliver chemotherapy into the arteries supplying the cancer. Chemotherapy can also be directly applied to tissues involved with cancer. Hyperthermic intraperitoneal chemotherapy is a technique in which the abdominal cavity is rinsed with a heated chemotherapy solution after all visible tumor is removed (debulking). It is used for certain advanced-stage tumors that have spread throughout the abdomen and may not be completely resectable, most commonly cancer of the appendix, ovarian cancer, and colorectal cancer. A similar technique is used in the thoracic cavity to treat mesotheliomas and other cancers affecting the lining of the lung.

The delivery of radiation therapy can also be facilitated by surgery. Brachytherapy is a form of radiotherapy in which radioactive “seeds” are introduced in or near the tumor. This is a commonly used modality in prostate and cervical cancer, in which the surgeon places the seeds directly into the involved organ with the aid of a special applicator. This is often done in lieu of removing the tumor. In other instances, the tumor is surgically removed, and one or more specialized catheters are placed in the cavity to allow subsequent delivery of the radioactive seeds. This is seen in breast cancer treatment, where radiation plays an important role in preventing recurrence after resection. In selected cases, radiation can also be directly applied to the cavity during surgery through a device temporarily introduced into the wound by the surgeon.

Reconstruction
During the treatment of cancer, the surgeon must always balance complete removal of the tumor with cosmetic and functional outcome. The ultimate goal is survival, but restoration of normal function and appearance and preservation of the quality of life of the patient is of paramount importance. In intestinal cancer surgery, bowel continuity is interrupted, and must be reconstituted to allow normal eating and elimination. Surgery for cancer of the bile ducts and pancreas results in interruption of the flow of digestive juices, and requires complex reconstruction to reestablish digestion. In surgery for breast cancer, careful placement of the incision and removing the minimum amount of tissue necessary for clear margins are used to ensure the best possible cosmetic result. Similar concerns apply for tumors of the skin, especially in the facial area. Sometimes, the operation needed to remove a cancer is so extensive that more elaborate procedures are needed to restore form and function. Cancer of the bladder may necessitate removal of that entire organ and creation of a new bladder from intestinal tissue. A diseased esophagus must be removed from the neck down to the abdomen, with a new conduit created from the patient’s stomach or intestine.

Plastic surgeons often play an important role in the treatment of cancer. Resection of large tumors involving skin, muscle, or bone can leave significant wounds that cannot be closed by conventional methods. Plastic surgery techniques of mobilizing flaps of tissue from adjacent and sometimes remote areas of the patient’s body are an indispensable tool in these situations. At times, plastic surgeons are called on to do more than close wounds; they must restore normal appearance after cancer surgery. Removal of cancers of the head and neck region can result in significant deformity and loss of function. Microvascular free flap techniques, in which portions of skin, muscle, or even bone are removed from a distant part of the body, such as the forearm, and transplanted to the facial area by connecting miniscule vessels with the aid of a microscope, have revolutionized reconstructive surgery in this area. Breast reconstruction is another advancement in which either the patient’s tissue or manmade implants are used to recreate the normal breast contour, improving quality of life in breast cancer survivors treated with mastectomy.

Palliation
Even when surgery is no longer curative, it can still have a role in improving a patient’s pain, function, and overall quality of life. Large tumors of the breast, skin, muscle, and bone that are ulcerated and painful
can be excised to treat distressing symptoms. Similarly, cancer of the colon and small intestine that have already become metastatic are removed if they cause bleeding or obstruction of the flow of bowel contents. Advanced kidney tumors are taken out to prevent pain and blood loss in the urine.

Palliative surgery goes beyond the removal of tissues involved with cancer, and can address many of the sequelae of advanced disease. Obstruction of the flow of intestinal contents can be seen in the late stages of a number of cancers, including ovarian cancer and malignancies of the stomach and bowel. This may require intestinal surgery to bypass the obstructing areas or drain the blockage through permanent openings created in the stomach or bowel. Obstructing cancers of the biliary tract can cause severe jaundice, itching, and recurrent infection, and a bypass procedure can be used to relieve these symptoms if less invasive methods fail. Transabdominal placement of feeding tubes into the stomach or small intestine often plays a role in the management of tumors causing blockage of the upper digestive tract, especially advanced tumors of the head and neck region and esophagus.

Another symptom of advanced cancer is the accumulation of malignant fluid in a patient’s body cavities. When this happens in the chest, the fluid collapses the lung and makes breathing very difficult. Surgeons can place a catheter into the chest cavity for intermittent drainage, or alternately perform an operation to obliterate the space around the lung, thus preventing reaccumulation of fluid. Cerebrospinal fluid accumulating around the brain because of obstruction by a tumor causes a rise in pressure inside the skull, resulting in headaches, nausea, and altered consciousness. It can even be life threatening. In these circumstances, a neurosurgeon can place a ventriculo-peritoneal shunt, which is a drainage tube within the skull that is then tunneled out under the patient’s skin to empty harmlessly into the abdominal cavity.

Surgeons and Cancer
From the dawn of surgery as a distinct specialty within medicine, surgeons have devoted themselves to the understanding and treatment of cancer. Many of the cancer operations that are still used today were developed in the late 19th century, and still carry the names of the surgeons who described and refined them. The German surgeon Theodore Billroth is considered one of the founding fathers of modern abdominal surgery, and pioneered the safe removal of the larynx, esophagus, and stomach for cancer. Other landmark surgeons include Jan von Mikulicz (abdominal cancers), Charles Mayo and Theodor Kocher (thyroid cancer), Frank Lahey (rectal cancer), George Crile, Roswell Park, and Hayes Martin (head and neck cancer), and John G. Clark and Ernst Wertheim (cervical cancer).

Today, surgeons continue to be innovators, developing new procedures for the treatment of malignancy. Sentinel lymph node biopsy is one such advancement. Up until the late 20th century, lymph node staging for breast cancer and melanoma (skin cancer) was achieved by routinely removing all of the adjacent nodes, resulting in permanent limb swelling in about 15 percent of patients. The work of Donald Morton (melanoma), David Krag, and Armando Giuliano (breast cancer) demonstrated that a gatekeeper or “sentinel” lymph node could be identified by injecting a blue dye or radiolabelled substance close to the tumor, allowing for successful staging with removal of far fewer nodes. After designing and carrying out the trials needed to prove that the new technique was safe and accurate, they were able to alter the surgical management of these diseases forever.

Practitioners of surgery have also contributed to scientific knowledge about the causes and development of cancer through work in the laboratory. The first environmental cause of cancer was described by British surgeon Percivall Pott in 1775, when he noted that cancer of the scrotum was a common disease among chimney sweeps, and he theorized that the ash and soot they were exposed to had carcinogenic properties. In the 1860s, German surgeon Karl Thiersch showed that cancers metastasize (spread) through circulating malignant cells, and not through a liquid, as was thought at the time. In England, Stephen Paget noted that while cancer cells could travel in the blood and lymphatics, they could only grow in certain organs. He gave the inspired analogy of metastatic cancer cells as “seeds (that) are carried in all directions, but they can only live and grow if they fall on congenial soil.”

Surgeons who specialize in cancer care are known as surgical oncologists, and have usually undertaken an extra two or three years of focused training beyond general surgery residency. The surgical subspecialties such as orthopedics,
The Future of Cancer Surgery

Advances in surgical techniques, medical technology, and the understanding of human physiology are enabling cancer operations unfathomable in the time of Halstead and Billroth. Cancers previously considered unresectable are now becoming targets of curative surgery. Minimally invasive techniques are applied to large cancer operations, and procedures previously considered highly risky, like removal and reconstruction of large blood vessels involved with cancer, are becoming more commonplace. This is a reflection not only of newer technology and improved outcomes because of better surgical care, but also of the development of more effective chemotherapy and radiation. Application of these therapies before surgery can shrink tumors and improve the chance of complete removal. Additionally, for complex surgical procedures such as those for the treatment of pancreatic cancer, outcomes are closely related to surgical and institutional volumes. This has spurred an initiative to direct those patients to high-volume “centers of excellence,” and is expected to continue to improve outcomes for these types of procedures.

At the same time that some cancers are treated with increasingly complex operations, others are requiring less surgery. A multimodality approach, in which local therapies such as surgery and radiation and systemic therapy like chemotherapy are utilized together, has been very successful in the management of many cancers. The extent of surgery for lymph node spread in breast cancer, for example, continues to decrease as these therapies are used more effectively together. As the understanding of the biology of cancer improves, so does the ability to predict which patients will benefit from more aggressive surgery, and which will not. Ultimately molecular analysis of an individual’s tumor will allow surgical and other therapies to be tailored to provide the best chance of cure.

Ingrid Marie Lizarranga
University of Iowa

See Also: Bladder Cancer; Bone Cancer; Osteosarcoma/Malignant; Breast Cancer; Colon Cancer; Esophageal Cancer; History of Cancer; Ovarian Epithelial Cancer; Society of Surgical Oncologists.

Further Readings

Survivors of Cancer

The past 30 years have seen a dramatic increase in the survival rates of most types of cancer, and cancer in general, in the United States. This has resulted in an increased interest in survivors of cancer, the long-term effects of the illness and its treatment, and how survivors view themselves. The National Cancer Institute’s recent Surveillance, Epidemiology, and End Results (SEER) report indicates that the five-year survival for all cancers is now above 66 percent. Survival rates for several of the most common cancers among adults, such as breast, colorectal, and prostate cancer, are now at 89, 65, and 99 percent, respectively. By comparison, in 1985, the survival rates for breast (78 percent),
colorectal (58 percent), and prostate (75 percent) cancers were lower. The increasing survivability of most types of cancer has generated a new discourse on cancer, one that focuses on living with cancer, rather than dying from it, and has changed the orientation from victimization to survivorship.

**From Victim**

When long-term survival from cancer was rare, the notion of survivorship was unrealistic for most diagnosed with cancer. For many patients, their families, and friends, the diagnosis was considered a death sentence. Cancer patients often chose to hide their diagnoses from others for as long as possible out of fear of negative responses and possible discrimination. As Paul Little and colleagues note, “A few decades ago, cancer illness was a topic shrouded in social silence . . .” In fact, many could not or would not even use the word “cancer” when discussing the illness. Even with increasing survival rates, public perceptions have lagged behind the realities of medical progress.

Research by Gary Deimling and colleagues at the Cancer Survivor Research Program (CSRP) found that as recently as 15 years ago, the “victim” label was endorsed by nearly 30 percent of older adults in their study of older adults previously diagnosed with cancer. However, even as perceptions of victimization have faded over time, there continue to be negative psycho-social responses to cancer that persist. Some of these are related to the individual's sense of self and identity.

Cancer may also have an impact on the self and identity by placing strain on core roles, such as spousal and parental roles. This type of role strain is more likely, and may be especially problematic, if cancer has caused long-term disability. Research has documented the long-term impact of cancer on physical functioning. This may be the result from the effects of the disease itself, or the greater number of health problems/comorbidities and illness symptoms that survivors report that result from treatment. During or after treatment, cancer patients may also experience difficulty with or a loss of other valued roles and activities. These may include work, hobbies, and recreation and social activities. This loss of valued roles may be compounded for older adults who have faced other role losses that are traditionally associated with aging (e.g., retirement, or the death of a spouse). Sex-specific cancers such as breast or prostate cancer may impact aspects of the self through gender identity, especially if cancer or its treatment impact sexual performance/satisfaction or body image. To the degree that those diagnosed with cancer believe that their behaviors may have increased their susceptibility to the disease (e.g., smoking and lung cancer, diet and colon cancer), the resulting self-blame can have a negative impact on their self-esteem. Self-blame may be heightened by feelings of stigma they perceive in the reactions of others to their illness.

In addition to the potentially negative effects of cancer on the individual's sense of self, research on the psychosocial effects of cancer has documented that cancer-related worries persist among those who have survived cancer, even those who have survived for an extended period, and even after recurrence is unlikely. Importantly, cancer-related worries have been shown to be linked to broader mental health effects, such as depression and anxiety.

**Toward Survivorship**

Fortunately, the emphasis on the long-term difficulties and vulnerability of survivors is being replaced by a focus on survivorship. The concept of survivorship has its origins in the mid-1980s, in Fitzhugh Mullan's paper, “Seasons of Survival.” Organizations such as the American Cancer Society (ACS), National Coalition of Cancer Survivorship (NCCS), and the Office of Cancer Survivorship (OCS) of the National Cancer Institute (NCI) have helped to reinforce a survivor orientation. As defined by the OCS, a cancer survivor is “anyone who has survived even one day after diagnosis.” Research at the CSRP has reported that well over three-fourths of long-term survivors studied by that group have adopted this label when referring to their cancer experience. The emergence of the cancer survivor label to describe those who have been diagnosed with cancer provides another perspective on their illness, one that focuses on the more optimistic, and for most a more realistic outcome. Even for types of cancer that are not curable, many are highly treatable, altering perceptions that some forms of cancer are chronic.

The portrayal of survivorship in the media that has brought celebrity survivors into the public discussion of the illness (e.g., cyclist Lance Armstrong, and singer/songwriter Sheryl Crow) has served to further promote the adoption of the
survivorship orientation by the general public and those who have had cancer. This is a change toward a celebration of survival, rather than focusing on stigma and victimization. This allows those who have survived cancer to join the growing number of high-profile survivors, and to some degree see themselves as a celebrity. Research has shown that the positive orientation that survivorship engenders can have the added health benefit of reinforcing ongoing relationships with their primary care providers, promoting more careful symptom monitoring, and engendering a focus on better health maintenance.

Moreover, cancer may be viewed as an opportunity for personal growth and improved wellbeing, and can motivate reintegration of the self. Phrases such as “self-transformation” and “reformulation of identity” have been used to describe the cancer experience. Based on his research, Bradley Zebrack quotes a survivor who reflects on the integrative aspects of the experience by saying, “for a long time now, maybe four or five years, cancer has felt like it’s been part of a quilt . . . one of those patches is cancer.” As survivors are able to return to effective and enjoyable participation in previously valued roles and activities, a sense of identity continuity may return, which in turn can enhance overall quality of life. Further, the adoption of the survivor identity may have important implications in terms of the distress that continues to be experienced by many survivors, even long after the completion of treatment. Viewing oneself as a survivor may help to buffer an individual from a preoccupation with cancer-related worries, and as a result may play a role in reducing anxiety and depression.

Much of the above identifies the positive aspects of a survival/survivorship orientation among individuals who have had cancer. However, a darker side has also emerged with the growth of the survivorship orientation in public discourse. Some have suggested that the survivor label or identity ignores the inherent uncertainty of the cancer experience, and may be rejected by many because of realistic fears of recurrence, or another type of cancer. For others, cancer survival may come with a responsibility to present one’s self as a role model to other individuals with the disease, or to “survive well.” It may also generate a sense of obligation to share their survival experience with others. Not every survivor is ready or willing to accept these responsibilities.

Into the Future
The general public’s and survivors’ adoption of the orientation and language of survival/survivorship has broader implications for the quality of life after cancer. With the shift from cancer victimization toward a focus on cancer as a survivable, or even a transformative illness, those diagnosed with the disease are provided with a new way of viewing themselves and their future. This suggests that a shift in the discourse on cancer, focused on survival and survivorship, is important, complex, and pervasive. As Cynthia Mathieson notes, the major challenge now faced by those who survive cancer is “the work of living with cancer.”

Gary T. Deimling
Sherri Brown
Case Western Reserve University

See Also: Age; History of Cancer, Psychosocial Care/Support; Stress; Survivors of Cancer, Families of.

Further Readings

Survivors of Cancer, Families of

Finding out that a family member or loved one has cancer brings forth questions without immediate answers. How serious is this? Will they survive? What will the treatment be like? How will we manage? Who will assume the responsibilities of the diagnosed individual? Will they die? Families of cancer survivors find themselves in new roles, beginning as support systems and caregivers, throughout a process that challenges and redefines relationships, resources, spirituality, and roles. Children, parents,
spouses, and others become caregivers who need to multitask to process feelings about the person, the relationship, and the future while questioning their mortality. Many survive their cancer diagnosis with early detection and treatment. Recurrence is possible, and the word *remission* becomes filled with reassurance, but not as much as another, “cured.” Caregivers find their roles, family reconfiguration, and the return to previous norms challenged when the surviving member returns to their previous roles. Can individuals involved discuss their shared experiences and feelings? Will they be surprised again? How can I be angry with someone who has recovered from so much? How will I recover? What is the new normal? Can things ever be the same? Should they return to the way they were before, PC (pre-cancer)?

**Diagnosis**

Cancer can affect a tiny baby or a family elder. Surviving cancer is a medical success, yet there can be layers of loss, from a person’s fertility to a sense of immortality grabbed and replaced with awareness of one’s vulnerability and eventual mortality. A cancer diagnosis can bring seemingly endless fear to the person impacted, as well as affected friends and family. A range of overlapping and contradictory expectations arises in regard to what will unfold. Details about the diagnosis and prognosis may seem confusing. One hopes for the best outcome, but fears the worst. Support of the person diagnosed competes with self-protection by the loved ones who hope for the best, but begin mourning when they learn the news.

**New Beginning**

Surviving cancer treatment is multifaceted for the person recovering, as well as family members who are adjusting to their new roles and feelings. The person who is returning home with a positive prognosis needs to regain their strength and health, and to keep track of their symptoms and side effects from ongoing or recently completed treatment. They are likely to have conflicting feelings of wanting to put cancer behind them while being fearful of a recurrence. Family members are likely to feel awkward in trying to be thoughtful while taking their cues regarding expectations and degrees of intimacy as the recovering individual tries to answer these same questions. Recovery from cancer can impact how a person rejoins the family. Can they pick up where they left off? Can the wish to have a child be fulfilled? What are the fertility options? How has one’s body been impacted by the cancer treatments? Will they be desirable to an existing or future partner with a body that may bear scars? Family plans may be changed because of physical changes, financial burdens, and limitations in the cancer survivor. These can be challenging to family members who may experience frustration and anger while also wishing to be supportive and grateful that their loved one survived.

**Surviving Cancer as a Family**

Cancer is a very personal experience, replete with unknowns. Will one survive, die, or have a recurrence? Such challenging questions are often too great to pose. Cancer survival within a family can range from a prognosis of low to high risk of recurrence, or a very immediate health decline, which will quickly result in death. Regardless of the bounty of individuals providing support, someone diagnosed with cancer can experience a sequential journey, much like Elisabeth Kübler-Ross’ Five Stages of Grief, while anticipating treatment, life expectancy, losses, and feelings of being utterly alone, even within a crowd. This can be very challenging for spouses and children, as well as other family members who want to help, to be comforted about their reactions to the diagnosis and their fears of losing their loved one. To whom can a child turn for comfort about the diagnosis and journey of their primary caregiver? How can a parent process their feelings while addressing the needs of a dying child? Internal battles, as well as external ones, can prevail as one tries to balance personal needs with efforts to support the family member.

While all feelings are real, the family unit can be best served by acknowledging the disruption, dissonance, grief, and fear they share, consoling each other while prioritizing their wishes to be of support, as needed, when the diagnosed individual is ready. Small children and others may find this especially challenging. Frustrations may arise for the others involved in this family crisis; it can also be reassuring to be perceived as the source of strength and center of the family unit. The journey may be especially challenging as family wholeness and balance is sought. It is tempting to act as if everything is fine and normal, as it was prior to the intrusion of
the diagnosis and treatment. However, everything is different for the survivor and many others within the family. The fears and doubts ignited are not easily extinguished or reduced.

**Family Supports**
Regardless of the volumes of information published or preparation offered by professionals, changes in family dynamics and functioning will gradually unfold as challenges and successes present themselves. Working with professionals and peer-support groups of others who have been through this journey or are also experiencing recovery, caregiving, or grief, at the same or another stage can be beneficial for everyone. Outsiders with distance and perspective would do well to encourage the survivor and family to seek support during this complicated journey post treatment and a prognosis absent guarantees. While it is common to feel that one should know how to act or feel, it is more likely one will not know what to do in such a life-altering situation. The family unit experienced a frightening challenge to their future, social roles, goals, and dreams. How secure should they be about the future? Will there be another recurrence? Will it be the same cancer and/or in a different place, or another? Like many others, these unknowns can become part of family functioning as life moves forward.

**Planning a Future as a Family**
It is not uncommon for someone post diagnosis and treatment to feel depression and anxiety following their frightening life challenge. However, one can emerge from this experience with a new attitude and optimism about life and goals. Many who have survived cancer find that they wish to help others, create positive changes in their life, and become supportive of others with cancer or in other ways that may have long been of interest, but on the back burner for a time when scheduling would be easier. Such a life-altering experience presents choices and rethinking what one really wants to do with the rest of their life. Such a sudden diagnosis often presents one with a previously unanticipated mortality, a very personal consideration about their life’s end and urgent decisions. Regardless of the official prognosis, complicated by a plethora of unknowns, planning a future can include a variety of elements. Every minute takes on a new meaning, for the patient as well as friends and family members who most likely take their cues from the patient. How do they feel physically and emotionally? Will life ever be the same? Should it?

**Confusion About Death**
The unknowns of cancer can change everything or nothing. Some already live with optimism, not taking a moment for granted. Others lose track of moments, months, and years, which blend together without a review of personal choices. When a family member is diagnosed, they may die soon, from another malady, or after a full life. Mourning often begins at the moment of diagnosis, and the person with cancer, as well as friends and family, may be confused about what to say, anticipate, and do. Depression may result in anyone involved, and it is not uncommon for the diagnosed individual to support their supporters by giving permission for all
feelings, inviting discussion, or providing directives of what they want regarding care and/or interactions, as well as final arrangements. Many with any serious or critical diagnosis will wish to be treated as normally as possible. Some may wish to write letters to and/or spend time with individuals of their past and/or present in order to share important (re)connections or say goodbye.

Survival of an individual within a family, or alone, may be long term (lifelong) or very brief. Death or disability may come in response to cancer. Families must be prepared for the inevitable and unknown outcome. It becomes most challenging hoping for the best while protecting oneself and making family plans as a loved one is recovering. Is it a betrayal to consider how one might parent a family alone while simultaneously hoping for and encouraging a spouse to heed the promising prognosis and focus on good and healing things? When should children be told? Are they truly ignorant of the changes within the family dynamics? Do they see physical changes and overhear details that they may comprehend, even in part? Death may not come predictably, but may later or after a recurrence. In fact, everyone will die, but the very diagnosis of cancer, whether late stage and incurable or an easily remedied and cured type, brings to mind one's mortality and that of loved ones.

**Family Roles in the Face of Cancer**

A variety of changes often occur when someone is stricken with any sort of serious illness and prolonged treatment. In the case of cancer, aggressive treatments may require support, family care, and a shift in family roles. Perhaps a child will need to bathe and attend to a parent's intimate physical needs of hygiene, dressing, side effects, and more. What changes does such a child experience in their normal life? Perhaps extracurricular activities of a school-age child will be sacrificed to become a caregiver. Perhaps the role changes will result in caregivers giving up employment or relationships, no longer able to afford their homes, resulting in much-needed personal social support. How does a family address the financial challenges when most within the United States are barely surviving on existing incomes, and now must make important choices when economics betray monthly overhead? The process of healing or dying can take an unknown period of time. How does one survive the journey? With whom can fears and plans be shared? Support groups and therapy can be of priceless benefit to all involved.

**Conclusion**

Perhaps dreams have come true, and the person diagnosed has survived cancer and treatment. They have returned to their previous lives as they were before, or are differently abled. Maybe there is a permanent physical change. Maybe there are emotional transformations that have made everyone in the family reconsider the future. Perhaps the survivor has reevaluated what they want from their life following the shocking first-hand knowledge that cancer might have ended a life seemingly out of the blue.

Families are systems, which seek equilibrium at some cost to what was for what will be. Survivors of cancer live among the caregivers who stood and acted in support, those who bore witness to the journey, took care of children, paid bills, maintained homes, spirits, and challenged their hopes and doubts to surround the healing party with optimism. Families become redefined in their journey from cancer to recovery or loss. It is the challenge of the survivors to balance grief with guilt and relief of the stress of attending to the journey of the family member. It is also a challenge to consider one's mortality and cancer risks.

---

**See Also:** Childcare and Cancer Risk; Family Size; Survivors of Cancer; Unusual Cancers of Childhood; Women's Cancers.

**Further Readings**


Sweden

The northeastern European nation officially called the Kingdom of Sweden has roots tracing as far back as the Kalmar Union, which was a state that Queen Margaret I of Denmark formed in 1397, which included Swedish and other Scandinavian territories. Sweden was unified with Norway from 1814 to 1905, until Norway declared its sovereignty and left Sweden in its modern rendition, the Kingdom of Sweden. Before the 18th century, an incidence of cancer in Sweden was untreatable because of the lack of understanding on how to treat the disease.

In the 18th century, as surgeons across the continent became much more proficient in surgical operations involving amputations and tumor removals, the capabilities of Swedish physicians increased. As tumor removals became more technically plausible and less risky to execute, Swedish surgeons helped steadily improve the survival rate of cancer victims in the country. In contrast to the 17th-century European belief that cancer was incurable, many 18th-century surgeons in Sweden and the rest of the continent performed radical and innovative new surgeries on cancer patients in an effort to find new ways to combat the spread of the disease within the human body. For example, surgeons of the period devised a new method to treat colon cancer, by removing parts of the bowel and then rerouting portions of the abdomen.

Today, Sweden has the peak prevalence rate of cancer incidences in all of Scandinavian Europe, with 3,050 cancer incidences per 100,000 Swedish citizens. In spite of this, Sweden has some of the highest life-expectancy rates in the whole world, with the average male living to 76.5 years old, and the average female living to 81.5 years old; this is thought to be because Sweden has an excellent health care system that is well financed, and though there are not many official cancer hospitals in the country that are designated for the specific purpose of cancer care, citizens are often referred to nearby university hospitals for more focused treatments. The country has a nationwide cancer registry, established since 1958, which provides physicians with information regarding domestic trends in the disease.

The most prevalent forms of cancer in Sweden are bowel cancer, breast cancer, lung cancer, skin cancer, and malignant melanoma. Prostate, skin, and colon cancers are the most common forms of cancer incidences in males in Sweden; whereas breast, skin, and bowel cancers account for the most prevalent forms of cancer incidences in females. Within the past 15 years, the preventable diseases of skin cancer and malignant melanoma have increased in prevalence in both sexes, and account for almost 15 percent of all cancer cases in Sweden. The widespread usage of tanning beds by the Swedish population is the predominant reason for such a consistent increase in skin cancer cases in the nation. Over the past few years, incidences of lung cancer are down in females, whereas incidences of prostate cancer in males and breast cancer in females are rising, partially a result of better screening techniques.

Many famous Swedish citizens have experienced cancer. For example, Academy Award–winning actress Ingrid Bergman of Stockholm passed away from breast cancer in 1982. Anna Maria Lenngren, one of the most popular and well-known Swedish writers in the nation’s history, also died of breast cancer in 1817.

More recently, the Swedish journalist, radio host, and television anchor Jarl Martin Alfredius died in Stockholm in 2009 after succumbing to a year-long battle with prostate cancer. Sweden is known for having a very strong health care system, and is known for its quality of care and its many skilled cancer specialists who are particularly concentrated throughout the nation’s universities. For instance, Dr. Kjell Oberg lives in Uppsala, and is a foremost expert in endocrinology. He is a renowned professor at Uppsala University, for which he created the Endocrine Oncology Department where he now teaches. Also at Uppsala University is the well-known specialist Lars Pahlman, who is an expert in the field of colorectal cancer and surgery.

William M. Peaster
Independent Scholar

See Also: Bowel Cancer; Breast Cancer; Lung Cancer; Prostate Cancer; Skin Cancer.

Further Readings

Switzerland

The statehood of the central European nation officially termed the Swiss Confederation traces back to 1291, when regional cantons banded together to establish a confederacy. However, the modern state of Switzerland is considered to have been established in 1848, when the nation drafted a federal constitution. Currently, Switzerland is home to a population of over 8 million citizens. Switzerland has a long history in the field of cancer treatment and research. Paracelsus, who lived from 1493 to 1541, was a Swiss doctor and chemist who is viewed as the first person to conduct methodical chemotherapy treatments on cancer patients. He compiled various chemical elements, and distributed them to cancer patients for treatment. Several years after Paracelsus's death in 1541, his students compiled his writings on chemotherapy in De Grandibus. This text contains the first reported incidences of industrial cancer, documenting incidences of lung cancer in local miners and ore smelters. Another person of note in Switzerland's history of cancer research is Theophilus Boneti, who lived from 1620 to 1689. Boneti documented nearly 50 autopsies that modern researchers believe were mortalities resulting from cancer of the breast, lung, and kidneys. Boneti is also remembered for his research regarding nonmalignant tumors.

Switzerland is also a nation where promising research is currently being conducted in the battle against cancer. Millions of Swiss francs are poured into domestic research programs every year, and donations have consistently increased annually. There are many institutions dedicated to cancer research. The Swiss Group for Clinical Cancer Research recently conducted over 40 different cancer studies in 2012 alone. The National Institute for Cancer Epidemiology Registration is a Swiss organization that monitors trends in the incidences of cancer within the nation, as well as annually observing the quality of cancer care in the country. Another notable organization is the Swiss Pediatric Oncology Group, which consists of a group of physicians, researchers, and scientists whose common goal it is to combat domestic childhood and adolescent cancer.

The Swiss experience some of the highest rates of breast, bowel, and lung cancer in the world. Nearly 40,000 new incidences of cancer are diagnosed in Switzerland every year, and there are over 15,000 cancer mortalities annually. Cancer researchers in the country currently estimate that one out of every three Swiss citizens will be diagnosed with cancer at some point in their life. Fortunately, the medical progression of early screening techniques has led researchers to believe that over 50 percent of all Swiss cancer patients can be cured of their cancer; moreover, thanks to excellent treatment facilities and highly trained specialists, even Swiss cancer patients who cannot be entirely cured of their disease can usually have it effectively contained for several years. The most prevalent incidences of cancer in Switzerland have been bowel, breast, lung, prostate, and skin cancer. Bowel, lung, and prostate cancers have been the most prominent in males; whereas bowel, breast, and lung cancers have been the most prevalent in females. In the last decade, certain cancers such as skin, cervical, and stomach cancer have seen a nationwide increase in incidence in Switzerland.

Many famous citizens of the Swiss Confederation have had cancer. The internationally acclaimed Swiss kickboxer Andy Hug died in 2000 as a result of complications arising from leukemia. Winfried Hitzfeld, who was the brother of the current manager of the national Swiss soccer team, recently passed away after succumbing to his battle with blood cancer in 2014. With some of the highest cancer incidences in Europe, Switzerland is home to numerous cancer treatment facilities and world-renowned cancer specialists. Many cancer patients travel from around the globe to receive advanced treatment techniques in Switzerland; George Harrison of the Beatles and Apple cofounder Steve Jobs...
are examples of individuals who came to Switzerland for its excellent cancer care.

William M. Peaster
Independent Scholar

See Also: Breast Cancer; Lung Cancer, Small Cell; Prostate Cancer; Skin Cancer (Melanoma).

Further Readings


Syria

Syria is an Arab country in middle eastern Asia. It is bordered by Lebanon and the Mediterranean Sea on the west, Israel on the southwest, Jordan on the south, Iraq on the east, and Turkey on the north. Syria was formed after the defeat of the Ottoman Turks during World War I. The country was under French rule after 1920, from which it gained full independence in 1946. Between 1958 and 1961, Syria united with Egypt to form the United Arab Republic. In 1970, Hafiz Al-Asad, a member of the socialist Ba’th Party, overthrew the government and brought political stability to the country. Following the death of President Al-Asad, his son Bashar Al-Asad became president in July 2000. The Syrian Civil War began in 2011, and is ongoing. The death toll among Syrian government forces, opposition forces, and civilians is estimated at 100,000. In 2014, the Syrian Opposition Coalition and Syrian regime initiated peace talks at the United Nations-sponsored Geneva II conference.

The population of Syria was 17.95 million in 2014, spread over an area of 185,180 square kilometers. In a 2006 survey, it was estimated that 90 percent of the population were Muslim, and 10 percent were Christian. The capital of Syria is Damascus. Arabic is the official and most widely spoken language in Syria. In 2011, it was estimated that the health expenditure was 3.7 percent of the gross domestic product (GDP), with approximately 1.5 physicians and 1.5 beds for every 1,000 people. Syria’s health system focuses on primary health care at the level of villages, districts, and provinces. Most private hospitals are located in big cities such as Damascus, Aleppo, Tartus, and Latakia. In 2002, the highest incidence of cancer in males was reported to be bladder and lung cancer, and in females was breast cancer, uterine cancer, and leukemia. The highest incidence was found to be in southern Syria, in Al Souida. In 2012, Rasha Deeb and Safiah Eid reported that the major reasons for developing cancer among the Syrian population were their daily habits or practices, such as the type of jobs they had, diet, and smoking.

In Syria, as in most of the Middle East, water pipe smoking is commonly practiced. This form of smoking has existed for many centuries, and involves the tobacco smoke passing through water before being inhaled. Called by different names (e.g., sheesha, hookah, narghile, or arghile), water pipe smoking is associated with various health risks, including cancer. The Syrian Society for Countering Cancer reported that 60 percent of males and 23 percent females smoked, with close to 98 percent of people affected by passive smoking. In an effort to address this issue, the Syrian government passed many laws regulating tobacco consumption. In 1996, it banned advertising of tobacco; and in 2006, it banned smoking in government offices and public transport. In 2009, President Bashar Al-Assad signed an anti-smoking law, enforced in 2010, which outlawed smoking cigarettes, cigars, and waterpipes in public spaces such as restaurants, hospitals, and cinemas.

The Damascus University Al Bairouni University Cancer Center, established in 2006, and located in Harasta, Damascus, is the largest specialized hospital for cancer in Syria. The hospital has five divisions, including radiotherapy, cancer medicine, tumor surgery, laboratories, and histopathology. It has nine specialized units dealing with breast, bone and nerve tissue, gynecological, gastrointestinal,
head and neck, leukemia, pediatric, pulmonary, and urinary tract cancers. The Al Biruni Hospital reports receiving 70 percent of all Syrian patients with tumors, with daily visits of 800 to 1,200 patients. The hospital contains 525 beds, with 21 tumor specialists, 29 surgeons, and 13 physicians in other specialties. In an article published in *The Lancet Oncology* in 2014, Dr. Paul Spiegel from the United Nations High Commissioner for Refugees (UNHCR) reported that Syrian refugees and war victims were denied cancer treatment and care because of a lack of funds.

Famous Syrians who died of cancer in recent times are actor Khaled Taja, who died at the age of 73 from lung cancer in Damascus. Taja was listed as one of the top 50 actors worldwide by *Time* magazine. Syrian actor Wafiq Al-Zaeeem passed away in 2014 after a long battle with liver cancer. Recent research emerging from Syria includes findings from Frial Nizamli, Monireh Anoosheh, and Mohammadi Essah, who used a qualitative study to understand the chemotherapy experiences of women with breast cancer. Dr. Maher Saifo, who is an assistant professor in the Department of Gastro Intestinal and Lung Service at the Damascus University Al Bairouni University Cancer Center, has published many articles about cancer in Syria. The Syrian Cancer Society, a charitable society addressing cancer in Syria, is a member of the International Union Against Cancer. The first association to support children with cancer in Syria, Battling to Smile Again (BASMA), was founded in 2006. Dr. Al Moustafa Ala-Eddin is the director of the Syrian Cancer Research Center, which is a part of the Syrian Society against Cancer. The Middle-Eastern Association for Cancer Research (MEACR) was also founded by Dr. Al Moustafa in 2009.

**See Also:** Breast Cancer; International Union Against Cancer; Lung Cancer, Small Cell; Smoking and Society.

**Further Readings**


Taisho Pharmaceutical (Japan)

Taisho Pharmaceutical Co., Ltd. is a pharmaceutical company that is incorporated in Tokyo, Japan. The company was established in 1912 with the ultimate aim being the production of over-the-counter drugs. It was only in 1955 that the company diversified and invested in prescription drugs, research, and development. The success of the company through the years has since seen it listed at the Tokyo Stock Exchange, with principal ownership of the company being under the Uehara family.

The principal line of business for the company so far still remains over-the-counter medication, wherein it has been able to introduce and promote into the market brands such as Pabron, Lipovitan-D, and many others. In as far as successful operation in the industry is concerned, one of the most successful products that the company introduced to the industry was clarithromycin, a macrolide antibiotic. The branded drug was called Clarith and was introduced into the Japanese market in 1991. For distribution outside Japanese borders, the company licensed Abbott Laboratories to handle the distribution.

Taisho Pharmaceuticals faces competition in the industry from players such as Astellas Pharma Inc., Otsuka Pharmaceutical Inc., Chugai Pharmaceutical Company, Ltd., Mochida Pharmaceutical Co., Ltd., and Kissei Pharmaceutical Co. In 2011, the company made changes and transitioned into a holding company, Taisho Pharmaceutical Holdings Co., Ltd. This was done through a sole-share transfer.

The company has been at the forefront in pharmaceutical research in Japan for many years, and over the past few years, it has been working toward developing successful treatment alternatives for the aging population while, at the same time, making sure that these are available affordably. The country has a primarily active aging labor force, and unfortunately, it is also one of the countries in the world that has a very low birth rate.

Structural changes in the economy and the environment within which the company operates has since made it mandatory for the company to look into the possibility of changing the ultimate business sphere while, at the same time, working toward an increased and enhanced business foundation. It is as a result of this that the decision to turn the company into a holding company was made. With the intermediaries in Japan and overseas, it was necessary that this would happen sooner rather than later.

The mission of Taisho Pharmaceutical Holdings is to make sure that the population in the country and beyond is able to enjoy the benefits of the creation and availability of superior pharmaceuticals. At the same time, the company is also keen on
developing health products and health care information and services to help in enriching the lives of those within society.

Research and Development
The company focuses on three important areas to be able to meet the overall goals and missions: convenience, effects and safety. It is upon these three pillars that the structure of the company has been established along with their research and development philosophy.

Over time, the need to meet the demands of customers has become ever so important, and it is as a result of this that the company keeps studying consumer needs with respect to drugs in particular. Most of the time, consumers are looking for drugs that can be used safely, that are very effective, and that are convenient. It is upon these precepts that the company also runs the research and development section.

In as far as safety and effects are concerned, the company’s drugs have since been switched to over-the-counter drugs. In as far as convenience is concerned, Taisho Pharmaceuticals also has gone far in developing products that are convenient and able to meet the customers’ ease of use demands while, at the same time, still making sure that they are safe for use by consumers even without the presence of health care practitioners. There are three categories of over-the-counter drugs that have since been instituted by the company.

Research Center
The company’s research facility was structured near the Omiya Factory in 1974. It is here that the research and development divisions of the prescription drug section and the over-the-counter drugs are located. It is in the research facility that all the work regarding the development of prescription drugs is carried out. This includes all the work between the investigation stage and preclinical testing. The research facility also is equipped with some of the latest equipment.

Corporate Social Responsibility
The emphasis of the company lies in research in the fields of life sciences, the promotion of self-education, and the ability to contribute effectively to arts and sports as reputable members of Japanese society. There are several ways through which the company has been able to engage in social contributions to society.

Early in 1985, the Uehara Memorial Foundation was established in memory of the honorary chair of the company, Shokichi Uehara. This was in honor of his struggle to promote research in pharmaceuticals and other areas in life sciences with the ultimate aim of enriching the lives and welfare of consumers.

In line with their mission to promote life sciences, the company spends a lot of effort toward recognizing those who have made significant achievements in as far as excellent research is concerned. The company has provided scholarships to young researchers to encourage them to further their dreams either abroad or in Japan.

The company has also organized and hosted symposiums and seminars for professionals within the medical industry. The Taisho Toyama Pharmaceutical branch also has hosted annual symposiums where doctors give lectures to the professionals who are in attendance on some of the issues that are affecting the industry, most importantly, the current trends.

Taisho Pharmaceuticals is actively involved in environmental conservation, especially since the company started conducting business activities with the main aim of cutting down on emissions into the environment, in particular carbon dioxide. In line with this, Taisho Pharmaceuticals has been at the forefront in promoting energy-saving activities and addressing some of the necessary technical elements.

Michael Fox
Independent Scholar

See Also: Abbott Laboratories (United States); Astellas Pharma (Japan); Daiichi Sankyo (Japan); Eisai (Japan); Ono Pharmaceutical (Japan); Takeda Pharmaceutical (Japan).

Further Readings
Taiwan

Taiwan, formerly known as Formosa, is composed of a main island (Taiwan) and several smaller islands in East Asia. Taiwan claims status as an independent nation, but this is contested by China. At east longitude between 120 and 122 degrees and north latitude between 22 and 25 degrees, with the Tropic of Cancer running through the central and southern areas, Taiwan is close to the People's Republic of China to the west, Japan to the east and northeast, and the Philippines to the south.

Taiwan has experienced multiple wars and has been occupied by different countries in different historical periods. In 1621, at the Age of Discovery, the Dutch landed in southern Taiwan (today's Tainan). They then expanded farther south and to the north. Through interracial marriages between the Dutch and the locals, their offspring spread out all over the island. In 1626, the Spaniards arrived in northern Taiwan. There were turf battles between the two powerful players of international sea trading. Decades later, Koxinga, a Chinese military leader loyal to the Ming dynasty, escaped from mainland China to Taiwan in 1661. He expelled the Dutch and Spaniards and used the Taiwan area as a base to try to overthrow the Manchu dynasty at the time. Eventually, the Manchu dynasty was able to defeat Koxinga's successors and took over the Taiwan area in 1684.

Two centuries later, the Manchus were defeated by Japan. The latter demanded possession of Taiwan and surrounding islands and signed in the Treaty of Shimonoseki in 1897. The Taiwan area then became a Japanese colony for half of a century to come. The Japanese culture had a profound impact on Taiwan's education, including medical training and research. In 1911, during Japanese colonial times, the Taipei Hospital of Taiwan Governor-General's Office had a radiotherapy unit for treating tumors that did not need surgical removal, such as early-stage cervical, vocal cord, nasopharyngeal, and so on. By doing so, patients were able to retain their original organs. This was particularly popular among the Asians due to cultural implications. Some overseas Chinese traveled to Taiwan to seek such treatment approaches.

During the 1960s, the Cancer Prevention Movement emerged. The most well-known prevention and early cancer detection method was the Papanicalauo smear, or Pap smear, promoted by Julia J. Tsuei, M.D. The Pap smear was first published by American Dr. Georgios Papanicalauo in 1943 but did not gain much attention. Through Dr. Tsuei's tireless efforts, adoption of the Pap smear is now widespread in the world. Dr. Tsuei also invented the now commonly used cervical cancer staging, which helps to detect cervical cancer early on. In fact, precancerous lesions are able to be cured nearly 100 percent of the time.

In early-day cancer research, incidence rates were measured by the number of beds of cancer patients. In 1958, Chun-Jen Shih, M.D., advocated a cancer registry by implementing his experience at the Montreal Neurological Institute of McGill University in Canada. The three major public hospitals—the Western medicine reemerge. He opened a clinic in Taiwan Fu (today's Tainan) and trained the Taiwanese as medical assistants. The clinic thrived to become the Sin-Lau Hospital (Sin-Lau means new building in Taiwanese). His son was the first superintendent of the new hospital. The hospital still exists and is a major hospital and medical research center. Dr. Maxwell started Western medical education in Taiwan. During the Japanese colonial times, Japanese-style Western medical education was implemented as well.

After World War II, American aid to Taiwan (to fight against Communist China) also infused Western medicine. Hence, medical development in Taiwan has become a prototype of blending American and Japanese experiences. Prior to 1970, like the rest of the world, for lack of effective drugs, treating tumors in Taiwan was done mostly through surgery. The common types of cancer at the time were solid tumor, such as liver, stomach, nasopharyngeal, cervical, and breast cancer.

Prior to the popularity of chemotherapy, radiotherapy was the main method for treating cancer. In 1911, during Japanese colonial times, the Taipei Hospital of Taiwan Governor-General's Office had a radiotherapy unit for treating tumors that did not need surgical removal, such as early-stage cervical, vocal cord, nasopharyngeal, and so on. By doing so, patients were able to retain their original organs. This was particularly popular among the Asians due to cultural implications. Some overseas Chinese traveled to Taiwan to seek such treatment approaches.
Tri-Service Hospital, the Taiwan University Hospital, and the Veterans General Hospital—joined his efforts. In 1979, the Bureau of Health (today's Ministry of Health and Welfare) started a central cancer registry. The registry has achieved the standards for Registry Certification of the North American Association of Central Cancer Registries (NAACCR). The World Health Organization's (WHO's) International Agency for Research on Cancer (IARC) also includes the Taiwanese registry in the World Cancer Report. The WHO's cancer prevention initiative of 2003 also has had a long-term impact on cancer registries and effective care.

In 1984, internationally known cancer researchers Jacqueline Whang-Pend, M.D., and Cheng-Wen Wu, M.D., Ph.D., jointly pioneered a tumor specialist system. Then in 1987, the Academia Sinica established a medical oncology specialist training project. Drs. Paul Carbone, John Bennett, and B. J. Kennedy, the first wave of board-certified internal tumor specialists in the United States, were invited to help start a Taiwanese board certification program. Through this project, internationally known tumor specialists came to Taiwan to deliver the training. Both the trainers and trainees were able to interact and communicate with other medical fields. The interdisciplinary collaboration thus benefits not only the trainees but also the whole medical system in Taiwan in the area of comprehensive cancer research and treatment.

The most accomplished cancer researcher in Taiwan is Chi-Huey Wong at the Academia Sinica. He is a member of the American Academy of Arts and Sciences, the U.S. National Academy of Sciences, and the U.S. National Research Council on Chemical Sciences and Technology. He is also a recipient of numerous prestigious awards in the field of biochemistry. Dr. Wong was born in Chia-Yi (southern Taiwan). After finishing his education in Taiwan, he studied at the Massachusetts Institute of Technology (MIT) and earned his doctorate in chemistry in 1982. He then followed his mentor, George M. Whitesides, from MIT to Harvard University as a postdoctoral fellow for another year. He started his research and teaching career at Texas A&M University. In 2003, he returned to Taiwan to lead the Genomics Research Center at the Academia Sinica. His research team currently focuses on the possible correlations between cancer and carbohydrates, glycoprotein, and small-molecule probes, with the hope to develop new vaccines for treating cancer.

In addition to innovative cancer detection, treatment, and research, health insurance coverage is essential for cancer patients. The health insurance programs in Taiwan were developed incrementally by occupations that included laborers health insurance (1950), public employees health insurance (1961), and farmers health insurance (1985). Eventually in 1990, the national health insurance was implemented. Each insured patient carries an Integrated Circuit (IC) card that records office visits and medical records within the network's clinics and hospitals. The national health insurance program is particularly beneficial to cancer patients. Treating cancer is a time-consuming process, which in turn incurs economic burdens to the patients and their families. A cancer patient's IC card carries a mark of "serious illness," which means a waiver of certain medical expenses within five years of incidence. This provision has won international recognition.

Yung-Chia Chen
Kaohsiung Medical University
Paige Mayleen True
California State University, Monterey Bay

See Also: Cancer Drugs, Cost and Benefits; Chemotherapy; Insurance; Japan; Netherlands; Radiation Therapy.

Further Readings


Tajikistan

Tajikistan is a central Asian country of 8.0 million people that became independent following the breakup of the Soviet Union in 1991. Classified by the World Bank as a low-income country, Tajikistan spends 6.8 percent of its GDP on health care. Tajikistan's health care system was neglected during the Soviet years, with inadequate facilities and shortages of staff and supplies. However, more recently the government of Tajikistan, with assistance from the Aga Khan Development Network and other funders, has committed to a number of health promotion, disease prevention, and disease management programs, including policies to reduce tobacco use, reduce obesity, promote physical activity, and reduce harmful alcohol use. Other efforts relevant to cancer control include training members of the health care system and the indigenous population with respect to raising awareness about cancer, the different cancers that exist in society, with an emphasis on the most prevalent types, and the avoidable causes.

The Aga Khan Development Network

The Aga Khan Development Network (AKDN) provides leadership and services to help improve the health care system in Tajikistan and improve the health of the population. Among the reforms undertaken by the AKDN are the training of community health promoters; development of a national nursing curriculum; creation of a fund to provide high-quality, affordable drugs; rehabilitation of hospitals; and training of hospital staff. This includes the provision of general medical services and support for primary health care services to the population within the country. One of the main benefits that the country enjoys from working with the Aga Khan in particular is that the institution brings into play a worldwide network of policies and strategies that are applicable in cancer care and management while at the same time working with the indigenous players within the country to make sure that they are able to come up with scenarios for handling cancer in Tajikistan uniquely and for better efficiency.

Through the worldwide support network, the Aga Khan Hospital has been able to collaborate with the government and other relevant players in the industry, such as government hospitals that are located in Gorno-Badakhshan Autonomous Oblast and are able not only to rationalize but also to rehabilitate and work on improving the facilities that are available in the country for dealing with cancer effectively. This is in line with the need to provide clinical practice and services that are suitable to nursing and relevant care for cancer patients. One of the other points of note is that all of these partnerships are held in close collaboration with the other relevant Aga Khan support members, such as the Aga Khan University and the Aga Khan Foundation.

There are health care programs in place that have been designed in such a way that they are able to reach and support the vulnerable groups and communities within Tajikistan when it comes to cancer support. Of particular mention in these groups are the remote communities and the rural communities, while at the same time, they also cater to the needs of the low-middle class, urban families, and groups that are not able to gain access to the medical services that they require.

At each level of care, the Tajikistan government is committed to making sure that there is more than enough awareness, evidence-based practices, and most importantly, continuous and accurate education of health care service providers, such as doctors, nurses, and their assistants. The government has been working with a number of professionals and volunteers to help champion its support for and the need to highlight the plight of cancer support societies along with the need for awareness of cancer.

Khorog General Hospital

The Khorog General Hospital is one of the main facilities in the country that is devoted to helping the society deal with cancer in the best way possible. This hospital has a 550-bed capacity, which is supposed to cater to the more than 40,000 residents that reside in Khorog. This already indicates that the facilities are simply not big enough to be able to handle the needs of a society that keeps expanding with time.

One of the other challenges in as far as the health sector in Tajikistan is concerned is that there is never enough financing for the health sector, especially with respect to resource-intensive cases such as cancer research. There have been a lot of questions with regard to the public health sector reforms.
and in particular in regard to the commitment of the government in as far as providing primary health care at the basic level. This, coupled with the fact that there are basically insufficient treatment protocols in place at the regional levels is just one of the main concerns that the government has had to deal with over time.

Palliative care standards are lacking in Tajikistan, and as a result, there are concerns as to the effectiveness of the management of the human resources with respect to cancer research and facilities. One of the main problems that keeps coming up is the fact that preventive medicine is still a pipe dream, especially for those who are not able to afford mainstream medication or those who are not able to gain immediate access to the services that are offered to those with the capacity to afford them without requiring any support from the government.

As has been the case in so many other places, cancer can be effectively managed only if it is detected early enough and if there are procedures in place to handle the situation. However, early screening in Tajikistan is still one of the main challenges that the government has to deal with because of the lack of facilities.

Cancer alone has led to a global mortality rate of 414.6 deaths for every 100,000 people, which in Tajikistan is 33.7 for every 100,000 people, and this loosely translates to 8.1 percent of the population. More than 30,000 lives are lost every year in Tajikistan, with cancer taking close to 3,000 people annually. At close to a 10 percent fatality rate, this is a situation that is spiraling out of control unless other parties step in to help avert a crisis.

Michael Fox
Independent Scholar

See Also: Government; Hospitals; World Health Organization.

Further Readings


Takeda Pharmaceutical (Japan)

Takeda Pharmaceutical Co. is a Japanese pharmaceutical corporation with, as of early 2014, 31,255 employees worldwide including subsidiaries. It was, in terms of sales as of 2011, the largest Japanese pharmaceutical corporation and the 14th-largest pharmaceutical corporation in the world. Takeda has the core therapeutic areas of cardiovascular and metabolic conditions, oncology, the central nervous system, immunology and respiratory conditions, general medicine, and vaccines.

In terms of turnover, Actos (marketed as Glustin in Europe) for the treatment of type 2 diabetes has for a long time been one of the main products. In 2011, it accounted for approximately 27 percent of the corporation’s total revenues. However, it lost its exclusivity in August 2012, and the current Takeda top seller Blopress (candesartan cilexetil) for hypertension treatment sold for ¥169.6 billion compared to ¥122.9 billion for Actos/Glustin in fiscal year (FY) 2012. Other products with large-volume sales include Takepron (Prevacid in the United States) for gastric and duodenal ulcers, Leuplin (Enantone in Europe) for prostate and breast cancer and for endometriosis, and Velcade for treating multiple myeloma.

Corporate Philosophy and Recent Strategic Initiatives
Takeda started out as a seller of traditional medicines in Osaka, Japan, in 1781. After the long period of Japanese seclusion policy until the late 1800s, Takeda started importing Western medicines. The company marketed its first multivitamin in 1952 and started overseas activities in 1962. In the early 2010s, Takeda regarded its corporate development as being in a transformation period. The overall corporate philosophy is titled Takedaism and lists its core values as: ethics (the highest ethical standards), challenge (discover new potential, and make the most of one’s ingenuity), progress (pursue
individual growth, and always push oneself further), teamwork (act as a team, and develop ties of mutual trust and respect), and steadfastness (seek what matters, and embrace a simple, steady approach). The corporation implemented a Vision 2020 plan in 2011 containing a new Takeda operating model to be achieved by 2020, divided into the core principles globalization, diversity, and innovation.

Takeda pursues what it calls a holistic approach when it comes to policies for corporate social responsibility (CSR). Takeda is concerned about both creating as well as sustaining corporate values and thus strives to operate cases conducted alone as well as cases called producer-type activities together with other companies.

Takeda has in recent years acquired several other companies. In 2008, Takeda acquired the Cambridge, Massachusetts, corporation Millennium Pharmaceuticals, and the subsidiary was later called Millennium: The Takeda Oncology Company. The subsidiary has got approximately 1,200 employees. Millennium developed the first version of Velcade, one of Takeda’s current core products, approved by the Federal Drug Administration in 2008. This pipeline product, also intended for the treatment for multiple myeloma, builds on the proteasome inhibition technique, which began with Velcade and is in the development phases, called MLN9708. It was the first oral proteasome inhibitor to enter clinical trials. In 2011, Takeda acquired the Swiss company Nycomed because it was conceived of as having a strong fit with Takeda’s overall growth strategy. At the time of Takeda’s acquisition, Nycomed had approximately 11,800 employees worldwide, and it was the 29th-largest pharmaceutical company worldwide based on global sales in 2010.

The company had its own commercial network throughout most countries in Europe. Its expansion has been remarkable when it comes to its presence within fast-growing, emerging markets, and operations in these markets accounted for about 40 percent of Nycomed’s total net turnover in fiscal 2010. In addition to these business aspects, the acquisition was envisioned as beneficial to Takeda’s efforts at achieving an internationalized corporate culture through the injection of diverse talents. Some other acquisitions and efforts at reorganizing include the 2005 acquisition of the San Diego-based company Syrrx, specializing in X-ray crystallography, and the 2008 acquisition of TAP Pharmaceutical Products. The latter was formed in 1977 as a joint venture between Takeda and Abbott Laboratories. Abbott, acquired in 2008, split the U.S. rights to the drug Lupron, whereas Takeda received rights to both the marketed drug Prevacid as well as TAP’s pipeline candidates. In 2012, Takeda acquired Philadelphia-based URL Pharma. The motive behind this acquisition is said to be obtaining the gout therapy drug Colcrys, and the non-Colcrys generic business was subsequently spun out to a subsidiary of Sun Pharmaceutical. Takeda also purchased the Brazilian pharmaceutical company Multilab in 2012.

Research and Development
Takeda’s expenditures for research and development (R&D) were 20.8 percent in FY 2012, when calculated as a percentage in relation to total sales. This was a slight increase from the previous year. There were 21 different R&D sites worldwide as of 2013, whereas the global research network hub is considered to be the Shonan Research Center, established in eastern Japan in 2011. It is a combination of functions previously held by the former Tsukuba Research Center and the Osaka Research Center. Takeda announced a new organizational framework regarding R&D in May 2013. Within this framework, a chief medical and scientific officer would lead the global R&D organization, and the oncology R&D function of Millennium Pharmaceuticals would be integrated into the global R&D organization. This move was...
considered to be in line with Takeda's commitment to enhance R&D operational excellence worldwide. Takeda also has efforts aimed at accelerating innovation in drug discovery. One such effort is to attempt a diversification of methods for identifying novel targets by way of harnessing the basic technologies that they acquire through partnerships.

One recent controversy involving Takeda concerns the 2011 release by the U.S. Federal Drug Administration warning that using Actos for more than a year may be associated with an increased risk of bladder cancer. The first Actos-related bladder cancer suits were filed the same year.

Terje Grønning
University of Oslo

See Also: Astellas Pharma (Japan); Daiichi Sankyo (Japan); Eisai (Japan); Ono Pharmaceutical (Japan).

Further Readings

Tamoxifen

Breast cancer represents the most common malignancy for women in the United States, with 70 percent of these breast cancers being estrogen receptor positive. For this reason, many therapies focus on hormonal ablation, antagonism of estrogen receptor signaling, and inhibition of estrogen synthesis. The drug tamoxifen treats hormone receptor-positive breast cancer after an individual undergoes surgery for complete removal of the breast cancer. This medication lowers the chance of cancer returning later, reduces the risk of a new cancer in the other breast, and prolongs survival after the initial episode of cancer. Tamoxifen falls into the category of a nonsteroidal antiestrogen drug (called selective estrogen receptor modulators [SERMs]) that thwarts the effects of estrogens in tissues. The exact mechanism of action remains unknown, but it is thought to connect with and blockade estrogen receptors on the surface of cells, precluding estrogens from binding and stimulating the cell. The Food and Drug Administration (FDA) reviewed the first formulation of tamoxifen in December 1977. The original multiple uses of tamoxifen ranged from preventing breast cancer in high-risk women (up to 50 percent in individuals 35 years and older); lowering the risk of acquiring invasive breast cancer in women with ductal cancer in situ (DCIS); preventing cancer from returning after aggressive treatment with surgery, radiation, and chemotherapy; and dealing with advanced breast cancer.

Examples of chemopreventives that have exhibited anti-promotional activity include tamoxifen (an antiestrogen), retinoids, and carotenoids, which are also inhibitors of proliferation.

Historical Background
Researchers described the initial notion of SERMs action first in the late 1980s and later on perfected and defined it as a balance of receptors and co-regulators. A cooperative group of physicians in the United States formed to carry out clinical trials on individuals with breast and colorectal cancer. This trial became known as the National Surgical Adjuvant Breast and Bowel Project (NSABP). From April 1992 to 1998, the NSABP group studied 13,388 women and discovered that women with a high risk of breast cancer could significantly reduce the risk of developing the condition by taking tamoxifen.

A second key breast cancer prevention trial started in 1998, titled Phase III Randomized Study of Tamoxifen and Raloxifene (STAR), and compared
Raloxifene to tamoxifen in preventing breast cancer in postmenopausal women. V. G. Vogel and colleagues published results showing that raloxifene and tamoxifen equally reduce the chance of developing invasive breast cancer, but raloxifene demonstrates a reduced risk of side effects and a higher risk of noninvasive breast cancer. In 2010, Vogel and colleagues published a longer-term follow-up of the STAR study. The results demonstrated that both raloxifene and tamoxifen represent good choices for prevention of breast cancer for postmenopausal women.

Since the earlier trials, aromatase inhibitors came into being to treat postmenopausal patients, but tamoxifen continues to be an inexpensive, lifesaving drug for premenopausal patients. Breast cancer returns, so patients need to continue adjuvant tamoxifen for five years to reduce recurrence by 50 percent. The effect of tamoxifen continues long after the first five years, but the issue of resistance contributes to breast cancer returning. C. Davies and colleagues recently showed that continuing tamoxifen to more than 10 years further reduces recurrence and mortality.

How Does the Drug Work?
As a unique form of a hormone drug, tamoxifen attaches to estrogen receptors in the body, where it prevents the action of estrogen. The drug is referred to as antiestrogen or a SERM. It works efficiently in breast cancers that need estrogen to grow because, with tamoxifen present to block the receptors, the cancer cells cannot get estrogen, and then the cancer stops growing and dies. Of course, tamoxifen works only for breast cancers that are estrogen-receptor positive. Remarkably, while the drug produces antiestrogen activity in the breast, it operates like an estrogen in the bones and the endometrium, or surface of the uterus. Biochemically, tamoxifen produces its cytotoxic influence primarily through cytostasis, a process associated with the accretion of cells in the G0/G1 phase of the cell cycle. Apoptotic activity also can be triggered by tamoxifen and involves cleavage of caspase 9, caspase 7, caspase 3, and poly-ADP-ribose polymerase (PARP). Downregulation of antiapoptotic proteins Bcl-2 and Bcl-XL and upregulation of proapoptotic proteins Bax and Bak appear to also occur.

Researchers explained the importance of the enzyme pathway of CYP 2D6 for tamoxifen. Tamoxifen activation transpires through two pathways to the final active form of endoxifen, a product 10- to 100-fold more efficient in obstructing estrogen receptors than tamoxifen. The primary channel ensues first through N-desmethyI tamoxifen (NDM) via CYP 3A and subsequently endoxifen through CYP 2D6. The lesser pathway encompasses 4-hydroxytamoxifen through CYP 2D6, CYP 2B6, CYP 2C9, and CYP 2C19, and consequently to endoxifen through CYP 3A. The meaning of CYP 2D6 genotypes for tamoxifen therapy to treat disease and monitor relapse-free survival for breast cancer remains an ongoing debate due to studies demonstrating both benefits and no value. R. Ter Heine and colleagues developed population pharmacokinetic models showing that not only CYP 2D6 but also CYP 3A enzyme activity affects the change of tamoxifen to the metabolite endoxifen in breast cancer patients.

According to researchers, if pharmacogenomics testing for tamoxifen became routinely available, patients with poor metabolizing of the drug could be switched to a different medication (like aromatase inhibitors) after the onset of treatment. In the scenario with premenopausal patients who are extensive metabolizers and receiving tamoxifen, therapeutic drug monitoring for endoxifen steady state could be used to predict outcomes.

S. Darakhshan, A. Bidmeshkipour, K. Mansouri, H. M. Saeid, and A. Ghanbari carried out studies in vitro on the effect of tamoxifen and the antiallergic tranilast drugs on CXCL12 and CXCR4. CXCL12 and CXCR4 enzymes both increase survival and proliferation of malignant cells. This preliminary work demonstrated that tranilast elevated the anti metastatic effect of tamoxifen. The research showed that the synergistic action of tranilast fails to be estrogen dependent. The data further suggests that CXCL12 and CXCR4 are key targets for drug therapy.

How Effectively Does Tamoxifen Work?
Tamoxifen effectively lowers the risk of the breast cancer recurrence, especially in women with one breast already removed. Researchers found a two-stage treatment with two different drugs may be a superior treatment in postmenopausal women. First, tamoxifen is given, followed by an aromatase inhibitor (e.g., anastrozole, exemestane, or letrozole).

Research shows that age influences the effectiveness of tamoxifen. Females less than 40 years old exhibit the least response to the drug, ages 40 to 50 years show some response, and women over
Tamoxifen

50 years profit the most from tamoxifen. As a matter of fact, early-stage breast cancer patients over age 50 years treated with the drug before surgery may reduce the tumor size so much that a lumpectomy can be performed instead of a mastectomy. In addition to preventing breast cancer recurrence, tamoxifen exhibits beneficial estrogenic effects. Tamoxifen reduces serum cholesterol and safeguards against bone loss and cardiovascular disease.

Prognostic Biomarkers for Tamoxifen Resistance
Recent research by T. Gao and colleagues explored the prognostic capability of the gene CCNA2 in estrogen receptor positive (ER+) breast cancer. CCNA1, or CyclinA2, present in almost all tissues in the human body, plays a key role in the control of the cell cycle. Previous research demonstrates the overexpression of the gene CCNA2 in literally dozens of cancer types, indicating its possible role in cancer transformation and progression. Gao and colleagues showed the predictive power of CCNAs in survival of ER+ breast cancer and closely associated with tamoxifen resistance. Their research suggests that CCNA2 is a biomarker for the prognosis of ER+ breast cancer and the monitoring of tamoxifen efficacy. Multicenter, randomized, controlled clinical trials still will be needed before this finding can be used in the clinical arena.

Possible Side Effects
Discussion with the health care provider must occur prior to prescribing tamoxifen to determine the risks and benefits of the treatment. The benefits need to outweigh the risks. The provider also needs to cover all the possible side effects that may occur with the medication so that the patient truly can make an informed decision about whether to take the medication. Common side effects consist of hot flashes and sweating, which occurs in about 45 percent of women on the drug; premenopausal women can experience irregular periods or stopping of their periods (periods start again after treatment ends); vaginal dryness, discharge, or itching transpires in 10 percent of women; fatigue occurs in 25 percent of women; light-headedness; eye problems such as cataracts and eyesight changes can occur; and diminished sex drive has been reported.

In about 10 in 100 people, occasional adverse effects occur. Fluid can build up in the ankles or fingers, causing swelling or weight gain. The sensation of feeling or being sick can take place at the initiation of treatment with tamoxifen but usually subsides after a few days to weeks. Tamoxifen can alter components of the blood (e.g., thrombocytopenia, leukopenia, or neutropenia). About 10 percent of individuals exhibit a change in their mood that produces sadness or depression. Hair thinning ensues in some individuals but generally triggers only slight, nonnoticeable hair loss. Individuals on tamoxifen may complain of bone pain or pain in the area of the tumor. Headache and leg cramps ensue in some individuals. Walking or stretching the muscles helps relieve leg cramps.

Rare side effects transpire in less than one in 100 people. Serious or life-threatening, but less likely, side effects include blood clots within the blood vessels of the eyes, damage to the retina of the eye, blood clots in the legs or lungs, stroke, ovarian cysts, liver abnormalities (hepatitis), liver cancer, and cancer of the lining of the uterus. Because ovarian cysts and cancer of the lining of the uterus possibly arise, patients are advised to undergo annual pelvic examinations yearly or more often.

Negative Interactions With Other Drugs
Tamoxifen possesses the ability to interact with other drugs that cause a lowering of the effectiveness of the tamoxifen, altering the efficacy of the other drug or producing a negative consequence in the human body.

Practitioners use selective serotonin reuptake inhibitors (SSRIs) to reduce the side effects of menopause, but unfortunately, this drug group blocks the CYP2D6 enzyme that activates tamoxifen to the more active endoxifen, leading to an increase in mortality. The effectiveness of tamoxifen can be reduced by as much as 40 percent. The drug fluoxetine, used for depression, also acts on the CYP2D6 enzyme and produces a decrease in efficacy of tamoxifen. This problem can be remedied easily by switching to venlafaxine, a selective norepinephrine reuptake inhibitor (SNRI). A Canadian study showed that venlafaxine decreased the mortality in breast cancer.

J. P. Kitzmiller, D. K. Groen, M. A. Phelps, and W. Sadee describe the inhibition of CYP2D6 by many different drugs. The drugs known to inhibit CYP2D6 and decrease the effectiveness of tamoxifen include the following:
C. B. Givens, D. K. Groen, M. A. Phelps, and W. Sadee carried out a systematic review of the literature on warfarin and tamoxifen. Patients concomitantly receiving both warfarin and tamoxifen demonstrate a higher risk of bleeding episodes. The exact mechanism of the interaction of the two drugs remains unknown, but one theory purports that tamoxifen inhibits the CYP2C9 enzyme involved in the metabolism of the S-isomer of warfarin. The combined use of the two drugs remains contraindicated, but if given together, highly vigilant and careful monitoring must be enforced. Recently, H. Ruhl and colleagues studied tamoxifen-induced activated protein C (APC) resistance. Researchers measured blood levels of APC before adjuvant treatment with tamoxifen for breast cancer on 25 women and monthly after treatment initiation. The study showed for the first time acquired APC resistance with tamoxifen use. Scientists believe the acquired APC resistance might explain the elevated thrombotic risk with tamoxifen treatment. Further research is needed to evaluate this effect.

A. Patel, E. B. Schwarz, and the Society of Family Planning published guidelines on contraceptive practices among breast cancer survivors using tamoxifen. Women of childbearing age, being treated for cancer, are advised to stay away from mixed hormonal contraceptive methods (containing estrogen and progestin) as these further elevate the risk of venous thromboembolism. Of course, the recommended contraceptive for individuals taking tamoxifen is the levonorgestrel-containing intrauterine system (IUS) because it reduces endometrial proliferation (a side effect of tamoxifen).

Recently, the FDA approved paroxetine (brand names: Brisdelle and Noven) in a dosage of 7.5 milligrams (mg) for menopausal hot flashes despite the fact that this drug interacts negatively with tamoxifen. Paroxetine strongly inhibits the cytochrome P-450 CYP2D6 enzyme. According to R. J. Orleans and colleagues, this enzyme converts tamoxifen to endoxifen, an important metabolite for the pharmacological activity of tamoxifen. Research shows that the concomitant administration of paroxetine (10 mg per day) in females using tamoxifen can reduce the plasma concentrations of endoxifen to 64 percent, but the risk of breast cancer relapse and death remains unknown.

Researchers studied the influence of Chinese herbal products (CHP) and tamoxifen intake on endometrial cancer risk among female breast cancer subjects. Y. T. Tsai, J. N. Lai, and C. T. Wu used a population-based study of 20,466 subjects to look at this interaction. Half of the subjects in this population-based study used one of two CHPs (Jia-Wei-Xiao-Yao-San or Shu-Jing-Huo-Xue-Tang), the most commonly used CHPs in China. The researchers found that, among the tamoxifen therapy group, CHP consumption decreased the risk of developing endometrial cancer.

Contraindications
A few other conditions produce negative reactions with tamoxifen. Since tamoxifen intensifies the risk of blood clots in the leg or arm, the lungs, or brain, individuals with a history of blood clots, heart attacks, or stroke may not take tamoxifen. Because this drug may cause harm to the fetus, tamoxifen must not be taken during pregnancy or breastfeeding.

Neutral Interactions With Other Drugs
Because tamoxifen provokes intolerable hot flashes in some women, W. L. Yeh, H. Y. Lin, H. M. Wu, and D. R. Chen studied the interaction of risperidone with tamoxifen to find drugs that could be used when women take tamoxifen. Risperidone failed to inhibit tamoxifen's cytotoxic impacts in vitro and in vivo. As risperidone does not interfere with the efficacy of tamoxifen, it warrants further research.

Resistance to Tamoxifen
Long-term adjuvant therapy with tamoxifen significantly improved breast cancer survival over the last 40 years. However, acquired resistance to tamoxifen
occurs in 40 percent of breast cancer patients and 25 percent of patients die from their disease. P. Fan and V. C. Craig describe laboratory studies in vivo that demonstrated three phases of acquired SERM exist. Cancers with phase I resistance undergo stimulation by both SERMs and estrogen; phase II resistance gets triggered by SERMs, but estrogen inhibits it by apoptosis. Phase III suggests that short-duration, low-dose estrogen may purge phase II-resistant breast cancer cells. This novel information provides a new direction to trial estrogen therapy after long-term anti-hormone therapy.

**Alternative Drugs**

Studies show that the drug raloxifene, originally approved for osteoporosis, acts similarly to tamoxifen as an antiestrogen drug in breast tissue, but it causes less cancer of the uterus and blood clots than tamoxifen. S. Zervoudis and colleagues summarized the comparison of tamoxifen and raloxifene by stating that postmenopausal women can decide on tamoxifen, the most effective drug, accepting its toxicities, or can chose raloxifene with slightly less efficacy but more tolerable side effects.

P. Y. Maximov, T. M. Lee, and V. C. Jordan reviewed the newer SERMs for breast cancer treatment. Research on arzoxifene demonstrated it to be effective in treating metastatic breast cancer and in reducing risk of invasive breast cancer with favorable response to bone health. The drug produces the same side effects as tamoxifen for venous thrombotic events, endometrial cancer, and hyperplasia, as well as hot flashes in 56 percent of research subjects.

Aromatase inhibitors (AI) recently became the gold standard as the primary therapy for females with hormone receptor-positive breast cancer in place of tamoxifen. They also may be employed sequentially with tamoxifen for postmenopausal women. These inhibitors focus on the estrogen biosynthetic pathway and take away the growth-promoting influence of estrogen from the cancer cells. The AIs lower the body’s estrogen by barring an enzyme called aromatase from changing androgen into estrogen. The AIs really provide a major benefit for disease-free survival of breast cancer. The AIs reduces estrogen-like effects such as endometrial cancer and thromboembolic disorders that are problematic in patients taking tamoxifen. A downside of AIs consists of osteopenia, osteoporosis, bone loss, and the risk of fractures. Bone loss can be managed with the use of bisphosphonates or other interventions (e.g., calcium, exercise, or vitamin D). The third-generation AIs currently on the market include anastrozole, letrozole, and exemestane.

**Conclusion**

Tamoxifen started out as a failed contraceptive, but progressed to be used to deal with all stages of breast cancer and to be employed as a chemoprevention agent for women at high risk for breast cancer, and proved to exert advantageous effects on bone density and serum lipids in postmenopausal women. Plus, the effects of tamoxifen continue for a decade after the drug is stopped. At the same time, the negative effects of thromboembolic disorders and uterine cancer ought to be kept in mind because tamoxifen must be given over a long time to treat and prevent breast cancer.

Sharon A. Takiguchi  
Independent Scholar

**See Also:** Anticancer Drugs; Breast Cancer; Chemotherapy; Drugs.

**Further Readings**


Tanzania

The United Republic of Tanzania, which was formerly known as German East Africa and then as Tanganyika, is situated in eastern Africa. It is bordered on the north by Uganda and Kenya, on the east by the Indian Ocean, on the south by Mozambique, Malawi, and Zambia, and on the west by Rwanda, Burundi, and the Democratic Republic of the Congo. It is the seventh-most populous country in Africa and 35th-most populous country in the world, with a population of more than 36 million. Kiswahili is the de facto national language, and there are 126 living indigenous languages still spoken by respective ethnic groups in Tanzania; the most widely spoken ethnic languages include Bena, Gogo, Haya, Hehe, Makonde, Nyukyusa, and Sukuma. Each ethnic group has its own rich traditions of ethnomedicine. For example, a traditional healer who uses medicinal plants for treating ailments is known as mganga in Kiswahili, and medicinal plants are called miti shamba.

Traditional medicine and associated beliefs continue to play a significant role, particularly in rural areas of Tanzania. Traditional medicine is typically less expensive and more readily accessible than the public health system. Many Tanzanians continue to believe that traditional healers are more powerful and holistic than Western practitioners. Accordingly, when someone dies of cancer in a rural village, it is not uncommon, even today, for local...
inhabitants to assert a superstitious explanation, such as that of witchcraft or a malevolent curse.

There are many traditional medicinal preparations still commonly used in Tanzania. Most of these incorporate use of local plant materials, many of which have shown medicinal properties in laboratory studies. For example, extracts from several medicinal plants used in Tanzania, such as *Garcinia senescens*, demonstrate cytotoxic specificity and may be a future source of antitumor compounds. Research suggests that use of certain plants may actually help protect against cancer by reducing oxidative stress and stimulating enzymes and other processes that help the body fight carcinogens. For example, an extract from *Salvia nilotica* demonstrated considerable antioxidant activity, as did extracts from root and stem bark of *Allanblackia ulugurensis*, and extracts from leaf, stem bark, and roots of *Combretum schumannii*.

Medicinal plants are used in Tanzania traditionally to treat many health problems associated with cancers and associated conditions. For example, the Zigua of the Bagamoyo District traditionally drink a root decoction of *Anchomanes diff formis*, which they call *cheho*, for joint pain. A leaf decoction of *Aloe lateritia*, which the Chagga call *mrature*, the Nyakyusa call *ibugubugu*, the Pare call *kithapa*, and is called *mlalangao* in Kiswahili, is traditionally drunk for treating hepatitis. The Digo take a leaf decoction of *Aloe rabaiensis*, which they call *jolanji*, for traditionally treating an enlarged spleen.

There are serious deficiencies of modern pharmaceutical supplies, as opposed to traditional preparations, and medical services in Tanzania. Tanzania has a relative shortage of medical doctors, with about 300, and in 2009, there were 640 licensed pharmacists. Due, in part, to the shortage of medical services and supplies, health problems are endemic in Tanzania. On the other hand, modern cancer treatments, such as chemotherapy and radiotherapy, are generally available in the public health system in Tanzania. Nevertheless, the 10 leading causes of mortality in Tanzania, in rank order, are complicated malaria, uncomplicated malaria, human immunodeficiency virus (HIV) and acquired immune deficiency syndrome (AIDS), tuberculosis, anemia, sickling disease, pneumonia, poisoning, diarrhea, and cardiac failure. The average number of cancer cases annually are 87.2 per 100,000 of the population.

Cancers account for a substantial amount of disability and suffering among impacted populations. According to the International Agency for Research on Cancer, in 2012 the five most common types of cancer for men in Tanzania were prostate cancer (estimated age-standardized incidence rate of 34.6 per 100,000 population), Kaposi’s sarcoma (22.8 per 100,000), and cancers of the esophagus (12.9 per 100,000), lip and oral cavity (6.8 per 100,000) and larynx (4.3 per 100,000). For women, the most common cancers were cancers of the cervix and uterus (estimated age-standardized incidence rate of 54.1 per 100,000 population, breast (19.4 per 100,000), Kaposi’s sarcoma (9.9. per 100,000), and esophageal (6.1 per 100,000) and colorectal cancer (5.8 per 100,000).
Modern pharmacological supplies, as opposed to traditional preparations, are generally, if available at all, in short supply in Tanzania. Both prescription and over-the-counter products often are unavailable. Consequently, health problems are endemic and limit development. For example, an estimated 1.6 million people live with HIV in Tanzania, which ranks the country eighth-highest in Africa and ninth-highest in the world. Debate continues on the relative risks in Africa for respective cancer types for those infected with HIV. The mortality rate for tuberculosis in 2008 was 13 per 100,000 of the population and that for malaria in 2006 was 98 per 100,000, while that for cancers in 2009 was 150 per 100,000. Furthermore, according to the WHO’s Global Health Observatory Data Repository, in 2008, the age-standardized estimates of deaths from all cancers was 79 per of the 100,000 of the population for males and 74 per 100,000 for females. As a consequence, life expectancy is only 44.88 years, which ranks Tanzania 38th in Africa and 209th in the world. There is a clear and urgent need for improved cancer awareness, early detection programs, and health services infrastructure in Tanzania.

Victor B. Stolberg
Essex County College

See Also: Burundi; Congo, Democratic Republic of; Developing Countries; Kenya; Malawi; Mozambique; Rwanda; Uganda; Zambia.

Further Readings

**Taxation**

Taxation of specific cancer-causing products or practices is, in the United States, on one level, a compromise between two values critical to the national self-image: the preservation of freedom of choice of the individual and concern for the health of the individual and of the public. If the issue were only about these two values, it might be a stalemate. But the reality is that purchases of cancer-causing products are an individual choice with an impact beyond the individual. Products that cause cancer in the consumer, like cigarettes, alcohol, or indoor tanning, nevertheless pass on parts of the cost of that cancer to the public, whether in the form of Medicare and Medicaid, public funds for cancer research, or simply by raising everyone else’s insurance premiums. Health-related behavior simply exacts a cost that is not contained to the individual, which is an important reality of public health policy that we as a country are not yet adept at acknowledging or discussing but which is reflected in cancer-related taxes and to a lesser degree in other taxes or tax proposals constructed with public health in mind.

Furthermore, not every purchase of carcinogens will have its carcinogenic effects limited to the individual purchaser. This is certainly true of cigarettes, given how much we know about the dangers of secondhand smoke. It is also true of gasoline, which contributes to carcinogenesis through its effect on
the environment and thence on the public at large, not simply on the individual driver.

As part of the Patient Protection and Affordable Care Act, effective July 1, 2010, the federal government imposed a 10 percent sales tax on indoor tanning. The tax offsets the public costs of health care for those who develop skin cancer as a result of this luxury service. Tanning beds use ultraviolet (UV) radiation, a combination of primarily UVA radiation and a smaller amount of UVB, in order to tan the skin. UV radiation exposure is a cause of cataracts, immune system problems, skin aging, and perhaps most importantly, skin cancer. UVA specifically, which makes up 90 to 100 percent of the radiation used by tanning beds, is the primary cause of melanoma, skin cancer that forms in the melanocytes and causes 75 percent of skin cancer-related deaths. The average tanning session is 10 minutes, providing the equivalent of 30 minutes of natural sunlight, but devoted tanners may go two or three times as long on a near-daily basis. Each session costs $15 to $30 in different parts of the country. Regular tanners are 4.5 times more likely to develop melanoma, 2.5 times more likely to develop squamous cell carcinoma, and 1.5 times more likely to develop basal cell carcinoma, compared to people who do not use tanning salons.

Like most taxes, the indoor tanning tax was met with controversy. Tea Party congressman Ted Yoho of Florida decried the tax as “racist,” because it targeted a service used almost exclusively by light-skinned people. Expected to generate $2.7 billion over 10 years—compared to the $18 billion that will be spent on treating skin cancer in that same period—it was enacted to offset costs of health care reform, but tanning salon owners complained they were unfairly targeted. Interestingly, Botox injections and elective (not reconstructive) plastic surgery was originally going to be taxed instead, but lobbying from the medical industry forced the change. While a tax on plastic surgery would have raised revenue, it would not have accomplished the additional goal of disincentivizing an activity that elevates cancer risk and results in significant public health costs.

Once the indoor tanning tax was proposed in Congress, the arguments in its favor were easy to make due to the relative success of cigarette tax. The Centers for Disease Control (CDC) says that, for every 10 percent price increase, cigarette consumption drops 3 to 4 percent in adults and 6 to 8 percent in young people. The doubled decrease among young people is likely due to increasing the cost for first-time or new smokers who are not yet addicted and thus find it easier to quit, whereas adult smokers include many longtime smokers who are not only physically addicted but have developed emotional and psychological attachments to smoking and their identity as smokers.

While the indoor tanning tax is an ad valorem tax—a tax proportional to the sale price of the service, as 10 percent of the price—most taxes on cancer-causing products or services are per-unit excise taxes, meaning that the amount of tax is a constant in dollars and cents and one that is levied in addition to any percentage-based sales tax that may also apply as part of a general sales tax for the jurisdiction. Excise taxes are often used as motivators or disincentives, such as taxes on gambling or prostitution—in this context, they are sometimes called a sin tax, usually pejoratively, though it is hard to stretch that term to encompass tanning. In the United States, excise taxes are levied both by the federal government and by most state governments as well as some local governments. For instance, the city of Anchorage, Alaska, has a $1.30 per pack excise tax on cigarettes, which is in addition to the federal and state taxes.

Excise tax on tobacco was first levied during the Civil War, after a failed attempt decades earlier by then-Secretary of the Treasury Alexander Hamilton. These first tobacco taxes were simple revenue generators with no motivating component, and for a brief period of time, tobacco tax was the government’s largest source of income. (The financing of government was a very different thing in the 19th century than it is today.) From 1921 to 1969, every state along with the District of Columbia adopted a tobacco excise tax—nearly always specifically on cigarettes—for a variety of reasons. Cigarette taxes, though they are always greeted with complaint, are a good way to increase revenue because they are an optional activity that no one will argue is necessary and so, in theory, present less cause for complaint than a general sales or income tax.

The federal tax on cigarettes increased from 39 cents per pack to $1.01 per pack in 2009, as part of the Children’s Health Insurance Program Reauthorization Act. This provided some of the revenue to fund the State Children’s Health Insurance Program (SCHIP), which provides aid to impoverished children and expanded its coverage in this reauthorization to include working and lower middle-class...
families at three times the federal poverty level, as well as children from eligible families in New York and New Jersey who are above that income threshold, in addition to expanding coverage to include dental and mental health benefits and services for immigrant children.

The arguments over the SCHIP cigarette tax increase illustrate the economic and ethical complexities of cigarette taxation.

Economists, for instance, pointed out that increasing the federal cigarette tax is likely to decrease state cigarette tax revenue. Cigarette price increases, whether from taxes or other factors, decrease consumption, as mentioned. That decreased consumption means fewer cigarette sales for the states to collect their individual taxes on. Cigarette taxes are also considered a regressive tax, de facto if not by design, in that half of cigarette smokers are in low-income households, who are thus disproportionately affected.

However, both of those facts have ethical and health-impact dimensions that are more complicated than simple sales figures. If a high federal cigarette tax reduces cigarette smoking, for instance, how can this be anything but good? This reduces cancer, reduces heart and lung disease, reduces the carcinogenic effects of secondhand smoke, and reduces the public health toll and expense of smoking. Further, the working class is the group least able to absorb the economic impact of an increase in cigarette cost and so the most likely to be dissuaded from smoking. They also possess the worst health coverage and are more likely to be at risk of cancer for reasons related to their workplace or carcinogens in their residential environment. Reducing cancer risks for the poor by making it more difficult for them to smoke may not be ethically clear-cut but neither is it as purely exploitative as a regressive tax sounds.

Studies consistently support the link between cigarette tax increases and cigarette smoking decreases. The federal government and 49 states also tax several categories of noncigarette tobacco products. The federal government, for instance, has specific excise taxes for snuff, chewing tobacco, pipe tobacco, roll-your-own loose tobacco, large cigars, and small cigars.

In addition to the federal cigarette tax and taxes levied by local or county governments (notably New York City and Chicago), state excise taxes vary widely and usually do not include the state or local sales tax:

- Alabama: $0.0425
- Alaska: $2.00
- Arizona: $2.00
- Arkansas: $1.15
- California: $0.87
- Colorado: $0.84
- Connecticut: $3.40
- Delaware: $1.60
- District of Columbia: $2.50
- Florida: $1.339
- Georgia: $0.37
- Hawai‘i: $3.20
- Idaho: $0.57
- Illinois: $1.98
- Indiana: $0.995
- Iowa: $1.36
- Kansas: $0.79
- Kentucky: $0.60
- Louisiana: $0.36
- Maine: $2.00
- Maryland: $2.00
- Massachusetts: $3.51
- Michigan: $2.00
- Minnesota: $2.83
- Mississippi: $0.68
- Missouri: $0.17
- Montana: $1.70
- Nebraska: $0.64
- Nevada: $0.80
- New Hampshire: $1.68
- New Jersey: $2.70
- New Mexico: $1.66
- New York: $4.35
- North Carolina: $0.45
- North Dakota: $0.44
- Ohio: $1.25
- Oklahoma: $1.03
- Oregon: $1.31
- Pennsylvania: $1.60
- Rhode Island: $3.50
- South Carolina: $0.57
- South Dakota: $1.53
- Tennessee: $0.62
- Texas: $1.41
- Utah: $1.70
- Vermont: $2.62
- Virginia: $0.30
The United States is not the only country that taxes cigarettes and other tobacco products. The World Health Organization Framework Convention on Tobacco Control was adopted by the 56th World Health Assembly in 2003 and is legally binding in 179 countries. It calls for signatories to act to "protect present and future generations from the devastating health, social, environmental and economic consequences of tobacco consumption and exposure to tobacco smoke," such as by limiting production and consumption through regulations on sales, production, and advertising and by taxing tobacco products. It is the most significant international public health agreement that does not deal with a contagious disease, malnutrition, or clean water access. It limits tobacco industry lobbying, calls for taxation as a demand reduction strategy, creates an obligation to protect the public from secondhand smoke, bans tobacco advertising, and requires a health warning on tobacco products that occupies at least 30 percent of the visible surface area of the packaging.

The United States, however, is one of the few United Nations members that is not a party to the WHO framework convention on tobacco control. President Bush elected not to send it to the Senate for consideration. Not only is the country not bound by the treaty, but it actually has sought to change various of its provisions—succeeding in removing from the treaty a ban on free tobacco samples and redefining its use of the term *minor* for purposes of restricting sales to such in order to protect the interests of American tobacco producers and their export revenues. The United States also attempted to oppose the requirement that warning labels be written in the language of the country where the tobacco product is sold.

One of the reasons for demand reduction of tobacco products, as mentioned, is the danger of secondhand smoke, also called environmental tobacco smoke or passive smoking. Secondhand smoke is the smoke released into the air from the burning of tobacco products, which lingers in the air for hours afterward and is inhaled by nonsmokers and smokers alike. There is no established safe level of exposure to secondhand smoke, which in the short term impacts blood platelets and the linings of blood vessels in ways that increase the risk of heart attacks.

Cumulative exposure to secondhand smoke, in the long term, increases both heart disease and lung and breast cancer risk as well as respiratory infections, asthma, ear infections and even hearing loss, dementia in patients over 50, and atopic dermatitis. In children and pregnant women, secondhand smoke increases the chance of brain tumors and damages carotid arteries and can result in low birth weight. Children are also at elevated risk for asthma and ear infections from secondhand smoke. There is increasing evidence that secondhand smoke is a factor in Sudden Infant Death Syndrome, tooth decay in young children, bronchitis and pneumonia in prepubescents, and the development of Crohn's disease in young children.

Alcohol is taxed at the state level with an excise tax applicable to off-premise sales (i.e., not drinks served in bars or restaurants) of distilled spirits of at least 40 percent alcohol by volume, which includes all whiskeys, brandies, rums, vodkas, and so on. That tax rate varies considerably by state:

- Alabama: $18.23
- Alaska: $12.80
- Arizona: $2.00
- Arkansas: $6.57
- California: $3.30
- Colorado: $2.28
- Connecticut: $5.40
- District of Columbia: $5.37
- Delaware: $3.75
- Florida: $6.50
- Georgia: $3.79
- Hawai‘i: $5.98
- Idaho: $10.92
- Illinois: $8.55
- Indiana: $2.68
- Iowa: $12.43
- Kansas: $2.50
- Kentucky: $6.76
- Louisiana: $2.50
- Maine: $5.80
- Maryland: $4.41
- Massachusetts: $4.05
- Michigan: $11.91
- Minnesota: $8.71
- Mississippi: $7.41
- Missouri: $2.00
- Montana: $9.34
- Nebraska: $3.75
- New Hampshire: $0 (Beer taxed at $0.30)
- New Jersey: $5.50
- New Mexico: $6.06
- New York: $6.44
- Nevada: $3.60
- North Carolina: $12.36
- North Dakota: $4.66
- Ohio: $9.32
- Oklahoma: $5.56
- Oregon: $22.73
- Pennsylvania: $7.21
- Rhode Island: $3.75
- South Carolina: $5.42
- South Dakota: $4.68
- Tennessee: $4.46
- Texas: $2.40
- Utah: $12.19
- Vermont: $5.86
- Virginia: $19.19
- Washington: $35.22
- West Virginia: $1.87
- Wisconsin: $3.25
- Wyoming: $0

In many states, different rates or rate modifiers apply according to the size of the container, place of production, alcohol content, and whether the alcohol is sold on board an airline.

Fuel exhaust is one source of atmospheric carcinogens. Diesel exhaust in particular is tied positively to lung cancer and likely implicated in bladder cancer as well. Emissions standards are one way to reduce the danger, but many countries use a fuel tax as a way to make the use of carcinogenic fuels more expensive and encourage the private sector to find other means while, at the same time, recovering revenues that offset the public health costs of these carcinogens. France, for instance, recently adopted a new tax to make diesel fuel more expensive than gasoline for this reason (unlike the United States, the majority of France's passenger cars are diesel). Gas taxes often are criticized as impacting the cost of other goods and so, theoretically, introducing a drag on the economy. On the other hand, in many sectors, goods are only transported as far as they are because of a long history of transportation fuel prices that have been kept artificially low compared to those of Europe; for instance, considerably more fuel per calorie of food is spent in bringing food to market now than in the 1940s, more than 10 times as much. Decentralized distribution would make this unnecessary, with the incidental benefit of reducing the scale of some of the country's food contamination crises.

The federal government imposes a $0.184 per gallon tax on gasoline and $0.244 per gallon on diesel. Aviation gasoline is taxed separately at $0.194 per gallon, while jet fuel is taxed at $0.219 per gallon or $0.044/gallon when used for commercial flights. State taxes vary, with gasoline listed first:

- Alabama: $0.393, $0.463
- Alaska: $0.308, $0.371
- Arizona: $0.374, $0.514
- Arkansas: $0.402, $0.472
- California: $0.713, $0.74
- Colorado: $0.404, $0.449
- Connecticut: $0.677, $0.793
- Delaware: $0.414, $0.464
- District of Columbia: $0.419, $0.479
- Florida: $0.544, $0.568
- Georgia: $0.459, $0.553
- Hawai’i: $0.665, $0.745
- Idaho: $0.434, $0.494
- Illinois: $0.575, $0.693
- Indiana: $0.592, $0.757
- Iowa: $0.404, $0.479
- Kansas: $0.434, $0.514
- Louisiana: $0.384, $0.444
- Maine: $0.484, $0.556
- Maryland: $0.454, $0.522
- Massachusetts: $0.449, $0.509
- Michigan: $0.598, $0.642
- Minnesota: $0.47, $0.53
- Mississippi: $0.368, $0.424
- Missouri: $0.357, $0.417
- Montana: $0.462, $0.529
- Nebraska: $0.457, $0.511
- Nevada: $0.516, $0.53
- New Hampshire: $0.38, $0.44
- New Jersey: $0.329, $0.419
- New Mexico: $0.373, $0.473

Fuel exhaust is one source of atmospheric carcinogens. Diesel exhaust in particular is tied positively to lung cancer and likely implicated in bladder cancer as well. Emissions standards are one way to reduce the danger, but many countries use a fuel tax as a way to make the use of carcinogenic fuels more expensive and encourage the private sector to find other means while, at the same time, recovering revenues that offset the public health costs of these carcinogens. France, for instance, recently adopted a new tax to make diesel fuel more expensive than gasoline for this reason (unlike the United States, the majority of France’s passenger cars are diesel). Gas taxes often are criticized as impacting the cost of other goods and so, theoretically, introducing a drag on the economy. On the other hand, in many sectors, goods are only transported as far as they are because of a long history of transportation fuel prices that have been kept artificially low compared to those of Europe; for instance, considerably more fuel per calorie of food is spent in bringing food to market now than in the 1940s, more than 10 times as much. Decentralized distribution would make this unnecessary, with the incidental benefit of reducing the scale of some of the country’s food contamination crises.

The federal government imposes a $0.184 per gallon tax on gasoline and $0.244 per gallon on diesel. Aviation gasoline is taxed separately at $0.194 per gallon, while jet fuel is taxed at $0.219 per gallon, or $0.044/gallon when used for commercial flights. State taxes vary, with gasoline listed first:
Technology, Imaging

Imaging modalities are central to the treatment of cancer given as they play integral roles in its early detection, diagnosis, and treatment. The different techniques available are applicable to different tumor types and locations, often providing unique benefits and disadvantages. Tools such as computed tomography (CT) scans and single-photon emission computed tomography (SPECT) can aid in the detection of tumors, while ultrasound and other techniques can guide treatment. Familiarity with present state and future advances in the imaging field is crucial to understanding the options for cancer detection and treatment.

Cancer Imaging for Diagnosis and Detection

Radiography is one of the oldest available imaging techniques, using X-rays and measuring the absorption of these light waves by different components of the body. Soft tissues tend to absorb very little of the radiation, while bones tend to absorb more. This difference can be used to distinguish between different organs and tissues to create a 2-D representation of the internal body structure. These images can be used by themselves to detect tumors, as in the case of cancer of the lungs or bones. X-ray imaging can also be used with injected contrast agents, which absorb X-rays, to visualize structures such as blood vessels. This may be indicative of the presence of a tumor in regions such as the breast, as in a contrast-enhanced mammogram.

While radiography usually provides 2-D images, computed axial tomography (CAT) uses multiple X-ray scans that penetrate at different depths to
create a 3-D representation of the body in the form of multiple slices. The multi-slice technique achieves higher resolution by using a system capable of scanning several parallel sections simultaneously. In both cases, computer algorithms reconstruct the 3-D structure based on the multiple X-ray images. This technique provides a noninvasive means of cancer detection in environments such as the colon.

Ultrasound has a very different mode of operation, relying on high-frequency (above 20 kHz) sound waves that are emitted into the body and reflected back by the internal structures. The reflected waves that are collected can then be used to construct an image of those internal structures. For example, transvaginal ultrasonography can be used to detect endometrial cancer.

One of the most powerful and expensive imaging techniques is magnetic resonance imaging (MRI), which uses a strong, oscillating magnetic field to align the nuclear spins of hydrogen atoms and measure the resulting patterns to create a high-resolution, 3-D image. MRI can be used to locate, visualize, and stage cancers in various soft tissues, including the brain. However, use of MRI is restricted by the effects that the magnetic field would have on implants and prostheses.

Finally, nuclear imaging works by using small amount of radioactively labeled chemical tracers that localize to specific tissues of the body, including tumors. Positron emission tomography (PET) creates a 2-D image of a region of the body based on the changing distribution of a radioactively labeled molecule, such as a sugar. This technique can serve to detect a tumor in a tissue, such as the brain, because the cancerous cells will have high metabolic demands and take up a large amount of the labeled sugar. SPECT, while yielding a lower resolution than PET scanning, creates a 3-D image by reconstruction from multiple images taken from different angles. This can be utilized in conjunction
with labeled antibodies that bind specifically to cancerous cells in order to visualize tumors.

**Cancer Imaging in Treatment**
The usefulness of the above imaging techniques is not limited to diagnosis and detection; these methods frequently play roles in guiding the treatment of various cancers. Procedures such as biopsies, resections, and tumor ablations all can be facilitated through the use of imaging techniques that reveal the locations of tumors, their severity, and even real-time changes in their conditions.

Biopsies of cancer cells provide histological information critical to staging a tumor and informing a plan of treatment. Extraction of a biopsy from a tissue deep in the body requires accurate knowledge of the location of the tissue of interest and the ability to insert the needle directly into the region of interest. Needle placement can be guided by modalities such as radiography, CT, and ultrasound as these techniques can distinguish between a tumor and its background. Surgical removal of a tumor is an important means of cancer treatment. Similar to a biopsy, it requires spatial information for planning and conducting the surgical removal. This is particularly important in delicate regions like the brain, where the surgeon must be guided to remove the tumor with minimal damage to the surrounding noncancerous tissue. In addition, it is important to ensure that every cancer has been removed. MRI can fulfill this role by providing the surgeon with high-resolution views of the structure of the brain and target tumor.

Ablation offers another, minimally invasive means for the elimination of cancer from the body. This involves the use of energy sources outside the body, such as ultrasound, to destroy the targeted diseased tissues. In techniques such as image-guided focused ultrasound (FUS) ablation, the ultrasound beams that destroy tissue are accurately directed toward the cancer through spatial information derived from MRI or ultrasound imaging.

**Future of Cancer Imaging**
Although the above techniques are well-established in their current uses, it is important to look to the future of the field for improvements in diagnosis and treatment. These advancements come in the form of new uses of imaging modalities as well as in integrative approaches that combine two or more of these techniques. In addition, novel computational approaches to extract maximal information from the derived images is currently a strong area of focus.

There is much relevant information to be derived from novel uses of existing imaging technologies. For examples, diffusion tensor imaging (DTI) uses nuclear magnetic resonance (NMR) to determine restrictions in the diffusion patterns of water in a tissue. Such restrictions are indicative of changes in the tissue structure and can be used for the detection of cancer in tissues such as the prostate and breast. Another promising advancement lies in the use of nanoparticles (molecules with at least one dimension below $10^{-9}$ meters) that selectively localize to cancerous tissues where they can be detected by MRI, PET, SPECT, and ultrasound. This provides greater resolution and improved detection capabilities for traditional imaging modalities.

The combination of existing techniques can improve biopsy and surgical treatment by providing both a detailed structural overview of the region for reference along with a dynamic representation of the same areas during the procedure. For example, the combination of MRI and ultrasound imaging can provide an accurate structural map for locating a tumor using the former technique as a general guide for biopsy, while the latter can help the surgeon as he or she guides the needle directly to the site. In addition, there are a number of emerging imaging modalities based on biophotonics such as optical coherence tomography (OCT), light scattering, multi-photon, Raman spectroscopy, and infrared spectroscopy; however these tools have not yet progressed to widespread clinical use.

In short, cancer imaging informs detection, diagnosis, and treatment through multiple modalities. The current techniques and recent advances in the field provide important tools for dealing with cancer and will continue to do so in the future.

Michael J. Walsh
University of Illinois at Chicago

**See Also:** Neutrons; Technology, New Therapies; X-Rays.

**Further Readings**
Technology, New Therapies

Cancer therapies have been continuously researched since the 19th century, and because cancer refers to a type of disease rather than a single illness, there will likely never be a silver-bullet cure for cancer but rather many treatments, some of them even cures or preventatives, for many types of cancer. Further, it has become commonplace, even standard, to employ multiple modalities in treating the same cancer: frequently surgery, if possible and advisable, combined with chemotherapy and radiation therapy.

Each of those modalities, in turn, may have side effects that necessitate their own treatment, such as the nausea induced by chemotherapy. As a result, there are numerous areas in which researchers continue to explore new cancer therapies. In 2014, the Pharmaceutical Research and Manufacturers of America (PhRMA) listed 771 new drugs in development, either in clinical trials or awaiting Food and Drug Administration (FDA) approval in addition to the drug discovery underway in labs throughout the scientific community, research into new combinations of existing chemotherapy treatments, new combinations of modalities, experimental forms of radiation therapy, and work on biologics and non-pharmaceutical treatments.

Among the experimental drugs or drug approaches in development, Human Alpha-lactalbumin Made LEthal to Tumor cells (HAMLET) has an interesting potential as a chemotherapy drug. HAMLET is a protein compound derived from human breast milk and in tests has induced cell death in several pathogens, including pneumococcus bacteria and human lung carcinoma cells. It also has demonstrated that it is useful in helping antibiotics kill off antibiotic-resistant bacteria (MRSA), which is of interest in the treatment of immunocompromised cancer patients, who are often left vulnerable to infection after radiation treatments or chemotherapy and spend a good deal of time in hospitals, which are rife with MRSA. Studies are applying the use of HAMLET to cancers of the lung, throat, kidney, colon, prostate, and ovaries, as well as leukemia, glioblastomas, and melanoma.

One rich area of research is the use of bacteria as cancer drugs because anaerobic Clostridia bacteria offer the potential to attack the interior of tumors, after which they die harmlessly in the oxygen-rich system of the body. There are several approaches that are possible here. C. novyi has been extensively researched as a cancer therapy for solid tumors, the interior cells of which are resistant to radiotherapy and chemotherapy. A genetically modified form of C. novyi, C. novyi-NT, infects and lyases hypoxic tumor cells but is ineffective against the cancer cells of the tumor surface.

An obvious solution to this is to use C. novyi-NT in combination with chemo- or radiotherapy, each addressing the other’s weaknesses. Radioactive monoclonal antibodies (mabs) also may be used with C. novyi-NT, with the benefit of sparing a greater amount of healthy tissue than traditional radiotherapy. C. novyi-NT also could be modified further to produce prodrug-converting enzymes to deliver to the tumor site or liposomes carrying anticancer drugs in order to increase the dose of chemotherapy experienced by the tumor cells without increasing the absolute dose and its damage to healthy cells. Alternately, the tumor can be pretreated with drugs like dolastatin, which widen the hypoxic core so that the C. novyi-NT can kill a greater percentage of the tumor. Techniques using

multiple administrations of *C. novyi*-NT also have been suggested, especially if this proves to be as effective as chemotherapy, with fewer of chemo’s debilitating side effects.

A relatively new form of cancer therapy is gene therapy, which was proposed in 1972 but saw little success until the 2000s. Originally conceived of as a treatment for hereditary diseases, gene therapy in the 2000s and 2010s has shown a great deal of promise as a cancer treatment. There are several forms of gene therapy used to treat cancer, all of which package DNA that encodes a specific protein into a vector—such as a virus—which is then introduced to the body or the target site. The DNA is delivered to a mutated gene, which it then replaces, causing the new DNA to release the protein that has been encoded. This has been used to successfully treat leukemias and myelomas in clinical trials.

Viruses can be used in other ways. In 2004, University of Texas researchers programmed a cold virus to attack cancer cells, and an engineered version of the herpes virus later made it into phase III clinical trials for the treatment of melanoma. Such viruses are called oncolytic viruses and kill cancer cells by infecting them and destroying them through lysis, the viral breakdown of a cell. In 2014, almost a dozen different groups of viruses were undergoing clinical trials as cancer treatments.

Cancer cells also can be killed by heat, and there are several methods by which heat can be applied to cancer cells. Photodynamic therapy is one method in which photosensitive agents are delivered to the tumor and exposed to light; they absorb and turn into heat in order to burn the tumor cells away. There is also renewed interest in whole-body hyperthermia therapy, long used to treat severe or recurrent cancer and, in recent years, becoming more popular as an adjuvant therapy. In whole-body hyperthermia, the patient’s whole body is heated until the body temperature reaches a certain threshold. There is no widespread agreement about that threshold, with researchers in Japan and Russia targeting 109 to 111 degrees F, and researchers in the West targeting somewhere between 104 and 107 degrees.

These few degrees make significant differences, both in technique and, many would argue, in the risk of toxicity to healthy cells. That said, the reason hyperthermia works is that tumor cells, though they excel at propagating throughout the body, are nevertheless not as efficient as healthy tissue in other respects, and in particular their inefficient vascular structure makes it difficult for them to shed excess heat. Healthy tissue is much more adept at it, and so while both sets of tissue are exposed to a temperature that is dangerous to them, the cancer cells consistently lose the battle first. Nevertheless, hyperthermia recipients must be closely monitored; damage from overheating can be severe and can lead to organ damage, exactly as with a very high fever.

As an alternative to whole-body hyperthermia, local hyperthermia can be conducted through magnetic hyperthermia, in which magnetic nanoparticles are injected that generate heat when the body is exposed to an alternating magnetic field. This poses fewer risks than whole-body hyperthermia. Similarly, nanoparticles made of gold or carbon can be injected and heated through exposure to radio waves.

The rapid cell division of cancer cells can be disrupted with Tumor Treating Fields (TTFs), electromagnetic devices marked by Novocure and approved by the FDA in 2011. The first systematic review of TTF’s effectiveness, in 2013, found that it was as effective as standard chemotherapy, with different side effects—primarily skin rashes caused by the electrodes, as opposed to the nausea, hair loss, and sometimes myelosuppression of chemotherapy.

Bill Kte’pi
Independent Scholar

See Also: Chemotherapy; Experimental Cancer Drugs; Radiation Therapy.

Further Readings
After World War II, America saw a surge in smoking. Returning GIs brought back with them smoking habits many did not have before their service; the new medium of television invited major tobacco companies to sponsor programs; women, many joining the workforce or wanting to make a statement for gender equality, began the habit; workplaces were foggy with smoke; doctors and nurses smoked; celebrities advertised cigarettes in splashy magazine and newspaper layouts.

The tobacco industry estimated just under half of adult Americans smoked. Although scratch medical research had indicated that prolonged use of tobacco caused lethargy, physical and mental, and could create peculiar side effects if it was stopped entirely, few public health advocates acknowledged more serious health impacts from cigarettes. In the 1950s, however, research began to suggest causal links between tobacco use and a variety of lung ailments, including bronchitis, emphysema, and heart disease. In 1957, Leroy Burney, then surgeon general, issued a largely ignored memo that first publicly linked smoking to lung cancer.

Seven years later, his successor, Dr. Luther Terry, would issue a far bolder, far broader indictment of smoking, calling it a public hazard and linking it definitively to a host of terminal diseases, most prominently lung cancer. That landmark report, the product not of zealous crusading or some antitobacco agenda (Terry himself was a smoker until a few months before the release of the report, when he switched to a pipe and even then never smoked publicly) but rather of Terry’s own determination to alert the American public of a critical health threat, now stands among the most important public health documents of the 20th century.

The son of a country doctor who worked with families across three counties in rural southern Alabama, Luther Leonidas Terry, born September 15, 1911, in the town of Red Level (population 612), grew up watching his father helping patients one on one and learned the responsibility of doctors when their patients were healthy and that prevention was far more practical than treatment. There was never a doubt he would be a doctor. Earning his bachelor’s in science from Birmingham–Southern College in 1931, he completed his M.D. four years later at Tulane University in New Orleans. After a number of medical appointments at prestigious facilities and university professorships specializing in the cardiovascular system, Terry decided research facilities and university classrooms were too divorced from the real work of helping people maintain their health. In 1943, he joined the United States Public Health Service—and over the next decade, he headed up the service’s medical offices in Baltimore, Maryland. He was a model bureaucrat—the offices ran efficiently and issued specific warnings and guidelines, largely concerning healthy heart habits, that were distinguished by their unbiased, matter-of-fact tone and their use of up-to-date medical data.

President John Kennedy (a cigar smoker, although seldom in front of cameras as he feared contributing to Irish caricatures) tapped Terry to be the nation’s ninth surgeon general, the chief of the National Health Service, the government’s official mouthpiece responsible for directing significant medical data to the public to prevent and treat diseases. There was little doubt where Terry would begin. Smoking was rapidly attracting more and more attention within the international medical community as a likely cause of lung cancer and bronchitis as well as general pulmonary-cardio distress. But the tobacco industry had long fended off such research as inconclusive and biased. Terry decided it was well within the purview of his office to study the reliability of the data and to reach a sound and unbiased conclusion.

Terry, determined to reach out to the widest range of the medical community, selected a 10-person, blue-ribbon committee; Terry personally vetted hundreds of doctors, cardiovascular researchers, public health officials, and pharmaceutical company representatives. To ensure the committee’s reliability, Terry even gave the tobacco industry representatives the power to veto any appointment to the committee. More than half of the final committee smoked. The committee worked diligently under Terry’s guidance for more than 14 months. The committee did no original research or fund specific data gathering—rather it became a kind of clearinghouse, investigating the reliability of data (more than 7,000 research documents) that had been published over more than 30 years. When the report was ready to be issued, close to 400 pages, Terry knew the report would be a bombshell. He timed the press conference to announce the results
of the report carefully—a Saturday, January 11, 1964—a day when the alarming news could not impact Wall Street, with its heavy tobacco industry presence, and would dominate Sunday morning newspapers and Sunday morning news programs on television.

The report, although massive in size, made a very clear and specific point: Unquestionably, smoking caused lung cancer. The death rate from lung cancer was astronomically higher among smokers than nonsmokers. In addition, data indicated irrefutably that smoking caused chronic bronchitis, emphysema, and heart disease. The report made no recommendations for action—Terry was determined to put the facts in front of the American people, certain the data would be sufficient to convince them. The tobacco industry representatives were quick to dismiss the report as it offered no original research. Although there had been public pronouncements before concerning the risks of smoking, *Smoking and Health: Report of the Advisory Committee of the Surgeon General of the Public Health Service* used a far more emphatic tone, describing smoking a public health hazard. In addition, Terry himself was perceived as no fiery antismoking lunatic fringer—his demeanor was calm, he was soft-spoken, he came across as reliable, and his data were carefully weighed, his conclusions sound and logical.

Terry spent the rest of his tenure as surgeon general (he served until 1965) tirelessly promoting the dangers of smoking. Before Terry came into office, Gallup surveys indicated less than 40 percent of Americans believed in a causal link between smoking and cancer; in 1968, nearly 80 percent believed it. In the year following the report’s release, estimates suggested nearly 20 million Americans quit smoking. Largely through Terry’s efforts, cigarette packaging was required to indicate that the product was a health risk. Terry, who accepted a teaching appointment at the University of Pennsylvania, would remain a public advocate for smoking bans, specifically the effects of secondhand smoke in the workplace, until his death, from a heart attack, March 29, 1985.

Joseph Dewey
Broward College

See Also: Environmental Tobacco Smoke; Passive Smoking; Smoking and Society; Tobacco Smoking.
Testicular Cancer

Testicular cancer (TC) forms in one or both testicles, often in young men. The American Cancer Society estimates that about 8,430 new cases of TC will be diagnosed in the United States in 2015, and about 380 men are expected to die of TC in that time. Half of these cases occur between the ages of 20 and 34. Because TC is rare, highly curable, and can be discovered at an early stage, most men have only a one in 5,000 lifetime risk of dying from the disease.

TC is typically detected by the male, an intimate partner, or a medical practitioner as a painless lump on, or swelling of, the testicle. Most cases are diagnosed following a physical examination, an ultrasound of the testicle, blood tests for tumor markers, or pathology reports following an orchiectomy. If left untreated, TC can spread along a predictable path through abdominal lymph nodes upward toward the lungs and outward to the liver, brain, and elsewhere. Treatment decisions for TC include orchiectomy in most cases, and radiation, chemotherapy, or surgery to remove abdominal lymph nodes if the cancer has spread beyond the testicle. Treatment can cause infertility, diminished sex drive, and additional concerns.

While TC rates have been increasing around the world for several decades, researchers are unsure of the causes. Few risk factors for the disease are currently known. However, psychosocial challenges during TC survivorship, barriers to early detection, and racial and ethnic disparities in TC outcomes are well documented.

Psychosocial Concerns

Because TC is highly treatable and the most common form of cancer in young men, most TC survivors live the majority of their lives facing a number of related psychosocial concerns. At the time of diagnosis, young men are already undergoing a number of normative life transitions that are less of a concern for older adults and younger children (e.g., finishing school, forming intimate relationships, beginning a career, starting a family, achieving independence, establishing an identity, and planning for the future). Young males also must work to initiate and maintain social relationships with family, friends, and peer support systems that are often less established than at other stages of life.

A TC diagnosis delays and sometimes prevents the achievement of these plans and milestones, and it often disrupts the initiation and maintenance of close relationships. Many TC survivors hesitate to disclose their illness to other men because they are afraid to be perceived as different, less masculine, and more vulnerable and incomplete. However, TC survivors have said that the use of humorous slogans, often on clothing and accessories (e.g., “Don’t be a punk, check your junk”), can serve as effective icebreakers in promoting a sense of normalcy and raising TC awareness among friend and peer groups.

Many single men experience lasting concerns about forming intimate relationships due to changes in physical appearance and function, fear of recurrence and death, and diminished finances. Although partnered TC survivors sometimes report that their cancer diagnosis helped to increase their relational closeness, both partners often experience uncertainty about possible infertility and an altered sexual relationship. Additionally, conflicts about primary caregiving roles and duties are common between newly formed romantic partners and the young man’s mother. Although psychosocial services and support programs are available specifically to address the unique concerns of a young adult with cancer, many TC survivors are unaware that these programs exist.

Barriers to Early TC Detection

Successfully persuading males that they are at risk for TC and that they should perform monthly testicular self-examinations (TSE) are challenges currently facing scholars and practitioners. Perhaps as a result of TC’s perceived limited susceptibility and severity,
males know little about TC and do not engage in regular TSE. Males’ uncertainty regarding their ability to reliably perform TSE is one of the most prevalent barriers to conduct effective screening. Beneficial conversations about TC and TSE often do not take place within male relationships due to normative expectations of masculinity, which also discourage men from engaging in TSE, seeking health information, and using health care services to address symptoms. Men may perceive such conversations and behaviors to violate stereotypical expectations of masculinity such as strength and stoicism.

Males are more likely to perform TSE if they are properly educated about TC risk and believe that TSEs are an easy and effective means of detecting abnormalities. Because this disease strikes primarily in young men, high schools and universities are often the targets of interventions intended to increase knowledge and foster positive attitudes toward TC prevention. A recent TC communication campaign called Check Yo Nutz increased college males’ intent to conduct TSE, search for TC information, and schedule appointments with their doctors. The campaign featured unique and humorous messages about TC and TSE disseminated through a wide range of communication channels, including on-campus events, printed shower cards, and a smartphone video game application called Nut Warz.

However, few TC mass media campaigns have been implemented and evaluated on a wider scale in the United States. Entertainment—education programs like MTV’s The Tom Green Cancer Special, which aired in the United States in 2000 and documented the comedian’s TC diagnosis and surgery provide opportunities to create TC awareness and normalize among at-risk males.

Racial and Ethnic Disparities

Males within racial and ethnic minority groups in the United States demonstrate even less knowledge and risk of TC compared to whites. Minority males’ tendency to maintain lower socioeconomic status, education level, income, health literacy, and access to health care often leads to delayed medical visits, which results in higher TC stages at diagnosis and higher rates of mortality.

Although TC is rarer in the black community than it is among whites, black men experience significantly lower five- and 10-year survival rates than whites with similar tumor types, and they have significantly higher stages of cancer progression upon diagnosis. Black men display the lowest TC education among all American racial and ethnic groups, and they are most likely to endorse traditional attitudes regarding health and masculinity. Many researchers agree that more effective health education and promotion programs for young minority men are needed at the interpersonal, organizational, and mass media levels to counter these disparities.

Nicholas T. Iannarino
University of Michigan–Dearborn

See Also: Age; Cancer Communication; Sex; Surgery; Survivors of Cancer.

Further Readings


Textile Dyes

The art and practice of dyeing clothing to meet individuals’ preferences and tastes is a long-standing tradition across many human cultures. In fact, historical evidence suggests that Neanderthal man was the first to use dye some 180,000 years ago. For the vast majority of human history, dyes were derived from organic materials—namely plants, minerals, animals, and insects. However, since the first discovery of synthetic dye in 1856, the art and practice of using dye has changed dramatically. This has included the overwhelming practice of using synthetic dyes for a number of reasons. This entry
explores this development, the concerns and scientific evidence connecting synthetic dyes to cancer incidence, the conflicts of interest in textile manufacturing, and how regulations are crucial toward improving both the human and environmental risks posed by such chemicals and introduces a few potential solutions and improvements to the current state of textile production.

**Development of the Synthetic Dye Industry**

For most of human history, the production of dyes to color clothing and goods was a highly labor- and land-intensive production. Much organic material had to be used and cultivated to produce a relatively small amount of dye. However, in the mid-19th century, this began to change with the discovery of the first synthetic dye, mauveine. This discovery enabled dyes to be produced on a much larger scale and also began to expose textile workers to new chemicals and chemical intermediates formed in the clothing manufacturing process at considerable levels. Regulations and testing for chemical toxicity at this time were largely nonexistent, and it was not until many textile workers years later began to suffer from bladder cancer at alarming rates did manufacturers and health policy pundits in society begin to take notice and question the safety of certain textile dyes, especially those such as fuchsine, auramine, benzidine, and 2-naphthylamine.

Once this information began to spread throughout the textile industry and slowly into the medical community, responsible textile manufacturers ceased use of such carcinogenic dyes and replaced them with safer alternatives. However, regulatory testing and safety for chemical dyes in general continued to be lacking well into the mid to late 20th century. Recognizing this shortcoming, the colorant and textile industry of western Europe began to step up and is credited for being the first organization to systematically examine and test textile dyes for safety and toxicology on a large scale. This eventually led to the formation of the Ecological and Toxicological Association of Dyes and Organic Pigment Manufacturers (ETADOPM) in 1974, which developed safety data sheets on chemicals typically used in the textile manufacturing process. These safety data sheets have since spread worldwide and have become commonplace in the textile industry. However, unfortunately, this has not meant that the process of dyeing clothing and consumer goods is now an entirely safe one because a number of issues still extant in the industry globally.

**Synthetic Dyes, Health Risks, and the Cancer Connection**

Over the last 40 years since the genesis of the ETADOPM organization, testing of textile dyes has become much more stringent and regulated across much of the globe, especially in Western countries. Unfortunately, this has not meant that all dyes used in textile manufacturing are necessarily safe nor are the regulations and safety findings always enforced, especially in developing countries. It is conceivable and perhaps not coincidental then why so many major clothiers wishing to avoid stringent regulations largely have outsourced their manufacturing operations to such locales. Subsequently, this has created a perilous situation in such countries due to the increased chemical exposure, which threatens the health and welfare of individuals (such as textile workers exposed to large amounts of chemicals and dyes in the manufacturing process), communities, and the environment at large.

Due to the plethora of scientific studies and epidemiological data going back decades now, it is not so much the issue that there is much debate as to whether certain textile dyes or chemical intermediates may be risky for both consumers and textile workers alike. Rather it is the case of what to do about manufacturing plants trying to illegally cut costs at the expense of their workers’ health and the environment and how to protect consumers and textile workers from exposures in the meantime that may threaten their health.

While safety data sheets have suggested that, on average, many problematic dyes (such as disperse dyes) may have low potential for acute toxic effects, these averages have seemed to run counter to the consistent reports by many dermatologists and consumers. Moreover, dyes used in the manufacturing process that are not left in the end clothing product but are part of the dyeing process (such as those termed reactive dyes) have been implicated in many allergic and dermatological reactions for textile workers.

Specifically related to genotoxicity and mutagenicity, certain textile dyes have been identified as especially concerning, such as certain classes of azo dyes. While many subtypes used in years past have been generally outlawed or phased out of usage due
Textile Dyes

to health concerns, this class of dyes is still used prolifically on a global scale, accounting for some 50 percent of the some 1 million tons of dyes produced annually, especially in developing countries in the textile manufacturing process. It is important to realize that both the dye itself or the metabolites of dyes can be carcinogenic. Thus, even though an initial dye itself may be considered safe in the manufacturing process, subsequent wearing, washing, and treating the dye in the garment later on can cause the dye to transform into dangerous metabolites that have the potential to be absorbed through the skin or the air or contaminate the water supply.

In the case of the azo dyes, this has been studied extensively. Interestingly, just slight chemical differences in the dyes can make dramatic impacts on their relative risk to humans and animals alike. For instance, the class of azo dyes called 4-aminoazo dyes were noted in studies in the 1980s to all be carcinogenic, whereas the 2-aminoazo dyes were not. This is explained by their different capacities to create different reactive metabolites through their differing degrees of solubility with solvents. Studies conducted in the 1970s and 1980s further illustrated that textile workers were often developing health problems and bladder cancer in particular due to the reactive metabolites of these types of dyes, not the original dyes themselves.

While some of these subcategories of chemicals have been substituted for and abandoned by manufacturers over time, this is not the case in many instances, especially in developing countries. Moreover, other problematic chemicals used in the manufacturing or the fabric finishing process still continue to be used with known health or cancer risks such as: azo dyes (class III A1 and A2 in particular), dioxin, heavy metals such as copper, chrome, zinc, nonylphenol ethoxylates (NPEs), and formaldehyde.

Other Dyes Used in Textile Manufacturing and Their Relative Health Risks

While azo dyes represent the largest class of textile dyes, other dyes have been used and also examined for potential toxicity and safety over the last number of decades. The second-most important class of dyes used in the textile industry has traditionally been the anthraquinone class (although they have diminished in importance in recent years). Interestingly, they have shown a similar pattern when compared to the azo dyes as they relate to health and carcinogenic risk. For example, those that are classified as solvent or disperse dyes containing amino- or methylamino-groups have the potential to metabolize into mutagenic or carcinogenic compounds.

Industry Conflicts of Interest and Problematic Regulatory Testing

All of these issues are compounded by the fact that, while manufacturers today are much more attentive and aware of health risks of chemicals as compared to decades ago, oftentimes the testing of chemicals is not always done thoroughly enough before a new dye is introduced into the commercial marketplace. Then, as the case is often with many pharmaceutical drugs, ill effects are often discovered after the fact once it has been introduced into general usage. This was the case with the dye Amaranth, which was introduced, then discovered to be carcinogenic, and then subsequently withdrawn.

Other times, companies, in pursuit of cutting costs, greater profits, and quicker turnaround times in garment manufacturing, have continued to use already banned dyes and chemicals. Greenpeace International recently commissioned a study to investigate many popular clothing manufacturers’ use of known hormone-disrupting and potentially cancer-causing compounds called NPEs. Independent labs found two-thirds of clothing items testing positive for these compounds. While these compounds are banned in the European Union (EU) and parts of North America, many international clothiers, as noted earlier, outsource to developing countries where regulatory testing and regulations are more lax.

Needless to say, this situation creates an especially concerning situation for residents and textile workers in these countries who are unwittingly being exposed to potential dangerous levels of such chemicals. Furthermore, these chemicals also often are being released into water supplies through either illegal dumping of wastewater or via ill-suited water treatment plants in such locales unable to filter out such chemicals. Thus, aquatic life and those dependent on using local waters for recreation, drinking, or bathing are being endangered due to such practices.

Studies such as those funded by Greenpeace, furthermore, have illustrated the plethora of dangerous and hazardous chemicals being released into wastewater and water treatment supplies, such as
Thailand

Thailand is a country located in the Indochina peninsula in southeast Asia and is made up of four areas: the north, northeast, south, and central regions. It was once deeply rooted in its indigenous medical practices, which stem both from the Buddhist belief system as well as those of indigenous tribes: the Mon and Khmer. In addition to these medical practices, Western medicine has become increasingly popular and advanced over the last 60 years.

By the 1900s, there was a large influx of migration of peoples from regions in southern China—what we know today as the Thai people. With this migration came new beliefs about medical practices. Western medicine was adopted, and many renounced the effectiveness of traditional, indigenous medical practices. Eventually, traditional medicine found its way back into validity in Thailand. Currently, there are two main strains of traditional medicine. The first is called Traditional Thai Medicine (TTM), which refers to traditional practices that are regulated by the Ministry of Public Health. The second is called Traditional Medicine of Thailand, which adopts its practices from ancient texts and is practiced throughout the country, although it is not systematized by the Ministry of Public Health, which oversees and regulates medicine and health care practices throughout Thailand.

While Thailand has been largely untouched from much Western influence, as it was not colonized like other parts of southeast Asia, Western medicine became more prevalent throughout the 1900s, and medical practices were largely advanced and refined by the 1970s. Western medical treatments for cancer are widely used and available throughout Thailand, with the rise of cancer treatment clinics, medical journals, and studies.

Cancer has been an increasing problem in Thailand over the last 15 years. People are most commonly subject to cholangiocarcinoma, a type of cancer that affects the liver and parts of the gastrointestinal tract.

Cholangiocarcinoma is also referred to as bile duct cancer, and it is caused by the consumption of raw fish from various regions in northeast Thailand. The fish oftentimes are infested with either a parasite or a liver fluke, which in turn affects the human host, leading to recurring incidents of infectious disease, which ultimately lead to cancer. Bile duct cancer typically has a poor prognosis and is rare in Western countries.

In a 2001 study conducted by the Japanese Journal of Clinical Oncology, it was reported that cancer was the leading cause of death overall in Thailand. In 2001, liver cancer or cholangiocarcinoma was

perfluorinated chemicals (PFCs) and alkylphenols. Solutions do exist thankfully, however, to change such situations through combined efforts of better regulation, forcing greater accountability on textile manufacturers and parent companies, and through the substitution of more natural dyes as well as well-tested synthetic substitutes such as the 2-aminoazo dyes instead of the 4-aminoazos.

Part of the challenge here has been companies who have been reticent to comply or be proactive in adopting more stringent guidelines when it comes to chemical use and proven health risks, which include many major clothing manufacturers popular with many consumers globally including Adidas, Abercrombie & Fitch, Calvin Klein, Nike, Ralph Lauren, and others. Moving such initiatives along continues to be an ongoing struggle of pitting health and environmental advocacy groups and concerned consumers against manufacturing plants and parent clothing manufacturers, with governments often stuck in the middle of it all in many countries.

Eric Wood
Hawthorn University

See Also: Bladder Cancer; Developing Countries; Lung Cancer, Non–Small Cell; Pollution, Water.

Further Readings
the leading cause of cancer-related deaths in both men and women. Thailand's incidence of liver cancer is much higher than any other region in the world due to liver flukes that correlate with the consumption of raw seafood. Because of increases of this disease in recent years, Thai political officials have been canvassing to promote dietary and health education to limit the consumption of raw and potentially infested foods.

Dr. Tanasanvimon is an oncologist at King Chulalongkorn Memorial Hospital in Bangkok. Even with Thailand's advances in Western medicine, specifically in the field of cancer, there are still few well-known oncologists. Dr. Tanasanvimon specializes in the study of cholangiocarcinoma and other gastrointestinal cancers. Because cholangiocarcinoma is the leading cause of cancer-related deaths in Thailand, Dr. Tanasanvimon has dedicated much of his research and practice to the branch.

Much of Dr. Tanasanvimon's research has substantiated claims that cholangiocarcinoma is caused by nitrate contamination and parasitical infestation of local seafood. Dr. Tanasanvimon recently received a grant in 2013 to continue his research, which he hopes will provide himself and other oncologists the ability to narrow treatment options and provide for earlier prognosis. In addition to his research, he perpetuates the political message of the importance of a healthy diet.

In addition to breakthroughs promoting dietary education, there also is a national dialogue of the benefits of screening for both cervical and breast cancers in women. While incidents of breast and cervical cancer among Thai and Asian women in general is lower than in other ethnic groups, the screening practice of these cancers is relatively low. The lack of self-screening among Asian women corresponds to the social attitudes and beliefs about the subject in those regions.

While the risk for these types of cancers seems to be a lower concern for Thai women, the mortality rate for these cancers is higher than would be expected as most women do not regularly practice self-screening.

Religious beliefs also play a large role in health care and health practices in Thailand. Buddhism is the official religion and has influence over a great deal of people's lives, specifically regarding alternative medical treatment.

Buddhist mind power healing is an avenue that the people of Thailand may consider exploring, especially if they already actively practice Buddhism. Most people who turn to this method operate on the belief that the disease was caused by some wrongdoing or bad will on their part in an earlier time during their lives.

This practice, though not uncommon, is typically reserved for those in the later stages of cancer who are seeking an alternative treatment after already undergoing traditional, Western methods like chemotherapy and radiation.

Wat Kampramong is another holistic approach rooted in TTM. Wat Kampramong was created by a Buddhist monk and largely targets cancer patients in later stages of the disease, much like Buddhist mind power healing. Wat Kampramong does not employ any Western strategies, and instead, the treatment consists of various mixtures of herbs and teas. While there is no empirical evidence to support the effectiveness of Wat Kampramong, many patients have described a feeling of overall well-being after they have taken part in the treatment.

Haylee Massaro
Independent Scholar

See Also: Breast Cancer; Cervical Cancer; Liver Cancer, Adult (Primary).

Further Readings


Thymoma, Childhood

The majority of the reports that describe the benefits of thymectomy involving juvenile myasthenia gravis (MG) were inferred from adult cases, whereas those relating to pediatric cases are minimal. This situation has thus prompted research groups to investigate the outcome of thymectomy in children diagnosed with thymoma. Recent studies have shown that pediatric thymoma patients within the age range of one to 15 years old at disease onset can present with various stages of thymoma, ranging from stage II to IV.

Furthermore, the use of the Osserman classification scheme has facilitated in the staging of pediatric cases of thymoma. Research investigations also have shown that screening for antibody titers for anti-acetylcholine receptor assists in the design of a personalized treatment scheme for a child diagnosed with thymoma.

MG pertains to a neuromuscular disorder characterized by dysfunctional transmission of signals due to damage in the postsynaptic endplates of nerve cells. The damage is mainly due to the responses of the immune system, thus resulting in variable degrees of muscle weakness and rapid fatigue in an individual. The extent of muscle types involved in MG varies among patients and also can change during the course of the disease. Mild MG often involves the muscles of the eyes, whereas more severe forms present generalized muscle weakness that is usually coupled with respiratory failure and bulbar symptoms.

In the Western parts of the world, almost 20 percent of patients diagnosed with immune-mediated MG develop their first symptoms prior to age 15. Although MG extensively varies in terms of its epidemiology and progress, the pathophysiology of its juvenile-onset stage is similar to that of adult-onset cases. Researchers have thus suggested that the treatment regimen for MG, regardless of age of onset, should be similar because of its identical pathophysiological characteristics. Furthermore, antibody titers for the acetylcholine receptor are commonly detected in approximately 85 percent of patients presenting generalized MG. On the other hand, only 50 percent of patients with mild MG, and thus showing only ocular involvement, test positive for the acetylcholine receptor.

In the case of patients who test negative for acetylcholine receptors, antibodies against muscle-specific kinase can be screened, which has been observed in approximately 30 percent of patients who test negative for this receptor protein. Previous studies also have suggested that the thymus plays an important role in the generation of an immune response, which in turn induces the production of antibodies against the acetylcholine receptor in MG patients. The relationship between MG and thymic hyperplasia also has been confirmed in thymoma, although this disorder rarely occurs in children.

Since the 1940s, thymectomy has been utilized as the treatment scheme for MG. The choice of thymectomy as the effective approach for MG treatment is based mainly on the reported improvement in the condition of MG patients after the procedure. The evidence-based findings from a significantly high number of reports support this treatment scheme, despite the absence of randomized controlled trials. Retrospective studies of MG have shown that, when thymectomy was conducted during childhood, the improvement was observed in 68 percent of the pediatric patients. In addition, half of this subpopulation was taken off their medications for MG after thymectomy. However, caution should also be exercised in this retrospective study because the pediatric MG patients presented heterogeneous symptoms, which in turn reflects potential variations in their responses to thymectomy. Studies have shown that the specific age of the pediatric patient also can influence the outcome of thymectomy; therefore, one cannot immediately generalize the outcomes of pediatric MG patients. Other factors that also could directly or indirectly influence pediatric patient outcome
after thymectomy include the specific surgical technique employed, the administration of immune therapies that are simultaneously administered with the surgical procedure, and the time interval between the thymectomy and the follow-up visit to the attending physician.

It is also important to consider that the majority of the pediatric MG patients is acetylcholine receptor antibody-negative, whereas some of these patients are muscle-specific kinase antibody-positive. Other cases might have unrecognized congenital-type myasthenic syndromes, which are often unresponsive to surgical techniques such as thymectomy due to their particular genotypic constitution. Several studies have thus examined the effect of thymectomy on juvenile MG. Most hospitals offer thymectomy as a standard treatment scheme for pediatric juvenile MG patients who are acetylcholine antibody-positive based on their generalized symptoms and their uncontrolled condition using medications alone. These studies have shown that pediatric patients with juvenile MG have higher rates of remission (38 percent) regardless of the presence or absence of treatment using medications. On the other hand, pediatric patients who did not undergo thymectomy had significantly lower remission rates (7 percent), irrespective of the administration of medications.

The severity of MG is determined by the Osserman classification scheme, which has been used extensively in juvenile MG studies for years. This classification system commonly is applied to clinical studies that focus on the effects of thymectomy on pediatric patients with juvenile MG. Examples of classification groups using the Osserman system after thymectomy include in remission, condition improved, disease unchanged, condition worsened, or dead. Other clinicians also include modifications in the medications received by the patient. A more detailed scheme for classifying MG was developed by the Myasthenia Gravis Foundation of America; however, this system has not been validated in pediatric patients.

Factors that significantly contribute to patient outcomes in using thymectomy include the selection of acetylcholine receptor antibody-positive pediatric patients, a relatively short interval between onset of MG and surgery, the use of the transternal technique in surgery that facilitates in the visualization as well as the excision of the thymus, and the administration of immune-modulating agents after thymectomy. Previous studies have shown that, when thymectomy is conducted early on, the patient often achieves a higher chance of achieving remission. An earlier study involving 85 pediatric MG patients showed that 61 percent of the patients who underwent surgical removal of their thymus within a year of disease onset were observed to be in remission at three-year follow-up. On the other hand, 24 percent of the patients who did not undergo thymectomy within a year were in remission by the third year of follow-up. The effects of thymectomy gradually occur, and thus, the entire general outcome might not be evident until at least one year after the surgical procedure.

Rhea U. Vallente
Independent Scholar

See Also: Childhood Cancers; Surgery; Thymoma and Thymic Carcinoma.

Further Readings

Thymoma and Thymic Carcinoma

Thymic carcinoma is a rare tumor involving the mediastinum and is generally considered as an orphan disease based on its relatively low prevalence. The current histological classification of thymic carcinomas consists of three categories, namely thymomas, thymic carcinomas, and lastly, neuroendocrine thymic tumors. The earliest research reports on thymic tumors were based mainly on
Thymoma and Thymic Carcinoma

single-institution cases that were diagnosed and treated in the past few decades. These long-term studies were conducted due to the rarity in the occurrence of thymic carcinoma, and thus, several years of collection of case reports were required to create a study population of acceptable size. In the past decade, the interest in thymic carcinoma has increased, which resulted in the establishment of a thymic working group that closely looked into various clinical aspects of this particular malignancy. The European Society of Thoracic Surgeons (ESTS) is an organization consisting of general thoracic surgeons from various countries who are dedicated in establishing a platform for studies on the clinical aspects of thymic carcinoma.

Thymic tumors are relatively rare tumors that occur in adults and involve the anterior mediastinal compartment. These tumors are highly heterogeneous, thus resulting in its further classification into subgroups based on histological features, namely, thymomas, thymic carcinomas, as well as neuroendocrine thymic tumors. Thymic malignancies have long been considered as orphan diseases. However, there has been a recent increase in interest in these malignancies, thus resulting in the creation of internationally based thymic interest groups in various countries around the world.

In the United States, the incidence of thymic tumors is 0.15 cases for every 100,000 person-years. Thymic carcinomas are the most common anterior mediastinal tumor that occurs in adults; however, these tumors also can develop at any age. A significant peak in incidence during the age range of 30 to 40 years has been reported for thymomas associated with myasthenia gravis, whereas the age range of 60 to 70 years of age was associated with the highest incidence of thymomas that were not associated with myasthenia gravis.

The incidence of thymic carcinoma is similar among males and females. Approximately 30 percent of patients diagnosed with thymoma are asymptomatic, whereas 60 to 70 percent of patients with thymic carcinoma and neuroendocrine thymic tumors show symptoms upon presentation. The most common symptoms recorded in any type of thymic tumor are often local, which include chest pain, difficulty or shortness of breath, and cough. In the case of invasive thymic carcinomas, the most common presentations include superior vena cava syndrome, paralysis of the hemidiaphragm with involvement of the phrenic nerve, and hoarseness of voice, possibly due to recurrent infiltration of the laryngeal nerve. Thymic carcinomas that have reached pleural spreading often present symptoms of pleural effusion coupled with chest pain.

Thymic malignancies often are associated with paraneoplastic or parathymic diseases. The most prevalent paraneoplastic disease among thymoma patients is myasthenia gravis, which has been observed in almost 50 percent of patients. In paraneoplastic syndromes not associated with myasthenia gravis, pure red cell aplasia or hypogammaglobulinemia is often observed, usually occurring in 5 percent of thymic carcinoma patients. These particular carcinomas are rarely associated with myasthenia gravis, and its prevalence ranges from 0 to 30 percent, often depending on the series being examined. Thymic carcinomas have very rarely been observed in cases of polymyositis, dermatomyositis, and erythrocytosis. Neuroendocrine thymic tumors often are associated with approximately 30 percent of endocrinopathies, which include Cushing’s syndrome and multiple endocrine neoplasia type 1. Wermer syndrome associated with parathyroid tumors, pancreatic islets cells, as well as the pituitary gland have also been associated with neuroendocrine thymic tumors. There also are cases in which the excessive production of growth hormone-releasing hormone associated with ectopic acromegaly have been associated

A basaloid type thymic carcinoma. Thymic carcinomas are the most common anterior mediastinal tumor that occurs in adults; however, in general it is a rare tumor. (Wikimedia Commons)
Thyroid Cancer

with neuroendocrine thymic tumors. Other rare syndromes linked to neuroendocrine thymic malignancies consist of prolactin secretion, multiple endocrine neoplasia type 2, peripheral neuropathy, myasthenia gravis, Eaton-Lambert syndrome, and carcinoid syndrome.

Thymoma patients generally have a twofold higher risk of developing second malignancies. Thymic tumors are generally diagnosed after clinical examination, radiographic imaging, and collection of a biopsy specimen for histological analysis. Clinical examination of the patient facilitates in the identification of symptoms of parathyroid syndromes. The use of computer tomography (CT) imaging also has been considered as an imaging standard for the initial assessment of patients with thymic malignancies. CT imaging is also the preferred procedure during follow-up monitoring of thymic carcinoma patients. On the other hand, magnetic resonance imaging (MRI) is apparently of little use in the diagnosis of thymic carcinomas, except in cases involving possible infiltration of the large vascular tissues and the heart. Positron emission tomography (PET) scanning also has been employed for the differentiation between thymic hyperplasia and thymoma, as well as low- and high-risk thymomas, and thymoma versus thymic carcinoma.

The cytohistological assessment of a biopsy specimen often is required for the diagnosis of thymic carcinoma. However, this has been less frequently employed in the previous decade. The significant improvement in imaging technologies has, since then, improved the diagnostic capability of histological assessment; and therefore, the utilization of this technique has increased in the past several years. A consensus, however, has been reached that assessment of a biopsy specimen would be required only in cases wherein the results of CT scanning are vague or seem to be unable to fully classify the tissue of interest or when the target tumor has been determined to be unresectable prior to initiation of chemotherapy or chemoradiotherapy.

Unfortunately, there is currently no established classification system for thymic carcinomas. The governing body mandated to define specific malignancies, Union of Internationale Contre le Cancer, in collaboration with the American Joint Commission on Cancer, has proposed a preliminary classification scheme. However, no official system has so far been identified. The most frequently used classification system for thymic carcinomas is the Masaoka staging system, which was first presented in 1981. Minor modifications to the classification system were incorporated in 1994. The Masaoka staging system uses four stages of disease progression, although the N factor is often of little value to the scheme. The new tumor, node, metastases (TNM) system is anticipated to be released in 2017, through the collaborative efforts of the International Thymic Malignancies Interest Groups together with the International Association for the Study of Lung Cancer.

Rhea U. Vallente
Independent Scholar

See Also: Chemotherapy; Technology, Imaging; Thymoma, Childhood.

Further Readings

Thyroid Cancer

The term thyroid cancer refers to cancer that originates in the thyroid gland, the butterfly-shaped gland located in the neck responsible for hormones that regulate major systems of the body (including the cardiac, digestive and reproductive systems). Thyroid cancer is the fastest-increasing cancer in adults in the United States and is rising throughout the world. Two main risks that increase the chances of thyroid cancer are genetic predisposition and exposure to radiation (environmental or medical). Most thyroid cancer responds well to treatment if caught early and treated effectively.
Risk, Prevalence, and Outcomes
Though thyroid cancer can develop without any specific identified cause, there are known risk factors. Nuclear accidents are known causes of thyroid cancer due to exposure to radiation and radioactive iodine (which can be prevented with potassium iodine). Exposure to external radiation through medical treatment is known to increase the risk of developing thyroid cancer.

Thyroid cancer is more common in areas where diets are low in iodine. Individuals with thyroid disorders or a family history of thyroid disorders or cancer are also at higher risk of thyroid cancer, and genetic mutations have been identified that may lead to development of thyroid cancer over the life span. The risk of thyroid cancer increases with age, and females are more likely to develop thyroid cancer than males. Children are much less likely to develop thyroid cancer and tend to have very good outcomes.

Thyroid cancer is typically slow growing and responds well to treatment, and long-term prognosis for patients undergoing treatment is positive. Studies of thyroid cancer patients over many years have shown that the vast majority, estimated between 90 and 100 percent, survive at least 10 years after diagnosis. Individuals under the age of 45 and those with small tumors and limited or no metastases usually have the best chance of a cure, though those over 45 also have a positive prognosis, though with a higher risk of recurrence.

Types of Thyroid Cancer
Thyroid cancer can be either differentiated (having relatively normal cell structures), including papillary and follicular thyroid cancer, or undifferentiated (having abnormal cells lacking typical cell structure), including medullary and anaplastic thyroid cancer.

Papillary cancer is the most common form of thyroid cancer in both adults and children, accounting for more than 85 percent of new cancer diagnoses. This form of cancer begins in the follicular cells and grows slowly. The risk of papillary cancer increases with exposure to external radiation (most commonly from medical treatment), although some researchers believe that carcinogens may affect the thyroid and increase the chance of thyroid cancer. Genetic mutations also have been linked to thyroid cancer of all types. The prognosis for papillary cancer, when diagnosed early, is very positive with a strong possibility of a cure.

Individuals with papillary thyroid cancer may have metastases (cancer that has spread to other parts of the body) to the lymph nodes, lungs, and bones, though thyroid cancer can spread to other areas of the body.

Follicular cancer is much rarer than papillary cancer but remains the second-most common form of thyroid cancer. Most people respond well to treatment and have positive outcomes. Follicular cancer is more aggressive than papillary and often invades the vascular system, which can lead to metastases in the lungs and bones. Even so, most individuals with this form of thyroid cancer do well with appropriate treatment. The majority of individuals diagnosed in early stages can be cured, and those in later stages have a positive prognosis, although reoccurrence is possible.

Medullary thyroid cancer, an undifferentiated thyroid cancer, is an uncommon, slow-growing cancer, which typically can be controlled if caught and treated before it metastases (spreads) to the rest of the body. Medullary cancer may run in families, passed from parent to child through changes in the genes. Outcomes for medullary thyroid cancer are dependent on how extensive the cancer has spread and how well the individual responds to treatment.

Anaplastic thyroid cancer is the rarest form of thyroid cancer but has the poorest outcome. Anaplastic thyroid cancer tends to occur most commonly in those over 60, and cancer cells grow and spread quickly. This type of cancer is hard to control and does not respond easily to treatment.

Symptoms and Detection
Thyroid cancer usually is diagnosed when a nodule, or mass, is found on the thyroid. Most nodules are benign, with between 10 and 30 percent being cancerous. Most cases of thyroid cancer are found during a standard doctor’s appointment, when a mass is felt or seen in the throat or neck. Thyroid cancer is usually painless, though in more advanced cases, nonspecific symptoms also may be present, including difficulty swallowing, difficulty breathing, or shortness of breath and persistent hoarseness.

If a mass is found during a physical exam, typically it is followed by tests including a neck ultrasound and needle aspiration. Blood work often is
used to identify issues in thyroid functioning. Other tests that may be done include chest X-rays, computed tomography (CT) scans, and thyroid scans to check for the extent of the cancer and to determine if it has spread to other parts of the body.

Treatment
Once identified, thyroid cancer is treated through surgical removal of the thyroid. Radioactive iodine often is used a few weeks after surgery to destroy any remaining thyroid tissue. The thyroid gland absorbs iodine, and a dose of radioactive iodine will destroy thyroid tissues. Other forms of treatment may be used, especially if thyroid cancer has metastasized throughout the body.

Conclusion
Thyroid cancer is a primary cancer of the thyroid, which can occur in any age group, but is very rare in children and adolescents and occurs more frequently in older individuals. Most forms of thyroid cancer are identified during routine health visits after a nodule has been identified and biopsied (most nodules are benign). Treatment for thyroid cancer is typically surgery followed by radioactive iodine, and long-term prognosis for those with thyroid cancer is generally positive, with favorable outcomes in most cases, including the possibility of a cure, especially for those under 45 years old, in early stages, and with the most common two forms (papillary and follicular). Thyroid cancer is rarely found in children.

Bridget Lepore
Kean University

See Also: Parathyroid Cancer: Radiation Therapy; Thyroid Cancer, Childhood.

Further Readings
Thyroid Cancer, Childhood

for the large majority of thyroid cancers, or undifferentiated (having abnormal cells lacking typical cell structure), including medullary and anaplastic thyroid cancer. These four main types of thyroid cancer are described by the appearance of the cells using a microscope.

Papillary cancer is the most common form of thyroid cancer in both adults in children, accounting for more than 85 percent of new cancer diagnoses in adults and children. This form of cancer begins in the follicular cells and grows slowly. The risk of papillary cancer increases with exposure to external radiation (most commonly from medical radiation), although some researchers believe that carcinogens may affect the thyroid and increase the chance of thyroid cancer. Genetic mutations also have also been linked to thyroid cancer of all types. The prognosis for papillary cancer, when diagnosed early, is very positive, with a strong possibility of a cure. Many children with papillary thyroid cancer will have metastases (cancer that has spread to other parts of the body), most commonly to the lymph nodes of the neck. Between 10 and 20 percent of these will have metastases that have spread elsewhere, most commonly to the lung. In spite of this, children typically respond well to treatment with a high possibility of a cure with appropriate treatment.

Follicular cancer is much less common, even rarer in children, and is a slow-growing cancer in the follicles. Diagnosed early, children respond well to treatment, with positive outcomes, although more aggressive treatment may be required due to the fact that follicular cancer is more aggressive and often invades the vascular system, which can lead to metastases in the lungs and bones as well as other areas of the body. Even so, children with this form of thyroid cancer do well with appropriate treatment, most with a cure, though recurrences is possible.

Medullary thyroid cancer is an uncommon, slow-growing cancer, which typically can be controlled if caught and treated before it spreads to the rest of the body. Medullary cancer may run in families, passed from parent to child through changes in the genes. Medullary cancer typically requires more aggressive treatment and has a higher risk of recurrence, though most children with this form of cancer respond well to treatment.

Anaplastic thyroid cancer, which is not found in children, is a very uncommon, aggressive, and highly lethal form of thyroid cancer.

Symptoms and Detection
Thyroid cancer is usually diagnosed when a nodule, or mass, is found on the thyroid. Most nodules are benign, but between 10 and 30 percent of all nodules are cancerous. Most cases of thyroid cancer are found during a standard doctor’s appointment, when a mass is felt or seen in the throat or neck. Thyroid cancer is usually painless, though in more advanced cases, symptoms may be present including difficulty swallowing, difficulty breathing, or shortness of breath and persistent hoarseness.

If a mass if found during a physical exam, typically it is followed by tests including a neck ultrasound and needle aspiration. Blood work is often used to identify issues in thyroid functioning. Other tests that may be done include chest X-rays, computed tomography (CT) scans and thyroid scans to check for the extent of the cancer and to determine if it has spread beyond the thyroid.

Treatment
Treatment for thyroid cancer in children is the same as that in adults. Once identified, thyroid cancer usually is treated through surgical removal of the thyroid. Radioactive iodine often is used a few weeks after surgery to destroy any remaining thyroid tissue. The thyroid gland absorbs iodine, and a dose of radioactive iodine will destroy thyroid cells, including cancer cells.

Thyroid cancer usually responds readily to therapy, with positive outcomes for the majority of those diagnosed. Thyroid cancer can reoccur, and those diagnosed and treated for thyroid cancer must be monitored throughout their lives.

After thyroid removal, patients must go on levothyroxine (thyroid hormone replacement therapy) in order to maintain their health. Levothyroxine also suppresses thyroid stimulating hormone (TSH), which helps in preventing recurrance of cancer. Children typically receive a dose of levothyroxine, which is measured to keep TSH in the lower normal range in order for optimal health and growth.

Conclusion
Thyroid cancer is a rare cancer in children, occurring slightly more frequently in adolescents, especially females, that responds well to treatment with a high possibility of a cure. Treatment of thyroid cancers typically involves surgery followed by radioactive iodine and then hormone replacement.
Individuals with a history of thyroid cancer need frequent monitoring throughout their lifetime as thyroid cancer can reoccur and usually presents few symptoms. Some cases of thyroid cancer can be prevented by protective measures during radiation exposure and proper dietary iodine levels.

Bridget Lepore  
Kean University

See Also: Childhood Cancers; Parathyroid Cancer; Thyroid Cancer.

Further Readings

Tobacco in History

The smoking of tobacco first took place as early as 5000 B.C.E. and grew over time from its roots in the Americas to a worldwide phenomenon. Struggles over the cultivation and sale of tobacco have shaped and colored many other significant events throughout history, including wars, slavery, territorial disputes, and trade battles. Across time and place, tobacco has been used in multiple cultures for religious purposes and pleasure. The sale and marketing of tobacco has been and remains a major source of global revenue. Although German scientists identified a link between tobacco smoking and health as early as the 1920s, this practice continues in much of the world, causing a variety of health problems. As the link between tobacco and a variety of health concerns, including cancer, has grown, efforts to reduce its availability or ban it outright have grown.

Background
Tobacco was first cultivated as a crop in South America approximately 7,000 years ago. Tobacco often was used as part of shamanistic religious rituals, with it being burned as other civilizations burned incense during religious rituals. Over time, the use of tobacco expanded to include smoking the substance, either by itself or in combination with various hallucinogenic drugs. Tobacco also was seen as having certain medicinal benefits and was sometimes used in an attempt to ameliorate a variety of conditions, such as earaches, toothaches, and as a cure for the common cold.

European explorers first were introduced to tobacco by the indigenous Americans, and its use soon became popular with them. Tobacco use was introduced to Europe around 1600 C.E. and met with widespread opposition from political and religious leaders. This opposition led to a variety of measures intended to curtail its use, from large taxes being assessed upon the sale of tobacco to outright bans of the substance. Despite these efforts, however, tobacco use had become widespread by the mid-17th century. In London alone, more than 7,000 tobacco shops were doing business, and a variety of other outlets for its sale existed across the European continent. Snuff and pipe tobacco were the most popular ways of using tobacco, although other ways of consuming the product were also known.

John Rolfe, an early settler in the English community of Jamestown in Virginia, is credited as being the first European to cultivate tobacco as a cash crop. Strong demand in Europe soon led to tobacco being planted widely in Virginia and other American colonies. The tendency of tobacco to rapidly deplete the soil in which it is planted, however, led to a push from many tobacco farmers for further westward expansion as fresh soil was needed for tobacco cultivation.

As a labor-intensive crop, tobacco also presented planters with labor issues as it was difficult to secure the number of workers needed while still permitting its cultivation to be profitable. Indentured servants were used first, and then slaves were imported from Africa. Tobacco generated large tax revenues for the British government, sometimes in excess of £300,000 pound per year. The American Revolution greatly affected the tobacco market as the British significantly interrupted the export of tobacco to Europe. This caused many farmers to
turn to crops other than tobacco for the duration of the war.

**Growth Era**

In the years following the American Revolution, changing tobacco usage patterns affected tobacco farming. Certain European markets for American tobacco, such as Great Britain and France, never recovered from the blockades produced as a result of the war, and consumers there turned to other sources, such as Turkey and Africa, for tobacco. Domestic use of tobacco in the United States, however, grew markedly, and chewing tobacco became increasingly popular with this market. Overall, smokers began to switch from pipes to cigars, which slightly altered the types of tobacco planted. Cigarettes, which had been around since the early 19th century, saw an exponential increase in demand after 1881, when a machine that could manufacture them was created, greatly reducing their cost. The ability to produce cigarettes inexpensively and in large quantities led to the rapid growth of cigarette manufacturing companies. The American Tobacco Company, for example, had annual sales of approximately $25 million in 1890, a figure that had grown to exceed $300 million a decade later.

This growth in cigarette sales, combined with the development of color lithography, permitted tobacco advertising to grow exponentially during the 20th century. Advertising agencies engaged by the tobacco companies created slogans and advertising campaigns for specific cigarettes, with specific brands attempting to appeal to certain segments of the market. During the first decades of the 20th century, most advertisements were print based, and newspapers and glossy magazines were filled with these. Beginning during the 1930s, tobacco companies also began sponsoring specific radio shows, and certain celebrities became affiliated with certain brands of cigarettes, such as Jack Benny with Lucky Strike and Bing Crosby with Chesterfield. The use of endorsements from famous men and women was seen as a way of appealing to the public’s desire to affiliate with those seen as glamorous and successful. As television became popular after World War II, cigarette advertisements became common on that medium, with various brands seeking to create images that supported use of their cigarettes.

**Awareness of Health Concerns**

As early as the 1920s, German scientists became aware that certain health conditions, including lung cancer, heart disease, and emphysema, were strongly linked with tobacco use. On the basis of these studies, the National Socialist (Nazi) government of Adolf Hitler took a strong antitobacco stance. During this era, the Germans banned smoking on trams, buses, and trains, and organized antitobacco lectures for the public. The Nazis also placed severe restrictions upon advertisements for tobacco products and limited smoking in restaurants and other public spaces. Although forward thinking, Germany’s defeat in World War II, and its relative isolation beforehand, limited the spread of
this campaign to other nations. In the postwar era, German consumption of tobacco increased greatly.

Beginning in 1950, British physician Richard Doll began publishing a series of studies that strongly linked tobacco smoking to lung cancer. Unlike the earlier German studies, this research was influential in the United States and elsewhere. The popular American magazine *Readers Digest* ran an article disclosing this link to the general public in 1952. The health risks associated with tobacco smoking were highlighted in the widely disseminated British Doctors Study, which compiled more than 20 years of research linking tobacco smoking to cancer. In 1964, the United States surgeon general issued a report on smoking and health that greatly increased American public awareness of the health risks of tobacco. The Federal Communications Commission (FCC) began requiring television and radio broadcasters to air antismoking messages in response to cigarette commercials, and in 1971, the United States Congress banned tobacco advertising from the airwaves. During the next three decades, cigarette advertising was limited to newspapers, magazines, and billboards.

Although litigants had tried to sue the tobacco companies for health problems that had arisen as a result of their smoking cigarettes manufactured by these entities, these lawsuits were largely unsuccessful through the 1980s. During the 1990s, however, a series of lawsuits were brought by state's attorney generals in an attempt to defray the medical costs state and local governments had been forced to bear as a result of their residents smoking cigarettes. These lawsuits resulted in what is known as the Tobacco Master Settlement Agreement, entered into among the attorney generals of 46 states and R. J. Reynolds Tobacco Company, Brown & Williamson, Lorrillard Tobacco Company, and Philip Morris Companies. In exchange for an exemption from tort liability from private lawsuits, the tobacco companies agreed to pay out more than $200 billion over a 25-year period and to curtail or cease most advertising of their products. The Tobacco Master Settlement Agreement has created a fund that sponsors antismoking campaigns and smoking cessation programs.

Globally, tobacco is used daily by more than 3 billion people, including 49 percent of men and 11 percent of women. In the United States, rates of smoking have declined over the past five decades, from a high of approximately 40 percent of the population in 1965 to fewer than 20 percent of the adult population today. This decline has been especially significant among affluent, well-educated men. Tobacco use remains relatively high among lower-income groups, and among younger smokers, the percentage of women smoking is now nearly identical to the rate of men. Continued governmental efforts exist to curtail tobacco use, and the Federal Drug Administration (FDA) recently has been permitted to regulate tobacco sales.

---

Stephen T. Schroth
Towson University

**See Also:** American Cancer Society; American Lung Association; Environmental Tobacco Smoke; Smoking and Society; Tobacco Smoking.

**Further Readings**


---

**Tobacco Smoking**

According to reports by the United States surgeon general, cigarette smoking is a major cause of cancer mortality in the United States. Nearly one in five deaths in the United States can be attributed to tobacco use. Tobacco smoking is also the most preventable cause of death in this country because it is a choice to smoke.

**Centers for Disease Control and Prevention Statistics**

According to the Centers for Disease Control and Prevention (CDC) report, about 42 million, or
18 percent, of all adults were cigarette smokers in 2012. More cigarette smokers were in younger age groups in 2012, although these figures might be influenced by early deaths in older smokers. There has been a new trend in smoking among high school students. About 14 percent of high school students were smoking cigarettes in 2012, and an additional 13 percent of high school students were smoking cigars. The cigars have changed in appearance, looking more like cigarettes. They cost less and come in flavors, which make them more appealing to a younger population. Adolescents are smoking several a day and inhaling the smoke like they would cigarettes.

Tobacco smoking has a high mortality rate and is responsible for the deaths of about half of all Americans who keep smoking. In the United States, about 480,000 people die annually from illnesses related to tobacco use. Smoking cigarettes kills more Americans than alcohol, car accidents, suicide, acquired immune deficiency syndrome (AIDS), homicide, and illegal drugs combined. It is also linked to many forms of cancer and is responsible for about 30 percent of all cancer deaths. Smoking increases the risk of developing cancers such as lung, larynx, oral cavity, nose and sinuses, throat, esophagus, stomach, pancreas, cervix, kidney, bladder, ovary, colorectal, and acute myeloid leukemia. Lung cancer is one of the hardest cancers to treat and is the leading cause of cancer death. Tobacco smoking is responsible for about 87 percent of lung cancer deaths in men and 70 percent in women. Religious groups that promote or require nonsmoking in its members have much lower rates of lung cancer and other smoking-related cancers than other religious organizations. Sadly, as high as these figures are, cancer accounts for less than half of the deaths related to tobacco smoking each year.

Tobacco smoking also causes other health problems, some of which are deadly, including heart disease, aneurysms, bronchitis, emphysema, and stroke. It also can negatively affect female reproductive health and the health of an unborn fetus. Tobacco smoking has been associated with increased risk of miscarriage, premature birth, stillbirth, low birth weight, birth defects, and sudden infant death syndrome. Smoking can make pneumonia, asthma, and other respiratory conditions worse and can exacerbate other health problems, including gum disease, cataracts, bone thinning, hip fractures, and peptic ulcers. Smoking can cause or worsen poor blood flow in the arms and legs.

The smoke from cigarettes that is inhaled by nonsmokers, or secondhand smoke, also can have harmful health effects on those exposed to it. Adults and children can acquire health problems just from breathing in the secondhand smoke. Smoking affects longevity and quality of life. Tobacco smoking shortens the lives of smokers. Male smokers' lives are shortened by 13.2 years and female smokers' lives by 14.5 years. Tobacco smokers are more likely to die between the ages of 35 and 69. When individuals stop smoking before the age of 40, they reduce the risk of tobacco smoking-related fatalities by 90 percent.

In addition to tobacco smoking-related deaths, other less-fatal health issues can arise, including chronic bronchitis, emphysema, heart attacks, strokes, and cancer. Some studies also have linked tobacco smoking with sexual impotence in male smokers. Smoking-related illnesses limit a person's daily activities due to shortness of breath or trouble breathing, which can reduce the individual's energy or ability to engage in activities. When someone quits smoking, especially at a younger age, tobacco smoking-related disability risks are greatly reduced.

Misconceptions of Tobacco Smoking

All types of tobacco smoking are dangerous and addictive. While it is important to cut down on the number of cigarettes smoked, it still poses a risk. Some research indicates that smoking even one to four cigarettes a day still increases the risk of serious health problems, including heart disease and the likelihood of dying at a younger age. Light and low-tar cigarettes also pose serious health risks. Many individuals do not understand this and assume that these types of cigarettes are safer for them to smoke. As a result, the United States Food and Drug Administration banned the use of the words light, mild, and low as descriptors for cigarettes. This ban, however, has not been extended to the cigarette-like cigars.

Some individuals erroneously believe that hand-rolled cigarettes are a cheaper and healthier way to smoke, but they are no safer than commercial brands. The opposite seems to be true. Longtime hand-rolled cigarette smokers have been shown to have an increased risk of developing cancers of the larynx, esophagus, mouth, and pharynx when
compared with smokers of commercially made cigarettes. Cigarettes advertised as all natural are marketed as having no chemicals or additives and are rolled with 100 percent cotton filters. These products do not have a basis for health claims and contain agents that can cause cancer. There are also toxins that come from the burning of the tobacco, including tar and carbon monoxide. This is also true of herbal cigarettes that do not contain tobacco.

Menthol cigarettes are no safer and might present an increased risk. The added menthol tends to produce a pleasant sensation in the throat when the smoke is inhaled. This decreases the dry feeling in the throat often present in smokers. As a result, smokers tend to inhale more deeply and hold the smoke longer. Menthol cigarettes account for about one-third of all cigarettes sold in the United States, and they tend to be a popular option with child and adolescent tobacco smokers. The menthol tends to make cigarettes seem smoother and less harsh, making them easier to smoke for first use and harder to quit.

Chemicals in Tobacco Smoke

Tobacco smoke is harmful to both smokers and nonsmokers, causing various forms of cancer and other health issues previously listed. When smokers quit, they reduce the health risks caused by exposure to tobacco smoke because they are no longer ingesting harmful chemicals. Tobacco smoke contains chemicals that can negatively impact the health of smokers and nonsmokers who breathe in secondhand smoke, including hydrogen cyanide, carbon monoxide, ammonia, arsenic, formaldehyde, and cadmium. There are 250 known harmful chemicals in tobacco smoke, and at least 69 are currently believed to be cancer-causing agents.

Nicotine is a substance that is present naturally in the tobacco plant and is considered the primary source of addiction to tobacco products. The nicotine enters the lungs as smokers inhale and is quickly absorbed into the bloodstream, where it travels to the brain. This process occurs in just a few seconds, releasing brain chemicals in response. Tobacco smokers who inhale deeply are at greater risk than those who smoke a higher nicotine content and do not inhale as deeply. The way the person smokes the tobacco is more important than the content of the nicotine in the tobacco for determining how much nicotine gets into the body. The nicotine is absorbed in the lungs and the lining of the mouth, and inhaling deeply through frequent puffs presents the greatest absorption of nicotine.

Secondhand Smoke

Secondhand smoke is a combination of smoke exhaled by a smoker and smoke given off by the burning tobacco product. Secondhand smoke causes lung cancer in nonsmoking adults as they inhale the smoke of others. It is also implicated in an increased risk of heart disease and can cause low birth weight in pregnant women who inhale secondhand smoke. Children who are exposed to secondhand tobacco smoke face an increased risk of sudden infant death syndrome (SIDS), ear infections, colds, pneumonia, bronchitis, and more severe asthma. It can also slow the growth of the child’s lungs, causing him or her to have respiratory issues.

Tobacco Facts

Cigarette smoking is responsible for approximately 480,000 deaths each year in the United States, including approximately 49,000 deaths related to breathing in secondhand smoke. Lung cancer is the leading cause of cancer death among both men and women in the United States, and 90 percent of lung cancer deaths among men and approximately 80 percent of lung cancer deaths among women are due to smoking. Smokers also have an increased risk of heart disease and heart attacks. They are as much as six times more likely to develop these problems, and the risk increases with the number of cigarettes smoked. Smoking also causes most cases of chronic lung disease.

There has been an overall decline in tobacco smoking between 2005 and 2011 for adults between the ages of 18 and 24 years. While the decline is significant, there are still many people who are smoking. In an effort to further reduce tobacco smoking, policy makers have considered increasing the price of tobacco products, implementing smoke-free laws in workplaces and public places, increasing antitobacco campaigns in the media, increasing incentives to help quitting, and enforcing restrictions on tobacco advertising.

Although comprehensive tobacco control programs have been effective in decreasing tobacco use in the United States, they do not receive as much funding as they need. The Centers for Disease Control and Prevention (CDC) recently recommended what it believed to be appropriate annual funding levels for each state’s comprehensive tobacco control program. Unfortunately, only two states chose to budget in tobacco control programs at
Tobacco-Related Exposures

Exposure to tobacco is strongly linked to cancer. Such exposure can occur through ingestion of tobacco related products such as cigarettes, cigars, and smokeless tobacco. Exposure also can occur through secondhand smoke or through exposure to tobacco plants in the environment, such as the workplace. Despite the fact that death from tobacco related exposure is highly preventable, tobacco exposure causes thousands of deaths from various diseases and cancers each year.

Epidemiology

Approximately half of those who continue to smoke will die of a smoking-related illness, disease, or cancer. Cigarette smoke is responsible for approximately one out of every five deaths in the United States. The overall mortality in the United States is approximately three times higher among smokers than nonsmokers. The primary causes of the increased mortality rate among smokers are cancers and diseases related to smoking, such as respiratory and vascular diseases. It is estimated that 159,260 deaths from lung cancer will occur in 2014. Men who smoke are 23 times more likely to develop lung cancer than nonsmoking men. Women who smoke are 13 times more likely to develop lung cancer than nonsmoking women. Smoking also is related to cancers of the lip, oral cavity, pharynx, esophagus, pancreas, larynx, cervix, bladder, liver, stomach, ovaries, colon, and kidneys. Exposure to tobacco through cigarette smoke is also the cause of many diseases, such as chronic obstructive pulmonary disease and heart disease. A smoker who experiences cardiac arrest is at a greater risk of death than a nonsmoker who experiences cardiac arrest. Smokers are also at an increased risk of strokes and aneurysms than nonsmokers. Worldwide, exposure to tobacco results in 6 million premature deaths annually.

See Also: Drugs; Food and Drug Administration; Smokeless Tobacco; Tobacco in History.

Further Readings


Some chemicals found in tobacco smoke include cyanide, benzene, formaldehyde, methanol, acetylene, ammonia, tar, carbon monoxide, and nitrogen oxide. Nonsmokers also may be exposed to these chemicals through secondhand smoke. More than 7,000 cases of lung cancer and more than 33,000 cases of heart disease occur each year in the United States as a result of secondhand smoke.

The life expectancy of smokers is about 10 years shorter than it is for nonsmokers. The use of smokeless tobacco is linked to an increase in the risk of death from an irregular heartbeat. Secondhand smoke is responsible for about 42,000 deaths in the United States each year.

Middle-aged individuals who smoke are four times more likely to die from coronary heart disease than those who do not smoke. In both men and women, smoking also increases the risk of dying from emphysema, bronchitis, cancer of the trachea, lung, and bronchus. Women who smoke often have lower bone density and are therefore at greater risk of broken bones and hip fractures. Smoking weakens blood flow and is linked to the development of an abnormal heartbeat.

Many childhood diseases are related to tobacco exposure in the womb, often resulting from smoking or exposure to secondhand smoke during pregnancy. Smoking during pregnancy increases the risk of the child developing lung cancer, heart disease, emphysema, asthma, and allergies. Smoking during pregnancy is related to an increased risk of low birth weight, premature births, and infant deaths. Approximately 5 percent of infant deaths are caused by smoking during pregnancy. Infants who are born to parents who smoke have an increased risk of heart defects, cleft lip or palate, and other birth defects. Infants also can be exposed to tobacco related carcinogens through breast milk in mothers who smoke or use tobacco products. Secondhand smoke damages cells in the same way smoking does. Secondhand smoke exposure is dangerous for pregnant women, and it has been linked to an increase rate of miscarriages.

Smoking and Other Forms of Tobacco Consumption

Tobacco products such as cigarettes, cigars, and smokeless tobacco have been linked to lung, head, and neck cancers. The more an individual uses tobacco products, the greater the cancer risk.

Smoking cigarettes is one of the leading causes of cancer, including lung cancer. It is estimated that 221,200 new cases of lung cancer will occur in 2015. Smoking increases the risk of developing lung cancer by more than 25 times. Smoking is responsible for about 87 percent of lung cancer deaths in men and 70 percent of lung cancer deaths in women. Smoking increases the risk of developing cancer by damaging the lungs, weakening the immune system, and causing changes in the genes. Tobacco use is responsible for approximately 30 percent of all cancer deaths.

Those who quit smoking have a greater chance of recovering from cancer than those who do not quit. Individuals who have cancer and who continue to smoke may not respond well to treatment and increase their risk of developing secondary cancer.

Cigars, as well as cigarettes, contain many carcinogens, and cigar smoking is related to cancers of the lung, mouth, throat, larynx, esophagus, and pancreas. Like cigarettes and cigars, smokeless tobacco products contain carcinogens. The use of smokeless tobacco increases the risk of developing cancers of the mouth, throat, pancreas, and esophagus.

Snuff is ground tobacco packaged in pouches or cans and is placed between the lower lip and gum. Nicotine in snuff is absorbed through tissues in the mouth. Snus is a common form of finely ground, moist snuff. The use of snus is related to an increased risk of pancreatic cancer. Snus users often develop lesions in the mouth, where the product is placed. All forms of snuff and smokeless tobacco contain carcinogens.

Cancers related to smokeless tobacco include cancers of the mouth, tongue, cheek, gum, throat, esophagus, stomach, and pancreas. In addition to various forms of cancer, smokeless tobacco also is linked to an increase in risk of heart disease, heart attacks, stroke, high blood pressure, tooth loss, tooth decay, cavities, bad breath, tooth abrasions, bone loss around the teeth, receding gums, leukoplakia, and an increased addiction to nicotine.

Secondhand Smoke

Secondhand smoke exposure can occur in the home or the workplace, and such exposure increases the risk of lung cancer by 20 to 30 percent. Even for nonsmokers and those who have never smoked, exposure to secondhand smoke can cause lung cancer. Nonsmokers who are exposed to secondhand
smoke inhale the same carcinogenic substances as those who smoke. Secondhand smoke is responsible for about 3,400 lung cancer-related deaths each year in the United States. Exposure to secondhand smoke can damage cells, even if the period of exposure was brief. The longer a person is exposed to secondhand smoke, the greater the risk of developing lung cancer. Secondhand smoke is also responsible for about 42,000 deaths each year in the United States as a result of heart disease. Secondhand smoke results in exposure to nicotine and toxic chemicals. Asthma is commonly developed by children who are exposed to secondhand smoke.

**Workplace Exposure to Tobacco**

Green tobacco sickness (GTS) is a form of acute nicotine poisoning resulting from absorption of nicotine through the skin as a result of picking tobacco and working in tobacco fields. GTS is a unique occupational hazard for farmworkers. Symptoms of GTS include nausea, vomiting, headaches, and dizziness. Some studies indicate that more than 40 percent of farmworkers reported having suffered from GTS at least once during the harvesting season. Even for farmworkers who do not smoke cigarettes, those who work in tobacco fields have levels of nicotine in their bodies equivalent to levels in regular smokers. The dizziness and nausea associated with GTS can become so severe that workers often vomit in the tobacco fields. Working with wet tobacco or wearing wet clothing while working increases the risk of GTS. GTS is highly preventable and could be avoided if farmworkers were provided with the proper protective clothing. Children and adolescents are at a greater risk of GTS than adults.

**Symptoms**

Smoking is the number one risk factor for developing lung cancer. There are many symptoms of lung cancer, including: coughing, shortness of breath, hoarseness, trouble breathing, wheezing, chest pain, fatigue, weight loss, and coughing up blood. Swollen or enlarged lymph nodes between the lungs also sometimes occur as symptoms of lung cancer. Often, symptoms do not occur until the cancer is advanced, and not all those who have lung cancer will exhibit all of these symptoms.

Exposure to tobacco products increases the risk of heart disease. Symptoms of heart disease include chest pain, shortness of breath, pain or numbness in the arms and legs, fatigue, and irregular heartbeat.

Laryngeal cancer also is commonly related to tobacco products. Symptoms of laryngeal cancer include a sore throat, constant coughing, trouble breathing, trouble or pain when swallowing, ear pain, weight loss, or a lump in the neck.

Likewise, esophageal cancer can be caused by tobacco or cigarettes. Symptoms of esophageal cancer include difficulty swallowing, weight loss, chest pain, fatigue, pressure or burning in the chest, coughing or hoarseness, frequent choking, indigestion, or heartburn. However, the early stages of both laryngeal cancer and esophageal cancer may cause no signs or symptoms.

Tobacco use has also been associated with recurrence and death from gastric cancer, even after initial surgeries to remove the cancer.
Prevention
In the United States, smoking is responsible for approximately 90 percent of lung cancer deaths in males and approximately 80 percent of lung cancer deaths in females. Quitting smoking is the most effective way to prevent lung cancer and other forms of cancer related to tobacco exposure. Despite the dangers related to tobacco use, more than 20 percent of men and 15 percent of women smoke cigarettes in the United States. Quitting smoking before the age of 40 has been shown to reduce the risk of death from a tobacco exposure by approximately 90 percent. In addition to quitting smoking, secondhand smoke also should be avoided.

Regular medical checkups and cancer screenings can help detect early signs of cancer related to tobacco exposure. Early detection of cancer can increase the possibility of remission.

Treatment
Treatment for tobacco-related cancer depends on the stage at which the cancer is first identified. Treatment options include surgery, radiation therapy, chemotherapy, various drugs, or a combination of these treatments.

Depending on the type and stage of the cancer, surgical removal of the cancer is sometimes a possible treatment. Additionally, certain drugs can be used to shrink lymph nodes and kill cancer cells. Radiation therapy uses radiation to kill cancer cells and prevent cancer from spreading.

It is important to quit smoking during treatment as exposure to tobacco can interfere with the success of the treatment. Secondhand smoke and smokeless tobacco products also should be avoided. It is important for both patients and clinicians to play a role in reducing the burden of tobacco-related cancers by engaging with tobacco cessation treatment.

Mark D. Sherry
Laurie Michaels
University of Toledo

See Also: Oral Cavity Cancer, Lip and; Lung Cancer, Non–Small Cell; Smokeless Tobacco; Tobacco Smoking.

Further Readings

Togo

The Republic of Togo is situated in western Africa. It is the 33rd most populous country in Africa and 108th globally, with a population of more than 5.6 million. French is the statutory national language, and there are 39 living languages spoken in Togo by respective ethnic groups. The most widely spoken include Ewe, Kabiye, Moba, Moore, and Nawdm. Each ethnic group has its own traditions of ethnomedicine. For example, a traditional healer who uses medicinal plants for treating cancers and other ailments is called agbawola in Ewe, lintou in Kasem, and tip-tiim in Moore.

Many in Togo typically would rely upon traditional medicines more than modern pharmaceuticals for dealing with health concerns. This is due to the fact that traditional medicines are generally more accessible and less expensive as well as that many have greater familiarity with and trust in traditional practices. Accordingly, there are many traditional medicinal preparations used in Togo. Most of these incorporate use of local plant materials, many of which have been shown to have medicinal properties in laboratory studies.

For example, an extract from Cymbopogon citratus demonstrated cytotoxic activity. Research also suggests that use of certain plants may help protect against cancer by reducing oxidative stress and stimulating enzymes and other processes that help the
body fight carcinogens. For example, an extract from leaves of *Annona senegalensis*, as well as extracts from *Momordica charantia*, *Parinari curatellifolia*, and *Entada africana* demonstrated antioxidant activities.

Medicinal plants are used widely in Togo to treat cancers and associated conditions. For example, breast cancer traditionally is treated by rubbing the breast with grated twigs of *Cissus quadrangularis*, which the Kabre call *kodia*.

There are serious deficiencies of modern pharmaceutical supplies, as opposed to traditional preparations, and in modern medical services for cancer and similar conditions. According to the World Health Organization's Health System Response and Capacity, as of 2010, there was no general availability of either chemotherapy or radiotherapy in the public health system in Togo. Togo is a signatory to the Single Convention on Narcotic Drugs, Convention on Psychotropic Substances, and UN Convention Against Illicit Traffic in Narcotic Drugs and Psychotropic Substances; consequently, laws exist to control narcotic and psychotropic substances and precursors. Annual consumption of controlled substances is regulated to curtail abuse. Accordingly, annual consumption of morphine is 0.071 milligram per capita (mg/capita), fentanyl 0.000011 mg/capita, pethidine 0.036 mg/capita, and phenobarbital 82.1 mg/capita. These factors make providing palliative care for cancers and other conditions very difficult.

The average number of cancer cases annually are 101.5 per 100,000 population. In a review of more than 5,000 cancer cases in Togo from 1984 to 2008, the average annual frequency was 210 cases. These had a male-to-female sex ratio of 0.9; average age of occurrence was 46.9 for males and 43.8 for females, with an overall average age of occurring at 45.3. The most frequent cancers for men were prostate cancer at 12.9 percent, non-melanoma skin cancer at 10.4 percent, and gastric cancer at 10.3 percent.

With respect to prostate cancer in 2002, the estimated age-standardized rate of new cases annually was 19.3 per 100,000 population, and estimated age-standardized number of deaths annually was 16.0 per 100,000; by 2011, prostate cancer reached 0.60 percent of total deaths, which accounted for an age-standardized death rate of 19.96 per 100,000, which ranks Togo 48th globally. In west Africa, the region to which Togo belongs, it is estimated that about 23.3 percent of women in the general population harbor the human papillomavirus (HPV) at any given time and that 51.4 percent of invasive cervical cancers are attributable to HPV 16 or 18. The most common cancers in children were Burkitt lymphoma at 27.9 percent and retinoblastoma at 8.5 percent of the cases; average age of occurrence of childhood cancers was 8.1 years with a sex ratio of 1.5 (218 cases in boys, 146 in girls). Histologically, carcinomas accounted for 68.1 percent of cases, sarcomas for 11.2 percent, and non-Hodgkin's lymphomas for 12.6 percent.

Despite the abundance of traditional and modern medical products and services, health problems are endemic in Togo. The 10 leading causes of death, in rank order, are malaria, human immunodeficiency virus (HIV) and autoimmune deficiency syndrome (AIDS), anemia, cerebrovascular disease, pneumonia, septicemia, hypertension, cardiac diseases, meningitis, and diarrhea. For example, there are an estimated 110,000 people living with HIV in Togo, which ranks it 30th highest in Africa and 47th globally. Debate continues on the relative risks in Africa for respective cancer types for those infected with HIV. Furthermore, according to the World Health Organization's Global Health Observatory Data Repository, in 2008, the age-standardized estimates of deaths from all cancers was 86 per 100,000 for males and 91 per 100,000 for females. As a consequence, life expectancy is 53.05 years, which ranks Togo 90th in Africa and 189th globally. There is a clear and urgent need for improved cancer awareness, early detection programs, and health services infrastructure in Togo.

Victor B. Stolberg
*Essex County College*

**See Also:** Benin; Developing Countries; Ghana.

**Further Readings**


Town Plans

Town planning, more commonly referred to as urban planning or simply planning, is the professional discipline tasked with making civic improvements. During the past decade, the dialogue between the urban planning and public health sectors became increasingly intersected as research revealed the links between disease and place.

Many of these links were discovered with the help of new information technology, particularly geographic information systems (GIS), which uses geography as the common foundation. Allowing large and multiple datasets to be visualized, it has facilitated health data, including cancer, to more readily be examined within the context of the natural and built environments. These data and spatial layers, combined with socioeconomic data, provided new knowledge about housing, industry, and other planning issues affecting health status.

As a result, the planning and public health industries are converging around issues of population health. Additionally, planning tools are helping health practitioners examine cancer rates beyond the aggregate or merely in terms of race, gender, age, and income. With GIS software, they are now able to identify clusters of certain types of cancer and identify potential causes, such as industrial waste, air pollutants, housing proximity to cancer-causing agents, and so on. Industry, housing patterns, transit networks, and the location of public-good facilities (e.g., schools, hospitals, grocery stores, etc.) are all part of town planning. Understanding placement and proximity to carcinogens helps inform planning decisions and reduce risk of cancer as an unintended consequence of development.

The Historical Link Between Public Health and Town Planning

Planning dates to the beginning of civilization. In its most fundamental form, it is the attempt to create orderly human settlements while meeting the needs of the residents. This includes maintaining population health. For example, once it was discovered that corpses spread disease, cemeteries were relocated farther from water sources and housing. Function, more than form and aesthetics, were primary.

When new manufacturing processes led to the Industrial Revolution, cities grew quickly and exponentially. The lack of modern transportation forced workers to live within close proximity of factories, slaughterhouses, and other generators of pollution and carcinogens. The housing was often substandard and lacked sources of fresh air. Furthermore, these workers often lived long distances from open spaces and fresh air. In the late 1880s, social reformers, such as Jane Addams and Jens Jensen, worked to address the social and health needs of the ever-growing urban working class. Jensen, a landscape architect, helped design Chicago’s parks and fought for a park system that allowed workers to escape overcrowded, polluted areas without having to travel to the country. Although rarely credited in the history of town planning, he played a significant role in the field by arguing that people need to be connected to nature in order to be healthy. This was the same ideal behind the Garden City Movement, which was a 19th century town planning scheme aimed at using nature to buffer citizens from urban center industry.

By 1900, industrialization and rapid urban growth had compounded the problems of cities. Unsafe working conditions, overcrowded housing (often without fresh air access), sanitation, and other health risks led social reformers to push public health initiatives and the passage of housing statutes. This, in turn, led architects to become more involved with social needs through design. Shortly thereafter, planning emerged as an autonomous profession, and many of the early planners aimed to address all major urban components at
once. They were often reformers who held the belief that social and physical planning could not, and should not, be separated from one another. Eventually, social and physical planning separated as town planning increasingly became about design and the creation of purely functional places or beautiful spaces.

**Public Health and Planning**

Public health practitioners regularly utilize GIS to map data to understand patterns of disease, whereas planners use it for a variety of reasons. Some of these have direct and indirect impact on public health, such as location of health facilities, zoning between residential areas and industry, and maintenance of contaminated land and natural resources. While the technology is new, the use of mapping in health is not.

Epidemiology, the cornerstone of public health, is the medical specialty that studies patterns, causes, and effect of health and disease conditions in defined populations. In the mid-1800s, Dr. John Snow (considered the father of epidemiology) led the way in linking health to town infrastructure. During the 1854 London cholera outbreak, 500 people died within 10 days. Using simple mapping techniques, he identified water pumps as the source of the outbreak. This led to the construction of improved sanitation facilities throughout the world. Today, epidemiologists work with a variety of diseases, including cancer. With diagnosis data sets, they now use mapping technology to identify clusters of certain types of cancer. When overlaid upon planning maps, they can more readily identify causes of the disease or even the cause of a particular type of cancer. A classic case is that of breast cancer in Cape Cod, Massachusetts. Cancer data (1982–1990) showed an incidence rate up to 130 times higher than in other areas of the state, leading researcher to seek causation. Using other geographic data, they discovered the disease was linked to pesticides used in cranberry bogs, including former bogs that were now housing and industry sites.

**Planning and Cancer**

Cancer can be a direct or indirect consequence of planning decisions that shape places and how people function within them. A recent Centers for Disease Control (CDC)—funded study of 3 million malignant tumors in 16 states linked poverty with higher mortality cancers. This study claims to be the most comprehensive assessment of the relationship between cancer, socioeconomic status, and place. People living in census tracts with higher poverty rates were found to have a prevalence of rarer cancers with high mortality rates. Likewise, lower-income people are more likely to die of cancer. The researchers hypothesize that the disparities may be due to behavioral and economic factors, such as substance abuse and access to medical care or healthy foods. Access is increasingly a planning issue to guide private resources to better meet the needs of lower-income communities. It is also these types of data that have driven the environmental justice and social justice movements. These movements help raise the voice of those most likely to suffer negative consequences of development decisions.

While zoning was an early, effective tool for separating housing from industrial pollution, other advances and urban shifts have resulted in other public health concerns. For example, along with suburban development came industrial decentralization. Many of these former industrial sites provided the space for office buildings and large public housing developments.

Like the Cape Cod example, workers and residents on some of these sites have higher rates of certain types of cancer as well as other illnesses. As public health informs the planning industry, new statutes and practices are put into place. Among these are federally mandated environmental impact assessments, a formal process aimed at not just protecting the environment but mitigating environmental damage that could be detrimental to health. Health impact assessment is also an emerging methodology to deal specifically with potential population health effects. In fact, the CDC and American Planning Association partnered to develop a free Web-based training.

Economically driven, the private sector lacks the motivation to plan comprehensively; however, public-sector planning attempts to achieve this through master planning. The process is largely ideological as politics and private capital are often the drivers of decisions. Planners help guide and inform the decisions and regularly deal with natural resource management, transportation, utilities, industry, housing, and the location of health resources, from hospitals to healthy foods.
Toxic Mold

Mold is a type of fungus, distinct from yeasts in that molds are multicellular while yeasts are unicellular, and distinct from mushrooms in that molds are microbes, while mushrooms are the fruiting bodies of large funguses. All funguses are distinct from plants, belonging to a separate kingdom. Many molds are involved in the biodegradation of natural materials, and mold spores (the means by which they reproduce), molds themselves, and compounds produced by molds all may have adverse health effects on humans who come into contact with them or inhale them. Molds also have been the source of significant medical advances, though—penicillin, one of the first antibiotic drugs, is derived from penicillium mold, and molds of the Aspergillus species are used in the production of soy sauce, sake, Katsuobushi, and miso and help to preserve foods against bacterial spoilage. The powdery white mold Penicillium nalgiovense provides a similar service to Italian dry salami, and Geotrichum candidum provides the natural bloomy rind of Camembert cheese. More recently, cholesterol-lowering statins and immunosuppressant drugs have been derived from molds; cyclosporine, for instance, is used to prevent and treat graft-versus-host disease in bone marrow transplants of cancer patients receiving radiation treatments. It was derived from a fungus found in Norwegian soil. Other fungal derivatives are used as cytotoxins, antibiotics, antimalarials, diabetes treatments, and even as treatments for fungal infections.

Molds are present virtually everywhere. When they are able to grow unchecked, like in parts of buildings out of reach of cleaning (inside walls or under floorboards), the dense concentration of mold spores can be a serious health problem. Toxic mold refers to molds that produce mycotoxins, but otherwise harmless molds can still cause allergic reactions, irritation, respiratory problems, headaches, migraines, coughing, and sleep disorders when people regularly inhale too many of their spores. Outdoor molds are a contributor to seasonal allergies for many people, and indoor molds may be found in dark or humid areas of the house, especially those with poor ventilation.

Mycotoxins are secondary metabolites produced by molds. Many mycotoxins are produced by more than one kind of mold, and similarly, many molds produce more than one kind of mycotoxin. The evolutionary explanation for mycotoxins is not clear because they do not seem to be involved in the mold’s growth or development. Mycotoxin levels generally only become high enough to matter when the conditions are right for the mold to thrive and form colonies. While most houses, especially in

Even within the planning field, the debate continues about whether the ultimate goal of planning is to create beautiful cities or generate better quality of life for residents and visitors. Inside this debate, planners are becoming increasingly specialized, and health planning is emerging as a new category. Today, much of the town planning conversation around health aims at increasing physical activity (e.g., bike lanes, increasing walkability, and improving park utilization) and improving living conditions in low-income communities (e.g., access to community facilities, healthy food options, and crime reduction). With more emphasis on the intersection between planning and public health, planners are increasingly challenged with creating attractive physical spaces that also meet the economic and social needs of people. Generating positive health impacts and mitigating negative health consequences and health disparities has now become part of the complicated work of designing places.

Denese M. Neu
National Louis University–Chicago

See Also: Daily Life; Environmental Justice and Cancer; Exercise; Poverty.

Further Readings
humid climates, likely have some amount of mold growing somewhere in them, and that may include a mold producing a mycotoxin, in most cases, the mycotoxin levels will not be sufficient to have health effects, either in the short term or cumulatively. When a plumbing leak leads to a buildup of stagnant water between the walls, on the other hand, and black mold thrives, an entire household can suddenly develop respiratory problems.

Mycotoxins are superbly resilient and not only resist decomposition but often survive being ingested, so when toxic molds infect crops and produce mycotoxins, those toxins not only remain in the crops throughout their processing into food, but if they are then turned into animal feed, they can remain in the meat or dairy products that result as well. Some mycotoxins further survive cooking or freezing. There is a great deal still to learn about molds, mycotoxins, and the mechanisms by which they interact with other organisms and so impact human health. Ergotism was once a serious recurring food supply problem for many civilizations, for instance. These alkaloids were produced by molds that were found among the various grass species used as cereal grains, including wheat and its ancestors. The alkaloids survived threshing, grinding, and baking, resulting in a supply of tainted bread that either turned its victims’ limbs gangrenous or induced convulsions. In the modern world, ergotism virtually has been eliminated as a human health concern (it still impacts livestock feed), but aflatoxin infestations have caused several recent food crises, including the 2013 aflatoxin contamination that impacted countries in Europe and the Americas.

Aflatoxin disease can cause acute hepatic necrosis and cirrhosis of the liver or liver cancer, but chronic aflatoxin exposure at subclinical levels also has dangerous effects. Children so exposed may experience delayed puberty, stunted growth, and hormonal imbalances or low production of certain hormones. Adults and children alike face an increased risk of liver cancer, though a diet with sufficient consumption of members of the apiaceae family—celery, carrots, parsley, cumin, cilantro, dill, fennel, and asafoetida, among other herbs—significantly reduces this risk, which may in fact have played a role in the adoption of those herbs and vegetables in the diets of ancient aflatoxin-vulnerable populations.

Groups of mycotoxins include ochratoxins, which are produced by some Aspergillus and Penicillium species, and can sometimes be found in red wine, cereals, coffee, and dried fruit. It accumulates in the meat of animals, is toxic to the kidneys, and is a suspected human carcinogen. Fumonisins are produced by Fusarium molds and found mainly in corn and wheat.

They are toxic to the liver and kidneys and believed to increase risk of cancer of the esophagus. Studies have found that poorer populations with less varied diets have a greater incidence of esophageal cancer the more dependent that diet is on corn. Patulin is produced by a number of molds and often found in rotting apples. Because it is a suspected carcinogen—there is not sufficient epidemiological data to investigate, and this suspicion is grounded on comparisons to other mycotoxins—the Food and Drug Administration (FDA) has set a limit on the acceptable levels of patulin in apple cider. This may have been premature because subsequent tests of patulin as an antibiotic against the common cold, while unsuccessful in that effort, found no ill effects from patulin consumption.

One of the best-known toxic molds is *Stachybotrys chartarum*, a black mold that can be found in soil or grain (it can infest silos) but is best known for its insidious presence in damp or water-damaged buildings. *S. chartarum* thrives in cellulose-rich building materials like damp wallpaper and is a frequent problem in homes that are recovering from flooding, whether from natural sources or plumbing accidents. Some studies have suggested that *S. chartarum* is a major factor in sick building syndrome, but more work is required. *S. chartarum* is toxic to both people and pets, producing satratoxin-H, a mycotoxin that can cause nosebleeds, bleeding in the lungs, headaches, chronic fatigue, rash with ulcerations, and hyperthermia. It is lethal in large quantities, such as when used as a chemical weapon, and symptoms can result either from ingestion or inhalation or simply from physical contact with the mold.

Bill Kte’pi
*Independent Scholar*

**See Also:** Daily Life; Pesticides; Pollution, Air.

**Further Readings**
Transportation

The causes of all types of cancer are not fully understood, but researchers know that pathogens, age, genetics, behavior, and environmental contaminants are factors in the development of the disease. The role of transportation in relation to cancer is complex. In order to understand the correlation, transportation as a cause and transportation as an intervention must be examined. Beyond direct exposure to air pollutants and chemicals, the link also must be examined within the context of lifestyle choices, socioeconomics, modernization, public policy, and urban planning trends. All of these impact transportation options, choices, and exposure to risk. A mode of transportation should not be viewed as a direct cause or intervention. Rather, each mode has direct and indirect health consequences that can help combat or contribute to the development of cancer.

Modes of Transportation and Associated Risks

Different modes of transportation serve different lifestyles, needs, and geographic areas. For example, the transit needs of an older person living in a rural area are different than those of a young, urban professional. The most traditional modes of transportation include automobiles, public transit (e.g., buses and trains), cycling, and walking. Each has associated merits and risks for health outcomes, including cancer, injuries, fitness levels, and exposure to environmental hazards.

The direct exposure to cancer risks is the simplest correlation to understand. These risks include exposure to air pollution (e.g., toxic outputs from fossil fuels), carcinogens at street level, and ultraviolet radiation. Although there is no evidence that exposure to gasoline causes cancer, long-term exposure to high levels of benzene (a component of gasoline) has been linked to an increased risk of leukemia (a form of cancer). Furthermore, researchers have identified a link between lung cancer and diesel exhaust, a major component of air pollution. Another direct cause is increased sun exposure while engaging in active transportation modes, such as walking or cycling.

The indirect causation is more complicated and difficult to identify or fully understand. However, this link between transportation and cancer is largely related to sedentary lifestyle, obesity, and higher stress levels. Each of these increases a person’s risk for developing certain types of cancer, particularly colon and breast cancer. Higher stress levels are known to impair immune response, contributing to the development and progression of some types of cancer. There is a direct correlation between physical activity, healthier body weight, and lower stress rates. Combined, these can help the body combat the onset of disease. Many people use active transportation to save money while also building exercise into their daily routines for both physical and mental fitness. Alternatively, active transportation increases exposure to environmental risks. Thus, modes of active transportation can decrease some cancer risks while increasing others.

Other forms of transportation are passive and may be contributing factors to sedentary lifestyles, obesity, and even increased stress. In the Western world, people most often utilize automobiles for their daily transportation needs. Many believe that car culture and urban sprawl are direct causes of obesity, but scholarly research examining these has not been conclusive. While the rise of car ownership, obesity, and cancer rates have steadily
increased since the 1950s, so too has American life expectancy. In fact, some research suggests that people with weight problems (thus at higher cancer risk) are more apt to live in areas requiring frequent utilization of a car. Therefore, car ownership may not be the direct cause of health problems but a contributing factor for people who do not actively engage in healthy lifestyle choices.

The conversation about health and cities often centers on walkable cities being healthier than auto-oriented suburbs. While this is true for some populations and places, it is an oversimplification for understanding the relationship between health and the built environment, especially for conditions that increase cancer risk. Data shows that many inner city areas, with high rates of public transit utilization, also have high rates of obesity and disease. Whereas cars are blamed for suburban health problems, food deserts (i.e., areas lacking of access to fresh fruit and vegetables) is noted as the primary cause of poor health outcomes for low-income people. This too is an oversimplification for understanding health disparities.

Distance decay theory suggests that the farther people are from what they need, the less likely they are to access that resource. Regardless of socioeconomic status or residential location, transportation provides access to resources. This includes health care, healthy food, and jobs. Certainly, car ownership provides more flexibility, and while it may increase the risk of a sedentary lifestyle, it also reduces transit burden. Personal finances, transit availability, residential location choice, and even health status are key factors in closing the spatial gap between person and resources. It is within this framework that transportation becomes a social determinant of health. For example, people with high transit burdens are more likely to consume convenience food, such as fast food and high-calorie processed foods. They are also less likely to seek preventive care, such as cancer screenings.

The Role of Policy Makers, Planners, and Architects

Until recently, transit policy has rarely incorporated health effects into decision making. This is changing as researchers are taking a more comprehensive approach to understanding the social and health impacts of the built environment. This approach helps decision makers understand the complexities of communities and transportation networks. Viewed as an intricate web of systems,
policy makers and planners more readily can see opportunities for improving access and ultimately population health.

At the macro level, transportation planning plays a key role in the implementation of greenhouse mitigation strategies. Better design can reduce the number of vehicle hours driven (or at least curtail an increase of vehicle hours). In turn, this may result in large-scale health benefits through the reduction of air pollution and protection of the Earth’s ozone layer, the atmospheric protection against ultraviolet radiation that causes skin cancer. At the micro-level, planners and architects can design streets and spaces to encourage walking and cycling.

Transportation planning and transit options are part of larger land use and urban planning decisions. They are also largely dependent upon the commitment of public funds. Although controversial, public monies are used to subsidize the operations of public transit systems. This keeps this option affordable for low-income households while also helping to promote ridership regardless of socioeconomic status. In fact, due to better planning, promotion, and increased gasoline and parking costs, public transit ridership has steadily increased in the past decade, and public transit utilization rates have reached the same utilization rates as in the 1950s, when car ownership rates began increasing.

Public transit systems reduce carbon emissions, and higher utilization rates encourage improved routing to serve a variety of population needs better. Some systems have integrated active transportation by installing bike racks on buses and in train stations. Some cities have constructed bike commuter stations with showers and lockers. Initially, the intent was to reduce traffic congestion; these programs also have become part of the larger public health initiative. Other transportation interventions with health benefits include interstate sound-pollution barriers, creation of bike lanes, bike share programs, and street-level beautification. In addition to transit systems, planners and architects are also creating urban design strategies as part of the larger public health initiative to reduce obesity and disease. Popular ideas include developing transit-oriented designs in which people live near public transit hubs (thus reducing dependency on cars), improving urban neighborhoods to increase walkability, and creating bike transit networks, so cyclists can navigate city streets more safely.

Even with increased awareness of health consequences associated with the built environment and transportation options, there is still much to be learned. Large transit projects can take years to plan, fund, and implement, and this process rarely incorporates health implications in evaluation of design and policies. To encourage health as a component of decision making, the U.S. Centers for Disease Control has endorsed Health Impact Assessment (HIA). This new method uses a variety of data sources and analysis but has yet to be adopted widely for transportation planning. As more researchers and practitioners become aware of health consequences associated with the built environment, health will increasingly be considered within the framework of transportation options and systems. Although not likely to reduce cancer rates, better options can be included in a series of crucial health interventions.

Denese M. Neu
National Louis University–Chicago

See Also: Exercise; Gasoline; Obesity; Pollution, Air; Sedentary Occupations; Western Diet.

Further Readings


Trichopoulos, Dimitrios

Dimitrios Trichopoulos was one of the great living academicians of the century. He was a professor of cancer prevention and professor of epidemiology at Harvard University, chair professor of epidemiology at the Medical University of Karolinska in
Stockholm, and member of the Academy of Athens. Born in Athens in 1938, Trichopoulos studied medicine at the University of Athens and specialized in internal medicine, microbiology, public health, and epidemiology at the Universities of Athens, London, Harvard, and Oxford. Since 1989, he served as a professor and the director of the Department of Hygiene and Epidemiology, Harvard School of Public Health (HSPH). Since 1992, he also served as a professor of cancer prevention and the director of the Center for Cancer Prevention, Harvard University. Trichopoulos died on December 1, 2014.

Having grown up in Athens, Greece, his education began there in 1963; he received his doctorate in medicine at the University of Athens Medical School. In 1968, he graduated with a master’s in science from HSPH. He furthered his education in his native Athens, and in 1971 he became a professor at the University of Athens Medical School.

In his native Greece, Trichopoulos served as chair of the Interuniversity Center, the State Council of Occupational Diseases, the State Population Committee, and other committees; as rapporteur of the State Health Planning Committee; and as a member of more than 40 state committees.

His ability was recognized internationally, and he served in various capacities and organizations. He served as a temporary advisor and consultant to the World Health Organization (WHO) on several topics, including the epidemiology of various diseases and conditions, health statistics, health services research, and cancer etiology and prevention. He also served as a faculty member in several graduate or postgraduate courses of the International Agency for Research of Cancer (IARC), the European School of Oncology, and several other universities.

At the international level, he also served as a member of the Panel of Social Medicine and Epidemiology of the European Community (EC) and of the EC Working Group of Epidemiology and Biostatistics, and as an organizer of several EC projects, including those dealing with cancer control, passive smoking, and teaching and epidemiology.

Outside Greece, but not at an international level, Trichopoulos served in the United States in several organizations and institutions at varying leadership levels. Among the many positions he held in the United States are chair of the Tobacco Related Diseases Epidemiology Program (University of California), member of the Environmental Epidemiology Group of the American Health Foundation, and a key member of the Department of Energy review group that studies the use of electromagnetic fields.

Trichopoulos made many breakthroughs in the area of cancer and in particular malignant tumors, which is what he investigated. As he noted, malignant tumors are what scare most people. Although cardiovascular diseases contribute to about half of human deaths, the majority of these are myocardial infarctions, and about 20 percent are malignant tumors (this statistic might have changed due to advancement in technology and the innovation of more effective cardiovascular treatment—today, cancer is the biggest killer). Having realized the threat of cancer, Trichopoulos set out as a youth to investigate this killer. In what could be regarded as his contributions, Trichopoulos made several discoveries, among them viral etiology of liver cancer; probably the most popular of his discoveries—that passive smoking causes lung cancer; and a focus on breast cancer, on which he developed a theory that is gradually becoming more widely accepted, in which the roots of cancer can be traced at a very early stage. Based on this discovery, Trichopoulos proposed that we cannot deal with cancer successfully simply with various preventive measures in adulthood.

Through his work, Trichopoulos has authored or coauthored more than 1,000 scientific publications, including research papers, commentaries, monographs, books, reviews, and reports. Through his work, the role of passive smoking in the causation of lung cancer and chronic obstructive lung disease has been brought to the fore. Other discoveries courtesy of his research include the quantification of the association between psychological stress and coronary heart disease and the identification of several dietary issues, the elucidation of the etiology of hepatocellular carcinoma, and other important risk factors in the etiology of a number of cancers and other diseases. Prior to his death, it is believed he was working on a major hypothesis that he developed concerning the etiology of breast cancer.

The recognition of his research work in the field of cancer has been recognized at several levels through awards. Trichopoulos was a recipient of the International Cancer Medal. Trichopoulos, a Vincent L. Gregory professor of cancer prevention at HSPH, was awarded the Medal of Honor from the IARC, which is part of the WHO. The medal was due to Trichopoulos’s research and contributions to
cancer etiology. Trichopoulos accepted the award at a ceremony in 2007 at the IARC headquarters in Lyon, France.

Other honors awarded to Trichopoulos include: Cutter Lecturer at HSPH (1982), Eleanor Roosevelt Fellowship, Member of the Delta Omega Honorary Public Health Society, United States, Ipsen Lecturer at the Institute of Social Medicine of Aarhus University (1987), European or International Scientific Societies, Chair of the EC Health Group and the EC AIDS Group during the Greek Presidency (1988) of the European Community, Distinguished Lecturer in the Japan Cancer Research Center (1992), Honorary Doctor of Medicine at the University of Uppsala (1994), Officer with the Palmes Academiques in France, and a member of medicine academies in France and Belgium, among other places.

Michael Fox

Independent Scholar

See Also: Breast Cancer; International Agency for Research on Cancer; World Health Organization.

Further Readings


Trophoblastic Tumor, Gestational

Gestational trophoblastic tumors (GTT), also known as the gestational trophoblastic disease or gestational trophoblastic neoplasms, are cancers seen rarely in women, where abnormal cellular proliferation is observed in the tissues formed after conception. These tumors start inside the uterus of the woman from the trophoblast layer, a layer of cells normally surrounding the embryo. Trophoblast cells, under normal circumstances, grow and surround a fertilized egg in the uterus and help in connecting the fertilized egg to the uterine wall and in the formation of the placenta. GTT does not develop from uterine cells; instead, these tumors start in the cells that would normally develop into the placenta during pregnancy. In GTTs, the development of the embryo may or may not take place. Often, the development of the embryo is flawed, resulting in the termination of the pregnancy. GTT is extremely rare in Europe and North America. The incidence of GTT is highest in southeast Asia, with one in 200 to one on 300 live births.

Gestational trophoblastic tumors are classified into two types: the hydatidiform mole and choriocarcinoma. Hydatidiform mole (also referred to as the molar pregnancy) is the most common type of GTT and involves the development of grapelike cysts once the sperm and the egg cells have fused. Hydatidiform moles do not metastasize outside of the uterus and account for almost 80 percent of GTT cases. Hydatidiform moles further can be classified as complete or partial. A complete hydatidiform mole results when a sperm fertilizes an abnormal egg lacking mother’s DNA or a nucleus and has a higher risk of becoming cancerous. A partial hydatidiform mole begins when two sperms fertilize a normal egg, resulting in two sets of DNA from the father. There is no system of staging for hydatidiform moles. Hydatidiform moles can be treated by surgery to remove the tumor. The levels of hormone β-hCG (beta human chorionic gonadotropin) are checked weekly after tumor removal to evaluate the status of the patient. In cases where the levels of β-hCG do not go back to normal levels, it indicates an incomplete removal of the mole or, in rare cases, if the mole has become cancerous.
A choriocarcinoma may initiate as a hydatidiform mole or from the tissue remaining in the uterus after an abortion or delivery of a baby. Choriocarcinomas can spread to other parts of the body. Approximately 15 percent of women with hydatidiform moles develop choriocarcinoma and GTT. Choriocarcinomas can be classified into four stages, that is, stage I through stage IV. Stage I refers to the period when the tumor is localized to the uterus. Stage II involves the spread of tumor to the ovarian tissue, the fallopian tubes, and other parts of the female reproductive system. Stage III GTTs spread beyond the reproductive system into the lungs, and in stage IV, the tumor generally has spread farther in the body. An extremely rare gestational trophoblastic tumor can initiate in the uterus at the site of placenta attachment and is called as the placental-site trophoblastic disease.

### Symptoms

GTT may remain undiagnosed in the early stages as the symptoms resemble early stages of a normal pregnancy. Generally, the symptoms associated with GTT are vaginal bleeding during or after pregnancy, a larger than expected uterus during pregnancy, severe nausea or vomiting during pregnancy, high blood pressure and headaches early in the pregnancy, pain in pelvic area, abdominal swelling, and unexplained weight loss.

### Risk Factors and Diagnosis

A history of oral contraceptive use has been associated with the increased risk of hydatidiform moles. Women with a prior history of spontaneous abortion are also at a two- to threefold higher risk of mole development. Genetic factors such as a missense NLRP7 gene mutation on chromosome 19q are also associated with an increased risk of development of moles. Hydatidiform mole is a single most important risk factor for the development of choriocarcinomas, and maternal ABO blood group also has been linked to an increased risk of development of GTT.

In their initial stages, GTTs are difficult to locate as they show the symptoms associated with normal pregnancies. The identification of tumors can be done by ultrasound tests, which have been shown consistently to be safe, sensitive, and reliable. Ultrasound tests alone are not sufficient for diagnosis and are always used in combination with the levels of the hormone β-hCG, which is present during normal pregnancy.

### Treatment Options

Low-risk GTTs may be treated using chemotherapy using either a single drug or a combination of drugs until the levels of the hormone β-hCG return back to normal. High-risk metastatic GTTs may be treated by a combination chemotherapy and radiation therapy, depending on the site of metastasis. As β-hCG is a highly sensitive biomarker for GTT, 90 percent of GTTs are curable due to early diagnosis and management of the tumors. Prognosis and treatment depend on the factors such as general patient health and if the tumor is metastatic.

Bill Kte’pi
Independent Scholar

### See Also

Gestational Trophoblastic Tumor; Lymphoma, Non-Hodgkin’s, During Pregnancy; Pregnancy and Breast Cancer.

### Further Readings


### Tunisia

Cancer in the north African nation of Tunisia is one of the country’s leading causes of mortality and morbidity, with roughly 12,000 new cases of cancer reported annually among its 11 million inhabitants. The incidence of cancer is increasing...
due to population growth in the country, population aging, industrialization, increasing Westernization of diet and lifestyle, and the pervasiveness of tobacco smoking. The increase in diagnoses also may, in part, be due to the result of more sophisticated diagnosis practices among oncologists as well as awareness among patients. The most common cancers in the nation for men are lung and prostate cancer, while the most common for women is breast cancer, with 1,500 new cases reported each year and incidence ranging from 27 to 30 of 100,000; further, breast cancer causes high morbidity and mortality among Tunisian women.

Gynecological malignancies include cervix uteri, corpus uteri, and ovary. Urological malignancies include bladder, kidney, prostate, and testis; however, incidence of testicular cancer is low. Other types of cancers, such as colorectal cancer and hematological malignancies, including leukemia, Hodgkin’s lymphoma, non-Hodgkin’s lymphoma, and multiple myeloma have seen increasing incidence. Colorectal cancer is ranked the fifth overall cancer for Tunisian males and third among Tunisian women. The incidence rates remain relatively low, which may be due to the Mediterranean diet, characterized by high intake of fruits and vegetables. Risk factors for colorectal cancer tend to be correlated with economic development and Westernization, most notably Western dietary norms.

Health Care During and Since Transitions in Governance
The health care infrastructure in Tunisia is one of the best across the African continent. During French colonial rule (1881–1956), Tunisian medical practitioners were trained in European techniques, and health care in the French protectorate came to be well regarded abroad. In the decades since independence, the health care sector continued to be one of the best across the African continent, with a mix of public and private institutions, the latter of which grew in scope and number in the past few decades. In addition, international partnerships and collaborations with cancer specialists and members of the pan-Mediterranean, pan-Arab World and international organizations such as the Arab Medical Association of Cancer, l’Association Internationale des Registres du Cancer, la Société Internationale de Chirurgie Hépato-Pancréato-Biliaire, la Fédération Pan-Arabe de Chirurgie, la Fondation Française de Carcinologie Digestive, and la Société Française de Cancérologie have enhanced expertise and practice in this most northern African nation.

In the past four years, given political and governmental unrest during and since the so-called Arab Spring, which many attest began on December 10, 2010, in the provincial Tunisian town of Sidi Bouzid, the Tunisian health care system has not seen the development and modernization for which it was previously known. Before the citizen uprisings of 2010 and 2011, the Tunisian government appropriated robust funds to the nation’s Ministry of Public Health, which in turn, expended roughly half its annual expenditure on tertiary care with the remaining half split between primary and secondary care. Recovery has been evident, however. For example, in 2013, the Minister of Health, Dr. Abdellatif Mekki, approved a collaboration with the International Atomic Energy Agency (IAEA) Programme of Action for Cancer Therapy (PACT) to conduct a national cancer control assessment, imPACT mission. Further, despite resource concerns during and since the 2010 to 2011 unrest, Tunisia still achieves a considerable level of development despite needs of modernizing health care infrastructure and given that the epidemiological profile of Tunisia is changing with increases in noncommunicable diseases such as cardiovascular diseases, diabetes, and cancer.

Cancer-Specific Health Care Infrastructure
Along with the growing health care infrastructure more generally, the cancer-specific health care infrastructure is developing. Given the National Strategy on Cancer Control, which will cover a five-year period, Tunisia has made major advances in cancer control. National organizations include l’Association Tunisienne de Lutte Contre le Cancer, located in the capital city of Tunis. Broader organizations include Societe Tunisienne des Sciences Medicales. Note-worthy clinics with specialization in oncology and radiotherapy include Institute Pasteur de Tunis; le Service de Radiothérapie, l’Hôpital Universitaire Farhat Hached at l’Université de Sousse, in Sousse, Tunisia; l’Institut Salah Azaiez in Tunis; Laboratoire d’Immuno-oncologie Moléculaire; and Faculté de Médecine de Monastir, in Monastir, Tunisia.

Population-based cancer registries in Tunisia and those of neighboring nations Morocco, Algeria, Libya, and Egypt have increased in number
from one to nine and cover at least 13 percent of the total regional population. One of the first population-based cancer registries in Tunisia, reporting on incidences of cancer in the central region of Tunisia, was established in 1987 in partnership with the International Agency of Research on Cancer (IARC) in Lyon, France, and located in the Pathology Department of l'Hôpital Universitaire Farhat Hached at l'Université de Sousse. This and other cancer registries in the region and in the country, such as the Cancer Registry of Tunis at the National Cancer Center of l’Institut Salah Azaiz, the main cancer treatment center in the nation, and the Cancer Registry of Sfax, housed at the pathology department of l’Hôpital Universitaire Habib Bourgiba at l’Université Habib Bourgiba in Sfax, which registers cases in the southern region of the country, have provided important information on cancer patterns over the previous years.

The quality of the data provided by the cancer registries is considered to maintain quality levels from acceptable to good, according to available indicators. The pattern of risk shown by north African cancer registries is exceptional in that the total cancer burden in the region ranges from one-third to one-half of what is observed in western Europe. The pattern of consistency between north Africa and western Europe diverges entirely from that of sub-Saharan central and southern African countries, where infection-related cancers are predominant.

Tobacco use continues to be an important risk factor for lung cancer. A World Health Organization study reported that 58 percent of adult men and 7 percent of women in Tunisia use tobacco. Risk for nasopharyngeal carcinoma in Tunisia and its north African neighbors is high; rates are 5.4 in men and 1.9 in women, which is 10 times higher than that in its European neighbors to the north of the Mediterranean. Standard treatment in Tunisia of locally advanced undifferentiated carcinoma of the nasopharyngeal type is chemotherapy followed by loco-regional radiotherapy.

Researchers have reported striking geographic variations in the incidence of inflammatory breast cancer (IBC). There is a higher occurrence of IBC in north African countries, most notably in Morocco, Algeria, Tunisia, and Egypt, where IBC incidence ranges from 10 to 15 percent. It should be noted, however, that cancer registries may have a variance of conceptual definitions used to diagnose IBC.

Nevertheless, IBC incidences have been rising throughout Africa; that is the case in Tunisia as well as in its neighboring north African nations. Research from centers including le Faculté de Médecine de Monastir, in Monastir, Tunisia, reports IBC, an inadequately understood and particularly aggressive form of breast cancer, makes up a larger proportion of breast cancer cases in north Africa than in the United States. Across north Africa, there is a high frequency of IBC diagnosed at relatively late stage as well as cancers that are either estrogen receptor negative (ER−) or triple negative (ER−, progesterone negative, and human epidermal growth factor receptor-2 negative), which tend to occur at younger ages.

Research in Tunisia, most notably from research practitioners at le Faculté de Médecine de Monastir, in Monastir, has found that there exists inadequate knowledge of breast cancer and screening methods as well as low levels of practice of breast cancer screening methods of among women in the region of Monastir. Further, the Tunisian l’Office Nationale de Famille et de la Population (National Office of Family and Population) has instructed pilot public health initiatives focusing on breast cancer mass screening using mammography in particular villages, such as Ariana, which is on the outskirts of Tunis. While improving, there remains an urgent need for updating public health education to raise women’s awareness and adherence to breast self-examination programs in Tunisia.

Lara Lengel
Catherine Cassara
Bowling Green State University

See Also: Age; Algeria; Breast Cancer; Developing Countries; Disparities Within Nations (Elimination of Cancer); Egypt; France; Global Health Issues and Cancer; International Agency for Research on Cancer; Libya; Lung Cancer, Non–Small Cell; Lung Cancer, Small Cell; Morocco; Passive Smoking; Poverty; Smoking and Society; Tobacco Smoking; Tobacco-Related Exposures; Western Diet; Women’s Cancers; World Health Organization.

Further Readings


---

Turkey

Turkey Republic, which was founded in 1923, is at the crossroads of Europe and Asia but mostly located on Asia with the population of 75.6 million. The country was headed by the Ottoman empire till 1923, and health services were not for the public but for the court and army. In the 19th century, the Ottoman empire made some progress in health, such as opening a medicine school and preparing laws, regulations, and rules regarding health services. Relations with Western countries in that period definitely affected those improvements in health services.

As of the establishment of the Turkey Republic, health services became a primary responsibility, which is still conducted by the Ministry of Health. Constitution and provision of health care centers, generation of health policies, and production and implementation of national health strategies were the main duties of the Health Ministry. The private sector and blue-collar public sector workers were provided health insurance by 1946, when Sosyal Sigortalari Kurumu (SSK; social insurance organization) was established. Following SSK, other social security organizations were founded in 1950 (Government Employees’ Retirement Fund [GERF], or Emekli sandığı) and in 1971 (Social Insurance Agency for Merchants, Artisans and the Self-Employed, or Bag–Kur). The Ministry of Health also focused on preventive public health programs to control communicable diseases such as tuberculosis, malaria, and leprosy.

Despite the economic recession, the health care system and health policies have progressed quickly in Turkey. After employing liberal policies for both economic and social life in the 1980s, healthy lifestyles, quality health service delivery, and environmental health came into prominence. The Ministry of Health focused on general health insurance and family practitioner schemes in 1990s but failed to carry out those reforms. After elections in 2002, the new government took office with many reforms, including health. The Health Transformation Program was introduced, and accordingly, all health insurance facilities were consolidated under the management of the Ministry of Health. So, the government became the major provider of health services. Projects regarding family practitioner schemes and preventive and primary health care were put into practice, respectively. National programs were planned with respect to noncommunicable diseases, such as cardiovascular diseases, diabetes, respiratory diseases, and cancer, in addition to enhancing primary health care.

Cancer has become one of the prominent public health problems as well as in other countries all over the world. Following cardiovascular diseases, cancer is the second-highest cause of death in Turkey. Although efforts related to cancer have not been conducted in an extensive and coordinated way, there have been positive strides to improve
cancer care, increase awareness, and provide infrastructure and equipment.

As a part of the Health Transformation Program, early diagnosis, screening, and training centers (KETEM) were established in 81 provinces across the country in 2012. Considering statistics regarding cancer screening, in comparison to 2012, it can be seen clearly that rates of breast (9 percent) and cervical cancer (23 percent) screening have been on the rise through 2013 by force of KETEM. The aim of the center is to extend cancer screening to all cancer groups by the end of 2015.

According to the Health Statistics Yearbook (2012) published by the Ministry of Health, cancer deaths in Turkey increased from 12 to 20 percent between 2002 and 2009. The most frequent types of cancer diagnosed among males are lung, trachea, and bronchial cancer (84.9 percent) and breast cancer (45.1 percent) among females.

The latest scientific studies and drug developments in the field of cancer disease has indicated some reasonable progress related to producing local medications. In addition to this, home production of 33 cancer medications for Turkish patients is seen as a research and development success by the Ministry of Health. Also, there is continuing study on cancer in the Black Sea region regarding the potential impact of the accident at the Chernobyl nuclear plant in 1986.

Cancer incidence and mortality rates being on rise prompted the government to develop powerful public health strategies. The National Cancer Control Program has been developed by the Ministry of Health with support of international institutes and agencies such as the World Health Organization (WHO), International Association for Cancer Registry (IACR), International Union Against Cancer (UICC), National Cancer Institute (NIC), and Middle East Cancer Consortium (MECC) in 2012.

**National Cancer Control Program**

The rising burden of cancer and its negative impact on the health status of communities and on financial expenditures have led to an extensive strategy for all phases of the disease. The National Cancer Control Program developed by the Ministry of Health in 2012 has been trying to enhance the registration system and reduce the incidence of preventable cancers. In a report from the Ministry of Health regarding application of the membership of IARC, other specific aims of the program are as follows:

- To reduce the consumption of tobacco as well as prevention of new smokers and passive smoking due to being one of the main risk factors for cancer.
- To control the lifestyle factors such as obesity and inactivity.
- To focus on environmental and occupational factors so as to reduce the frequency of cancers.
- To establish a delivery chain structure for the diagnosis, treatment, and scientific research for cancer.
- To establish a national organization structure for cancer.
- To extend palliative care services countrywide.

Decreasing the incidence of noncommunicable diseases and risk factors are some of the main targets of the Health of Ministry’s 2013 to 2017 strategic planning. Expanding the capacity related to technology, education, and infrastructure to enhance the National Cancer Program outcomes shows that the program is an ongoing process. Raising awareness of early diagnosis of cancer among the public by using famous role models and improving cancer screening...
programs are also accepted as essential duties to be fulfilled between 2013 and 2017.

Ezgi Eyüboğlu
Maltepe University

See Also: International Agency for Research on Cancer; Screening, Access to; World Health Organization.

Further Readings
Ministry of Health Turkey. Admission of a New Participating State Report for IARC. Ankara: Ministry of Health Turkey, 2011.

Turkish Society of Haematology

As one of the oldest societies in Turkey, the Turkish Society of Hematology (TSH) was founded in 1967 by Sedat Tavat, Arif Ismet Çetingil, F. Reimann, Seref Inceman, Orhan N. Ulutin, Ayhan Çavdar, Burhan Say, Nail Tartaroglu, and Mustafa Karaca, and by 2014, the society has reached more than 700 members. The society is run by seven members of the board of directors and scientific subcommittees that operate under them.

The scientific subcommittees consist of Hemophilia, Homeostasis–Thrombosis, Laboratory Standards, Red Blood Cell Disorders and Hemoglobin, Multiple Myeloma, Infectious Diseases and Supportive Therapies, Bone Marrow Failure, Hemapheresis, Blood Banking and Transfusion, Acute Leukemia, Molecular Hematology and Cytogenetic, Chronic Myelocytic Leukemia and Chronic Myeloproliferative Disorders, Lymphoma, Hematopathology, Stem Cell Transplantation, Stem Cell Biology, and Research Scientific Subcommittees.

The objectives of the society are to increase the level of hematology education and standardize it throughout the country; to create a network for hematology workers for cooperation, collaboration, and communication; and to develop and support research in the field of hematology. In the scope of these objectives, TSH organizes conferences and educational events, publishes a journal, provides grants and scholarships, and promotes national and international cooperation in the field of hematology.

In the scope of educational activities, TSH organizes a number of events including courses, seminars, workshops, conferences, and training programs both at the national and international level. The Annual Hematology Congress is the main national conference, and since its foundation in 1967, TSH has hosted 40 conferences as of 2014. This annual congress addresses new research and developments in the field and brings hematology workers together. The society also organizes the National Bone Marrow Transplantation and Stem Cell Therapies Congress every two years since 1996. This event aims to highlight recent developments in bone marrow transplantation and stem cell therapies. The society also organizes an international event called the International Congress on Lymphoma–Leukemia–Myeloma, which aims to create a platform for the international exchange of knowledge, practices, and ideas in the field.

Another major activity of the society is the Turkish School of Hematology. The school was launched in 2008 with the purpose of filling the gaps in hematology education in Turkey. The duration of the school is three years, and 12 courses are offered during this period. The school also aims to be a bridge for the European Hematology Association (EHA) passport accreditation; thus, the content of the courses are in line with the EHA curriculum and CV passport. The courses are held on weekends in different parts of the country, the first being held in Edirne in 2008. Apart from medical knowledge and skills, the school aims to inform the participants about other EHA & European Society of Hematology (ESH) courses and conferences and encourage them to participate.

The society also organizes various training programs that target different populations for different purposes. The HEKHEP training program aims to train medical doctors on basic and up-to-date
principles of hematology in the cities where hematologists do not exist. Another program called HALKHEP aims to inform patients and their relatives about new developments in hematology to support them during their treatment processes. TSH also organizes training programs for those who work in the pharmaceutical industry.

TSH also initiates public campaigns to raise awareness about blood diseases and provides information about prevention, early diagnosis, and treatment of blood diseases. For instance, in 2013, TSH started a public campaign called Blood Is You to create awareness about various blood diseases. Another campaign was implemented to raise awareness about chronic myeloid leukemia in 2011. The society also has broadcast a national TV video to inform the public about the reasons for and consequences of anemia. Apart from the training programs and campaigns, TSH tries to educate the public through both printed material and the digital press. On the society's Web site, there is an online library that provides information and education for hematology workers, patients, and their relatives. Moreover, TSH has more than 50 educational books published, including handbooks, atlases, and dictionaries.

The society has its own peer-reviewed periodical journal called the Turkish Journal of Hematology, which is a continuation of the New Istanbul Contribution of Clinical Science, established by Professor E. Frank in 1951. The journal is published quarterly in English and indexed in SCI, PubMed Central, EMBASE, SCOPUS, CINAHL, Index Copernicus, GALE, EBSCO, DOAJ, and the Turkish Medicine Index. The Turkish Journal of Hematology aims to publish high-quality research papers on clinical hematology as well as educational materials, reviews, editorial notes, and case reports.

TSH provides a number of grants and awards to junior, basic, and clinical researchers to support hematological research. These funding programs include the hematology fellow international training grant (HAUD), research project awards, international congress grants, TSH annual congress awards, the international scientific publication award (UYDO), fellowship grants, and THD-industrial sponsored grants.

Finally, TSH is an internationally recognized society, and it operates under the Europe–Africa branch of the International Society of Hematology (ISH). Since 2004, TSH is accredited with continuing medical education (CME) accreditation points for participating in scientific and educational programs. TSH also carries out educational and training events with other societies, such as the European Group for Blood and Marrow Transplantation (EBMT) and the International Society on Thrombosis and Homeostasis.

Burcu Ozdemir  
Ankara University

See Also: American Society of Hematology; Turkey.

Further Readings

Turkmenistan

The Republic of Turkmenistan is located on the western part of the Caspian Sea. It is bordered by Iran to the south and southwest, Afghanistan to the southeast, Kazakhstan to the northwest, and Uzbekistan in the north. In 2014, the population was estimated to be more than 5.1 million with a median age of 26.6. Turkmenistan occupies 488,100 square kilometers (188.456 square miles). More than 70 percent of Turkmenistan is covered by subtropical desert called Karakum or Garagum (meaning black sand in Turkmen), which holds the world’s fourth-largest natural gas resources in the world.

Present-day Turkmenistan has been conquered by Persian empires, the Greek Kingdom of Macedon by Alexander the Great, Muslims, Turkic tribes, and Russians. Turkmenistan is a relatively young country, with a rich history and culture that dates back to the 8th century, when Turkic (Oghuz) tribes moved from Mongolia to central Asia. The current Turkmenistan region Mary (historically called Merv) was on the crossroads of the historic Silk Road. Around the 10th century, Oghuz tribes accepted Islam and started to be called Turkmen.
Some Turkmens migrated westward into present-day Iran, Azerbaijan, and Turkey, spreading Turkic culture and living as part of the Seljuk empire. Later around 13th century, Turkmens forced to move southward formed new tribes when Mongols invaded most of their lands. In the late 19th century, the Russian empire occupied Turkmenistan. In 1924, it was part of Soviet Union. On October 27, 1991, upon the dissolution of the Soviet Union, Turkmenistan declared its independence after a national referendum to leave the Soviet Union.

Due to limited funding after independence in 1991, the health system was in poor condition with limited hospital beds and medical facilities, poorly trained medical personnel, and a low ratio of doctors to patients. There are major health factors such as poor diet, polluted drinking water, and contaminated soil, especially in the northeastern, rural areas. In addition, there is a significant income inequality between urban and rural communities in terms of accessing quality health care and medical centers.

Turkmenistan has several environmental issues, from contamination of the soil and groundwater to decreasing water levels in rivers (e.g., Amu Darya) and lakes (e.g., Sarygamymsh Koli). Drinking water sources are improving, especially in urban settings (2011 estimates); for instance, 89.1 percent of the population in urban settings can access improved-quality waters. On the other hand, 46.3 percent of the population in rural settings do not have access to quality drinking water.

According to United Nations Human Development Index, Turkmenistan is ranked 145th in the world. There are different estimates for life expectancy. According to the World Health Organization (WHO) 2011 data, life expectancy is 63.4 (59.8 for males and 67.1 for females), coming in 142nd on the World Life Expectancy ranking. The Central Intelligence Agency (CIA) World Factbook reports 69.47 years (66.48 for males and 72.61 females), ranking Turkmenistan 155th in the world. On the other hand, the State Statistics Committee of Turkmenistan, in 2011, reported the average life expectancy as 70.6 years (67.7 for males and 73.5 for females), which indicates an increase since 1990 (66.4 years) as well as decreasing infant mortality.

According to the CIA World Factbook, Turkmenistan spends 2.7 percent of gross domestic product (2011) on health, ranking 183rd in the world; there are 2.44 physicians for 1,000 people (2007) and 4.1 beds per 1,000 population (2011).

As part of the World Health Organization (WHO) Europe Region, the government of Turkmenistan hosted the WHO European Ministerial Conference on the Prevention and Control of Non-communicable Diseases (NCDs) for Health 2020 on December 3 and 4, 2013, in Ashgabat.

In comparison to other eastern European countries, cancer mortality rates are lower in Turkmenistan. However, cancer is one of the most common causes of death in Turkmenistan as well as cardiovascular and respiratory diseases. Common cancer types among men are stomach, lung, esophagus, liver, and colon; among women, they are breast, esophagus, cervical, stomach, and colon or rectum cancer. There is a high mortality rate for liver and lung cancers. The overall ratio of mortality to incidence is 72 percent among the Turkmen population.

Esophageal cancer is the eighth-most common cancer in the world, and according to GLOBOCAN 2012, Turkmenistan is listed among the highest incidences of esophageal cancer in the world.

According to the WHO April 2011 data, there are 341 or 0.90 percent of total deaths due to breast cancer in Turkmenistan, which ranks Turkmenistan 87th in the world for breast cancer. In the last two decades, while female populations increased by approximately one-third, there is a twofold increase (108 percent) in breast cancer (from 195 to 406) cases. The International Agency for Research on Cancer (IARC) predicts higher cases of breast cancer in Turkmenistan as demographics and life change with higher caloric intake, less physical activity, and limited access to mammogram screening.

According to the Human Papillomavirus (HPV) Center fact sheet, cervical cancer ranks as the fourth-most common cancer among women, with the fifth-most common cancer incidence among females 15 to 44 years old in Turkmenistan. It is estimated that 129 females die annually from cervical cancer out of 324 diagnosed cancer cases. In addition, WHO 2011 data lists 451 deaths or 1.19 percent of stomach cancer-related deaths, which ranks Turkmenistan 33rd in the world with lung cancers deaths at 377 or 1.00 percent of total lung cancer-related deaths, which ranks Turkmenistan 100th in the world.
Even though there are limited data and statistics available in the field of health and medicine through the Turkmen government, there is a significant effort to rebuild the country, increasing resources in health and medicine and increasing involvement in international organizations and projects. With a median human development index of 102nd out of 186 countries in the world, Turkmenistan has been welcoming the scientific research and conferences in the field of medicine and health education. The Ministry of Education and the Ministry of Health and Medical Industry collaborate on the implementation of a number of health programs (e.g., immunization, human immunodeficiency virus [HIV] prevention, and prenatal care). Since 1996, the Ministries of Education and Health have developed textbooks and integrated health education into the kindergarten through grade 12 curriculum.

Melda N. Yildiz  
*Kean University*

**See Also:** Afghanistan; Breast Cancer; Cervical Cancer; Colon Cancer; Esophageal Cancer; Kazakhstan; Liver Cancer, Adult (Primary); Lung Cancer, Non–Small Cell; Stomach (Gastric) Cancer; Uzbekistan; World Health Organization.

**Further Readings**


Uganda

The Republic of Uganda is located in eastern Africa. It is bordered on the north by South Sudan, on the east by Kenya, on the south by Rwanda and Tanzania, and on the west by the Democratic Republic of the Congo. It is the 11th-most-populous country in Africa and 44th most populous in the world, with a population of over 26.4 million. Although English is the official national language, most Ugandans learn a local language before English. Ganda is the de facto national language, while Kiswahili is the statutory national working language; there are also 41 living indigenous languages still spoken by respective ethnic groups in Uganda. The most widely spoken ethnic languages include Chiga, Konzo, Lango, Masaaba, Nyankore, Soga, and Teso. Each ethnic group has its own rich traditions of ethnomedicine. For example, in Kiswahili, a traditional healer who uses medicinal plants for treating ailments is known as mganga, and medicinal plants are called miti shamba.

There are many traditional medicinal preparations used in Uganda. Most of these incorporate myriad local plant materials, many of which have shown medicinal properties in laboratory studies. For example, extracts from Podocarpus sensu demonstrate significant anti-tumor activity. Research suggests that the use of certain plants may help protect against cancer by reducing oxidative stress and stimulating enzymes and other processes that help the body fight carcinogens. For example, an extract from Nymphaea lotus, locally referred to as lora, demonstrates substantial antioxidant potential. This quality is also found in extracts of Kigelia africana (which the Gbe-Gen call nyakpokpo, the Luganda call mussa, the Tem call abilu, and the Vhe call niagpe) as well as in extracts of Hallea rubrostipulata and Zanthoxylum chalybeum.

Medicinal plants are used in Uganda to treat many health problems associated with cancers. For example, the So of northeast Uganda traditionally drink a root decoction of Ackanthera spp. to treat “white urine.” The So also apply the leaves of Rhoicissus tridentata, which they call robol-e, as a plaster to treat wounds.

Unlike traditional preparations, there are serious deficiencies of modern pharmaceutical supplies in Uganda. Uganda is a signatory to the Single Convention on Narcotic Drugs, the Convention on Psychotropic Substances, and the UN Convention against the Illicit Traffic in Narcotic Drugs and Psychotropic Substances; consequently, laws exist to control narcotic and psychotropic substances and precursors. The annual consumption of controlled substances is highly regulated to curtail abuse. Accordingly, the annual consumption of morphine is 0.7416 mg/capita, and the consumption of pethidine is 0.2090 mg/capita. In 2010, the annual prevalence of opiate use by the population aged
15 to 64 years was 0.05 percent, one of the lowest rates in the world. This creates a serious lack of access to basic palliative care that makes cancer experiences in Uganda very different from those elsewhere in the world.

Due, in part, to the shortage of medical services and supplies, health problems are endemic in Uganda. The 10 leading causes of mortality, in rank order, are malaria, HIV/AIDS, anemia, pneumonia, tuberculosis, septicemia, diarrhea, respiratory infections, injuries, and perinatal conditions. The average number of cancer cases annually in Uganda is 171.9 per 100,000 population.

There are also serious deficiencies in modern medical services for cancer and similar conditions in Uganda. According to the World Health Organization’s “Health System Response and Capacity,” as of 2010 there was no general availability of either chemotherapy or radiotherapy in the public health system in Uganda.

Cancers account for a substantial amount of disability and suffering among impacted populations. According to the World Health Organization’s “Disease and Injury Country Estimates” for 2004, the ten most prevalent cancers in Uganda were esophageal cancer, at 193 per 100,000 population; prostate cancer at 163 per 100,000 population; cervical and uterine cancers at 121 per 100,000 population; lymphomas at 98 per 100,000 population; stomach cancer at 85 per 100,000 population; breast cancer at 80 per 100,000 population; liver cancer at 77 per 100,000 population; colon and rectal cancers at 76 per 100,000 population; mouth and oropharynx cancer at 60 per 100,000 population; and trachea, bronchial, and lung cancers at 53 per 100,000 population.

Modern medical services and supplies, as opposed to traditional preparations, are generally in short supply in Uganda, if available at all. Both prescription and over-the-counter products are often unavailable. Consequently, health problems are endemic and limit development. For example, an estimated 600,000 people live with HIV in Uganda, ranking the country 11th highest in Africa and 16th highest globally. The mortality rate for HIV/AIDS is 209 per 100,000 population. Debate continues on the relative risks in Africa for respective cancer types for those infected with HIV. The mortality rate for tuberculosis is 27 per 100,000 population, and for malaria it is 145 per 100,000 population, while for cancers it is 138 per 100,000 population. Furthermore, according to the World Health Organization’s “Global Health Observatory Data Repository,” in 2008 the age-standardized estimates of deaths from all cancers was 127 per 100,000 population for males and 140 per 100,000 population for females. As a consequence, life expectancy is only 50.43 years, which ranks the Uganda 23rd in Africa and 194th in the world. There is a clear and urgent need for improved cancer awareness, early detection programs, and health services infrastructure in Uganda.

Victor B. Stolberg
Essex County College

See Also: Developing Countries; Kenya; Rwanda; Tanzania.

Further Readings


Ukraine

The eastern European nation officially termed Ukraine has experienced many variations in its statehood over the past several centuries. This has led to confusion even among contemporary historians regarding the nation's proper history, but what is known is that the roots of the modern state of Ukraine can be traced back to the ninth-century federation of tribes called the Kyivan Rus. The region underwent many political variations in the ensuing millennia. In 1922, Ukraine became the Ukrainian Soviet Socialist Republic and was incorporated into the Soviet Union until the nation declared its independence in 1991 after the Union's dissolution, and thus arrived at its modern rendition.

With regard to Ukraine's battle against cancer, the infamous disaster that occurred in April 1986 at Chernobyl's nuclear power plant has had repercussions on the rate of cancer incidences in the country, especially in adolescents. Improperly trained staff members and mistakes in the facility's design led to a nuclear meltdown at the facility that caused nuclear fallout to be expelled high into the atmosphere. The fallout drifted over portions of Ukraine, Belarus, and Russia, and in the years following the disaster, a tangible increase in the incidences of thyroid cancer diagnosed in children from regions near Chernobyl has led specialists to believe that fallout from the nuclear accident is likely to blame. Specifically, scientists believe that the radioactive isotope I-131 that was present in the nuclear fallout from the disaster is the main reason for the noticeable increase in thyroid cancers in the region's youth. Thyroid cancer rates in the area continue to be closely monitored by domestic and international scientists.

In the past 25 years, Ukraine has initiated an overhaul of its medical system by striving to give the nation's medical students the best possible cancer-education resources. Prospective cancer specialists can go to one of 19 state-run medical universities for their education, and, if they graduate, they can follow up their training at one of three post-graduate training academies. Incidences of cancer have been consistently trending upwards in Ukraine in recent years, so the Ukrainian Ministry of Health has been going to great lengths to ensure that the country will have an adequate amount of highly trained cancer specialists to combat the disease in forthcoming decades. On average, there are currently only four cancer specialists in the country for every 100,000 Ukrainian citizens.

The most prevalent forms of cancer in Ukraine are lung cancer, breast cancer, skin cancer, prostate cancer, and stomach cancer. Lung, skin, and prostate cancers make up nearly half of all cancer incidences in males in the nation, while breast, skin, and uterine cancers are the most prevalent cancer incidences in females. Within the past 10 years, certain cancers such as skin cancer, stomach cancer, uterine cancer, lung cancer, and thyroid cancer have seen a nationwide increase in prevalency, while incidences of gallbladder cancer have steadily been declining. Certain parts of Ukraine experience more cases of specific cancers than other parts of the country; there are higher incidences of thyroid cancer in the youth of the region that was affected by the Chernobyl nuclear disaster in 1986 than in the rest of the nation.

As in all nations, many citizens of Ukraine have had cancer throughout the country's history. The Kiev-born and world-renowned tennis athlete Elena Baltacha passed away after a two-month battle with liver cancer. The Ukrainian Vladimir Shevchenko, who famously filmed the immediate aftermath of the Chernobyl nuclear disaster, died in 1987 from complications resulting from cancer induced by the accident's radiation fallout. Volodymyr Sabodan, who was the primate of the Ukrainian Orthodox Church, passed away in July 2014 at a hospital in Kiev after his own battle with cancer.

Ukraine is home to 27 cancer specialist centers. The nation is also home to numerous medical academies and university hospitals that function in similar capacities. Ukrainian cancer specialists are well
Ultraviolet A Radiation

Exposure to ultraviolet (UV) radiation is a major risk factor for the development of many skin cancers. Sunlight is the main source of UV rays, but tanning lamps and beds also produce UV rays. People who get a lot of UV exposure from these sources are at greater risk for skin cancer. UV rays are only a small portion of the sun's rays, but they produce the main harmful effects of the sun as they damage the DNA of skin cells. When the sun's UV ray damage affects the DNA of the genes that control skin cell growth, the body is vulnerable to the development of skin cancer.

Not all UV rays are the same. There are three main types of UV rays, ultraviolet A (UVA) rays, ultraviolet B (UVB) rays, and ultraviolet C (UVC) rays. UVA rays are responsible for aging skin cells and damaging skin cell DNA. UVA rays have been linked to long-term forms of skin damage, including wrinkles. These rays also have a part in the development of some skin cancers. Most of the tanning beds on the market give off large amounts of UVA radiation, which is one reason these beds pose a skin cancer risk. UVB rays are the rays mainly responsible for sunburns and produce direct damage to skin cell DNA. UVB rays are often implicated as a causal agent in most forms of skin cancer. UVC rays are absorbed by the Earth's ozone layer and do not reach the Earth's surface. As such, these rays do not normally play a large part in the process of skin cancer development. Most of the UV rays that come in contact with humans are UVA, with a smaller amount of UVB. While both UVA and UVB rays damage skin and cause skin cancer, UVB rays are thought to be the more potent of the two, and more heavily involved in causing at least some skin cancers. Fortunately, some UVB rays are also absorbed by the Earth's ozone layer. Other UVB
rays, however, are not absorbed and are able to pass through and affect humans. Overall, there are no safe UV rays. They are all harmful. The amount of UV exposure a person gets depends on the strength of the rays, the length of time the skin is exposed, and whether the skin is protected with clothing or sunscreen.

**Effects of UV Rays**
Sun is often thought of as the main causal agent in skin cancers, and it is classified as a human carcinogen. If people get too much sun, they increase their risk of skin cancer. Yet, there are other effects of UV exposure. Sunburn and tanning are the short-term results of too much exposure to UV rays, and they are the overt signs of skin damage. Long-term exposure can cause early skin aging, wrinkles, loss of skin elasticity, and dark patches known as age spots. Long-term exposure can also cause precancerous skin changes, including dry, scaly, rough patches called actinic keratosis.

The sun's UV rays can also increase a person's risk of cataracts and other eye problems. UV rays can also suppress the skin's immune system. Darker-skinned people are generally less likely to get skin cancer than light-skinned people, but they can still get cataracts and immune suppression. UV rays from the sun are not the only harmful source. UV radiation is also transmitted from tanning beds, classifying it as a source of human carcinogen. Other sources of UV radiation include mercury vapor lighting; halogen, fluorescent, and incandescent lighting; and some types of lasers. Additionally, certain oral and topical medicines, such as antibiotics, birth control pills, and benzoyl peroxide products, as well as some cosmetics, may increase skin and eye sensitivity to UV rays in all skin types.

**The UV Index**
The amount of UV light reaching the ground in any given place depends on a number of factors, including the time of day, time of year, elevation, and cloud cover. The UV Index was designed by the National Weather Service and the Environmental Protection Agency (EPA) to provide an indicator of the strength of UV rays on any given day in any given area. The scale runs from 1 to 11+, with a higher number indicating greater risk of UV ray exposure. The greater risk of exposure also increases the chance sunburn and skin damage that could potentially lead to skin cancer. Local changes in cloud cover and other factors may change the actual UV levels experienced.

**UVA**
All radiation is a form of energy, most of which is invisible to the human eye. UV radiation is only one form of radiation, and it is measured on a scientific scale called the electromagnetic (EM) spectrum. UV radiation is only one type of EM energy. Radio waves that transmit sound from a radio station's tower or between cell phones; visible light that is emitted from the lights in a home; and X-rays like those used in hospital X-ray machines are all forms of EM energy. Like all forms of light on the EM spectrum, UV radiation is classified by wavelength. Wavelength describes the distance between the peaks in a series of waves. Of the three types of UV rays, UVA rays have the longest wavelengths, and UVC rays have the shortest wavelengths; UVB rays fall in between the two. The longer wavelength of UVA rays is able to penetrate the middle layer, or dermis, of human skin.

UVA is the most commonly encountered type of UV light. Most humans are exposed to large amounts of UVA throughout their lifetime. UVA rays account for up to 95 percent of the UV radiation reaching the earth's surface. Atmospheric ozone absorbs very little of this part of the UV spectrum. UVA is needed by humans for synthesis of vitamin D; however, overexposure to UVA has been associated with toughening of the skin, suppression of the immune system, and cataract formation. UVA light is often called black light. Most phototherapy and tanning booths use UVA lamps.

Although they are not as intense as UVB rays, UVA rays are 30 to 50 times more prevalent. They are present with relatively equal intensity during all daylight hours throughout the year, and they can penetrate clouds and glass. UVA, which penetrates the skin more deeply than UVB, has long been implicated in skin aging and wrinkling. UVA exposure has an initial pigment-darkening effect (tanning) followed by erythema if the exposure is excessive. Initially, scientists believed UVA did not cause significant damage in areas of the epidermis where most skin cancers occur. Recent studies, however, show that UVA damages skin cells called keratinocytes in the basal layer of the epidermis, where most skin cancers occur. UVA radiation contributes to and may even initiate the development of skin cancers.
UVA is the dominant tanning ray. Tanning in any form, whether outdoors or in a salon, causes cumulative damage over time. A tan results from injury to the skin’s DNA; the skin darkens in an imperfect attempt to prevent further DNA damage. These imperfections, or mutations, can lead to skin cancer. Tanning booths primarily emit UVA. The intense sunlamps used in tanning salons emit doses of UVA as much as 12 times that of the sun. Not surprisingly, people who use tanning salons are 2.5 times more likely to develop squamous cell carcinoma, and 1.5 times more likely to develop basal cell carcinoma. According to recent research, exposure to tanning beds in youth increases melanoma risk by 75 percent.

**Factors Influencing UVA Levels**
The level of UV radiation reaching the earth’s surface can vary. The amount of UV rays the ozone layer absorbs varies depending on the time of year and other natural events. The sun’s angle changes with the seasons, which affects the intensity of the UV rays. The UV rays tend to be more intense in the summer months. Time of day is also a consideration. The sun is highest in the sky around noon. The sun’s rays pass directly through the atmosphere from the shortest distance, causing levels to be at their highest. In the early morning and late afternoon the sun’s rays are slanted, and the intensity is reduced. The sun is most directly overhead around the equator, which makes the sun’s rays strongest in this area. The rays do not have to travel as far through the atmosphere.

Ozone also is naturally thinner in the tropics compared to the mid and high latitudes, so there is less ozone to absorb the UV radiation as it passes through the atmosphere. At higher latitudes, the sun is lower in the sky, so UV rays must travel a greater distance through ozone-rich portions of the atmosphere and, in turn, expose those latitudes to less UV radiation. In addition to location, the ozone layer has been affected by environmental concerns. The ozone layer is thinner than it used to be due to ozone-depleting chemicals used in industry and consumer products. These chemicals are being phased out, but the ozone layer is not predicted to return to pre-1980 levels until mid- to late century. This allows the UV rays to reach the earth with less filtering.

Higher altitude levels also increase the intensity of UV radiation because there is less atmosphere to absorb the damaging rays. The risk to skin and eyes increases in high-altitude locations. Cloud cover also reduces the UV radiation that reaches the earth’s surface. Thinner cloud cover, even on colder days, can still allow UV radiation in strong enough doses to burn skin. Surfaces like snow, sand, pavement, and water reflect much of the UV radiation that reaches them. Because of this reflection, UV intensity can be deceptively high even in shaded areas.

The photochemical effects of UV radiation can be exacerbated by chemical agents including birth control pills, tetracycline, sulphathiazole, cyclamates, antidepressants, coal tar distillates found in antidandruff shampoos, lime oil, and some cosmetics. Protection from UV is provided by clothing, polycarbonate, glass, acrylics, and plastic diffusers used in office lighting. Sun-blocking lotions offer limited protection against UV exposure. Accidental overexposure might not be detected because the
UV radiation is invisible and does not produce an immediate reaction. Yet, this radiation can injure individuals. Labeling on UV sources usually consists of a caution or warning label on the product or the bulb packaging cover, or a warning sign on the entryway.

Constance M. Dolecki
Independent Scholar

See Also: Ultraviolet B Radiation; Ultraviolet C Radiation; Ultraviolet Radiation Related Exposures.

Further Readings

Ultraviolet B Radiation

Exposure to ultraviolet (UV) radiation is a major risk factor for development of many skin cancers. Sunlight is the main source of UV rays, but tanning lamps and beds also produce UV rays. People who receive a lot of UV exposure from these sources are at greater risk for skin cancer. UV rays are only a small portion of the sun’s rays, but they produce the main harmful effects of the sun because they damage the DNA of skin cells. When the sun’s UV ray damage affects the DNA of the genes that control skin cell growth, the body is vulnerable to the development of skin cancer.

Not all UV rays are the same. There are three main types of UV rays, ultraviolet A rays (UVA), ultraviolet B rays (UVB), and ultraviolet C rays (UVC). UVA rays are responsible for aging skin cells and damaging skin cell DNA. UVA rays have been linked to long-term forms of skin damage, including wrinkles. These rays also have a part in the development of some skin cancers. Most of the tanning beds on the market give off large amounts of UVA, which is one reason these beds pose a skin cancer risk. UVB rays are the rays mainly responsible for sunburns, and produce direct damage to skin cell DNA. UVB rays are often implicated as a causal agent in most forms of skin cancer. UVC rays are absorbed by the Earth’s ozone layer, and are not based in sunlight. As such, these rays do not normally play a large part in the process of skin cancer development. Most of the UV rays that come in contact with humans are UVA, with a smaller amount of UVB. While both UVA and UVB rays damage skin and cause skin cancer, UVB rays are thought to be the more potent of the two, and are more heavily involved in causing at least some skin cancers. Fortunately, some UVB rays are also absorbed by the Earth’s ozone layer. Other UVB rays, however, are not absorbed, and are able to pass through and affect humans. Overall, there are no safe UV rays. They are all harmful, and the longer someone is exposed, the greater the risk. It is also important to look at the strength of the rays, and whether the skin is protected with clothing or sunscreen.

Effects of UV Rays
Sun is often thought of as the main causal agent in skin cancers, and is classified as a human carcinogen. The more sun that an individual receives, the more they increase their risk of skin cancer. Yet, there are other effects of UV exposure. Sunburn and tanning are the obvious short-term signs of too much UV ray exposure. Long-term exposure can cause early skin aging, wrinkles, loss of skin elasticity, and dark patches known as age spots. Long-term exposure can also cause precancerous skin changes, including dry scaly rough patches called actinic keratosis.
The sun's UV rays can increase a person's risk of cataracts and other eye problems. These rays are also responsible for problems with the function of the skin's immune system. People with lighter skin are at higher risk for developing skin cancer than people with darker skin, but people with darker skin are still at risk for developing cataracts and a suppressed immune system. UV rays from the sun are not the only harmful source. UV radiation is also transmitted from tanning beds, classifying them as a human carcinogen. Other sources of UV radiation include mercury vapor lighting; halogen, fluorescent, and incandescent lighting; and some types of lasers. Additionally, some medicines can increase susceptibility to UV rays and their harmful effects, including certain prescription and over-the-counter oral and topical medicines, and some types of cosmetics. These products can increase sensitivity for all skin types.

**UV Index**

The amount of UV light reaching the ground in any given place depends on a number of factors, including the time of day, time of year, elevation, and cloud cover. The UV Index was designed by the National Weather Service and the Environmental Protection Agency (EPA) to provide an indicator of the strength of UV rays on any given day in any given area. The scale runs from 1 to 11+, with a higher number indicating greater risk of UV ray exposure. The greater risk of exposure also increases the chance sunburn and skin damage that could potentially lead to skin cancer. Local changes in cloud cover and other factors may change the actual UV levels experienced.

**UVB**

UVB radiation is the chief cause of skin reddening and sunburn, which tends to damage the skin's more superficial epidermal layers. It plays a key role in the development of skin cancer, and a contributory role in tanning and photoaging. The intensity of UVB radiation varies by season, location, and time of day. The more intense amounts of UVB radiation occur in the United States between 10:00 A.M. and 4:00 P.M. from April through October. However, UVB rays can burn and damage skin throughout the year. Locations with higher altitudes are at greater risk, and snow and ice increase this risk because they reflect the sun's rays and bounce back up to 80 percent of the rays so that they hit the skin twice. UVB rays are not as able to cause damage through glass. UVB rays have a short wavelength that reaches the outer layer of the skin (the epidermis). UVB radiation that reaches the Earth's surface has the potential to create serious health effects, and can negatively impact the environment. Levels of UVB radiation are not as constant as UVA, but are more intense and capable of doing damage.

UVB radiation is typically the most destructive form of UV radiation because it has enough energy to cause photochemical damage to cellular DNA, yet not enough to be completely absorbed by the atmosphere. Some UVB radiation is needed to help synthesize vitamin D. Even with this benefit, harmful effects can occur, including erythema (sunburn), cataracts, and development of skin cancer. Individuals working outdoors are at the greatest risk of UVB effects, and should take precautions to minimize this risk. Most solar UVB radiation is blocked from reaching the surface by the ozone layer of the atmosphere. Thus, there are concerns that reductions in atmospheric ozone could increase the prevalence of skin cancer.

**Sun Exposure and UVB Radiation**

Since the invention of modern day sunscreens, a sunscreen's efficacy has been measured by its sun protection factor (SPF). SPF is not the amount of protection that a product provides. The SPF number provides a guideline for how long it will take for UVB rays to redden skin when using that level of SPF sunscreen, compared to how long skin would take to redden without the product. For example, someone using a sunscreen with an SPF of 30 will take 30 times longer to redden than without the sunscreen. An SPF 15 sunscreen screens 93 percent of the sun's UVB rays; SPF 30 protects against 97 percent; and SPF 50, 98 percent. The Skin Cancer Foundation maintains that SPFs of 15 or higher are necessary for adequate protection.

UVB radiation has some health benefits in addition to the risks. Exposure to UVB radiation helps the skin produce vitamin D3, which plays an important role, along with calcium, in bone and muscle health. The amount of UVB exposure necessary for this development and other potential health benefits depends on different factors, including the amount of vitamin D that the person takes in in other ways, darkness of skin color, sunscreen
Exposure to ultraviolet (UV) radiation is a major risk factor for development of many types of skin cancer. One of the most common sources of UV rays is sunlight, but tanning lamps and beds also use, clothing, geographical location of home (latitude and altitude), time of day, and time of year. At this time, the FDA has not cleared or approved any indoor tanning device for producing vitamin D using UVB radiation.

UV radiation is also present in lasers and UV lamps. Some topical medications used for certain diseases that are unresponsive to other forms of medical therapy can increase UV sensitivity. This process is called phototherapy. Phototherapy provides UV exposure, administered by a trained health care professional, under the supervision of a dermatologist. Studies suggest that phototherapy can help treat unresponsive and severe cases of several diseases, including rickets, psoriasis, eczema, vitiligo, and lupus. Phototherapy occurs by exposing a patient to a specific closely monitored dose of UV radiation administered at regular intervals on a set schedule. In some cases, effective therapy requires that a patient’s skin is first treated with a prescription drug, ointment, or bath that increases its UV sensitivity.

Factors Influencing UV Radiation Levels
The level of UV radiation reaching the Earth’s surface can vary. The amount of UV rays that the ozone layer absorbs varies depending on the time of year and other natural events. The sun’s angle changes with the seasons, which affects the intensity of UV rays. UV rays tend to be more intense in the summer months. Time of day is also a consideration. The sun is highest in the sky around noon. The sun’s rays pass directly through the atmosphere from the shortest distance, causing levels to be at their highest. During early morning and late afternoon, the sun’s rays are slanted, and the intensity is reduced. The sun is most directly overhead around the equator, which makes the sun's rays strongest in this area. The rays do not have to travel as far through the atmosphere.

Ozone also is naturally thinner in the tropics compared to the mid- and high-latitudes, so there is less ozone to absorb the UV radiation as it passes through the atmosphere. At higher latitudes, the sun is lower in the sky, so UV rays must travel a greater distance through ozone-rich portions of the atmosphere and, in turn, expose those latitudes to less UV radiation. In addition to location, the ozone layer has been affected by environmental concerns. The ozone layer is thinner than it used to be because of ozone-depleting chemicals used in industry and consumer products. These chemicals are being phased out, but the ozone layer is not predicted to heal to pre-1980 levels until mid- to late-century. This allows the UV rays to reach the Earth with less filtering.

Short exposure to UVB radiation generates vitamin D, but can also lead to sunburn, depending on an individual’s skin type. Fortunately, the ozone layer in the atmosphere shields some UVB radiation, but not all of it. UVB radiation is a potent danger if individuals do not take measures to minimize or prevent the possible damage. Since the benefits of sunlight cannot be separated from its damaging effects, it is important to understand the risks of overexposure, and take simple precautions to protect oneself.

Constance M. Dolecki
Independent Scholar

See Also: Ultraviolet A Radiation; Ultraviolet C Radiation; Ultraviolet Radiation Related Exposures.

Further Readings


Ultraviolet C Radiation
Exposure to ultraviolet (UV) radiation is a major risk factor for development of many types of skin cancer. One of the most common sources of UV rays is sunlight, but tanning lamps and beds also

Factors Influencing UV Radiation Levels
The level of UV radiation reaching the Earth’s surface can vary. The amount of UV rays that the ozone layer absorbs varies depending on the time of year and other natural events. The sun’s angle changes with the seasons, which affects the intensity of UV rays. UV rays tend to be more intense in the summer months. Time of day is also a consideration. The sun is highest in the sky around noon. The sun’s rays pass directly through the atmosphere from the shortest distance, causing levels to be at their highest. During early morning and late afternoon, the sun’s rays are slanted, and the intensity is reduced. The sun is most directly overhead around the equator, which makes the sun's rays strongest in this area. The rays do not have to travel as far through the atmosphere.

Ozone also is naturally thinner in the tropics compared to the mid- and high-latitudes, so there is less ozone to absorb the UV radiation as it passes through the atmosphere. At higher latitudes, the sun is lower in the sky, so UV rays must travel a greater distance through ozone-rich portions of the atmosphere and, in turn, expose those latitudes to less UV radiation. In addition to location, the ozone layer has been affected by environmental concerns. The ozone layer is thinner than it used to be because of ozone-depleting chemicals used in industry and consumer products. These chemicals are being phased out, but the ozone layer is not predicted to heal to pre-1980 levels until mid- to late-century. This allows the UV rays to reach the Earth with less filtering.

Short exposure to UVB radiation generates vitamin D, but can also lead to sunburn, depending on an individual’s skin type. Fortunately, the ozone layer in the atmosphere shields some UVB radiation, but not all of it. UVB radiation is a potent danger if individuals do not take measures to minimize or prevent the possible damage. Since the benefits of sunlight cannot be separated from its damaging effects, it is important to understand the risks of overexposure, and take simple precautions to protect oneself.

Constance M. Dolecki
Independent Scholar

See Also: Ultraviolet A Radiation; Ultraviolet C Radiation; Ultraviolet Radiation Related Exposures.

Further Readings


Ultraviolet C Radiation
Exposure to ultraviolet (UV) radiation is a major risk factor for development of many types of skin cancer. One of the most common sources of UV rays is sunlight, but tanning lamps and beds also
produce UV rays. People who are exposed to the UV rays from these sources face higher risks of developing skin cancer. UV rays make up a small amount of the sun's rays, but they produce the main harmful effects of the sun because they damage the DNA of skin cells. When the sun's UV ray damage affects the DNA of the genes that control skin cell growth, the body is vulnerable to the development of skin cancer.

Not all UV rays are the same. There are three main types of UV rays: ultraviolet A rays (UVA), ultraviolet B rays (UVB), and ultraviolet C rays (UVC). UVA rays are responsible for aging skin cells and damaging skin cell DNA. UVA rays have been linked to long-term forms of skin damage, including wrinkles. These rays also have a part in the development of some skin cancers. Most of the tanning beds on the markets give off large amounts of UVA, which is one reason why these beds pose a skin cancer risk. UVB rays are mainly responsible for sunburns, and produce direct damage to skin cell DNA. UVB rays are often implicated as a causal agent in most forms of skin cancer. UVC rays are absorbed by the Earth's ozone layer, and are not based in sunlight. As such, these rays do not normally play a large part in the process of skin cancer development. Most of the UV rays that come into contact with humans are UVA, with a smaller amount of UVB. While both UVA and UVB rays damage skin and cause skin cancer, UVB rays are thought to be the more potent of the two, and are more heavily involved in causing at least some skin cancers. Fortunately, some UVB rays are also absorbed by the Earth's ozone layer. Other UVB rays, however, are not absorbed, and are able to pass through and affect humans. Overall, there are no safe UV rays. They are all harmful. The extent of harmful UV exposure normally depends on the strength of the rays, how much time the exposure to the skin occurs, and what type of protection is on the skin, including clothing or sunscreen.

**Ultraviolet C Radiation**

UVC is very rarely observed in its natural state because it is absorbed completely by the carbon dioxide and ozone in the atmosphere. This is a good thing because UVC rays are very dangerous, and even short exposure to any quantity of UVC is very harmful to the eyes and causes severe sunburn. In essence, the shorter the wavelength, the more potentially dangerous the ultraviolet radiation. UVC radiation is extremely dangerous for humans; some forms are produced on the Earth's surface by such processes as arc welding. It is part of the far regions of ultraviolet radiation, with wavelengths between 200 and 290 nanometers, or wavelength range, all of which is filtered out by the ozone layer and does not reach the Earth's surface. UVA and UVB have larger wavelength ranges, and are thus able to permeate the atmosphere and affect skin by exposure to sunlight. The shorter wavelengths produce ozone in air (oxygen). Differences in size of wavelength can produce differences in what occurs with them. For example, the wavelengths at the bottom of the spectrum radio have radio waves with photons containing low energies. This causes wavelengths with long peaks that are farther apart. The photons of microwaves have higher energies, followed by infrared waves, UV rays, and X-rays. At the top of the spectrum, gamma rays have photons with very high energies and short wavelengths, with peaks that are close together. The shorter gamma ray wavelengths present the greater danger with exposure to humans.

UVC light tends to be utilized through manufactured means, rather than impacting humans in its natural state. When humans are exposed to UVC radiation, it is absorbed in the outer dead layers of the epidermis. UVC overexposure creates the potential for corneal burns, which is also called welders' flash, and snow blindness. This results in a severe sunburn to the face. While UVC injury usually clears up in a day or two, it can be extremely painful. UVC wavelengths are not produced by the ultraviolet radiation sources utilized by the indoor tanning industry.

UVC radiation has properties that have the ability to kill bacteria. The shorter-wavelength, higher-energy UV radiation associated with the UVC category is very strongly absorbed by most organic materials. This makes it a good candidate for use in treatment of certain diseases. UVC is used in germicidal lamps in medical facilities. Light in the UVC wavelength can be used for disinfecting water, sterilizing surfaces, destroying harmful microorganisms in food products and in the air, and is also used in ultraviolet phototherapy. UVC radiation, in the range of 255 to 275 nanometers, renders harmful microorganisms such as bacteria and viruses ineffective by destroying the genetic information
in DNA. The microorganisms are unable to reproduce, which leads to the death of the microbes. The germicidal nature of UV is well suited to treat parasites that are extremely resistant to chemical disinfectants, such as Cryptosporidium or Giardia.

UVC radiation is aggressive enough that individual photons may produce chemical bond breakage and ionization of some atoms and molecules. The preferential absorption of particular energy photons by materials, both organic and inorganic, is evident throughout the electromagnetic spectrum, from microwaves through infrared and visible light, ultraviolet, X-rays, and gamma rays. The absorption at particular wavelengths may be associated with resonance-type effects in which the gaps between certain energy states in an atom or molecule are nearly matched by the energies of the incoming photons. Atomic or molecular excitation may occur as a result of the absorption, or an electron may be ejected from an atom when the incoming photon energy exceeds the binding energy of the electron in the atom. There is a pattern to photon absorption by particular atoms or molecules that could begin small at a given energy, increase with increasing energy, and then decrease again at yet higher energies, so it is not surprising that some higher-energy UV radiation may be more strongly absorbed than lower-energy UV.

UVC radiation has not been implicated as a cause of human skin cancer or other types of human cancer, although some experiments with mice have demonstrated a causative link between squamous cell cancer and UVC irradiation. The dead skin on most of the human body is sufficient to absorb UVC radiation almost completely. In areas of reduced dead-skin thickness and intense radiation, however, UVC radiation might reach live skin tissue, and could produce erythema and possibly other undocumented effects. This would be true especially in an abraded area of skin, or in the region of a significant flesh wound.

Since UVC radiation is greatly diminished by atmospheric gases, no significant irradiation of human beings on Earth results from natural sources. With increasing germicidal uses of man-made UVC radiation, especially in hospital settings where there is a strong concern about the spread of harmful bacteria, it is likely that more human exposures will occur, and future studies may show some links with disease that have not been identified as yet. UVC radiation can damage the superficial tissues of the eye, and care must be taken to avoid excessive exposures of the eye to this form of radiation. While eye exposures to UVC may cause extreme discomfort, the symptoms usually subside within a rather short time, and no evidence of any lasting malignant effects has been discovered at this point.

**Ultraviolet Germicidal Irradiation**

Shortwave UVC radiation is also called ionizing radiation because it has enough energy to quickly destroy important molecular bonds, such as those found in deoxyribonucleic acid (DNA), the molecular blueprint of all living cells. By creating random breaks in DNA, UV radiation can introduce mutations, and in most microorganisms, this causes cell death. Ultraviolet germicidal irradiation (UVGI) is one of the most adaptable and effective ways of sterilizing an object without causing damage and without generating harmful byproducts. Because of its versatility and safety, UVGI has been used to sterilize air, drinking water, aquariums, ponds, laboratory equipment, medical instruments, food, and beverages. The UVGI process uses short-wavelength UVC in a contained area to kill microorganisms such as viruses, bacteria, and molds, some of which can cause human disease and are called pathogens. The pathogenic microorganisms normally resistant to other forms of sterilization, including chemical forms, are destroyed using UVGI. UVGI is also effective when the use of heat sterilization is not feasible. Each microorganism has a different level of sensitivity to UVC radiation. Some microorganisms require only a small amount of UVGI to break apart its DNA and prevent reproduction, whereas others require more.

**Arc Welding**

Another place where radiation in the UVC range can be found is in welding. It is present in the arc of a welding torch. This has given rise to the term “welder’s eye,” referring to optical damage caused by UVC light. UVA and UVB light can cause similar skin and eye damage, but much higher levels and much longer exposure times are required. The short distance between the arc and the welder’s skin may not be sufficient to absorb most of the UVB and UVC radiation, allowing it to remain at a higher concentration for human exposure. As a result, arc welders may be at significantly increased risk of
developing actinic skin and ocular damage, including malignancy, particularly if they have inadequate protection. Additionally, thermal burns from hot metal can occur when welding, contributing to this risk. Welders can be advised regarding appropriate clothing and be encouraged to choose sunscreens that include UVC protection. Workers welding aluminum risk the highest exposures to artificial UV, and should take extra precautions. The lack of quality studies on UVC exposure means there is uncertainty about the risk of skin cancers from arc welding operations, and further investigations are needed.

While UVC radiation is not as prevalent on the Earth's surface as UVA and UVB radiation, the shorter wavelength creates the potential for more severe harm when contact is made. Most of the UVC radiation is created synthetically, rather than occurring naturally from the sun. This does not make it any less potent. There are benefits to UVC radiation because it has been shown to be helpful in eradicating certain types of germs that are resistant to other antibacterial measures. Jobs that expose individuals to UVC radiation should provide safety measures that will effectively prevent employees from risk to exposure and painful consequences. Arc welders must learn about and use recommended safety equipment in order to reduce their risk.

Constance M. Dolecki  
Independent Scholar

See Also: Ultraviolet A Radiation; Ultraviolet B Radiation; Ultraviolet Radiation Related Exposures.

Further Readings


Exposure to ultraviolet (UV) radiation is a major risk factor for development of many types of skin cancer. One of the most common sources of UV rays is sunlight, but tanning lamps and beds also produce UV rays. People who are exposed to the UV rays from these sources face higher risks of developing skin cancer. UV rays make up a small amount of the sun's rays, but they produce the main harmful effects of the sun because they damage the DNA of skin cells. When the sun's UV ray damage affects the DNA of the genes that control skin cell growth, the body is vulnerable to the development of skin cancer.

Not all UV rays are the same. There are three main types of UV rays, ultraviolet A rays (UVA), ultraviolet B rays (UVB), and ultraviolet C rays (UVC). UVA rays are responsible for aging skin cells and damaging skin cell DNA. UVA rays have been linked to long-term forms of skin damage, including wrinkles. These rays also have a part in the development of some skin cancers.

Most of the tanning beds on the markets give off large amounts of UVA, which is one reason why these beds pose a skin cancer risk. UVB rays are the rays mainly responsible for sunburns, and produce direct damage to skin cell DNA. UVB rays are often implicated as a causal agent in most forms of skin cancer. UVC rays are absorbed by the Earth's ozone layer, and are not based in sunlight. As such, these rays do not normally play a large part in the process of skin cancer development. Most of the UV rays that come in contact with humans are UVA, with a smaller amount of UVB. While both UVA and UVB rays damage skin and cause skin cancer, UVB rays are thought to be the stronger and more dangerous of the two types of rays, and are more heavily involved in causing at least some skin cancers. Fortunately, some UVB rays are also absorbed by the Earth's ozone layer. Other UVB rays, however, are not absorbed, and are able to pass through and affect humans. Overall, there are no safe UV rays. They are all harmful. The extent of harmful UV exposure normally depends on the strength of the rays, how much time the exposure to the skin occurs, and what type of protection is on the skin, including clothing or sunscreen.
Ultraviolet Radiation

All radiation is a form of energy, most of which is invisible to the human eye. UV radiation is only one form of radiation, and it is measured on a scientific scale called the electromagnetic spectrum (EM). UV radiation is only one type of EM energy. Radio waves that transmit sound from a radio station’s tower or between cell phones; visible light that is emitted from the lights in a home; and X-rays like those used in hospital X-ray machines are all forms of EM energy. Like all forms of light on the EM spectrum, UV radiation is classified by wavelength. Wavelength describes the distance between the peaks in a series of waves. UVA rays have the longer wavelengths, and UVC rays have the shortest wavelengths. UVB rays fall in between the two. The longer wavelength of the UVA rays is able to penetrate the middle layer, or dermis, of human skin.

Differences in size of wavelength can produce differences in what occurs with them. For example, the wavelengths at the bottom of the spectrum have radio waves with photons containing low energies. This causes wavelengths with long peaks that are farther apart. The photons of microwaves have higher energies, followed by infrared waves, UV rays, and X-rays. At the top of the spectrum, gamma rays have photons with very high energies and short wavelengths, with peaks that are close together. The shorter gamma ray wavelengths present the greater danger with exposure to humans. Both UVA and UVB, however, are able to penetrate the atmosphere, and play an important role in conditions such as premature skin aging, eye damage (including cataracts), and skin cancers. They also suppress the immune system, reducing an individual’s ability to fight off these and other maladies.

Effects of UV Rays

Sun is often thought of as the main causal agent in skin cancers, and is classified as a human carcinogen. If an individual receives too much sun, they increase their risk of skin cancer. Yet, there are other effects of UV exposure. Sunburn and tanning are the most evident short-term results of too much exposure to UV rays, and are the most obvious signs that the skin has been affected by this exposure. Longer exposure can cause more severe skin aging before its time, wrinkles, dry scaly skin, and age spots. Long-term exposure can also present precancerous skin changes, including dry scaly rough patches called actinic keratosis.

The sun’s UV rays can also increase a person’s risk of cataracts and other eye problems. These rays are responsible for problems with the function of the skin’s immune system. People with lighter skin are at higher risk for developing skin cancer than people with darker skin, but people with darker skin are still at risk for developing cataracts and a suppressed immune system. UV rays from the sun are not the only harmful source. UV radiation is also transmitted from tanning beds, classifying them as a human carcinogen. Other sources of UV radiation include mercury vapor lighting; halogen, fluorescent, and incandescent lighting; and some types of lasers. Additionally, some medicines can increase susceptibility to the UV rays and their harmful effects, including certain prescription and over-the-counter oral and topical medicines, and some types of cosmetics. These products can increase sensitivity for all skin types.

UV Index

The amount of UV light reaching the ground in any given place depends on a number of factors,
Ultraviolet Radiation Related Exposures

including the time of day, time of year, elevation, and cloud cover. The UV Index was designed by the National Weather Service and the Environmental Protection Agency (EPA) to provide an indicator of the strength of UV rays on any given day in any given area. The scale runs from 1 to 11-plus, with a higher number indicated greater risk of UV ray exposure. The greater risk of exposure also increases the chance sunburn and skin damage that could potentially lead to skin cancer. Local changes in cloud cover and other factors may change the actual UV levels experienced.

Exposure
Exposure to UV rays is linked to a number of harmful health conditions, including skin cancer. More than 1 million cases of nonmelanoma skin cancer are diagnosed in the United States each year. Most incidences of skin cancer appear in middle age or later, after the age of 50. Although it appears later, skin damage from the sun begins much earlier in life. Protection from overexposure to the sun's harmful rays should begin in childhood in order to prevent skin cancer later in life. This is difficult because children and adolescents do not see the consequences and might not heed warnings as a result.

Exposure to UV radiation can also cause photoaging, or premature aging of the skin. This is different from the chronological aging that is celebrated every year on someone's birthday. Sunbathers show photoaging earlier in life, often before they are 30 years old. Symptoms of the photoaging process include freckling, fine wrinkling, and dilation of capillaries. The photoaged skin frequently develops irregular pigmentation called liver spots in later years. Both photoaging and chronological aging cause wrinkling and loss of skin elasticity. However, these changes occur much earlier when skin has been overexposed to the sun.

Cataracts are classified as an eye disorder, and are characterized by a change in the structure of the crystalline lens that causes blurred vision. Cataracts are a leading cause of blindness around the world. One of the main risk factors associated with developing cataracts is excessive UV radiation exposure. Research indicates that individuals who spend more time in the sun may develop cataracts earlier than others. In an effort to decrease this risk, the American Academy of Ophthalmology now recommends wearing UV sunglasses and a wide brimmed hat to lessen exposure to ultraviolet rays. Additionally, corneal sunburn, growths on the outer surface of the eye, retinal-tissue damage, and other eye diseases are also known or are suspected to be related to long-term exposure to UV rays.

The skin is part of the body's natural defense system. Some research indicates that the UV radiation absorbed through the skin can negatively alter immune system functions, especially through invasion of skin cells. When UV radiation impedes the immune response of the system, it hampers an individual's ability to fight certain diseases, including skin cancer. Some health professionals have proposed that the overexposure of UV radiation also has the ability to interfere with the desired results of immunizations given through the skin. UV radiation has been a topic of concern for both the U.S. Departments of Health and Human Services as a proven human carcinogen. UV radiation is considered the main cause of nonmelanoma skin cancers (NMSC), including basal cell carcinoma (BCC) and squamous cell carcinoma (SCC). UV radiation has also been linked to melanoma, the most virulent and deadly form of skin cancer, by many professionals. They point to increased risk for people who have fairer skin tones.

Sunscreen Ingredients
Since both UVA and UVB are harmful, individuals need protection from both kinds of rays. Sun protection products are beginning to offer additional UVC radiation protection. Modern-day sunscreens are measured by sun protection factor (SPF) levels, which provide an individual with information on its effectiveness in protecting from harmful sun rays. SPF is not the amount of protection a product provides. The SPF number indicates how long it will take for UVB rays to redden skin when using a sunscreen, compared to how long skin would take to redden without the product. Someone using an SPF of 45 will be protected from reddening in the sun 45 times longer than if they did not use protection. An SPF 15 sunscreen screens 93 percent of the sun's UVB rays; SPF 30 protects against 97 percent; and SPF 50, 98 percent. The Skin Cancer Foundation maintains that SPFs of 15 or higher are necessary for adequate protection.

The photochemical effects of UV radiation can be exacerbated by chemical agents. Protection from UV is provided by clothing, polycarbonate,
glasses, acrylics, and plastic diffusers used in office lighting. Sun-blocking lotions offer limited protection against UV exposure. Accidental overexposure might not be detected because the UV radiation is invisible, and does not produce an immediate reaction. Yet, this radiation can injure individuals.

Constance M. Dolecki
Independent Scholar

See Also: Ultraviolet A Radiation; Ultraviolet B Radiation; Ultraviolet C Radiation.

Further Readings

Union for International Cancer Control

The Union for International Cancer Control (UICC), formerly named the International Union Against Cancer (IUAC), is the largest cancer-fighting organization in the world. It focuses on helping the global health community in its battle against cancer. The member organization includes approximately 815 organizations from 155 countries, from cancer societies and research institutes to government and international health organizations, patient groups, and corporate partners.

IUAC was established in 1933 when cancer researchers founded the organization to enhance the global sharing of knowledge and expertise. IUAC changed its name to UICC in 2014. Based in Geneva, Switzerland, UICC fosters the fight against cancer on a global scale. Its member organizations govern the organization, which has an executive body made up of 17 board of directors members. UICC’s longstanding partners include the National Cancer Institute, Centers for Disease Control and Prevention, World Cancer Research Fund Society, American Cancer Society, Swiss Cancer League, Norwegian Cancer Society, and World Health Organization (WHO).

UICC primarily focus on three interlinked pursuits: advocacy, convening member meetings, and running building projects. The organization has stated that its specific purpose is to bring together the international cancer community to reduce the burden of cancer on an international scale. Other goals include promoting greater equity in cancer research and care and fostering the inclusion of cancer control issues in the agendas of world health and development organizations.

UICC is the administrator of the International Cancer Fellowship program, and its official publication is the International Journal of Cancer. In terms of advocacy efforts, UICC oversees various advocacy efforts and education initiatives designed to have the greatest impact on reducing the cancer burden. Its advocacy efforts include providing support to increase resources to fight cancer with a special focus on developing countries, which are most at risk of cancer overwhelming their health systems and hindering economic growth.

Advocacy campaigns include efforts such as improving access to cancer medicines via the WHO Model List of Essential Medicines, increasing the availability of radiotherapy for cancer control in low- and middle-income countries, and setting cancer prevention and control priorities for global health and development projects. These advocacy efforts typically include communication programs to disseminate important information about cancer; sharing data on cancer prevention and control concerning specific countries, and developing UICC authored or coauthored position papers, factsheets, and other written contributions.

UICC helps coordinate global cancer programs, such as the Global Education and Training Initiative, to help meet the growing global shortage in the health care workforce. The organization’s Global Access to Pain Relief Initiative is a joint program with the American Cancer Society to ensure
the universal availability of essential cancer pain medicines by 2020. The Cervical Cancer Initiative focuses on reducing the development of cervical cancer in women, as well as death from the disease.

UICC’s Childhood Cancer (ChiCa) program is dedicated to increasing the number of children who survive cancer in low- and middle-income countries by providing guidance on developing prompt, essential treatment initiatives in these countries, with an emphasis on accessibility and affordability. The Global Initiative for Cancer Registry Development program is a multi-organizational effort led by UICC and the International Agency for Research on Cancer. The program focuses on increasing cancer registry efforts in countries to help effectively use available resources in areas such as cancer prevention, treatment, rehabilitation, and palliative care, as well as to set research agendas.

UICC also holds a general assembly every two years in collaboration with the World Cancer Congress. The assembly serves to bring together UICC members from around the world to foster discourse, advocacy, and cancer education. UICC and member organizations typically supply printed information, including news releases on topics discussed. For example, the 2012 meeting included releases concerning how lifestyle changes could prevent 50 percent of common cancer, including issues surrounding smoking and obesity, as well as how to protect against the main viruses associated with cancer.

UICC is also a cosponsor of World Cancer Day, which in 2014 focused on reducing the stigmas associated with cancer and dispelling myths about the disease. The four myths addressed were (1) people do not need to talk about cancer, (2) signs or symptoms for cancer do not exist, (3) nothing can be done about cancer, and (4) the belief held by some people, primarily in developing countries, that they do not have the right to cancer care.

Another convening program supported by UICC is the World’s Cancer Leaders’ Summit. Designed to bring key decision makers together, the summit is a high-level policy meeting that fosters debate on emerging cancer issues designed. A goal is to ensure that various cancer organizations around the world mount positive responses to support government initiatives. These meetings also feature time allotted for both organizations and individuals to make public commitments on various cancer control programs and projects.

The UICC Global Roundtable Series features roundtables focusing on key cancer issues in cities around the world. The roundtables typically bring together civil organizations, governments, and representatives from the private sector. The series fosters discussion of pressing issues such as the cancer information dilemma, understanding and curing prostate cancer, and the development of personalized cancer medicine.

In 2013, UICC joined forces with IBM to develop the largest and most comprehensive clinical dataset on cancer patients in the world. The effort focuses primarily on building cancer registries in developing countries. The initiative began in sub-Saharan Africa, where an 85 percent–plus increase in the area’s cancer burden is expected to take place by 2030. The effort is anticipated to extend to Southeast Asia and Latin America. The plan is to improve cancer registry data to show population-based trends that can help countries shape and adapt their cancer strategies.

David Petechuk
Independent Scholar

See Also: American Cancer Society; Cervical Cancer; Pain and Pain Management; World Health Organization.

Further Readings


United Arab Emirates

The country of the United Arab Emirates (UAE) lies on the southeast end of the Arabian Peninsula on the Persian Gulf. The country formed in December 1971,
with the combination of seven principalities or emirates. A hereditary emir governs each emirate, and the seven emirs comprise the Federal Supreme Council, which is the highest executive body in the UAE. The emirs select a president from their group. The conduct of national business occurs in Abu Dhabi, the capital city of UAE. Islam is the official religion, and Arabic is the official language. Since 1971, incredible financial and industrial progress with the exportation of oil occurred in the UAE, causing a change from the old-style seminomadic existence to a contemporary urbanized and technology-propelled lifestyle. Cancer is the second-largest cause of death globally, but it is the third-largest cause of death in the Emirates. In the beginning of the 1900s, the UAE demonstrated a very low incidence of cancer compared to developed countries, but since the 1970s, the country has gone through upheaval in the economic, social, and demographic platforms, leading to increased prosperity. These alterations resulted in significant increases in all chronic noncommunicable disease, including cancer. Deaths from cancer climbed to 10 percent of all deaths in 2010.

No national or regional population-based cancer registry currently exists in the UAE. With no cancer registry, the UAE produces no comprehensive information on the incidence of cancer. Despite this limitation, the Minister of Health gathered some data for the UAE to enter in the Globocan database and Gulf Cooperation Council-wide cancer registry report. The number of cancer deaths in the UAE for both sexes is 54.9 per 100,000 person years; whereas in the United States, the number of cancer death for both sexes remains at 104.1 per 100,000 person years. Despite the lower rates at this time, the rate of all cancers is anticipated to double by 2020. Researchers expect that aging and an elevated exposure to risk factors in a more Westernized society will trigger the increase in cancer rates.

Breast cancer is the most regularly occurring cancer in females in the UAE, and is the most prevalent cancer in both genders; whereas lung cancer remains the most commonplace cancer among males, but scarcely occurs in females (mirrored by the smoking rate: males 23 percent, and females 0.5 percent). Not only is breast cancer the most frequent cancer in females, the malignancy appears a decade earlier in UAE women than females in Western countries, with the majority of patients premenopausal. Because of social traditions, many females in the UAE fail to attend regular medical examinations until symptoms from advanced stages of the disease appear. The tumors appear with more aggressive histology and biology. The majority of tumors demonstrate vascular and lymphatic invasion. Gene (P53 and Her-2 neu) over-expression remains relatively high in breast cancer cases in the UAE. Elobaid and colleagues conducted a cross-sectional survey of women (≥ 40 years) in one city in the UAE. The study found that many women lacked information about breast cancer screening, with 44.8 percent never receiving a clinical breast exam, and 44.1 percent never undergoing a mammography. Contact with a health care practitioner represented the most important pathway for alerting women to the value of periodic breast screening.

Colorectal cancer is the second most frequent cancer in both genders, followed by leukemia and non-Hodgkin lymphoma. Pediatric cancers account for approximately 9.5 percent of all cancer events, with an average of 9.2 cases per 100,000 children in the UAE. Lymphoma occurs as the most frequent childhood malignancy, and accounts for nearly 60 percent of all childhood cancers. Prostate cancer is the second-most-common cancer among national males in the UAE.

The UAE hosted the 5th Pan Arab Human Genetics Conference jointly with the 2013 Golden Helix Symposium. The meeting revolved around nine sessions, consisting of cancer genomics and epigenetics, genomic and epigenetic studies, genomics of blood and metabolic disorders, cytogenetic diagnosis and molecular profiling, next-generation sequencing, consanguinity and hereditary diseases, clinical genomics, clinical applications of pharmacogenomics, and genomics in public health. Scientists discovered that cancer in the Arab world shows an increased homozygosity from consanguinity. Elevated homozygosity from consanguinity links to a high risk of cancer. One study reported on breast cancer in women accounting for 42 percent of all tumors. The study showed that triple-negative breast cancer (e.g., any breast cancer failing to express genes for estrogen receptor, progesterone receptor, and Her2/neu) remains more common in this area.

The UAE attended the Afro Middle East Asian Symposium in 2014 to present its current oncology situation and needs. The Middle East countries or Gulf countries represent only 1.2 percent of the
United Kingdom

The northwestern European nation currently termed the United Kingdom of Great Britain and Northern Ireland became a modern state in 1707, when the Treaty of Union was ratified by the various kingdoms of England, such as Scotland and Wales. Consequently, this treaty made the United Kingdom a single sovereign state. Nearly a century later, the United Kingdom ratified an Act of Union in 1800 that further added the Kingdom of Ireland to the United Kingdom.

In many western European countries in the 18th and 19th centuries, cancer was perceived to be a predominately female disease due to the high prevalence of breast and uterine cancers, and during this time period this belief was particularly dominant in the United Kingdom. At the time, many English social commentators believed that men could only contract cancer by emasculating themselves through eating excessive amounts of food and not exercising often enough. Even experts of the era, like Walter Hayle Walshe who was the author of a leading textbook on cancer in 1846, maintained that women were as much as three times more likely to experience an incidence of cancer than males were.

When incidences of cancer in males rose during this period, gender as a causing factor of the disease became refutable, and other avenues of causation were explored; some of the other sources that had begun to be explored as cancer-causing agents included physical trauma, sexual intercourse, masturbation, occupation, residence, unpleasant emotional states, and nutrition. In the early 19th century, doctors were extremely hesitant to perform surgery on cancerous tumors because it was believed that this would not treat the underlying constitutional cause of the cancer. Also, surgical techniques were still relatively crude at this time, and operations on tumors were considered more risky than beneficial. Patients deemed terminally ill were copiously prescribed opiates and were advised to shun any form of physical exertion.

Toward the end of the 19th century, physicians began to move away from the notion of gender, morality, or one's constitution as the causes of cancer; instead, as surgeons became more technically skilled and knowledgeable, cancer began to be understood as a disease that was localized in specific organs and tissues and that was caused by the degeneration of cells, and thus surgery became the most viable and dominant treatment option during the 1860s and onwards. Surgeons such as William De Morgan and Charles Moore became vocal leaders in the shift towards this modern understanding of the disease.

When the United Kingdom entered the 20th century, this new understanding of cancer helped lead its...
citizens to a strong social awareness of the dire need to combat the disease effectively. Over the past 100 years, numerous domestic research institutions have been created to contribute to the global effort to find a reliable cure. The United Kingdom Association of Cancer Registries was initiated in 1992 to provide a single and reliable source for important cancer information within the country. As a part of the global World Cancer Research Fund, the World Cancer Research Fund UK was begun in 1990 as a charity entirely focused on the domestic prevention of cancer. In 2013, Cancer Research UK discerned 80 novel genetic variations that increase the risk of certain cancers.

Currently, the most prevalent forms of cancer in the United Kingdom are bowel cancer, breast cancer, lung cancer, and prostate cancer. Bowel, lung, and prostate cancers make up over half of all cancer incidences in males in the United Kingdom, while bowel, breast, and lung cancers account for over half of all cancer incidences in females there. Within the past 10 years, certain cancers such as malignant melanoma, thyroid cancer, uterine cancer, liver cancer, and kidney cancer have seen a nationwide increase in prevalence, while incidences of bladder cancer have steadily but consistently dropped. Certain parts of the United Kingdom experience more cases of specific cancers than other parts of the country, such as the high incidence of lung cancer in Scotland due to higher levels of smoking there than the rest of the nation.

Unfortunately, many citizens of the United Kingdom have had cancer. The world-renowned musician and songwriter George Harrison (1943–2001) of the Beatles died from lung cancer that had spread to his brain; the popular broadcaster and journalist Alistair Cooke (1908–2004) also died from lung cancer that had spread to his bones. Moreover, the critically acclaimed British actor Sir Alec Guinness (1914–2000) passed away due to liver cancer. There are currently many gifted cancer specialists operating in the United Kingdom at world-class facilities. For instance, Dr. Nick Plowman is the Senior Clinical Oncologist at St. Bartholomew’s Hospital and the Hospital for Sick Children at Great Ormond Street; he is extremely well renowned in the field of cancer treatment for his seminal expertise in radiation therapies. Another renowned specialist is Dr. Nihal Shah, who is the Consultant Clinical Oncologist at the Mount Vernon Cancer Centre in London. He is a foremost expert in the treatment of breast, head, lung, and neck cancers, and Dr. Nihal also specializes in treating patients with unknown primary cancers.

William M. Peaster
Independent Scholar

See Also: Breast Cancer; Cervical Cancer; Lung Cancer, Non-Small Cell; Lung Cancer, Small Cell; Rectal Cancer.

Further Readings
United States

The United States is a former British colony that declared its independence from Great Britain in 1776 and was recognized as the new nation of the United States of America following the Treaty of Paris in 1783. During the late 18th, 19th, and 20th centuries, 37 new states were added to the original 13 colonies as the nation expanded across the North American continent and acquired a number of overseas possessions.

Two of the most traumatic experiences in the nation’s history were the Civil War (1861–1865), in which a northern Union of states defeated a secessionist Confederacy of 11 southern slave states, and the Great Depression of the 1930s, an economic downturn during which about a quarter of the labor force lost its jobs. Even with the challenge presented by the recession that started in 2008, the United States remains the world’s most powerful nation state. The economy has achieved relatively steady growth, low unemployment and inflation, and rapid advances in technology in global comparisons.

As one of the most developed countries in the world, the United States faces a tremendous cancer burden. The United States is one of the most populous nations with a 2013 population of over 318.9 million, and in 2013, there was an estimated 1,665,540 new cancer cases diagnosed and 585,720 cancer deaths in the United States. Cancer remains the second most common cause of death in the United States (after heart disease), accounting for nearly one of every four deaths. For every 100,000 people there are 250 physicians and 980 nurses, for all areas of specialization.

As a world leader in health care, the United States has many organizations on the forefront to fight cancer. The American Society of Clinical Oncology (ASCO) is one such organization. In their landmark report on the state of cancer care in America, they recognized that the demand for cancer prevention, screening, and treatment services is growing rapidly. The ASCO reports that by 2030, the number of new cancer cases in the United States will increase by 45 percent, and cancer will become the nation’s leading cause of death, largely as a result of the aging of the nation’s population. At the same time, the number of cancer survivors, which totaled 13.7 million in 2012, will continue to grow. Many of these individuals will require significant, ongoing care. After reviewing the current need for cancer care in America, the ASCO report examined and identified many future challenges to the U.S. cancer care system, and specifically addressed the need to increase the number of oncology workers and the racial and ethnic diversity of those workers.

Another issue identified, a problem similar to what other developing nations face, is access to quality health care for the poor or otherwise disenfranchised. In the United States, access to quality cancer care remains uneven, which is often reflected in various health disparities. Millions of people with cancer lack access to quality medical care, and rates of access to care are disproportionately lower for African Americans and Latinos. About 30 percent of Americans reported foregoing medical care due to cost in 2013, and those without a regular source of care are less likely to receive cancer screening. The Patient Protection and Affordable Care Act (ACA) is expected to provide millions more Americans with health insurance coverage in the coming years. However, the ACA alone may not solve disparities in cancer care as it places significant emphasis on expanding Medicaid coverage, which has been associated with poor outcomes for patients with cancer. The ACA is not a universal coverage plan, and in the first quarter of 2015, one year after implementation of the ACA, 11.9 percent of adult Americans (age 18 and older) were uninsured. Soaring costs have created an urgent need to improve the value of patient care. While costs are rising throughout the health care system, the trend is especially pronounced in cancer care as annual costs have risen from $104 billion in 2006 and are expected to reach more than $173 billion in 2020. This increase is a result of many factors, including the cost of many new cancer therapies. Access to high-quality cancer care will be sustained and expanded only if we address these rising costs, including the use of unnecessary or ineffective tests and treatments.

Cancer Scientists

Historically, many prominent cancer scientists have come from the United States or have received their training and education in the United States. John Collins Warren (1778–1856), one of the most renowned surgeons of the 19th century, wrote *Surgical Observations on Tumors, With Cases and Operations* (1837). Others were Nobel Prize winners for cancer research: Peyton Rous (1879–1970)
was awarded the Nobel Prize for Physiology or Medicine in 1966 for his work with sarcomas and how they could be transmitted; Ernest Orlando Lawrence (1901–1958) won the 1939 prize for Physics for his invention of the cyclotron, the first particle accelerator to achieve high energies, and was later involved in the use of neutron beams in treating cancer; and Salvador Luria (1912–1991), who won the Nobel Prize for Physiology or Medicine in 1969 for his work concerning the genetic structure of viruses, was later appointed director of the Center for Cancer Research at MIT.

In 2006, five Johns Hopkins Cancer Researchers, Bert Vogelstein, M.D., Kenneth Kinzler, Ph.D., James Herman, M.D., Stephen Baylin, M.D., and David Sidransky, M.D., were named doctors of the decade as their research has influenced modern scientific thought in oncology based on the number of citations their work has received. Vogelstein and Kinzler, both leading experts in molecular genetics, had over 50,000 citations. In 2014, Owen Witte, M.D., a prominent stem cell researcher, established a targeted therapy for chronic myeloid leukemia.

Cancer research is advancing in several areas, beginning with more targeted therapies. And as more is learned about the molecular biology of cancer, researchers will have more targets for their new drugs. Some of these areas include immunotherapy, in which drugs aimed at specific immune checkpoints are being developed to help the immune system better kill cancer cells; cancer genetics, in which scientists identify gene mutations that cause some patients to respond better to certain drugs; nanotechnology, which is a new technology for producing materials that form extremely tiny particles used in imaging to locate tumors; robotic surgery, which is used to remove tumors with less surgical trauma; expression profiling and proteomics, in which expression profiling identifies what proteins are present in cells, their behavior, and their aggression levels, which can help scientists predict the drugs a tumor will respond to; and proteomic methods, which is measuring the amount and type of protein in the blood that can be used for cancer screening.

Research and Advocacy Organizations
The United States is not only the leader in cancer research and treatment, the nation leads the world in patient-centered self-help and political advocacy groups. One grassroots political advocacy organization is the National Breast Cancer Coalition (NBCC), a nonprofit organization founded in 1991 with the goal of ending breast cancer, not just treating it. In 2010, the NBCC set a deadline of knowing how to end breast cancer by 2020, and it launched a plan to achieve this. Breast Cancer Deadline 2020 is their call to action for all stakeholders to focus efforts on knowing how to end the disease by the end of the decade. The Accelerating the End of Breast Cancer Act, S. 865 and H.R. 1830, defines an important role the federal government must play in this effort. The legislation complements and enhances the strategic work being done by NBCC to end breast cancer. Earlier grassroots advocacy work resulted in the Department of Defense Breast Cancer Research Program (DOD BCRP), which was created in 1992 to “eradicate breast cancer by funding innovative, high-impact
research through a partnership of scientists and consumers.” The DOD BCRP is widely viewed as an innovative, unique, and efficient medical research model, which has proven to be accountable to the public and has produced extraordinary results. NBCC seeks continued funding for this successful program.

Other important organizations include the American Association for Cancer Research, the American Cancer Society, the American College of Radiology, the American College of Surgeons, the American Society for Therapeutic Radiology and Oncology, the American Society of Clinical Oncology, the Arthur G. James Cancer Hospital Research Institute, the Black Women's Health Imperative, Campaign for Tobacco-Free Kids, the Cancer Treatment Centers of America, the Candlelighters Childhood Cancer Family Alliance, the C-Change: Collaborating to Conquer Cancer, the Centers for Disease Control and Prevention, the College of American Pathologists, the Fred Hutchinson Cancer Research Center, FORCE: Facing Our Risk of Cancer Empowered, the Gerald P. Murphy Cancer Center, the Kellogg Cancer Care Center, the LIVESTRONG Foundation, the Massey Cancer Center, the MD Anderson Cancer Center, the National Cancer Institute, the Oncology Nursing Society, the Smilow Cancer Center at Yale Hospital, the St. Jude Children’s Research Hospital, and the Susan G. Komen Breast Cancer Foundation. There are many others.

Annette Madlock Gatison
Southern Connecticut State University

See Also: American Association for Cancer Research; American Cancer Society; National Cancer Institute.

Further Readings


University of Alabama at Birmingham Comprehensive Cancer Center

The University of Alabama at Birmingham Comprehensive Cancer Center (UAB CCC) is one of the nation's leading cancer research and treatment centers. Established in 1971, it was the first National Cancer Institute (NCI)--designated center in the region. It is the only NCI-endorsed full-service cancer center in Louisiana, Mississippi, Alabama, Georgia, South Carolina, and Arkansas. The center treats approximately 5,000 new cancer patients annually. It has more than 330 scientists on its staff, comprised of researchers and physicians. In addition to treatment for cancer, the center also conducts research. The mission of the UAB CCC is to provide the highest quality of life for people diagnosed with cancer while advancing the world's understanding of cancer, and translating this knowledge into prevention, detection, treatment, and survivorship. The vision is to eliminate cancer as a major public health problem.

To achieve the mission and vision, the center has comprehensive research activities in the areas of immunotherapy, drug discovery and development, and gene therapy. Scientists in the center have been sourced from various professions to ensure that every aspect of cancer is involved in the treatment and research. These include the areas of immunotherapy, surgery, radiotherapy, chemotherapy, and nutrition. In each of these areas, the scientists have made considerable advances. Currently, scientists in the center are devising new antibiotic treatments for cancers of all sorts.

One of the strengths of the center is in the area of translational research. This strength is coupled with active programs of research and patient care in the
areas of ovarian, breast, pancreatic, and brain cancers. Patient care in UAB CCC is delivered in multidisciplinary clinics that also foster accrual to clinical trials with novel treatments. These novel treatment techniques use genetically engineered monoclonal antibodies, alone or in combination with radioactive isotopes, chemotherapy, or immunotoxins to specifically target a broad array of cancers. The team of researchers in the center is also developing a series of cancer vaccine trials using genetically engineered vaccine reagents. The UAB CCC has developed a number of therapeutic vaccine strategies. To develop an overall vaccine strategy, researchers at UAB CCC are exploring a broad array of approaches to induce an immune response to molecules prevalent in tumor cells.

To promote cancer awareness, one of the core elements in the mission of the center, the Deep South Network for Cancer Control, was formed. The Deep South Network for Cancer Control is a program of UAB that seeks to enhance outreach and collaboration, with the objectives of training, gathering cancer related data, and providing education to the 22 counties in Alabama and the Mississippi Delta. Toward this end, the UAB CCC has held hundreds of community events on the importance of cancer prevention, awareness, and cancer screening. To ensure that professional cancer information is available through the outreach program, the center uses trained volunteers as community health advisors to educate community members.

The ultimate goal of the Deep South Network is to build a community-based infrastructure that will aid in eliminating cancer health disparities in underserved African American communities. To fast track this initiative, the center has formed collaboration with local communities that has resulted in network collaborations with more than 300 community partners, including small businesses, industries, schools, faith-based groups, and other organizations to implement cancer prevention and wellness programs. Other organizations, including nonprofit organizations, state agencies, and media partners, have come onboard to help the Deep South Network in disseminating information to local communities.

The UAB CCC strives for excellence in its dual roles as a regional cancer referral center and a cutting-edge research entity. This is realized through having the information established in the research work translated to treatment and patient care. However, the first step toward realizing this is clinical trials. UAB CCC members actively participate in efforts to improve cancer therapy, diagnosis, and prevention through original research protocols and the NCI’s high-priority trials and multicenter research collaborations, including national cooperative group studies. This multifaceted approach towards research and clinical trials maintains the center’s connections with the national cancer research community while fostering the development of translational research linked to the UAB’s scientific resources.

Treatment of cancer patients at the UAB CCC is done through the practice of comprehensive cancer treatment. This practice requires that patients be treated not just by one doctor, but by a team of highly specialized professionals who work together to determine the best course of action for each patient. Through this practice, cancer patients seeking treatment at the UAB CCC can expect a visit by up to three specialists on the first day.

One of the outstanding treatments at the UAB CCC is mesothelioma cancer treatment. The diagnosis for this diseases is one of the most challenging because of its symptoms that include chest pain, cough, and fatigue—symptoms that are similar to other diseases. To provide treatment, it requires appropriate diagnosis, and the comprehensive cancer treatment practiced at the UAB CCC serves to increase the probability of a correct diagnosis. At the UAB CCC, patients suffering from the disease are treated at the Lung Health Center, which focuses on diagnosis, treatment, research, and innovations related to lung diseases. Treatment of mesothelioma at the UAB CCC consists of a combination of surgery, chemotherapy, and radiation. If a patient decides to take part in the clinical trial for novel treatment techniques, then they are treated using new treatments not yet available to the public.

In addition to mesothelioma treatment, the Cancer Vaccine Development program of the UAB CCC has been charged by the NCI with development of a series of vaccine trials using properly and professionally engineered vaccine reagents. So far, the center has successfully developed four therapeutic vaccine strategies: a vaccine that can control the development of tumors in those who have metastatic breast cancer that has been known to respond well to hormonal treatments and adjustments, a genetically engineered vaccine virus (smallpox) to eradicate colon cancer, a naked deoxyribonucleic acid (DNA) gene therapy vaccine for colon cancer,
and studies to test immunization to the carcinoembryonic antigen (CEA) for several different cancer sites, including the colon and breast.

Michael Fox

Independent Scholar

See Also: Mesothelioma, Adult Malignant; Mesothelioma, Childhood; National Cancer Institute.

Further Readings


University of California, Davis, Comprehensive Cancer Center

The UC Davis Cancer Center is designated as a National Cancer Institute (NCI) Comprehensive Care Center. The specialized team of doctors works to develop treatment plans for each cancer patient. The center is recognized nationally as a leader in research, treatment, and education. It is one of the largest and most comprehensive available on the West Coast.

The pediatric oncology section at the center is a member of the Children's Oncology Group (COG), a federally funded cooperative for the treatment of pediatric cancers. The center offers more than 40 pediatric cancer clinical trials at any given time and is one of only two Sacramento COG programs. The center provides diagnosis and management of all types of pediatric cancers and blood disorders. Specialists in neuro-oncology, radiation oncology, otolaryngology, ophthalmology, and urology are also available. Resources for patients and their families may include social support services, temporary housing, and case management.

Plastic surgery is also a key program available at the center. Plastic surgeons have been dedicated to patient care since 1975. They are trained as clinicians and educators and bring the highest standards of professional care. Services in plastic surgery include: facial aesthetic surgery; aesthetic surgery of the trunk and extremities; reconstructive surgery of the breast, trunk, and extremities; hand surgery; and skin care.

The Department of Radiation Oncology is nationally recognized for pioneering state-of-the-art technology and treatment methods for cancer patients. The ultimate goal of the department is the relief of symptoms and the eradication of cancer. The department includes research programs that advance technology through clinical trials and laboratory research. The department focuses on treating cancer patients using state-of-the-art technology and clinical trials...
on research in cancer stem cells, DNA repair, low-dose radiation, and new imaging technologies. The department also has residency programs in radiation oncology and medical physics. They are committed to expert patient-centered care, research, and quality teaching.

The UC Davis Stem Cell Transplant Program performed its first bone marrow transplant in 1993. The program currently serves adults and children and is the region’s only National Marrow Donor Transplant Program giving patients access to potential donors worldwide.

The Surgical Oncology Program provides highly skilled, board-certified, nationally recognized surgeons. The program assures that each patient’s surgical care is planned by a team of cancer specialists (i.e., radiation oncologists, medical oncologists, surgical oncologists, plastic surgeons, etc.); is comprehensive from diagnosis through treatment; is based on the most current knowledge of cancer disease and surgical applications; is appropriate after fully considering the risks and benefits; and is continued with regular follow-up. UC Davis Medical Center also offers robotic-assisted surgery in several specialties (i.e., gastrointestinal surgery, cardiothoracic surgery, gynecologic oncology, otolaryngology, and urology). The da Vinci robotic surgical system represents the latest in minimally invasive surgery while offering a broader visualization of the operative field and precision control of surgical instruments not available in traditional laparoscopic surgery. Benefits associated with the da Vinci system can include significantly less pain, less blood loss, less risk of infection, less scarring, shorter hospital stays, and shorter recovery times.

UC Davis Cancer Center offers research programs with researchers who are experts in a variety of fields and are interested in a related group of cancers. The Molecular Oncology Program seeks to unravel cancer’s molecular secrets to better diagnose and treat cancers. Seventy percent of cancer patients whose cancer involves treatment-resistant malignant cells can benefit from molecular oncology research.

In all cancers combined, the death rate is 25 percent higher for African Americans than for whites. White women have the highest rate for breast cancer, but African American women are more likely to die from breast cancer. Hispanic women have the highest cervical cancer rate. African American men have the highest rate for prostate cancer in the United States and are more than twice as likely as white men to die from this disease. Pacific Islanders and Asian Americans have the highest rate for liver and stomach cancer and are twice as likely to die from these diseases as whites. Alaska Natives and American Indians have higher rates and deaths for kidney cancer than any other racial or ethnic group.

UC Davis Cancer Center cites these disparities as the primary reason for the creation of the Cancer Disparities Research Program, which is dedicated to understanding why cancer affects people differently and how to eliminate disparities among ethnic and racial groups. The NCI defines cancer health disparities as adverse differences in the incidence, prevalence, mortality, and survivorship of cancer. These differences do not necessarily fall in racial or ethnic lines but can include: age, disability, education, gender, income, and geographic location.

The Comparative Oncology Program has an interest in comparative medicine approaches. Comparative oncology can include research in canine cancer, as it does at UC Davis. The effort to understand comparative oncology is critical as there is increasing difficulty in new successful drug treatment for cancer, and only five percent of new drugs investigated ever end up receiving approval from the Food and Drug Administration.

The Prostate Cancer Research Program at UC Davis is ranked third in the nation with regard to research grants. The program also ranks among the top three institutions receiving NIH funding over the previous three years.

The Cancer Therapeutics Research Program focuses on innovative methods for identifying new systems to treat cancer. As an example, the first chemotherapy agent was derived from mustard gas when somebody noticed those exposed to it were low on white blood cells. Researchers used this finding to treat lymphoma, a cancer of the white blood cells. The aim of the Cancer Therapeutics Research Program is to discover new drugs, take them through the necessary trials, and then get them into the clinic.

The Biomedical Technology Research Program researches innovative engineering technologies to solve cancer problems. For example, when a surgeon removes a tumor, a biopsy of healthy
tissue is removed from the edge of the tumor to be reviewed under a microscope to ensure that the entire tumor has been removed. If pathology is found, the surgeon removes more tissue, and the process is repeated until no further malignancy is evident. UC Davis researchers have been engaged in the development of a light tool that would assist the surgeon so that healthy tissue can be distinguished from malignant tissue during surgery, without the need for repeated checking with a microscope.

Jessica Anne Hammer
Independent Scholar

See Also: University of Hawai’i Cancer Center; University of Pittsburgh Cancer Center; University of Southern California Norris Comprehensive Care Center; University of Virginia Cancer Center; Vanderbilt-Ingram Cancer Center.

Further Readings

University of California, Los Angeles, Jonsson Comprehensive Cancer Center

The Jonsson Comprehensive Cancer Center (JCCC) began in 1974 as a cancer center started by scientists at the University of California, Los Angeles (UCLA). In 1976, the National Cancer Institute (NCI) designated it as a comprehensive cancer center. The UCLA Medical Center, in particular, has been ranked by U.S. News and World Report as the best medical center in the western United States and one of the best three hospitals in the country. As of 2013, it was ranked 11th nationally among cancer centers. JCCC received the comprehensive designation because it offers a wide range of services in terms of treatment, research, and support of patients in treatment and their families. Issues with regard to survivorship and prevention are also under the JCCC umbrella of services.

JCCC works closely with the UCLA School of Medicine. As such, JCCC lists more than 100 UCLA physicians who are considered to be among the best doctors in America. Interdisciplinary treatment of patients at JCCC also provides patients with care from more than 350 physicians and scientists from areas that include immunology, genetics, geriatrics, nursing, and dentistry. Services provided to patients include early detection, treatment, psychological care, guidance with nutrition and general wellness, as well as survivorship.

JCCC is located in California and has clinics in Westwood, Santa Monica, Alhambra, Irvine, Pasadena, Porter Ranch, Santa Clarita, and Simi Valley. Although clinics are located in California, through partnerships with other programs, JCCC is able to offer clinical trials throughout the United States. These partnerships were made possible by Dennis Slamon, M.D., who launched Translational Oncology Research International (TORI). TORI provides opportunities for UCLA physicians and scientists to partner with other researchers, health care providers, and research institutions to provide clinical trials of experimental medications and treatments. TORI also offers cancer patients the opportunity to search for experimental trials of medications and treatments on their specific cancer diagnosis, thus linking a more diverse population of cancer patients to cancer research. Patients can search and find clinical trials specifically through the JCCC Web site or by calling the Clinical Trials Hotline at (888) 798-0719. The TORI network has brought together more than 25 oncology practices, 130 physicians, and 5,000 patients throughout the United States in the fight against cancer.

The JCCC Web site offers a vast amount of information to patients, caregivers (including family and
friends), and health care practitioners. Information and support can be found based on specific cancer diagnosis and organ system affected. Survivorship support and opportunities for survivors to organize and fund-raise are included on the Web site. Further, patients and family and friends can find physicians at UCLA based on a search of their gender, language, and specialty.

Survivorship, in particular, is a focus of JCCC. Some of the programs survivors can participate in through JCCC include the UCLA–Livestrong Center of Excellence; Simm/Mann–UCLA Center for Integrative Oncology; Athena Breast Health Network; and UCLA Family Cancer Registry. For survivors who want to give back, the Jonsson Cancer Center Foundation provides a place for survivors to participate in cancer fund-raising events.

As the Jonsson Comprehensive Cancer Center Foundation is the primary sponsor of JCCC, it is active in fund-raising to continue research on and treatment of cancer. The foundation can be accessed through the UCLA Fights Cancer page on Facebook, Twitter, or YouTube. The JCCC Foundation, along with grants from other research organizations, supports a wide variety of research at JCCC and UCLA.

Research at JCCC focuses on eight program areas. These include cancer and stem cell biology; cancer molecular imaging; gene regulation; genitourinary oncology; healthy and at-risk populations; patients and survivors; signal transduction and therapeutics; and tumor immunology. Another program on nanotechnology is under development. The program areas were created to encourage interdisciplinary research across disciplines. Other research programs, called shared resources, focus on the prevention, diagnosis, and treatment of cancer and include: biostatistics, analytical support, and evaluation; embryonic stem cell/transgenic mice; flow cytometry; genomics; informatics; molecular screening; small animal imaging; and a translational pathology core laboratory.

Breast and ovarian cancer research at JCCC serves as an example of the cutting-edge research conducted there. JCCC received grant support from the Noreen Fraser Foundation. Both breast and ovarian cancers are not specific types of cancer but instead different forms of cancer that only have in common the organ where they can be found. Through the breast cancer research at JCCC, they have developed a medication presently called PD 0332991, which can be used to inhibit cdk-4/6 and thus stop the growing of estrogen receptor positive (ER+) breast cancer cells. The results to date are stronger when the new medication is combined with tamoxifen. A phase III trial is in the planning process for the new drug.

With regard to ovarian cancer, UCLA researchers have accumulated 41 human ovarian cancer cell lines and 225 clinical ovarian tumor samples. Through analyses of these specimens, they have found that there are specific subtypes of the cancers with unique signaling pathways that cause tumor growth. Further, they have identified one pathway, called IGF-1, and have developed a product to block IGF-1 signaling of cancer tumor growth. The drug is in initial testing but demonstrates the type of research conducted at UCLA–JCCC.

Other research conducted at JCCC focuses on health disparities. The Division of Cancer Prevention and Control Research (DCPCR) is a program at JCCC that supports research on cancer in specific populations. The program also works with community partners to provide cancer education to low-income and ethnic minority populations.

**Conclusion**

UCLA’s JCCC is an organization that focuses on cancer prevention, treatment, research, and survivorship. It has been designated a comprehensive cancer center by the NCI, and although it has several locations in California, it provides access to research or clinical trials throughout the United States.

Anne Hubbell

*New Mexico State University*

**See Also:** Breast Cancer; Chemotherapy; Clinical Trials; Disparities Within Nations (Elimination of Cancer); Drugs; Education; International Association of Cancer Registries; National Cancer Institute; Ovarian Cancer, Childhood; Ovarian Epithelial Cancer; Ovarian Germ Cell Tumor; Ovarian Low Malignant Potential Tumor; Poverty.

**Further Readings**

University of California, San Francisco, Helen Diller Family Comprehensive Cancer Center

Over 1 million Americans receive the diagnosis of cancer each year, with one in four dying from the disease. In the face of these statistics, cancer centers work to expand comprehension of cancer, make new therapies available, enhance quality of life, and bring new optimism to patients. The University of California at San Francisco’s (UCSF) Helen Diller Comprehensive Cancer Center follows this tradition. The UCSF Helen Diller Comprehensive Cancer Center opened in 1999. It is one out of 1,500 cancer centers in the United States designated by the National Cancer Institute (NCI), meaning that it receives core funding from the NCI. Despite its late designation as an NCI facility, this cancer institution moved to one of the top positions in California based on grant funding. The center underwent a name change in 2007, to the UCSF Helen Diller Comprehensive Cancer Center. The new name acknowledges Helen Diller, a long-term Bay Area resident, who motivated her neighbors and others to move beyond themselves to address the needs of their communities.

The UCSF Cancer Center provides a distinct program, with its concentration on biomedical research and graduate health-science education. The program places faculty and researchers in five principal campuses and multiple satellite locations. The UCSF located the newest campus and largest research university expansion to Mission Bay in San Francisco. The UCSF Cancer Center continues to expand, with construction that will house cancer programs on the prostate, kidney, and brain. The UCSF plans a new cancer hospital at this location in the future. The Helen Diller Family Comprehensive Cancer Center utilizes four San Francisco medical centers for care of cancer patients. The hospitals include UCSF Medical Center at Mount Zion, UCSF Medical Center at Parnassus, San Francisco General Hospital, and the San Francisco Veterans Affairs Medical Center.

About half of the UCSF Cancer Center’s multidisciplinary programs focus on disease, and the other half comprise leading programs in genetics, immunity, signaling, tobacco control, and society diversity and disparity. Three NCI Specialized Program of Research Excellence (SPORE) grants for breast, prostate, and brain tumor research remain housed under the UCSF Comprehensive Cancer Center. The National Cancer Institute allows the cancer center to employ the title of “comprehensive” because the program treats every form of cancer. The UCSF’s long tradition of prominence in cancer research includes the distinguished work of Nobel Prize winners J. Michael Bishop and Harold Varmus, who uncovered cancer-causing oncogenes. These individuals laid the groundwork for investigating genetic errors that cause cancer. Their pioneering work provided the background for breakthroughs occurring in cancer research today.

As one of the leading research institutions in cancer, the UCSF Cancer Center offers over 1,000 research trials at any one time. The NCI revolutionized its clinical research program in an effort to keep ahead of advances in the science of cancer. The NCI created the National Clinical Trials Network (NCTN) and the NCI Community Oncology Research Program (NCORP). The NCTN’s novel infrastructure permits investigators to start clinical trials more rapidly, complete results faster, and recommend patient studies at over 3,000 clinical trial locations. The mission of the UCSF Helen Diller Comprehensive Cancer Center’s clinical program delivers thorough care through multidisciplinary teamwork to provide innovative cancer therapies via clinical research, and to educate prospective physicians to treat cancer patients. The mutual approach to research and managing patient treatment remains a trademark of the cancer center’s program, procuring the involvement of surgeons, medical oncologists, radiation oncologists,
pediatric oncologists, radiologist, and pathologists. Working in conjunction with prominent UCSF scientists in disciplines varying from molecular biology and biochemistry to epidemiology, biostatistics, and public policy analysis, UCSF clinic specialists remain dedicated to transforming scientific visions into lifesaving experiences for cancer patients around the world.

The UCSF program sits at 6th place in receiving grants among all NCI grantee institutions, but it ranked first out of the 10 NCI-designated centers in California. Significant aspects of the center’s clinical program include premier bone marrow transplantation procedures; highly advanced radiation therapies (e.g., high-dose brachytherapy, conformal radiotherapy, and radio-immunotherapy); specialized therapy for AIDS-related malignancies; translational studies for managing cancers of prostate, breast, head and neck, colon, liver, lung, melanoma, and other solid tumors; and leadership in treating pediatric malignancies. The UCSF Cancer Center received one of the 53 community grants under NCORP. The cancer center sponsors the pioneers for investigating genetic, cellular, and immune-system triggers and responses to cancer. The UCSF possesses the nation’s largest brain tumor program, with state-of-the-art research and therapy for children and adults.

Carlo Maley, a scientist at UCSF Cancer Center, uncovered the reason for aspirin lowering the risk of some cancers in 2013. Aspirin and other non-steroidal anti-inflammatory drugs slow the accumulation of DNA mutations in abnormal cells. The aspirin exerts cancer-prevention by lowering mutation rates in cells. Maley and colleagues analyzed biopsies of tissue samples from patients with a precancerous condition called Barrett’s esophagus. The researchers studied the subjects with Barrett’s esophagus (both on and off aspirin) for 19 years. By looking at biopsies taken when subjects took aspirin, the investigators found that patients accumulated new mutations 10 times more slowly. Maley hypothesized that aspirin’s lowering of the mutation rate is probably because of the effect of reducing inflammation. The next area of research will focus on inflammation that leads to cancer in precancerous tissue. Maley and colleagues’ research represents just one of many molecular level studies in progress at the SCSF Cancer Center.

In prevention research at the SCSF Cancer Center, Sutton and colleagues set out to brainstorm alternative ways to look at prevention of breast cancer. The group proposed looking at the environment because it is a poorly utilized pathway to the prevention of breast cancer. A project called the California Breast Cancer Prevention Initiative became the focus for prevention research. This initiative set an agenda to investigate the environment, discrepancies, and prevention for exposures to chemicals, physical agents, and socially constructed situations. The outcome to this large task remains how to modify the world to attain a less carcinogenic milieu. The UCSF Helen Diller Comprehensive Cancer Center provides a two-prong approach to cancer by sustaining infrastructure for both biomedical research and clinical care for cancer patients. The cancer center maintains robust operations for both programs in the fight against cancer.

Sharon A. Takiguchi
Independent Scholar

See Also: Aspirin; California Blood Bank Society; National Cancer Institute.

Further Readings

University of Chicago Medicine Comprehensive Cancer Center

The University of Chicago Medicine Comprehensive Cancer Center (known by the acronym UCCCC) is a cancer research program headquartered in New Lenox, Illinois. Founded in 1973, the
program is comprised of 210 scientists and physicians who serve over 1,000 patients annually in over 200 varying comprehensive clinical trials.

The University of Chicago’s program is one of two cancer research programs in Illinois (including the Robert H. Lurie Comprehensive Cancer Center at Northwestern University) to be designated a comprehensive care program by the National Cancer Institute (NCI). The center’s new facility at New Lenox’s Silver Cross Hospital opened in 2012.

History and Facilities
The program was established as the University of Chicago Cancer Research Center in 1973 following the institution’s designation as a “Clinical Cancer Center” by the NCI. The name was changed in 2010 after the program received the NCI’s “Comprehensive Care Center” designation.

The center’s 2010 NCI “comprehensive” designation was awarded after the center expanded efforts in its cancer prevention and control research, as well as for its numerous clinical trials concentrating prevention and early detection and implementation of cancer awareness programs for the Chicago metropolitan area’s underserved communities.

The center conducts research at 13 disparate facilities in and around Chicago, the majority of which are housed at Silver Cross Hospital in the New Lenox, fifty miles south of downtown Chicago. The 560,000-square-foot facility is home to 289 beds in addition to state-of-the-art chemotherapy and radiation therapy. The facility was completed with a construction cost of $21.6 million.

The UCCCC’s numerous facilities include the Biostatistics Core Facility, dedicated to observational studies on patient data; the Human Immuno logical Monitoring-cGMP Facility that primarily investigates immune responses to cancer; and the Integrated Small Animal Imaging Research Resource, which specializes in clinical research trials involving tissue and organ and other animal-borne specimens.

Other major UCCCC facilities include the Image Computing, Analysis, and Repository Facility, which provides researchers with the latest in medical image viewing and processing technology, and the Human Tissue Resource Center, which specializes in the procurement, storage, distribution, and analysis of human biospecimens.

Landmark Programs and Researchers
The UCCCC has been the site of numerous landmark accomplishments and discoveries in cancer research since its inception. In 1972, Dr. Janet Rowley spearheaded the center’s work identifying genetic anomalies in leukemia patients. The discovery would eventually become a staple in modern medicine’s understanding of the link between genetics and cancer. Rowley received the Presidential Medal of Freedom in 2009 for her long career of groundbreaking cancer research.

A 1988 study based at the UCCCC led to the discovery of the mechanism that blocks the effects of estrogen in the spread of certain types of breast cancers. This discovery ultimately led to widespread use of the drug tamoxifen, regarded as one of the most effective cancer treatments available today.

Another one of UCCCC’s prominent researchers was Dr. Elwood Jensen, whose 35 years of research at the center culminated with the development of tests that could predict whether patients with certain types of breast cancer would benefit from hormonal therapy treatments.

Programs
The UCCCC research division is divided into six integrated programs, each specifically dedicated to a particular facet of the disease.

The Molecular Mechanisms of Cancer group focuses on how genetic and cell-signaling alterations impact the development of cancer. Doctors and students who comprise UCCCC’s Hematopoiesis and Hematological Malignancies concentrate on the molecular origin of hematological diseases, while those in the Immunology and Cancer program attempt to understand the relationship between immune systems and malignant tumors, in hopes of one day transforming their knowledge into clinical applications.

The center’s Pharmacogenomics and Experimental Therapeutics program works to develop new cancer treatment therapies while evaluating the interaction between chemotherapy and radiation. The UCCCC is also home to a research group dedicated to making improvements in Advanced Imaging and computer-aided cancer treatments and diagnosis, while the Cancer Prevention and Control program concentrates on potential behavioral, epidemiological, and population-based genetic research surrounding cancer in its many forms.
The UCCCC is also home to one of 11 of the NCI’s Specialized Programs of Research Excellence (SPORE) in Breast Cancer programs. In addition to investigating the global issues and trends related to the disparities of cancer types among varying ethnic and racial groups, UCCCC’s SPORE program also concentrates on genetic and imaging-based cancer prevention methods.

Community Support Initiatives
The UCCCC’s Cancer Resource Center, a partnership between the center and the American Cancer Society (ACS), stands as the facility’s flagship for community programs. Housed in the Duchossois Center for Advanced Medicine at the University of Chicago, the center offers patients and their families one-on-one counseling as well as seminars on information surrounding breakthroughs in the center’s research trials. In addition to their numerous cancer support groups, the UCCCC Cancer Resource Center also holds a regular schedule of networking seminars to allow interaction between families and patients who share a similar diagnosis.

The UCCCC’s Office of Community Engagement and Cancer Disparities (OCECD) spearheads the center’s efforts in engaging with its metro-Chicago community. The UCCCC has fostered a variety of outreach programs designed to increase the visibility of cancer treatment and prevention and to empower citizens to take necessary precautions such as screening to preempt and prevent the spread of the disease. The UCCCC’s Mentored Education Now Taking on Research (MENTOR) program encourages area undergraduate and graduate students to engage in research regarding health problems among specific populations, while the center’s Cancer Transitions program, operated in conjunction with the LIVESTRONG organization, helps to improve the emotional health and quality of life of patients who have recently completed their cancer treatment.

The UCCCC OCECD also hosts a rotating annual calendar of community-based and faith-based events aimed at cancer advocacy and outreach, including movie screenings, celebrity breakfasts, luncheons, walk-a-thons, and corporate-sponsored family wellness nights.

Publications
The UCCCC’s latest projects, staff developments, landmark trials, and role as a nationally renowned center for cancer research are profiled in its quarterly magazine Pathways to Discovery. The center also hosts a blog featuring staff and patient perspectives on emerging trends and treatments as well as information regarding the center’s latest philanthropic and fundraising events.

John Pritchard III
Independent Scholar

See Also: Breast Cancer; Chemotherapy; National Cancer Institute.

Further Readings

University of Colorado Cancer Center

The University of Colorado Cancer Center was founded in 1988 and is headquartered at the University of Colorado Anschutz Medical Campus in Aurora, CO. The CU Cancer Center is the only National Cancer Institute (NCI)-designated comprehensive cancer center in Colorado and the
Rocky Mountain region. The center is a consortium of researchers and physicians from three state universities and six institutions in the Colorado area. The mission of the CU Cancer Center is to discover, develop, and deliver breakthroughs in diagnosis, treatment, and prevention to improve cancer care locally, nationally, and globally.

The CU Cancer Center is part of the University of Colorado Hospital (UCH), the primary adult teaching hospital and the location where most of the CU Cancer Center clinical care is delivered and research is conducted. Each year, over 63,000 patients visit the center, and thousands more visit the UCH community satellite office; in 2013, UCH admitted 2,750 new adult patients for cancer treatment. In addition to the multitude of noteworthy achievements announced each year by the CU Cancer Center, U.S. News & World Report consistently ranks the CU Cancer Center among the top 25 cancer centers in the United States.

**Founding and NCI Designation**

Founded in 1988, the CU Cancer Center began under the leadership of Dr. Paul Bunn. Initially, the center began with the development of a statewide consortium cancer center, which included seven participating institutions. The CU Cancer Center grew under Dr. Bunn’s direction, and he served as its director until 2009. In July 2010, the CU Cancer Center welcomed its second director, Dr. Dan Theodorescu. In addition to Dr. Theodorescu, Dr. Andrew Thorburn serves as the deputy director, and Dr. S. Gail Eckhardt is the senior associate director; these individuals comprise the leadership of the institution.

The CU Cancer Center is one of 68 cancer centers with a consortium designation from the National Cancer Institute (NCI), and the only NCI-designated cancer center in Colorado. These institutions are dedicated to research and the development of innovative approaches to the prevention, diagnosis, and treatment of all types of cancer. All NCI-designated cancer centers engage in research that spans laboratory science, clinical research, and population-based research. In addition to research, the CU Cancer Center also has a clinical program that provides patients with cutting-edge treatments and access to experimental clinical trials. In order to become a NCI-designated cancer center, institutions must demonstrate that they possess advanced research facilities, faculty, and a clear track record of proven success in treating cancer patients. The CU Cancer Center received its first five-year NCI cancer center support grant in 1987 and the comprehensive NCI designation in 1997. In 2005, the CU Cancer Center was awarded a formal consortium designation that included three of the state universities and six cancer care and research institutions located in Colorado.

**Members of the CU Cancer Center Consortium**

Initially, the CU Cancer Center included full and associate members from the University of Colorado School of Medicine, National Jewish Health, University of Colorado Hospital, Denver Health, Denver Veterans Affairs Medical Center, and Children’s Hospital Colorado. Later, the Children’s Hospital Colorado merged with the University of Colorado School of Medicine, and researchers at both organizations became faculty at the CU Cancer Center. In 2005, when the CU Cancer Center received its formal NCI consortium designation, researchers from the University of Colorado Boulder, Colorado State University (including the Flint animal cancer center), and Kaiser Permanente Colorado also joined the cancer center to complete the current configuration of the consortium. All members of the consortium have access to shared resources from the CU Cancer Center, which are used by members from all of the associated sites. These resources include: clinical trials, flow cytometry, functional genomics, genomics, human tumor model-based databank, molecular pathology, pharmacology, protein production/tissue culture, research informatics, structural biology, and tissue biobanking and processing.

**Research and Special Departments**

As of 2013, the CU Cancer Center received $98 million in direct annual cancer research funding; received $24 million in direct annual NCI research funding; and had invested approximately $102 million in institutional cancer research since 2005. The CU Cancer Center has six research programs: in cancer cell biology; cancer prevention and control; developmental therapeutics; hormone-related malignancies; lung, head, and neck cancer; and molecular oncology. In 2013, the research programs at the CU Cancer Center produced 636 publications, of which 38% were collaborations with other institutions. The center has a strong
program of clinical trials; approximately 21% of patients diagnosed there were enrolled in treatment trials in 2013. The CU Cancer Center is also associated with the treatment of pediatric cancers and blood disorders; however, the majority of this treatment takes place through the center’s partner, the Center for Cancer and Blood Disorders at Children’s Hospital Colorado. This facility ranks as one of the top pediatric cancer centers in the United States.

As a regional leader in cancer care, the center provides multidisciplinary care within each subspecialty of oncology. The University of Colorado Hospital and Cancer Center treats patients suffering from all types of cancer; however, the center specializes in the following areas: breast cancer, lung cancer, gastrointestinal cancers, cutaneous oncology, neuro-oncology, head and neck cancer including thyroid cancer, gynecological cancers, developmental therapeutics urological cancers, radiation oncology, hematologic malignancies, and bone marrow transplants. The center is the coordinating center for the Lung Cancer Mutations Consortium, which is funded by a $5.3 million American Reinvestment and Recovery Act Grand Opportunities grant. Additionally, the CU Cancer Center serves as the home to three cancer survivorship clinics for the Rocky Mountain region: the TACTIC clinic for adult survivors of childhood cancer, the THRIVE clinic for transitioning adult cancer patients back to primary care, and the young adult survivors of cancer. CU Cancer Center is also one of the LIVESTRONG Survivorship Centers of Excellence.

As part of the University of Colorado Hospital (UCH), the CU Cancer Center provides training to students, residents, and fellows in the practice of medical oncology, hematology, radiation oncology, and many other medical subdisciplines. The center provides students with the opportunity to participate in several training tracks, which include: clinical investigation, disease-oriented basic science research, and bone marrow transplantation research. In addition to training at UCH, students also receive training at other members of the CU Cancer Center Consortium, including the Denver Veterans Affairs Hospital, the Children’s Hospital of Colorado, Denver Health, and National Jewish Health.

Accomplishments
The CU Cancer Center is home to many accomplishments and breakthroughs in the field of oncology. Each year the CU Cancer Center has some of the highest five-year cancer survival rates of any hospital and medical facility in the Rocky Mountain region. The center is especially noteworthy for the survival rates of patients who suffer from late-stage cancers. For instance, the center is home to one of the world’s best lung cancer research and treatment centers; one-year survival rates of patients suffering from stage-four lung cancer are more than two times the national average.

The Colorado Colorectal Screening Program has become a national model for individuals who meet specific financial and risk criteria to receive the necessary colorectal screening and follow-up treatment at no cost to the patient. The program is coordinated by the center and has more than 65 community partners throughout the state that offer endoscopy and colonoscopies to individuals who qualify for the screening program. The center is also noteworthy for its Phase I cancer clinical trials program. This program offers patients who are treated at the CU Cancer Center access to the largest number of cancer clinical trials as well as cutting-edge cancer treatments and care.

The Cancer Clinical Trials Office (CCTO) at the center coordinates clinical trials by ensuring the clinical investigators have the resources necessary to conduct successful clinical trials. The CCTO ensures that clinical trials can be translated from research into everyday basic knowledge for both patients and providers. Finally, the center’s shared resource, Structural Biology, houses the CU Cancer Center’s Nuclear Magnetic Resonance (NMR) Spectroscopy and X-ray facilities, which are considered to be some of the best in the world. The Structural Biology Shared Resource is one of only two NCI-designated centers with X-ray Crystallography, NMR, high-field NMR, and synchrotron.

Emily Hammad
David P. Tracer
University of Colorado Denver

See Also: Clinical Trials; Lung Cancer, Non–Small Cell; Lung Cancer, Small Cell; National Cancer Institute.

Further Readings
The University of Hawai‘i’s (UH) Cancer Center strives to be a world leader in eliminating cancer through improved patient care, education, and research. The university’s scientists and physicians focus on cancers that are of key impact to Hawai‘i while contributing to the global body of knowledge regarding cancer treatment and therapies. The UH Cancer Center collaborates internationally, from clinical trials conducted in the United States to partnership programs in Guam, Micronesia, and other parts of the Pacific. The university actively recruits new talent to develop new strategies for discovery, to drive findings into clinical practice, and to deliver optimal outcomes in patient treatment and recovery.

Hawai‘i is a geographically and demographically diverse state. It has the highest percentage of individuals with mixed-race ethnicity in the United States. Two of every 10 citizens of Hawai‘i describe themselves as mixed-race. Hawai‘i residents have the longest life span of any of the United States; yet, each year, more than 6,000 Hawai‘ians are diagnosed with cancer and another 2,000 die from cancer-related disease.

The UH Cancer Center, designated by the National Cancer Institute (NCI), is a consortium cancer center. The UH Cancer Center collaborates with The Queen’s Medical Center, Hawai‘i Pacific Health, Kuakini Medical Center, and UH Manoa’s John A. Burns School of Medicine. The common goal is the elimination of cancer through science. The consortium represents basic, translational, and clinical cancer research efforts to benefit all citizens of Hawai‘i and the Pacific Rim. The consortium’s vision is to substantially reduce the burden of cancer through the support of clinical and translational research. The consortium’s mission is to facilitate, support, and assure that high-impact patient research is efficient and safe and substantially reduces the burden of cancer.

The UH Cancer Center houses the central administrative and organizational structure of the Hawai‘i Cancer Consortium. It is the central authority that focuses and organizes the efforts of and resources for efficient accomplishment of the consortium’s goals. The Kuakini Medical Center’s Oncology Services uses a multidisciplinary approach to address the individual needs of each cancer patient. Services include prevention, early detection, treatment, medical care, education, and support. The Oncology Services members also participate in community activities and events while providing information, education, and free screenings. The Queen’s Medical Center offers comprehensive, multidisciplinary cancer treatment and research. It was designed to reduce the need to travel to the mainland for quality cancer care. It offers advanced technology in a patient-centered, comfortable setting. The John A. Burns School of Medicine seeks health solutions for Hawai‘i and the Pacific Rim’s multicultural society and the world. The school is the most culturally diverse in the United States, and its vision is A.L.O.H.A. (Attain Lasting Optimal Health for All).

The UH Cancer Center conducts research on prevention, treatment, and causes of cancer. Areas of focus include new therapeutic approaches, community-based interventions, quality of life for survivors, prevention, and epidemiology. The Cancer Biology Program seeks to discover mechanisms that drive cancer development and progression, then to translate those discoveries into better diagnostics and interventions. Program objectives include: providing better knowledge concerning the development and progression of cancer; developing new diagnostics and therapies; and initiating new clinical trials in Hawai‘i.

The Cancer Epidemiology Program seeks to understand the reasons underlying ethnic/racial differences in cancer incidence and mortality rates. The program studies the role of lifestyle (diet, obesity, exercise, etc.), genetics, and infectious agents to identify risk factors that can lead to successful interventions. The program places special research emphasis on the role of dietary nutrition and external factors (i.e., infectious agents, inherited factors,
etc.) related to the incidence of breast, prostate, colorectal, cervical, ovarian, and lung cancers.

The Cancer Prevention and Control Program aims to reduce cancer risk, incidence, morbidity, and mortality. Early screening and detection, elimination of tobacco use, increased physical activity, reduced unprotected exposure to sunlight and artificial light, and improved dietary consumption are all critical to reducing the incidence of cancer. Goals for the Cancer Prevention and Control Program include (1) advancing understanding of behavioral, psychosocial, biological, environmental, and social factors associated with cancer risk, incidence, morbidity, mortality, and survival; (2) testing interventions that reduce cancer risk, increase early detection, and improve survival rates; and (3) increasing knowledge on how to disseminate research so that it benefits multicultural, multiethnic, and underserved populations.

The Clinical and Translational Research Program seeks to translate discoveries into clinical applications, in order to generate innovative and high-impact research interventions. The program aims to identify interventions (i.e., agents, devices, and diagnostic tests) that, when applied, are more helpful than harmful, especially with regard to liver and breast cancer, which disproportionately impact Hawai’i’s population. The program also provides Hawai’i residents with access to clinical trials that are the most promising and contribute Hawai’i’s multiethnic population to nationally conducted trials. Participants get state-of-the-art care without having to leave the state.

The Natural Products and Experimental Therapeutics Program leads translational drug discovery and development research with an emphasis on identifying natural product-based therapeutics. There is a vast chemical diversity in the natural products unique to Hawai’i’s agriculture and environment. The program’s goals include (1) investigation of anticancer targets and pathways; (2) exploration and development of natural products and synthetics that modulate cancer pathways; and (3) design, pursuit, and analysis of natural products in innovative clinical trials.

Jessica Anne Hammer
Independent Scholar

See Also: Comprehensive Cancer Center of Wake Forest University; Ohio State University Comprehensive Cancer Center; OHSU Knight Cancer Institute; Purdue University Center for Cancer Research; University of California, San Francisco, Helen Diller Family Comprehensive Cancer Center.

Further Readings
collaborations since, but the UMCCC building remains a state-of-the-art treatment and research center.

Currently, over 350 University of Michigan faculty members as well as 27 clinics provide patient care. Of the 27 clinics, 17 are considered multidisciplinary in their approach to cancer treatment. UMCCC also has been rated by U.S. News and World Report as 34th on its list of the best hospitals for cancer treatment and is the only hospital in the state of Michigan to rank in the top 50.

Accreditations and certifications further demonstrate UMCCC’s commitment to excellent patient care. First, UMCCC has been accredited by the Joint Commission. The Joint Commission accreditation is voluntary and represents an organization’s demonstration of safe and comprehensive treatment of patients diagnosed with cancer (i.e., fully informing patients of all risks and options of treatments). UMCCC has also received a three-year certification from the Quality Oncology Practice Initiative for providing quality cancer treatment. UMCCC has even been designated as a Blue Distinction Center for Complex and Rare Cancers by the national Blue Cross and Blue Shield Association.

UMCCC is also a member of the Michigan Cancer Consortium, Big Ten Cancer Research Consortium, National Comprehensive Cancer Network, and Commission on Cancer of the American College of Surgeons. These associations represent collaborations among UMCCC members and other research and oncology care institutions. Through such collaborations, UMCCC and its partners can provide the newest information and treatments to patients.

Research
UMCCC’s focus with regard to cancer research is to seek to improve understanding of the genetic markers and triggers of cancer; researchers strive to understand cancer at its molecular level. UMCCC is one of the few centers in North America dedicated to cancer stem cell research. To that end, UMCCC has 22 research programs, which include six basic (or laboratory) science programs, 14 clinical trial research programs, and two programs devoted to the development and testing of prevention and control strategies. The Basic Science programs include: Cancer Cell Biology, Cancer Genetics, Experimental Therapeutics, Molecular Imaging, Radiation Sciences, and a Tumor Immunology and Host Response Program.

UMCCC research has also received three Specialized Programs of Research Excellence (SPORE) grants from the NCI. Another SPORE grant in sarcoma was awarded to UMCCC through its participation in the Sarcoma Alliance for Research through Collaboration (SARC). SPORE grants represent prestigious awards, which are only awarded to top institutions.

Patients benefit from the clinical research and trials at UMCCC and its partners. Some of the clinical research programs include: Breast Oncology, Childhood Cancers, Endocrine Oncology, Prostate Cancer, Neuro-Oncology, and Thoracic Oncology. Finally, the two prevention and control programs are the Biomedical and Socio-Behavioral Prevention programs. Patients can search through the UMCCC Web site for opportunities to participate in over 285 cancer research clinical trials.
**Patient Care**

According to the UMCCC Web site, in 2012 there were 93,319 outpatient visits to the clinic, 51,884 infusion treatments, 4,184 radiation consults, and 2,854 cancer patients admitted to hospitals. Of the cancer diagnosed and treated at UMCCC, the top five are: melanoma, breast cancer, prostate cancer, blood cancers, and lung cancer.

Although UMCCC is a leader in the treatment and diagnosis of common and rare forms of cancer, the institution also is a leader in the support of patients and families. UMCCC provides multiple levels of support for patients and families through prevention, detection, treatment, and survivorship. The Patient and Family Support Services Program (PFSS) at UMCCC, for example, offers more than 30 programs for patients and their family members. Social workers, psychology professionals, nutritionists, and other professionals trained in cancer treatment work with patients and families through PFSS to support patients and families through art therapy, financial management of cancer treatment, nutrition, and other programs. The U-M Cancer AnswerLine is another example of patient and family support; patients and family members can call and reach an oncology registered nurse to answer questions. Patients and family cannot receive diagnoses or recommendations for treatment through the AnswerLine but can receive information about their current treatments and concerns. UMCCC also provides genetic counseling to patients to determine if they are at risk of developing cancer so that they can enact behaviors, such as improved diet and exercise, to minimize the risk.

Other amenities and services offered to patients and families include the Overnight Accommodations program; the Guest Assistance Program; the Practical Assistance Center; and the Voices of Art Gallery, which features patients' and family members' artwork.

Patient support continues through survivorship programs at UMCCC. UMCCC maintains two clinics focused on the survivorship of those afflicted with breast or prostate cancer. Patients are referred to these clinics after treatment for breast or prostate cancer. At the clinics they receive another comprehensive health exam as well as opportunities to talk with health care practitioners about their real life concerns. Some topics discussed include the management of continued side effects from their treatments as well as their sexual health. Other survivorship programs at UMCCC include continued help with management of financial issues, occupational therapy, support groups, a blog for conversations related to cancer, and providing other online resources that patients and families can access.

**Outreach**

UMCCC provides extensive outreach to the community. One opportunity offered by UMCCC is the Physician Liaison Program, in which a UMCCC physician liaison will visit a health care practitioner's practice and offer support and information about new treatments and clinical trials. UMCCC also offers a Speaker's Bureau, Community Outreach Events, Minority Outreach Initiative with culturally targeted community events, free cancer displays and materials for health fairs, etc., and free cancer screenings. Finally, survivorship outreach is provided by UMCCC in the form of a yearly community event that celebrates National Cancer Survivors' Day.

**Training of Health Care Professionals**

UMCCC, through its partnership with the University of Michigan Medical School, offers an education in medicine through 20 clinical and nine basic science departments. Approximately 170 physicians graduate each year, and U-M Medical School alumni include Nobel Prize winners, leaders of Fortune 500 companies, as well as leaders at educational and research institutions.

**Conclusion**

UMCCC was one of the first cancer centers focused on the use of multidisciplinary teams in the fight against and research of cancer. The center has won several accolades for its dedication to providing quality care to patients, and research at UMCCC is focused on understanding cancer at the molecular level so as to improve knowledge about the genetic markers and triggers of cancer.

Anne P. Hubbell

*New Mexico State University*

**See Also:** Breast Cancer; Caregivers; Clinical Trials; Cost of Therapy; Diet and Nutrition; Disparities Within
Nations (Elimination of Cancer); Experimental Cancer Drugs; Genetics; Insurance; Oncology Nursing Society; Prostate Cancer; Screening, Access to; Survivors of Cancer; Survivors of Cancer, Families of; Technology, New Therapies.

Further Readings

University of Minnesota Masonic Cancer Center

The University of Minnesota Masonic Cancer Center serves as that institution’s premier institute for cancer research. As part of the University of Minnesota, the center seeks to create a collaborative research environment that concentrates on the causes, prevention, detection, and treatment of cancer. The University of Minnesota Masonic Cancer Center also works to apply this knowledge in ways that will improve the quality of life for patients and survivors and to share its discoveries with others, including students, scientists, researchers, medical professionals, and the community. Designated a comprehensive cancer center by the National Cancer Institute, the University of Minnesota Masonic Cancer Center collaborates with other individuals and institutions to make ongoing and significant advances in cancer research, treatment, and education.

Background
Founded in 1851, the University of Minnesota is a publicly funded research institution located in Minneapolis and Saint Paul, Minnesota. Organized into 19 different colleges and schools, the University of Minnesota has several units that engage in stem cell research. The College of Science and Engineering was organized in 1935 as the Institute of Technology and comprises the university’s departments of mathematics, engineering, and the physical sciences. The University of Minnesota Medical School is located in Minneapolis and Duluth and is one of two medical schools in Minnesota (the other being affiliated with the Mayo Clinic in Rochester). Dr. Robert A. Good of the University of Minnesota Medical School conducted the first bone marrow transplant between individuals who were not identical twins and is considered one of the founders of the field of immunology. The University of Minnesota College of Biological Sciences is located in Minneapolis and was the alma mater of Dr. Edward B. Lewis, who won the 1995 Nobel Prize in Physiology or Medicine. Lewis was a founder of the field of developmental genetics and was primarily responsible for discovering the Drosophila bithorax complex.

The University of Minnesota Masonic Cancer Center was founded in 1991. Representing a long tradition of Masonic support for cancer research within Minnesota, the center changed its name to honor the Masons in 2008, after a $65 million donation. The Masonic Cancer Center is part of the university’s Academic Health Center. The Academic Health Center includes the University of Minnesota’s Medical School, School of Dentistry, School of Nursing, College of Pharmacy, School of Public Health, and College of Veterinary Medicine.

Focused upon building a collaborative environment, the university’s Stem Cell Institute, the Center for Immunology, and the Center for Magnetic Resonance Imaging serve as some of the Masonic Cancer Center’s main research partners. The Masonic Cancer Center’s clinical research and treatment work is done in conjunction with the University of Minnesota Physicians, the University of Minnesota Medical Center, Fairview Hospital, and the University of Minnesota Amplatz Children’s Hospital.

Cancer Research and Treatment
Research at the University of Minnesota Masonic Cancer Center is organized to address several
themes identified as holding the most promise. These themes include the following:

- Prevention and etiology
- Carcinogenesis and chemoprevention
- Genetic mechanisms of cancer
- Tumor microenvironment
- Immunology
- Cell signaling
- Transplant biology and therapy

Teams working on each of these themes bring together scientists from different disciplines to discover processes and procedures that might affect cancer.

Scientists who work at the Masonic Cancer Center are making discoveries that are leading to better ways to treat and prevent cancer. Dr. Stephen Hecht and colleagues, working in the area of carcinogenesis and chemoprevention, are looking to identify chemical and molecular mechanisms of carcinogenesis, specifically in regard to tobacco, and to use this knowledge to develop and evaluate practical methods for cancer prevention. These practical methods have included examining the chemical and molecular mechanisms of carcinogenesis and how chemoprevention can be used to address these.

Other researchers, such as Dr. Anja Bielinsky and Dr. Peter Bitterman, are working to better define and understand the genetic changes that occur during cancer development. These include specific changes that drive tumor initiation and progression and those that influence a patient’s cancer susceptibility. Dr. Carol Lange and her colleagues, who examine cell signaling, are looking to improve their understanding of the spectrum of altered signaling pathways and their components that contribute to cancer initiation, promotion, and disease progression. Lange’s research group is engaged in the step-wide translation of this knowledge into strategies that will facilitate the prevention, early detection, diagnosis, and treatment of cancer.

Dr. Yoji Shimizu and other immunologists at the Masonic Cancer Center are seeking to define the basic mechanisms that control adaptive immunity. Gaining this understanding will assist researchers in developing immunotherapies that can overcome the significant barriers associated with generating a durable immune response against tumor-associated antigens. Researchers investigating prevention and etiology, such as Dr. Anne Joseph and Dr. DeAnn Lazovich, are working to increase understanding regarding the biological and behavioral factors in the etiology of cancer. In doing so, it is hoped that it will be possible to reduce those behaviors that may lead to cancer or to enhance those behaviors that decrease cancer risk. The research group has used a multidisciplinary approach that has demonstrated more progress than previous efforts. Dr. John Wagner and Dr. Daniel Weisdorf, who lead the transplant biology and therapy program, seek to reduce or eliminate factors limiting hematopoietic stem cell transplantation. Those factors include regimen-related toxicities, graft-versus-host disease (GVHD), and delayed reconstitution of immunity. The tumor microenvironment scientists, led by Dr. Kalpna Gupta and Dr. James McCarthy, are examining those critical molecular and cellular mechanisms through which alterations in the tumor microenvironment contribute to tumor-related factors in malignant progression. To this end, the program has been organized to concentrate upon three distinct but overlapping themes that might impact tumor progression in several ways. The ways in which tumor progression might be impacted include reducing tumor burden, limiting metastasis, and lessening cancer-induced pain. Each of these factors would affect morbidity and mortality in cancer patients.

The Masonic Cancer Center has also established a number of inter-programmatic and translational research work groups to promote new discoveries. Translational work groups use Masonic Cancer Center members from a variety of research programs. These groups are each designed to address site-specific cancers, foster collaborations, and provide the necessary scientific and clinical expertise to improve outcomes for the specific disease sites. In collaboration with medical professionals from across Minnesota and the United States, these work groups have had great success in translating research findings into changes in practice that positively affect patients and their families.

Stephen T. Schroth
Towson University

See Also: Mayo Clinic Cancer Center; National Cancer Institute; University of Chicago Medicine Comprehensive Cancer Center; University of Wisconsin Carbone Cancer Center.
Further Readings


University of New Mexico Cancer Research and Treatment Center

The University of New Mexico Cancer Center (UNMCC) was established in 1971 by New Mexico's state legislature. The legislature's intention was to create an advanced research and public service institution to serve the state as well as the southwestern U.S. region. In 2005, UNMCC received a designation as a National Cancer Institute (NCI) Cancer Center and is one of the 68 centers in the United States with this prestigious recognition. To achieve this designation, a cancer center must demonstrate a commitment to multidisciplinary research and treatment of cancer as well as provide training of medical professionals and prevention and control education efforts in the community. Participation in clinical trials is also required of NCI-designated cancer centers.

Currently, UNMCC is the only NCI cancer center in the state of New Mexico, but it has partnerships across the state and country. UNMCC is associated with over 100 board-certified oncology physicians covering every specialty in cancer treatment. Through partnerships with organizations like Johns Hopkins and the Mayo Clinic, the UNMCC research team works with over 130 cancer researchers who are supported with over $77 million in yearly funding. The main cancer center, located in Albuquerque, is a 206,432-square-foot facility that was designed to provide a peaceful and welcoming environment for patients.

The mission of UNMCC, as stated on the institution’s Web site, is to provide assistance to the people of New Mexico through exceptional diagnosis, treatment, and research. Service to the communities throughout New Mexico is included in the UNMCC mission statement as well. Training of future oncology health care practitioners through the UNM Medical School and other programs at UNM also is part of the center’s mission.

UNMCC also maintains several certifications and accreditations. One of the new certifications is the QOPI (Quality Oncology Practice Initiative) Certification. The certification is given to institutions that demonstrate a commitment to quality care. UNMCC has also received accreditations from the Joint Commission; the Commission on Cancer Accreditation from the American College of Surgeons; and the College of American Pathologists. Currently, UNMCC is working toward certification of the center’s radiation oncology and breast cancer suites.

Research
UNMCC actively participates in research and averages over 300 open clinical studies. In 2012, as an example, UNMCC maintained 345 research studies and recruited approximately 20 percent of their patients to participate in therapeutic research.

UNMCC has four main research programs that are aligned with NCI research categories. The research programs are: Cancer Control; Cancer Genetics, Epigenetics, and Genomics; Translational Cancer Biology and Signaling; and Cancer Therapeutics: Technology, Discovery, and Targeted Delivery. More than 125 researchers at UNMCC participate in research in these four areas. Partnerships with other organizations both outside New Mexico as well as in New Mexico provide further research opportunities. Some of the partnerships within the state include collaborations with scientists from: Sandia National Laboratories, Los Alamos National Laboratory, Lovelace Respiratory Research Institute, and New Mexico State University.

Researchers at UNMCC have also been recognized by NCI. Two UNMCC research teams won highly esteemed NCI Provocative Questions grants. One of the teams is exploring how RNA manufacture affects cancer, and the other team is studying why some non-steroidal anti-inflammatory medications have shown to have positive effects on cancer outcomes.

Patient Care
UNMCC is a unique cancer center with regard to the communities it serves. The multicultural
population of New Mexico includes tribal nations and pueblos, rural communities with limited health care access, Mexican Americans, as well as some undocumented populations. To provide education on cancer for the remote and underserved populations in New Mexico, UNMCC developed a Cancer 101 educational program that has been provided to communities throughout the state. The focus of this and other programs is to provide education on cancer as well as improve screenings and treatment so that cancer, when diagnosed, is treatable. Ethnic minorities in New Mexico tend to present with more advanced, or terminal, cancer, thus limiting treatment options. To improve cancer outcomes among the diverse populations in New Mexico, UNMCC has established collaborations with 19 of the pueblos, as well as the Jicarilla Apache Nation, the Navajo Nation, and Spanish-speaking communities in the state. UNMCC also is one of only three NCI-designated cancer centers that provides care to patients regardless of their ability to pay.

Through outreach to the state, UNMCC was able to provide care for over 65 percent of the cancer patients in New Mexico. This includes serving over 11,000 patients with over 124,000 clinic visits each year. Services provided to patients include: psychology services; oncology nutrition specialists; oncology social workers to help with logistics and financial concerns; a patient education resource library; a comprehensive Patient Guide to answer questions for patients and family members; support groups; clinical services; and other programs.

A unique newsletter, called El Oso Updates, is available online for patients and family members. It includes updates about new treatments, current treatments, and survivorship stories and events like the Think Pink Lobo Football game where fans wear pink to increase awareness and raise funds for cancer treatment and research.

Support groups both for those fighting cancer and survivors of cancer can also be found at UNMCC. Examples of these support groups include: Survivors Writing Together (a journaling support group); Arts-in-Medicine at UNM; Family and Friends of Advanced Cancer Patients; and Look Good...Feel Better for Women.

UNMCC works with the UNM Children’s Hospital to diagnose and treat children diagnosed with cancer. The UNM Children’s Hospital provides care to approximately 60,000 children and is a Children’s Miracle Network hospital. The hospital includes a pediatric oncology infusion center and Child Life Center. Patient rooms are large and comfortable to provide family and patients with a calm and secure environment during care. The Ronald McDonald House provides families with housing during extended treatments.

Training of Health Care Professionals
UNMCC, through its partnership with the University of New Mexico School of Medicine, offers training to future oncology health care specialists. The UNM School of Medicine excels at rural medicine and was ranked as second in the United States for its Rural Medicine Program by U.S. News and World Report.

Anne P. Hubbell
New Mexico State University

See Also: Association of Oncology Social Work; Caregivers; Clinical Trials; Diet and Nutrition; Disparities Within Nations (Elimination of Cancer); Experimental Cancer Drugs; Genetics; Screening, Access to; Survivors of Cancer; Survivors of Cancer, Families of; Technology, New Therapies.

Further Readings
Center in 1990, and the center is the only public comprehensive cancer center in North Carolina to have this designation. Since it was established, the aim of the center has been to reduce cancer occurrence and death through research, treatment, training, and outreach. UNC Lineberger is named after the Lineberger family of Belmont, North Carolina, because of the longstanding association between UNC and the Linebergers. In addition, four brothers of the Linebergers were key players in the creation of the Lineberger Cancer Research Center.

For the center to start operations, 315 members working at the center were drawn from more than 40 departments at the UNC and other institutions, including the College of Arts and Sciences, the Eshelman School of Pharmacy, and the Gillings School of Global Public Health. The UNC Lineberger Comprehensive Cancer Center is part of the university’s school of medicine, and the North Carolina Cancer Hospital is the focus of Lineberger’s clinical activities. The center has nine programs, through which it conducts interdisciplinary research. These programs are cancer epidemiology, cancer prevention and control, molecular therapeutics, breast cancer, cancer genetics, clinical research, cancer cell biology, virology, and immunology.

Research work by the Lineberger Center is more focused on breast cancer. Current projects in breast cancer studies are regularly supported by reports on associated molecular phenotypes, with an emphasis on the most difficult parts to treat and heal. These studies on cancer are in line with the center’s work on population studies, particularly with the African American community. Other areas of research are gastrointestinal cancer and colorectal cancer, with current research on genetic studies. Cancer is a complex disease, and it needs complex solutions: based on this realization, drug discovery scientists, physicists, oncologists, and chemists of UNC came together to create the Carolina Center of Cancer Nanotechnology Excellence (CCNE). Those who study here look to find new models used for the comparison of four critical nanoparticle formulations.

The UNC Lineberger Cancer Center is also the repository for Collaborative Cross. Collaborative Cross is an international effort investigating the genetic and environmental factors that contribute to cancer susceptibility. In the effort toward research on cancer, the UNC currently has more than 300 of the 600 inbred mouse strains that represent the genetic diversity of the human population, and is importing the remaining models in order to enable creation of population-level mouse models to inform cancer biology.

The Lineberger Center and the UNC Eshelman School of Pharmacy have established a partnership in Comprehensive Chemical Biology and Drug Discovery. Projects include potential treatments for renal cell carcinoma, gliomas, acute lymphoblastic leukemia, and basal-like breast cancer. The center is also working on the Cancer Genome Atlas (TCGA). Work through this program has been focused toward adjusting the form of breast cancer into several categories, based on how they are treated. The Lineberger Center extends its research mission by disseminating effective practices to the community. Treatment of cancer, screening for cancer, and prevention programs are provided and available at the North Carolina Cancer Hospital, where there is access to cancer clinical trials for patients.

The Lineberger Center’s clinical base, North Carolina Cancer Hospital, was completed in 2009. Through the hospital, the center is able to deliver cancer treatment to the public. The center’s physicians have offered multidisciplinary patient-centered care for more than a quarter century. The center provides patients the benefit of many medical and patient support specialists in one place, often in one visit. To ensure effective treatment, the center applies the latest technology to cancer diagnosis and treatment, offering intraoperative radiation therapy (IORT), advanced virtual and 3-D imaging for breast biopsies, intensity modulated radiation therapy (IMRT), PET scans, and laparoscopic and robotic surgeries for select surgeries. Other cancer treatment technologies used at the hospital include genetic counseling and testing for some cancers.

For North Carolina cancer patients, the Lineberger Center has support programs to ensure compassionate and effective support, not only to them, but also their family members. The mission of the support program is to provide outstanding clinical and educational programs for cancer patients and their caretakers, and a world-class training and research site for health care professionals who work with cancer patients. UNC Lineberger is not only focused on cancer research. It also has community initiatives that include programs for cancer prevention, early detection, and cancer survivorship. These programs extend throughout North Carolina, and the objective
is to reduce cancer incidence and mortality. The center also has cancer epidemiology and cancer prevention and control programs that examine patterns of cancer in the community to understand the complex interaction among biology, genetics, environmental exposures, and behaviors that cause cancer.

In the prevention of cancer, UNC research components form part of the Carolina Community Network that is funded by the National Cancer Institute (NCI). The purpose of the network is to reduce prostate, colorectal, and breast cancers in adult African Americans. In addition to the UNC, the network includes health promotion-oriented institutions and organizations and cancer treatment centers. The North Carolina–Louisiana Prostate Cancer Project is a longitudinal study of Caucasian and African American prostate cancer patients focusing on identifying reasons for racial differences in prostate cancer mortality. This project has received support from community advocates, prostate cancer survivors, state cancer registries, and the federal government through the U.S. Department of Defense Prostate Cancer Research Program. UNC Lineberger houses several international research programs in molecular carcinogenesis, virology, immunology, molecular therapeutics, cancer genetics, and cancer cell biology that investigate the genetic and molecular aspects of cancer. Researchers from the center are also conducting molecular-based analysis on cancers to establish cancer patients who stand to benefit the most from treatment. In addition, Lineberger Center researchers are seeking to identify molecular targets for new therapies and develop the methods appropriate for genetic therapy.

Michael Fox
Independent Scholar

See Also: Gene Therapy; Genetics; National Cancer Institute.

Further Readings

University of Pittsburgh Cancer Institute

The University of Pittsburgh Cancer Institute (UPCI) and the University of Pittsburgh Medical Center (UPMC) together form an integrated cancer care network that treats more than 74,000 patients annually. UPMC and UPCI partner as western Pennsylvania’s only National Cancer Institute (NCI) Comprehensive Care Center. UPCI is ranked 12th in NCI funding, including four Specialized Program of Research Excellence (SPORE) grants that focus on head and neck, lung, skin, and ovarian cancers. UPCI receives $173 million in peer-reviewed research grants.

Together, UPCI and UPMC represent more than 1,700 experts in: surgical, medical, radiation, and gynecologic oncology; otolaryngology; neuro-oncology; palliative care; behavioral medicine; scientists; and other health care professionals. There are 35 treatment centers in western Pennsylvania and Ohio associated with UPMC and UPCI, in addition to centers in Ireland, Italy, and Singapore.

The Hillman Cancer Center is the hub of the UPMC Cancer Center network. The Hillman Cancer Center was founded in 1985. It is a five-story facility that houses a full-service cancer center, disease-specific cancer centers, an education center, and a center for early detection and prevention of cancer. The Hillman Cancer Center also houses most of UPCI’s research laboratories.

There are nearly 400 research and clinical faculty who specialize in multiple disciplines including prevention, early detection, treatment, survivorship, and end-of-life care. Primarily, UPCI researchers work to advance understanding of the biological basis of cancer development and progression, develop novel treatments, and establish and implement preventive measures. There are hundreds of clinical trials available at UPCI and UPMC sites. UPCI plans
for growth with ongoing recruitment and planned expansion of clinical and laboratory space.

The Clinical Executive Advisory Committee consists of several members, which include the director of UPCI and the director of UPMC. The Research Executive Advisory Committee focuses on research-related issues. The committee is also responsible for academic activities. The primary focus of the committee includes: basic, translational, and clinical research; strategic planning; and assessment of opportunities and needs for infrastructure and recruitment. The UPCI External Advisory Board includes nationally and internationally recognized physicians, scientists, and cancer center directors. They annually review programs, shared facilities, and activities and provide detailed advice with regard to research, evaluation of programs, and recruitment. The UPCI and UPMC Cancer Center Council, which includes 50 of Pittsburgh's leaders, provides advice and support to the Clinical Executive Advisory Committee. They are ambassadors for UPCI and UPMC and promote the core missions of advancing the understanding of cancer; development of innovative methods for cancer prevention, diagnosis, and treatment; and provision of state-of-the-art cancer care. These members also help secure funding and promote relationships between UPCI and the business community that helps to guide technology.

Shared resources at UPCI are key in supporting cancer research through access to innovative and expensive technology and technical expertise while containing costs. The shared resources of UPCI are state-of-the-art and provide support in infrastructure, technology, and expertise to assist with basic, translational, and clinical cancer research. The goal is to provide outstanding service at a reasonable cost. Facility directors are available for expert consultation and may participate, in some cases, as researchers. Shared resources include the following: the Animal Facility (quality and humane animal care and services for research); the Biobehavioral Medicine Facility (biological changes associated with stress, psychological, and behavioral factors); the Biostatistics Facility (statistical and computer-related expertise); Cancer Bioinformatics Services (data management and access); the Cancer Biomarkers Facility (discovery and translation of relevant molecular biomarkers); the Cancer Pharmacokinetics and Pharmacodynamics Facility (pharmacology research services); the Cell and Tissue Imaging Facility (microscopic techniques and analysis); the Cell Culture and Cytogenetics Facility (cell culture services); the Chemical Biology Facility (potential anti-cancer compounds); Clinical Research Services (development, implementation, and completion of clinical research); the Cytometry Facility (analytical and imaging cytometry and cell sorting); the Hematopoietic Stem Cell Laboratory (therapeutic T-cell products and stem cell products); the Immunologic Monitoring and Cellular Products Laboratory (therapeutic cell product generation and banking of blood and tissues); the In Vivo Imaging Facility (MRI, PET, CT, optical, and ultrasound imaging); Investigational Drug Services (pharmacy procedures and processes); Tissue and Research Pathology Services (tissue and biological specimen procurement); and the Vector Facility (viral and non-viral vectors, cells, reagents, protocols, and technical assistance in AIDS cancer research).

Centers at UPCI include the Women's Cancer Research Center (WCRC), the Center for Environmental Oncology (CEO), and the Tumor Microenvironment Center (TMC). The WCRC is a collaboration between UPCI and the Magee Women's Research Institute (MWRI). Their mission is to reduce the incidence and number of deaths from women's cancers. The mission of the CEO is to protect public health and raise awareness regarding avoidable causes of cancer. They are committed to communicating the scientific evidence that links environmental exposures to cancer risks. The TMC is created by a collaboration between UPMC and UPCI. Preclinical and clinical scientists come together to translate basic knowledge of cancer cells' mechanisms of interaction and their microenvironment (i.e., immune, inflammatory, and patient-specific microenvironment factors).

UPCI researchers conduct laboratory-based, translational, and clinical cancer research in one (or more) of 11 UPCI programs. The Biobehavioral Oncology Program promotes innovative, interdisciplinary research on the role of the mind and brain in cancer. Goals include contributing to research that reduces the risk of cancer development, earlier detection, improved treatment response, reduced symptoms, and enhanced survival. The Breast and Ovarian Cancer Program personalizes prevention and treatment. Goals also include educating researchers, physicians, and the public about
advances in women's cancer and to train future women’s cancer researchers and physicians. The Cancer Epidemiology and Prevention Program promotes understanding the risk of cancer and innovative cancer prevention and control. Researchers are dedicated to identification, validation, and application of biomarkers, personal susceptibility, and early detection in relevant populations. The Cancer Immunology Program facilitates basic and translational research in immunoprevention, immunotherapy, and immunology. The Cancer Therapeutics Program develops innovative strategies for drug treatment of tumors and malignancies. The goal is to promote interactions along the continuum of basic, preclinical, and clinical research for novel approaches to drug treatment. The Cancer Virology Program seeks to identify and characterize cancer-causing viruses and to explore oncolytic viruses as treatment tools. The Head and Neck Cancer Program works to discover the biology of head and neck cancers and to design and implement new strategies to prevent, diagnose, and treat these cancers.

The Lung Cancer Program investigates the biology and genetics of lung cancer. Researchers work to improve the basic understanding of lung cancer and genetics and to apply this research. The Melanoma Program investigates cell biology and develops and implements new therapies. Goals include identifying and providing insight into the genes and proteins that play a role in melanoma. The Molecular and Cellular Cancer Biology Program researches the fundamental aspects of cancer cell biology. The goal is to make new discoveries about the cellular and molecular basis of cancer and cancer progression.

Jessica Anne Hammer
Independent Scholar

See Also: Ohio State University Comprehensive Cancer Center; Purdue University Center for Cancer Research; University of Alabama at Birmingham
Comprehensive Cancer Center; University of California, San Francisco, Helen Diller Family Comprehensive Cancer Center; University of Chicago Medicine Comprehensive Cancer Center.

Further Readings

University of Southern California Norris Comprehensive Cancer Center
The USC Norris Comprehensive Cancer Center has 200 members who investigate the origins and progression of cancers while developing prevention strategies and searching for cures. USC Norris is part of the Keck School of Medicine and is designated a Comprehensive Cancer Center by the National Cancer Institute (NCI). The center’s mission is to personalize patient care, educate, and integrate research in an effort to eradicate cancer. USC Norris Comprehensive Cancer Center describes its vision as innovation in the cancer field by setting a global standard of research and accelerating all programs that prevent, treat, or cure cancer. The center has created an inclusive and engaging culture of collaboration that revolutionizes an interdisciplinary approach to the prevention and treatment of cancer.

For more than 35 years, USC Norris Comprehensive Cancer Center has been fighting against cancer. In 1971, Dr. G. Denman Hammond, a pediatric oncologist at Children’s Hospital Los Angeles, founded the USC Cancer Center. Between 1971 and 1983, the center received $2 million for facilities and $5.6 million for research. County general funds, federal appropriations, private donations, grants, and a capital campaign funded the $37 million needed for a 96-bed hospital and 125,000-square-foot research institute. Five years later, the need for expansion presented itself due to the growth of the center and its reputation for quality care. The Dr. Norman Topping Tower, name in honor of a great champion of the cancer center and USC’s seventh president, included outpatient facilities, laboratories, and offices, and was dedicated March 21, 1996. In 2009, USC purchased the Norris Cancer Hospital and the Keck Hospital, made possible from a $25 million gift from philanthropist Henrietta Lee. USC Cancer Center then became the USC Norris Comprehensive Cancer Center.

Research at the center is organized into five thematic programs and five translational research programs. The five thematic programs are: molecular genetics, epigenetics and regulation, tumor microenvironment, cancer epidemiology, and cancer control research. The five translational research programs are: genitourinary cancers, gastrointestinal cancers, women’s cancers, leukemia and lymphoma, and developmental therapeutics. Research members currently hold grants in excess of $134 million in direct costs, with $53 million funded by the NCI.

Patient care at USC Norris Comprehensive Cancer Center is comprehensive and performed at affiliated hospitals and outpatient clinics. The center conducts hundreds of clinical trials (research that involves volunteer patients). Current trials focus on testing new therapies; optimizing existing therapies; improving quality of life before, during, and after diagnosis; and discovering prevention methods. In June 2014, USC and NYU scientists developed a potential cancer-fighting compound. The researchers patented a molecule that interferes in cancer progression. Also in June 2014, researchers discovered that cycles of prolonged fasting help protect the immune system from damage that occurs during chemotherapy.

Supportive services available to researchers include: BioInformatics (provides management, mining, analysis, and visualization of biological information utilizing computational tools and methods); Bioreagent and Cell Culture (provides reagents for cell cultures and prepares bioreagents that are grown in the facility); Biostatistics (meets the statistical needs of researchers); Cell and Tissue Imaging; Clinical Investigations Support Office (assists in infrastructure of clinical research); Flow Cytometry (addresses questions in cellular immunology, biology, radiology, and mechanisms of drug
actions); Immune Monitoring (offers advice, technical support, and equipment); Cancer Research Informatics Core (provides custom programming and software support); Molecular and Cell Biology Support (provides supervision and maintenance of centralized shared equipment); Molecular Genomics; Small Animal Imaging; Transgenic/Knockout Rodent; and Translational Pathology (provides normal and tumor tissue specimens).

Patient care at the USC Norris Comprehensive Cancer Center is affiliated with several local hospitals. The Kenneth Norris Jr. Cancer Hospital is a 60-bed inpatient and outpatient facility that is devoted to cancer research and treatment. It has a laboratory-to-bedside structure that means patients receive innovative therapies and treatments. The Keck Hospital is a 401-bed research and teaching hospital. It is designed to be a comfortable facility for patients to receive advanced services, including: transplantation, bloodless surgery, neurosurgery, cardiac catheterization, and interventional cardiology. Three floors are dedicated to cancer care, and surgical specialties include: cardiothoracic, esophageal, orthopedic, and reconstructive surgeries. The Children's Hospital Los Angeles has cared for pediatric patients with cancer and blood diseases for more than 40 years. It is the largest pediatric oncology/hematology program in the United States. Programs include: leukemia, hematopoietic stem cell transplantation, neuroblastoma, bone and soft tissue tumors, brain tumors, retinoblastoma, hemophilia, and sickle cell disease. Children's Hospital Los Angeles also participates in the only nationally and internationally collaborative research network for childhood cancers, Children's Oncology Group. The Los Angeles County + USC Medical Center is one of the largest academic medical centers in the United States, serving more than 50,000 inpatients and 750,000 outpatients annually.

The future of USC Norris Comprehensive Cancer Center includes continued participation in major national and international efforts regarding cancer research. The Harlyne J. Norris Research Tower has been added and provides five new floors for basic research, two floors for research in preventive medicine, and a conference center. Children's Hospital Los Angeles has recently completed a seven-floor, 317-bed building for medical and surgical care. It has an ER, imaging facilities, a cancer day hospital, a 48-bed acute cancer care unit, and a 14-bed bone marrow transplant unit. New faculty members specialize in a variety of research, including: clinical trials and translational studies for breast cancer via a personalized and multidisciplinary approach; molecular genetic analysis of common malignancies (breast, colon, and prostate); genetic risk factors; AIDS-associated cancers; biology of stem cells; and cancer drug resistance.

Membership in the USC Norris Comprehensive Cancer Center is divided into three types: full membership, associate membership, and affiliate membership. Full membership is for faculty who have had peer-reviewed support for their cancer-focused research and national leaders of cancer-focused programs who meet the criteria for peer-reviewed support. Associate members have not yet achieved independent support for their research and are typically new recruits, junior level scientists, and physicians (who have not met criteria for peer-reviewed support). Affiliate members have a significant focus on cancer research or demonstrate an interest in cancer research and contribute to the center’s mission. All members participate in center meetings and membership is reviewed annually.

Jessica Anne Hammer
Independent Scholar

See Also: University of Alabama at Birmingham Comprehensive Cancer Center; University of California, San Francisco, Helen Diller Family Comprehensive Cancer Center; University of Minnesota Masonic Cancer Center; University of Wisconsin Carbone Cancer Center; Vanderbilt-Ingram Cancer Center.

Further Readings
departments, and divisions that invest in clinical research, treatment, and public outreach. MDACC has had a rich history since its founding in 1941 and plays a role in the “War Against Cancer” declared by President Nixon in the National Cancer Act of 1971. MDACC’s extensive investment in a wide range of clinical and public health research has benefited the study of cancer and patients receiving cutting-edge care.

History
MDACC, located in the Texas Medical Center in Houston, Texas, was founded in 1941 and designated as one of the original three comprehensive cancer centers by the National Cancer Act of 1971. To meet federal requirements for comprehensive cancer center designation, MDACC maintains programs in laboratory, clinical, population-based, and transdisciplinary research. Comprehensive cancer centers must also sponsor professional and public educational outreach programs. The National Cancer Institute (NCI) Office of Cancer Centers is responsible for program designation and management.

The center adopted the current name in 1988, after going through four successive name changes. The previous names were Texas State Cancer Hospital and the Division of Cancer Research (1941), MD Anderson Hospital for Cancer Research of the University of Texas (1942), The University of Texas MD Anderson Hospital and Tumor Institute at Houston (1955), and The University of Texas System Cancer Center (1972).

Organization
MDACC is composed of six research institutes, 25 research centers, and 23 programs. The research institutes include: Duncan Family Institute for Prevention and Personalized Risk Reduction, Institute for Applied Cancer Science, Institute for Basic Science, Institute for Personalized Cancer Therapy, Institute for Cancer Care Innovation, and McCombs Institute for the Early Detection and Treatment of Cancer. There are over seven dozen additional departments and divisions that range from the Division of Anesthesiology and Critical Care to Veterinary Medicine and Surgery. There are approximately 50 labs that conduct basic and applied clinical research throughout the institution.

MDACC is based in the Texas Medical Center in Houston, Texas, but has additional locations throughout the state including: Bay Area, Katy, Sugar Land, The Woodlands, Bellaire, Memorial City, and Bastrop. MDACC also works with partner members at the Banner MD Anderson Cancer Center in Gilbert, Arizona, and MD Anderson Cancer Center at Cooper throughout New Jersey. Additional certified members and affiliates are spread throughout 11 U.S. states, Spain, and Istanbul.

Performance
MDACC is consistently ranked among the top cancer centers in the United States. MDACC was ranked “#1 Cancer Hospital” by U.S. News & World Report’s “Best Hospitals 2013–2014,” having been awarded the title 10 times since 2002. MDACC is also nationally ranked by U.S. News and World Report’s “Best Hospitals 2013–2014” in four specialties: ear, nose, and throat; gynecology; pediatrics; and urology. Additionally, MDACC’s specialties of geriatrics, nephrology, neurology and neurosurgery, orthopedics, and psychiatry are ranked as high performing. Professionally recognized leaders in medicine are among the hospital faculty and include seven members of the Institute of Medicine (IOM), two members of the National Academy of Sciences, and four fellows from the Academy of Arts and Sciences.

Staff Demographics
MDACC employs approximately 20,000 staff, including 1,700 faculty, 1,200 volunteers, and 6,500 trainees. The group of trainees is composed of physicians, residents, fellows, scientists, students, nurses, research trainees, and other health professionals. MDACC is among the 10 percent of medical colleges where faculty are required to reapply for tenure at the conclusion of seven-year term appointments. While tenure is traditionally reapproved in 92 percent of cases, most medical colleges do not require reapplication after full tenure has been awarded. These increasingly rare tenure practices have led to increased controversy in recent years. Nevertheless, MDACC is nationally ranked as a top company to work for by independent organizations such as the American Association of Retired Persons (AARP) and Glassdoor.

The 2014 MDACC staff demographics report indicates the following ethnic distribution: White (33 percent), Asian (26 percent), Black (25 percent), Hispanic (15 percent), and the remaining 1 percent
is categorized as mixed-race. Staff reported the following age demographics: born 1981 to 2000 (35 percent), born 1965 to 1980 (33 percent), born 1946 to 1964 (31 percent), and those born 1922 to 1945 (1 percent). Females represent 67.37 percent of all employees but only 38 percent of faculty; males represent 32.63 percent of all employees and 62 percent of faculty.

Patients, Research, and Finances
Since its first patient in 1944, MDACC has treated approximately 950,000 patients. Currently, approximately two-thirds of MDACC patients are from Texas, and one-third travel to Houston from outside the state to receive care. Those receiving inpatient treatments consistently rate MDACC highly on the Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) survey.

As of 2013, there were approximately 7,500 patients enrolled in about 1,000 clinical trials throughout the hospital system. MDACC remains the highest dollar recipient of grant funding from the NCI. Clinical trials are designed and approved through the standard rigorous Institutional Review Board (IRB) processes with U.S. Food and Drug Administration (FDA) oversight. Additionally, NCI-funded grants typically result in research partnerships between awardees and NCI scientists. MDACC conducts clinical research throughout the clinical trials process from animal and lab studies through Phase IV review.

During fiscal year 2013 (FY13), MDACC reported approximately $4 billion in revenue. About 77 percent of revenue was composed of patient payments; 12 percent came from grants, contracts, and philanthropy; 3.5 percent came from state government appropriations; 4.5 percent was from investments, and 3 percent came from auxiliary or other income. MDACC has a daily operating cost of approximately $9 million dollars.

The 2012 to 2013 annual budget was set at approximately $3.5 billion. During FY13, MDACC delivered about $225 million of uncompensated care to Texas citizens who did not have health insurance or were underinsured. During FY13, MDACC treated approximately 120,000 patients, and this number is expected to rise in the future.

Andrew J. Widener
University of Texas Medical School at Houston

See Also: Hospitals; National Cancer Institute; Nixon, Richard (War on Cancer).

Further Readings


University of Virginia Cancer Center
The University of Virginia Cancer Center has two priorities: strengthening ties between its clinic and cancer research laboratories and achieving NCI (National Cancer Institute) designation as a comprehensive cancer center. The cancer center is state-of-the-art and offers outpatient oncology care at the Emily Couric Clinical Cancer Center. Goals include building upon its affiliation network throughout the state, recruiting key clinical leaders and basic scientists who focus on translational research, and developing a population research center in preparation for NCI comprehensive status. The center’s mission includes: discovery of the fundamental causes of cancer; development of knowledge to increase tools for cancer treatment, diagnosis, and prevention; delivery of the most innovative and compassionate care; and distribution of tools for cancer prevention, detection, and treatment.

The University of Virginia Cancer Center has a rich tradition in research and academic oncology care and is a regional leader in cancer prevention, education, and screening programs. The center is committed to its partnerships with referring physicians and exhibits this with prompt and frequent communication. Providing unique and comprehensive treatment and programs that support patients and their families is also a commitment.
The cancer research center includes 23 departments (schools of medicine, nursing, engineering, arts, and sciences) with more than 160 faculty members. It is a NCI-designated cancer center with more than $75 million in research annually. The goal of the center’s research is to understand, at the most basic of levels, how cancer arises, grows, and spreads. A second related goal is to utilize the knowledge to develop ways to prevent, detect, diagnose, and treat cancer.

The center’s faculty members are divided into five research programs. Each represents an area of expertise to understand how cancer begins and to detect, diagnose, treat, and prevent cancer. The five research programs are (1) the cancer cell-signaling program, (2) the chemical and structural biology program, (3) the immunology/immunotherapy program, (4) the molecular genetics and epigenetics program, and (5) the women’s oncology program.

The cancer center shares resources with the University of Virginia Health System. State-of-the-art instrumentation, scientific expertise, and technology offer distinct advantages to cancer center members. The cancer center members are able to express their individual interests and expertise to meet the needs of the research community. The following facilities are available to center members: advanced microscopic facility, biomolecular analysis facility, biorepository and tissue research facility, flow cytometry facility, gene targeting and transgenic facility, molecular assessments and preclinical studies core facility, preclinical tumor analysis and imaging, biostatistics shared resource, office for clinical research, and the office of research core administration.

The University of Virginia Cancer Center treats people and their families through a unique, illness-specific, team approach. Cancer care teams were first created in 1995, made up of pathologists, surgeons, researchers, radiologists, and other health professionals. Each team is aware of the medical, physical, spiritual, emotional, and social needs of patients and their families. Each team is available to whatever extent the patient and/or family needs.

Team members typically consist of nurses, doctors, palliative care doctors, social workers, nutritionists, clergy, patient educators, the patient, and someone the patient designates to be a primary support. The primary support person can attend appointments to think of questions to ask, offer support, and help the patient remember what is said. Nurses can answer questions about care and provide advice; they are a good resource for educational materials and information. Doctors provide specialized care and any of the following may be present on the team: a surgical oncologist is a specialist who will provide expertise about surgical removal, if appropriate; a medical oncologist specializes in medicines used to treat the whole body in cases where cancer has spread; a radiation oncologist specializes in the use of radiation to treat cancer; a reconstruction surgeon specializes in reconstructing areas of the body affected by cancer treatment, typically by surgery; and a palliative care doctor specializes in managing side effects from treatment. Social workers who specialize in oncology are also members of the team, as are nutritionists who help ensure vitamin, protein, and calorie intakes are at optimum levels during treatment. Prayer and spiritual counseling may be useful for patients or families, therefore clergy are often members of the team. Finally, a patient educator can help with information prior to, during, and after treatment for the patient and family.

The center advocates for early detection and prevention as the best defenses against cancer. Cancer discovered in the first or second stage has an 80 to 90 percent survival rate at five years follow-up. The center sponsors and participates in programs that promote screening and education in the community at health fairs and other events. The center offers annual skin cancer screenings, as well as other screenings throughout the year.

The center also offers advice regarding risk factors under an individual’s control. For example, diet and exercise are important, as being overweight increases the risk for several types of cancer: breast, colon, prostate, esophageal, endometrial, and kidney cancers. Never smoking or smoking cessation also decreases the risk of smoking-related cancers. Smoking is related to at least 10 kinds of cancers and accounts for at least 30 percent of cancer deaths. Finally, exposure to the sun is another risk factor under an individual’s control. Skin cancer is the most common cancer and is diagnosed in more than one million people each year. Sunscreen and avoiding the sun during peak times (10 a.m. to 3 p.m.) can decrease the risks associated with sun exposure.

Jessica Anne Hammer
Independent Scholar
University of Wisconsin Carbone Cancer Center

The University of Wisconsin Carbone Cancer Center (UWCCC) is an integrated, collaborative center with a rich history in cancer research, education, and treatment. Beginning with the establishment of the McArdle Laboratory for Cancer Research at the University of Wisconsin, the university subsequently started the University of Wisconsin Clinical Cancer Center. The two facilities were combined in 1973 as the University of Wisconsin Comprehensive Cancer Center. In 2006, the center was renamed the University of Wisconsin Carbone Cancer Center for Dr. Paul P. Carbone, who served as director of the center from 1978 until 1997. The center now employs more than 2,400 staff, including 280 doctors and scientists, and sees over 30,000 patients per year. Spanning a period of over 70 years, the center has evolved into a facility at the forefront of cancer research and treatment.

The McArdle Laboratory for Cancer Research, funded largely by the donations of private area residents, was established during the 1940s as the first basic science cancer center at an academic institution in the United States. The cancer research program was created by Dr. Harold P. Rusch, the first director of the McArdle Laboratory. Dr. Rusch remained as director until 1972, and did much to solidify the laboratory’s prominence, chiefly by selecting a number of talented young scientists whose work helped gain the laboratory its international standing as a premiere institution for cancer research. Much of the early research conducted at the McArdle Laboratory focused on chemical carcinogenesis, that is, potential chemical causes of cancer, and how these chemicals created genetic changes in cells, resulting in cancer. Scientists also initially concentrated on the biochemistry of malignant cells, particularly focusing on the differences between cancer cells and healthy cells.

In 1951, Dr. Charles Heidelberger began the process of synthesizing and clinically developing 5-fluorouracil (5-FU), a drug used to this day in the treatment of basal-cell carcinoma, pancreatic cancer, breast cancer, rectal cancer, colon cancer, head and neck cancer, and stomach cancer. Dr. Heidelberger received a patent for the drug in 1959. 5-fluorouracil is on the World Health Organization’s List of Essential Medicines. In 1975, Dr. Howard Temin was awarded the Nobel Prize in Physiology and Medicine, along with Drs. David Baltimore and Renato Dulbecco, for the discovery of reverse transcriptase. His experiments provided evidence of the ability of retroviruses to perform DNA synthesis from RNA within cells, and led to a flurry of research into retroviruses. Dr. Temin was subsequently appointed to the national committee whose work formed the basis of the bill that became the National Cancer Act, signed into law by former president Richard Nixon.

In the 1970s, the center began conducting Phase I trials, that is, trials involving a very small number of participants in order to determine the safety, dose range, and side effects of a treatment. Phase I trials are the first step in evaluating, researching, and approving a drug for treatment. In 1973, the same year that the University of Wisconsin Carbone Cancer Center was formed, the center also received the National Cancer Institute (NCI) designation as a comprehensive facility, one of only six in the United States. To date, the center is the only comprehensive cancer center in Wisconsin. A total of 41 of the 68 NCI-designated cancer centers in the United States are comprehensive cancer centers. In order to gain
the title of comprehensive cancer center, the highest ranking given by the NCI, a facility must meet and adhere to specific guidelines. These include a strong basis in laboratory and clinical cancer research, along with translational research, which is the practical application of research findings. Additionally, the center must offer cutting-edge cancer treatments involving clinical trials, cancer prevention and control programs, training and instruction of health care staff, cancer information services, and community outreach and instruction.

Toward this end, the UWCCC is involved in a number of programs and research areas, not only to continue to meet the rigorous guidelines set forth by the NCI, but also to provide the best care possible for its patients. The center treats an array of cancers and related issues, from breast cancer, head and neck cancer, and lymphoma, to pediatric hematology and oncology. It also provides ancillary care including genetic counseling, integrative medicine, palliative care medicine, and psychology, social work, and spiritual care. Research scientists, academic faculty, and physicians collaborate across eight different research programs: cancer control, cancer genetics, chemoprevention, experimental therapeutics, human cancer virology, imaging and radiation sciences, nuclear signaling, and tumor microenvironment. More than 250 clinical trials are open to patient accrual in a wide variety of areas.

UWCCC is also involved in research involving outside facilities. The Wisconsin Oncology Network (WON) is one example. WON provides the opportunity for patients being treated at approved community treatment centers in Wisconsin and northern Illinois to enroll in certain clinical trials run by the UWCCC. The UWCC is also a member of the Wisconsin Network for Health Research, another similar network that promotes collaboration with researchers at other facilities throughout Wisconsin. With regard to cancer prevention and control, the UWCCC collaborates with the University of Wisconsin Center for Tobacco Research and Intervention (UW-CTRI).

UW-CTRI conducts tobacco research that is applied to tobacco treatment in health care clinics throughout Wisconsin. UWCCC is also a member of the Wisconsin Comprehensive Cancer Control Program. This program focuses on coordinating the efforts of public, private, and community-member institutions in order to facilitate a statewide method to best control cancer.

Additionally, UWCCC partners with two minority outreach programs. The first is the Partnerships with Underserved/Minority Populations, a program that uses established principles of community-based research to support successful research with its population of subjects. The project is investigating community preparedness for change and assessing quality cancer care in eight underserved communities. The second outreach program, the Spirit of Eagles, works to prevent and control cancer, and use research findings to improve health outcomes in American Indian/Alaska Native populations in Wisconsin. Since the program’s creation in 2000, the UWCCC has been a principle partner and subcontractor.

Lorna Rogahn
Independent Scholar

See Also: Chemoprevention; Chemotherapy; Clinical Trials; Experimental Cancer Drugs; National Cancer Institute; Nixon, Richard (War on Cancer).

Further Readings

Unknown Primary Site, Cancer of, Childhood

Cancer of unknown primary (CUP) is quite rare in children, representing less than 1 percent of solid tumors. CUPs are, by definition, metastatic cancers in which a primary tumor cannot be identified after routine workup. Thus, these tumors are unique in that they represent a failure to reach a conclusive diagnosis. This raises a number of issues for
the treating doctors and the patient's family. First, there is the perception that the diagnostic workup may have been deficient, which compounds the emotional suffering that the family will feel upon receiving the diagnosis. The idea that a child has a “hidden cancer” is troubling to both the family and the clinician. A second related issue is the question of just how far should doctors go in trying to locate the primary tumor. In patients who have a poor general condition and are unable to tolerate any proposed therapy, the value of extensive investigations is questionable.

The median age of diagnosis is about 8 years old. It affects boys and girls in approximately equal proportions. Cancer registry data are imprecise because of variations in the definition of CUP between countries, and even between studies. Accordingly, it is difficult to draw any meaningful conclusions regarding geographic differences in incidence. CUP is, however, a worldwide phenomenon, and the incidence appears to be falling, probably because of improved diagnostic methods. Because of the extreme heterogeneity of CUPs, it is not possible to identify risk factors or possible causes for their development. Symptoms often include general nonspecific complaints, such as generalized malaise, nausea, loss of appetite, and loss of weight or a failure to thrive (i.e., the child does not gain weight as expected). Symptoms from metastases may include lumps in the neck, armpit, or groin; pain; shortness of breath; and neurological complaints. On examination, there may be abdominal swelling from enlargement of the liver or ascites (fluid in the abdomen), anemia, jaundice, chest sign, and neurological signs.

A routine workup must already have been undertaken before the diagnosis of CUP is made. This will include a thorough medical history and physical examination of the patient. Furthermore, a tissue biopsy of the metastatic tumor must be obtained. Additional investigations will typically include routine blood counts, assessment of liver and kidney function, and urine and stool tests. Some form of imaging, such as a computerized tomography (CT) scan of the chest, abdomen, and pelvis will also have been performed. More sophisticated tests are carried out according to the clinical scenario. These tests may include gastrointestinal endoscopy and a thorough ear, nose, and throat (ENT) examination, including nasal and laryngeal endoscopy. Specialized scans, such as positron emission tomography (PET), are especially useful in locating head and neck tumors. Tumor markers, such as alpha-fetoprotein (AFP) and beta-human chorionic gonadotropin (beta-HCG), may be very useful in identifying primary liver cancers such as hepatoblastoma and hepatocellular carcinoma. B-HCG is also extremely useful in identifying possible germ cell tumors (tumors that arise from primitive embryonal cells). Urinary catecholamines are useful to identify neuroblastoma.

New molecular profiling techniques have reportedly been able to assign a tumor type to 60 to 85 percent of CUP tumors in adults. However, few studies have been performed to assess the validity of these diagnostic techniques in the pediatric population. Nonetheless, these advanced molecular profiling methods are likely to revolutionize the workup of CUP. Whether that translates to an improvement in patient outcomes remains to be seen. Depending on pathological findings, CUP is classified into several types. These types differ in the basic tissue type, for example adenocarcinoma, or squamous cell carcinoma, or germ cell tumors. Adenocarcinomas are cancers where the cells resemble glandular cells, squamous carcinomas have cells that resemble skin cells, and germ cell tumors have primitive cells that resemble those found in embryos.

Tumors that are more common in the pediatric population, such as melanoma, lymphoma, and embryonal tumors, are more frequently seen in CUP biopsies. Data is limited regarding the exact proportions, but according to one study, embryonal tumors are the predominant cancer type. Embryonal tumors arise from primitive cells that are seen during the development of the human embryo. Examples of embryonal tumors that are seen in CUP are rhabdomyosarcoma, neuroblastoma, and Ewing's sarcoma. Chemotherapy and radiotherapy are the primary modalities of treatment. Treatment depends on the histological type of tumor, the extent of disease, and the age of the patient. Embryonal tumors are mostly sensitive to chemotherapy, and even metastatic embryonal tumors can sometimes be cured with chemotherapy. Thus, treatment is often begun upon confirmation of the histology, without embarking on an exhaustive search for the primary tumor.

In some situations, where it is anticipated that radiotherapy will be useful, it is important to localize all tumor sites so that they may targeted by radiotherapy. Sometimes, if the primary site cannot
be found, a strategy of aggressive local control of the metastases is employed (using chemotherapy, local radiotherapy, and even surgery). This is then followed by a period of careful observation to detect the primary tumor, should it become apparent at a later stage. The prognosis of CUP is slightly better in children than it is in adults because of the relatively larger number of chemo-responsive tumors, such as lymphomas and germ cell tumors, which are more common in children. A five-year relative survival rate of 17 percent has been noted.

CUP is a failure to diagnose the primary underlying tumor, thus the chance of suboptimal therapy being administered is substantial. Additional work needs to be done to develop better diagnostic modalities, such as genetic profiling techniques, to further reduce the number of CUPs. More work also needs to be done to elucidate the underlying biologic mechanisms that drive these aggressive tumors.

See Also: Childhood Cancers; Extracranial Germ Cell Tumor, Childhood; Unknown Primary Site, Carcinoma of, Adult.

Further Readings
Carcinoma of unknown primary (CUP) represents about 3 percent of all cancers in adults. By definition, a carcinoma of unknown primary is a tumor that has spread from an original primary tumor, but routine investigations fail to reveal the site of the primary cancer. A diagnosis of CUP often generates a great deal of anxiety among both patient and doctor because it represents a failure to fully diagnose the cancer. The metastatic nature of the tumor, coupled with the generally poor condition of the patient, only adds to the stress. Moreover, a real diagnostic and ethical dilemma exists as to how far a diagnostic workup should be taken. In the United States, CUP represents 2 percent of all cancers. Internationally, the figure is about 3 to 5 percent. The median age at diagnosis is around 60 years old. There is no significant difference in incidence between men and women. As diagnostic techniques have improved over the years, the incidence of CUP has fallen, and this trend is expected to continue. Because CUPs are an extremely heterogeneous group, it is not possible to identify risk factors or specific causes for their development.

CUPs are generally aggressive tumors that show a propensity for early spread. In fact, they usually present with more than one site of metastasis. Additionally, the pattern of spread is often unusual. For example, metastatic prostate cancer with a known primary typically spreads to bone. However, when it presents as CUP, it tends to spread to the liver or lung. Patients usually present with nonspecific symptoms such as loss of appetite, loss of weight, nausea, and fatigue. Other symptoms are from the metastases and may include a lump in the neck, throat, armpit, or groin; bone pain or fracture; vomiting; and neurological complaints (e.g., weakness, double vision, headache, and convulsions). Physical examination may reveal ascites (fluid in the abdomen) or an enlarged liver. Anemia, jaundice, and enlarged lymph nodes may also be noted. Workup usually includes a biopsy (which proves that there is a malignancy), routine blood, urine and stool tests, a chest x-ray, and a computerized tomography (CT) scan of the abdomen and pelvis.

Once this routine workup fails to reveal the primary site, a diagnosis of carcinoma of unknown primary can be made. Doctors (and patients) are then faced with the ethical question of how far to pursue the diagnostic workup. Several studies have shown that exhaustive investigations yield only minimal benefit in terms of overall survival improvement, at a huge cost. Furthermore, patients have metastatic disease and are often weak and frail. The usefulness of such extensive investigations in patients who are unlikely to be fit enough to receive aggressive chemotherapy is debatable. Moreover, even after extensive investigations, a primary tumor is found in only about 20 to 30 percent of patients. Nonetheless, an extensive workup is usually undertaken in patients who have better general health. The aim of the workup is to select the minority (about 15 percent) of patients who may have a better prognosis. This extended workup relies on clinical suspicion as to the likely location of the primary. It may include a positron emission tomography (PET) scan, gastrointestinal endoscopy (upper and lower), panendoscopy of the upper airways, and tumor markers.

The pathologic examination is the cornerstone of the workup in CUP. The pathologist will typically use several techniques to gather more information, beginning with light microscopy, which may give basic information about the cell type and the degree of differentiation (resemblance to normal cells). However, this is unlikely to be sufficient to make a diagnosis. Other more sophisticated techniques such as immunohistochemistry (antibodies to certain cell components are used to verify the presence of these cellular components in the sample), electron microscopy, and chromosomal analysis are often used, but may fail to provide a conclusive diagnosis. A far more promising technique is molecular genetic profiling (DNA fingerprinting), to match the sample to known genetic profiles of various cancers. According to some studies, these genetic profiling techniques have succeeded in identifying a tumor type in 75 to 85 percent of cases of CUP. Whether identification of the primary cancer will actually lead
to an improvement in overall survival for patients remains to be seen.

After routine pathologic examination, CUP is usually divided into five subgroups, based on the general type of cell and the degree of differentiation (the degree of resemblance to normal tissue). The first group is moderate or well-differentiated adenocarcinoma (cancer that arises from glandular tissue). The second group is poorly differentiated carcinoma, with or without features of adenocarcinoma. The third group is squamous cell carcinoma (cancer cells resemble normal skin cells). The fourth group is neuroendocrine carcinoma (cancer cells are similar to nerve and hormone-secreting cells). The fifth group is undifferentiated neoplasm (cells that are so unusual that no determination of the cell type can be made). The pathological data are coupled with clinical data to place the patient in a defined clinicopathological group. These groups or subsets are known to have different outcomes to the usual (rather dismal) outcome seen in most patients.

The treatment of CUP depends on whether a patient belongs to one of these favorable subsets or not. If a patient belongs to a favorable subset, then specific therapy can be given. However, if the patient does not belong in one of these favorable subsets, a generic treatment approach is taken with the aim of palliation only. Examples of favorable subsets include women with axillary lymph nodes (i.e., lymph node enlargement under the arm) and adenocarcinoma histology (similar to breast cancer). These women are presumed to have an occult breast cancer, and are treated accordingly. Similarly, men with high prostate-specific antigen (PSA) and typical bone metastases are treated as prostate cancer. For patients who do not fall into these favorable subsets, chemotherapy is given blindly for palliation. Chemotherapy agents that are often used include cisplatin, carboplatin, paclitaxel, docetaxel, 5-fluorouracil, etoposide, and gemcitabine.

The overall prognosis of CUP is very poor, with median survival of 6 to 10 months in favorable subsets, and 3 to 4 months in the unfavorable subset. One-year survival is around 15 percent, and five-year survival is only about 5 percent. There is a need for better diagnostic modalities to identify the primary tumor so that specific therapy can be given. In addition, progress needs to be made to understand the underlying molecular biology of these tumors, which may harbor different biological mechanisms to their metastatic counterparts.

Emad Abdulhamid Eddokali
Independent Scholar

See Also: Lung Cancer, Non–Small Cell; Lung Cancer, Small Cell; Nasopharyngeal Cancer; Pancreatic Cancer; Prostate Cancer; Unknown Primary Site, Cancer of, Childhood.

Further Readings

Unusual Cancers of Childhood

Cancer among children was a rare occurrence in the past; however, the incidence of childhood cancer has increased in the last four decades. In the United States, cancer is the second-largest cause of mortality in children, after accidental injuries. An estimated 175,000 children develop cancer globally every year, and around 96,000 of these children do not survive. In 2010, the most commonly diagnosed cancers in the age group 0 to 19 were leukemia and brain and central nervous system cancer.
Prevalence of Childhood Cancer

In developed countries, around 0.5 percent of all cancers occur among children under 15 years. Whereas most adult cancers are carcinomas, cancers in children are varied and are classified based on histology. The International Classification of Childhood Cancer has identified common forms of cancer among children. The 12 major groups are leukemias, lymphomas, brain and spinal tumors, sympathetic nervous system tumors, retinoblastomas, kidney tumors, liver tumors, bone tumors, soft-tissue sarcomas, gonadal and germ-cell tumors, epithelial tumors, and other and unspecified malignant neoplasms.

Childhood cancer is a result of genetic alteration, possibly in utero, as studies on concordance between identical twins have confirmed. Besides the genetic factors familial aggregations have been studied that is the likelihood of one siblings suffering from cancer also increases the risk of cancer in the other sibling. Genetic syndromes such as Li-Fraumeni syndrome, neurofibromatosis, and Gorlin-cell syndrome are linked to childhood cancer. Children with Down's syndrome are more likely to have cancer. Retinoblastomas (a type of eye cancer) are caused by a faulty gene. The high incidence of certain childhood cancers in some regions of the world is linked with infections by viruses such as Epstein-Barr, hepatitis B, and human herpes virus 8.

Environmental factors shaping childhood cancer include exposure to prenatal obstetric irradiation; this factor was discovered almost 45 years ago, and the reduced use of diagnostic X-rays in pregnancy may have decreased the prevalence of cancer. Other factors include high levels of radiation; children who have undergone chemotherapy or radiation are more likely to develop cancer a second time. There is inconclusive evidence whether the exposure to ultrasound during pregnancy, exposure to magnetic field from power lines, use of pesticides, and occupational exposure of parents could lead to childhood cancer. Smoking habits of the father more than the mother increases the risk of a child to cancer. Little evidence exists on the relationship between viruses and childhood cancer.

There is considerable variation in the incidence of different types of childhood cancer in different regions of the world, and between ethnic groups in the same country. In some instances, a higher-than-average incidence of cancer can be easily explained: the high incidence of Kaposi's sarcoma in central and East Africa, for example, is related to the AIDS epidemic; the high incidence of thyroid carcinoma in Belarus is a result of the Chernobyl nuclear disaster. However, explanations for other differences in incidence are less clear: Why is the incidence of acute lymphoblastic leukemia (ALL) lower in developing countries? Why are children in developing countries at higher risk of retinoblastoma and Hodgkin's disease? Why do black children in the United States (but not in the United Kingdom) have a lower incidence of ALL than white children? Why is there a lower incidence of rhabdomyosarcoma among children in South and East Asia, as well as among Asian children in the United Kingdom, compared with white children?

Various tests and procedures are used for diagnosing cancer, such as a physical examination and learning the child's medical history. The study of blood chemistry includes testing of a blood sample to measure the substances being released into the blood by organs and tissues. Biopsy includes removal of cells or tissues so that they can be viewed under the microscope by the pathologist for cancerous cells. X-rays send an energy beam through the body. CT (computed tomography) scans produce detailed pictures of areas of the body taken from various angles. PET (positron emission tomography) scans use a radioactive substance called a tracer to find malignant tumor cells in the body. MRI (magnetic resonance imaging) uses a magnet and radio waves to give detailed pictures of the body from inside. An ultrasound exam is a procedure involving high-energy sound waves that generate internal pictures of the body.

Children who are suffering from symptoms are usually diagnosed by a pediatrician, a pediatric oncologist, or a pediatric hematologist who treats blood disorders. The treatment for childhood cancer includes a synthesis of surgery, radiation, and chemotherapy, depending on the type and stage of cancer. Treatment should be a coordinated effort by a team of doctors, nurses, and social workers. Because childhood cancers are uncommon, the outcomes are likely to be more successful if managed by specialized children's centers.

Cancer treatment in children can affect puberty and fertility, the heart, and lungs; cause hearing loss, kidney problems, intellectual development,
and education problems; and cause a second cancer. For young children, being away from family and friends can be difficult to cope with, and they might become clingy, argumentative, or difficult. Managing the situation with equanimity is important, along with maintaining the regular discipline. Treatment could cause weight loss or gain or hair loss, which might adversely impact the self-esteem of the child. Parents play an important role in keeping the child’s self-esteem intact. The British Childhood Cancer Survivor Study (BCCSS) is the first national population-based study of survivors of childhood cancer to be undertaken in Britain, assessing a wide spectrum of possible adverse health outcomes of childhood cancer and its treatment.

Keerty Nakray
Jindal Global Law School

See Also: Adrenocortical Carcinoma, Childhood; Esophageal Cancer, Childhood; Leukemia, Acute Myeloid, Childhood; Lymphoma, Hodgkin’s, During Pregnancy; Lymphoma, Non-Hodgkin’s, During Pregnancy; Salivary Gland Cancer, Childhood; Stomach (Gastric) Cancer, Childhood; Survivors of Cancer; Thyroid, Childhood; Visual Pathway and Hypothalamic Glioma, Childhood; Young Adult Cancer Prevention.

Further Readings

Ureter and Renal Pelvis, Transitional Cell Cancer

The ureter is a long tube connecting the kidney to the urinary bladder, and the upper part of the ureter is called the renal pelvis. The kidneys are responsible for the removal of wastes from the blood, collecting it in the form of urine. The urine collects in the renal pelvis, in the middle of each kidney, and is drained out of the body, passing through the ureter into the bladder, and finally exiting through the urethra. The renal pelvis and ureter is lined with specialized cells called transitional cells, which have an ability to be stretched and change shape depending on the bladder pressure, without any damage to the cells. Transitional cell cancer (TCC) is initiated in these cells, and TCC can affect the renal pelvis, or the ureter, or both. Tumors of the renal pelvis and ureter (upper urinary tract) are relatively rare. TCC of the renal pelvis accounts for only 10 percent of all urinary tract TCCs, whereas TCC of the ureter accounts for less than 2 percent of all TCCs of the urinary tract. TCC accounts for more than 90 to 95 percent of tumors of the upper urinary tract. Although the causes of TCC are unknown, the occurrence is higher in males, and environmental irritants are believed to play an important role in the development of the disease. Arsenic contamination in drinking water has been associated with the increased risk of developing TCC of the ureter and renal pelvis.

Symptoms associated with TCC include blood in the urine, back pain and pain between the lower ribs and hip bone, weight loss, and painful and frequent passage of urine. TCC may remain asymptomatic. Cysts may be discovered on the renal pelvis or ureter during imaging, often performed for other reasons. Once a cyst is discovered, urine cytology and urine analysis may be performed, along with a biopsy for further evaluation. A computerized tomographic (CT) scan or magnetic resonance imaging (MRI) may be recommended to evaluate the lesions, along with the recommendation of ureteroscopy, where a
thin flexible tube is inserted into the urethral opening up to the urinary bladder. Ureteroscopy allows the physician to view the cells lining the ureter and the renal pelvis for the presence of any lesions and cysts. The process also allows for quantitation of the number of lesions, and a section of the lesions or cysts may be removed to conduct a biopsy and gradation of the tumor.

TCC is classified into five stages, 0 through IV. During Stage 0, cancer cells are detected and remain localized to the transitional cells lining the ureter or the renal pelvis. In Stage I, cancerous cells spread to the underlying cellular layers. Once the cancer cells have spread to the surrounding muscle tissue, the cancer is classified as Stage III. In Stage III, the cancer cells may also invade the prostate gland in men, and the uterus in women. TCC is classified as Stage IV when the cancer cells invade the abdominal cavity and metastasize to the lymph nodes, followed by invasion into the blood stream. Abuse of medications for relieving pain, also called nephropathy, is considered a potential risk factor for the development of TCC of the ureter and renal pelvis. Certain occupations involving the exposure to a class of chemical compounds known as aromatic amines in the textile and leather industry and the plastics industry are also associated with an increased risk of development of TCC of the ureter and renal pelvis. Another common potential risk factor is smoking.

Nitrites and nitrates have also been associated with the risk of development of TCC of the renal pelvis and ureter. Certain genetic polymorphisms in high-risk individuals are implicated in the increased risk of cancer development when exposed to certain chemicals. Other than the above, chronic irritants such as catheters and recurrent infections of the urinary tract also increase the risk of development of TCC of the ureter and renal pelvis. Treatment of TCC of the renal pelvis and ureter is largely dependent on the individual case and stage of cancer. Kidney function and the presence of other conditions such as high blood pressure and diabetes are important factors determining the course of treatment. Low-grade localized tumors may be treated with specialized ureteroscopy to destroy cancer tissue. This is a minimally invasive technique, and does not involve surgery. Nephrostomy, involving the insertion of a thin tube into the kidney from the posterior end, may be performed for tumors that are larger in size. High-grade TCC of Stage III and above may involve the removal of an entire affected kidney and ureter via a procedure called nephroureterectomy. The procedure may be extended to remove associated lymph nodes in order to improve the prognosis and improve patient survival. Earlier detection of TCC results in better survival of the patient, with a five-year survival rate of 85 percent. However, most TCC of the renal pelvis and ureter are diagnosed at later stages, once they have spread beyond the site of origin.

Poonam Balani
Independent Scholar

See Also: Urethral Cancer; Uterine Cancer, Endometrial; Uterine Sarcoma.

Further Readings

Urethral Cancer

The urethra is present in both males and females and functions to connect the bladder to the outside of the body. Cancers arising from the urethra may be of multiple histologic subtypes, including squamous cell, urothelial cell, and adenocarcinoma. Treatments depend largely on location and stage of the tumor, and range from surgical resection in early disease to chemotherapy and radiation in more advanced cases. While cancers of the urethra account for only a small minority of cancers of the urinary tract, it is important for clinicians
and patients alike to be aware of the early symptoms, as advanced disease is associated with a poor prognosis.

Urethral cancers are malignant tumors that arise from the cells that line the urethra, the tube that carries urine (and also semen in men) from the bladder to the external environment. These cancers are exceedingly rare, accounting for less than 1 percent of all malignancies of the urinary tract. They occur at a rate of 4.3 per million men and 1.5 per million women. Due to the paucity of cases worldwide, the epidemiologic data is largely inconsistent between studies. As with many cancers, there is a direct correlation between incidence and age, with the mean age of presentation in men occurring at 60 years of age. In most studies in the United States, this cancer tends to favor African American race and male gender.

Risk factors for development of urethral cancers are generally associated with long-term irritation and inflammation of the urethra. A large proportion of patients have a history of urethritis (inflammation of the urethra typically caused by infection), urethral strictures, prior urethral surgery, trauma, or urethral diverticula in women (an out-pouching of the wall of the urethra). Additionally, human papilloma virus (HPV), the virus responsible for cervical cancer, has been found in the squamous cell variants of urethral cancers. There is also an increased incidence in patients with history of other sexually transmitted illnesses and other cancers of the urinary tract, including bladder and ureter. Chronic exposure to arsenic (typically found in water sources) has also been shown to increase risk of urethral cancer. No hereditary component has been identified in these cancers.

The major histologic subtypes of urethral cancer include squamous cell carcinoma, urothelial cell carcinoma (formerly known as transitional cell carcinoma), and adenocarcinoma. Most data suggest that the most common subtype is squamous cell carcinoma; however, some studies indicate urothelial cell carcinomas are more common. In rare cases, melanomas, lymphomas, and small cell carcinomas have also been reported to arise as primary urethral tumors. Anatomically, urothelial cell carcinomas and adenocarcinomas tend to arise in the proximal urethra (the portion closer to the bladder), while squamous cell carcinomas arise more often in the distal urethra. In men, tumors most commonly occur in the bulbomembranous urethra, that is, the portion of the urethra between the prostate and the penis.

Clinically, male patients most often present with symptoms of urine outflow obstruction. This may manifest as difficulty initiating urination, weak stream, or urinary retention. Other common symptoms include bloody urine, bloody or pus-filled discharge from the urethra, painful urination, and the presence of a lump in the penis. Men may infrequently present with swelling of the genitals and bloody ejaculate. Female patients more often present with symptoms resembling urinary tract infection, including painful urination, bloody urine, and increased urinary frequency. Less commonly, women may experience painful intercourse, a urethrovaginal fistula (a connection between urethra and vagina), and rectal pressure.

Diagnosis of urethral cancer requires a high index of suspicion, as presenting symptoms can easily be confused with other pathologies. Cytological evaluation of a urine specimen has relatively low sensitivity, and suspicious results must be confirmed by biopsy. Approaches should begin with cystourethroscopy and retrograde urethrography. Following diagnosis, an MRI is frequently used to determine the extent of local invasion. A CT scan is then utilized for assessment of distant metastases. Urethral cancer tends to spread locally into nearby soft tissues. At the time of diagnosis, a majority of patients will have locally invasive disease, whereas approximately 10 percent will have distant metastases. Metastasis occurs via lymphatics, with the most common sites being the lungs, bone, and liver. Cancers arising in the distal urethra are often diagnosed earlier and therefore have a more favorable prognosis than those of the proximal urethra, due in large part to earlier clinical presentation.

Treatment options are based on extent of local disease, presence of distant metastases, and location within the urethra. Surgical resection is the mainstay of treatment for anterior urethral tumors. Although outcomes data are limited, surgical resection for tumors of early stage offers good local treatment, with greater than 70 percent five-year survival rates. Several approaches to resection may be used, including transurethral resection, segmental urethral resection, or penectomy (removal of all or part of the penis) in men. Potential adverse
Endometrial cancer is the fourth-most-common cancer and the seventh-most-common cause of cancer death for women in the United States. Uterine cancer affects Caucasian women in higher proportions than black women; however black women are more likely to die from the disease, according to the American Cancer Society.

There are two primary types of uterine cancer: sarcomas and endometrial. Sarcomas are considered rare and more dangerous than endometrial cancer. Sarcomas arise from the muscles and supporting tissues of the uterus and are generally separated into three categories. The first, endometrial stromal sarcoma, is found in the supporting connective tissue of the uterus (stroma) and the endometrium. This form of cancer occurs in less than one percent of uterine cancers and is considered low grade (cancer cells appear closer to normal and tend to grow slowly).

The prognosis tends to be better than other uterine sarcomas. Undifferentiated sarcoma is a type of endometrial stromal sarcoma that is the most aggressive, also affecting less than one percent of females with uterine cancers, and is associated with poor clinical outcomes. Uterine leiomyosarcomas begin in the muscular wall of the uterus (myometrium), and they affect approximately two percent of women diagnosed with uterine cancer.

Endometrial cancer is considered more common than sarcomas and generally affects women....
aged 55 and older. Approximately 600,000 women are survivors of this type of cancer. Endometrial cancers begin in the cells that line the uterus and are mostly formed in the endometrium. The most common type is known as endometrioid adenocarcinoma (endometrioid), constituting 75 to 80 percent of all cases of endometrial cancer, and the less common types include squamous cell and undifferentiated carcinoma. The less common types are considered to be more aggressive and have poorer responses to treatment. Endometrioid cancer is divided into three grades, depending upon the similarity between cancer glands and normal healthy glands; the lower grade appears in glandular form, and the higher grade appears in a disorganized manner and not having a gland form. Grade 1 tumors have 95 percent or more of the cancerous-tissue forming glands, while grade 2 tumors have 50 to 94 percent; grade 3 tumors have 49 percent and below. Grades 1 and 2 tumors are identified as “type 1” endometrial cancers and are believed to be a result of excess estrogen, are less aggressive, and are slow to spread to other tissues. The high-grade tumors tend to be most aggressive and have poorer prognosis than grades 1 and 2 because it is believed that they are not caused by excess estrogen and are more likely to grow and spread outside the uterus.

**Treatment Options**

Treatment of uterine cancers, particularly endometrial forms, can range from surgery to radiation and chemotherapy, depending upon the severity and location of the lesion. Abnormal postmenopausal bleeding is the primary symptom that is most associated with type 1 endometrial cancer. If the cancer is primarily found in the uterine region and has not metastasized to other areas, then standard treatment involves total hysterectomy and bilateral salpingo-oophorectomy (TH/BSO). In some practices a pelvic/para-aortic lymphadenectomy, which involves the removal of the pelvis and the para-aortic lymph nodes, would be considered; however, the reliability of results are a point of debate.

There is evidence that the lymphadenectomy may increase the risk of lymphoedema with no added benefits. In a randomized trial conducted by National Cancer Research Institute (NCRI) and Medical Research Council (MRC) in the United Kingdom, females who underwent lymphadenectomy and adjuvant external beam radiotherapy (RT) had no increase in survival rates, so implementing it as a routine procedure was not considered therapeutically adequate.

Higher-grade cancers that spread further than the uterus can involve other forms of surgical treatment, including radical total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAH/BSO) and possible pelvic/para-aortic lymphadenectomy dissection, particularly if the cancer is in the cervical area. For those with intra-abdominal disease that involves the omental, nodal, ovarian, peritoneal, and ascites areas, treatment options such as TAH/BSO and maximal surgical debulking are considered. Those with metastatic disease involving the liver and lungs would be considered for palliative hysterectomy. Females with inoperable type 1 or 2 endometrial cancers may be treated with RT and/or brachytherapy (BT).

Black females diagnosed with uterine cancer and other chronic medical illnesses, such as diabetes or hypertension, are likely to be diagnosed later and less likely to have surgery. Radiation therapy is a primary treatment for black females with diabetes, and although chemotherapy is less utilized as a form of treatment for uterine cancer, it is more frequently used than surgery among some populations. Hormone replacement therapy has also been used to treat uterine cancer. According to a study that assessed 219 patients who underwent surgical staging, it was noted that blacks, who were less likely to use hormone replacement therapy, which was known to prolong the interval between the onset of symptoms and surgery, presented with higher prevalence of unfavorable features, even after controlling for hormone use.

**Health Disparities**

Health disparities exist in the diagnosis, treatment, and survival of women with uterine cancer. Black women tend to be diagnosed at later stages, have higher grades of uterine cancer, and have less favorable survival rates than their white counterparts.

Some researchers have begun to question if the presence of comorbid diseases like diabetes, obesity, and hypertension explain disparities in uterine cancer among black females. Obesity affects 34 percent of American females, of which 52 percent are black. Obesity is considered an antecedent of many chronic illnesses, including hypertension, diabetes, and some cancers. Body mass as noted by
BMI (kg/m²) influences the efficacy of treatment, prognosis, and survival of females with uterine cancer. Research indicates that issues related to access to care and later diagnosis potentially contribute to higher mortality rates for black women with uterine cancer. One study examining the role of socioeconomic status, race, and ethnicity in the diagnosis and treatment of women with uterine cancer found that black women were 41 percent more likely to be diagnosed with advanced stages of the disease. Delays between the onset of initial symptoms and diagnosis may result in black women’s presenting with more severe manifestations of the disease, which ultimately affects the course, efficacy, and success of treatment, and, subsequently, contribute to higher mortality rates. Delays in diagnosis and barriers to access to care may be influenced by multiple factors including sociocultural and socioeconomic determinants.

Racial barriers to health care access can, in part, be attributed to the general distrust that, historically, many blacks have with medical institutions and physicians. There is a significant history of the mistreatment of blacks in the United States by medical professionals (i.e., Tuskegee syphilis experiment). The history of overt and covert racism, discriminatory practices, and inequities between Caucasians and blacks also contribute to this distrust. Black patients may also have a communication and linguistic style that differs from their physician’s and may promote miscommunication and reduced efficacy of evaluations and cancer treatments. Black females with significant financial limitations and lack of health insurance have less access to preventative care, higher utilization of emergency health services, and later diagnoses of cancer.

In assessing a population-based Surveillance, Epidemiology, and End Results (SEER)—Medicare database, it has been noted that diabetes in both racial groups resulted in higher death rate for endometrial cancer. Interestingly, it was also found that hypertension in black women was correlated with greater rates of survival than their white counterparts.

Further Readings


Christopher L. Edwards
Keisha N. O’Garo
Abigail Keys
Duke University Medical Center

See Also: Endometrial Cancer; Uterine Sarcoma; Women’s Cancers.
Uterine Sarcoma

Uterine sarcoma ranks as the fourth-most-common cause of cancer-related death in women, and the number of cases diagnosed each year continues to increase. At this time, approximately 90 percent of patients diagnosed with uterine sarcoma are considered incurable and have an average survival rate ranging from six to 12 months. Based on the rapid deterioration of a uterine sarcoma patient and the lack of effective treatment strategies, an early detection method is imperative, which in turn may significantly improve patient outcomes.

Uterine sarcomas are rarely occurring neoplasms that involve the exocrine uterus cells (also known as islet cells or islets of Langerhans), which are responsible for generating chemicals that regulate specific activities of cells and organs, including the production of insulin for the maintenance of blood sugar levels. Uterine sarcomas rarely cause any symptoms, thus making it very difficult to diagnose. Furthermore, the details of its molecular pathogenesis remain elusive. In an effort to shed light on this disease, clinicians and researchers have embarked on molecular and genetic investigations to establish its mechanisms of development.

A few years ago, Giorgio Malpeli and colleagues conducted an investigation on gene silencing, mainly focusing on the Ras Association Domain Family 1 (RASSF1) gene, which is a putative tumor-suppressor gene that has been localized to chromosomal region 3p21.3. The protein product of the RASSF1 gene has been reported to suppress tumor growth using both in vitro as well as in vivo systems. RASSF1 has been regarded as a major component in the inhibitory effects of Ras on cell proliferation by regulating downstream agents, thus inactivating the entire Ras signaling pathway. The investigation was based on the fact that the RASSF1 gene harbors two CpG islands, one extending into the regulatory segment that occurs in gene types A, D, E, F, and G, whereas the other one is present in the regulatory segment of RASSF1 type C gene. The research study thus evaluated the possible role of methylation of the RASSF1A gene in regulating transcription in uterine sarcomas.

Another study involving methylation was conducted by Albertas Dauksa, who examined the significance of employing these specific epigenetic marks as predictive biomarkers in uterine tumors. In this particular study, methylation levels at specific sites within CpG-rich domains of the promoter sequences of various uterine sarcoma-related genes were assessed. The genes examined were ACIN1, APC, BCL2, CD44, DAPK1, p16, RARbeta, TNFR10C, and 30ST2. Using blood collected from
a total of 30 patients diagnosed with uterine sarcoma, methylation levels of selected CpG sites were assessed. The results of the investigation showed that several CpG areas were significantly highly methylated, whereas sites consisting of repeat sequences showed a slightly lower degree of methylation relative to that of the control. Furthermore, a positive correlation between the degree of methylation and risk for uterine sarcoma cancer was observed. Interestingly, the study also detected potentially useful correlations such as that between elevated methylation levels in TNFRSF10C and ACIN1 and a lower survival rate for a patient. This promising and significant finding could eventually be applied in clinics, although a larger-scale study should initially be conducted to further strengthen and validate this correlation. Should this be achieved in the near future, a simple blood test could assist clinicians in detecting uterine sarcoma, as well as predict the survival time of a patient.

A recent study conducted by Mingzhou Guo further strengthened the usefulness of epigenetic modifications in detecting and assessing neoplasms involving the exocrine, as well as endocrine, uterus. By extracting the DNA from a total of 48 paraffin-embedded uterine tumors, the levels of methylation were examined using nested methylation-specific polymerase chain reaction (PCR). The tissue samples used in the study consisted of acinar cell carcinomas (12 cases), adenocarcinoma (18 cases), and islet cell tumors (18 cases). This study was able to describe a methylation signature involving various uterine tumor-related genes. Thus, the pattern of methylation of specific genes involved in uterine sarcoma in a decreasing order was as follows: APC gene (50 percent), BRCA1 gene (46 percent), p16INK4a gene (35 percent), p15INK4b (35 percent), RARβ (35 percent), and p73 gene (33 percent).

In addition, a majority (94 percent) of the uterine tumors showed methylation in at least one of the studied genes, whereas 69 percent of the neoplasms showed methylation in two or more of the genes investigated in the study. Another significant finding of this particular study was that the patterns of methylation of these genes in uterine adenocarcinomas could be distinguished from those of uterine sarcomas. This difference could therefore be applied in clinics, specifically in diagnosing the type or subtype of uterine sarcoma. For decades, uterine sarcoma has been considered a very difficult neoplasm to detect, diagnose, and predict in terms of its progression. These molecular signatures involving methylation in specific genes may help in resolving the major challenges experienced by clinicians, particularly oncologists.

Rhea U. Vallente  
Independent Scholar

See Also: Endometrial Cancer; Uterine Cancer, Endometrial; Women's Cancers.

Further Readings

Uzbekistan

Uzbekistan is a unitary constitutional presidential republic, comprised of 12 provinces, one autonomous republic, and one independent city. Officially known as the Republic of Uzbekistan, the country is in central Asia. It is bordered by five countries: Afghanistan to the south, Kazakhstan and the Aral Sea to the north, Turkmenistan to the southwest, Tajikistan to the southeast, and Kyrgyzstan to the northeast. The country had a population of approximately 30.18 million in 2013. Since the Soviet era, the health care quality in Uzbekistan has plummeted. Between 1992 and 2003, spending on health care services and the number of hospital beds per capita both declined by almost half, and emigration from Russia reduced the number of physicians. As of 2004, Uzbekistan had 53 hospital beds per 10,000 people. Medical supplies such as antibiotics, anesthetics, and even needles became scarce. Even though all citizens are given free health care, bribery became a common way to navigate
the sluggish and severely limited state health care system. Early in the 2000s, policies were written that improved the quality of health care facilities and reduced the cost of inpatient facilities.

Disease in Uzbekistan is predominantly caused by polluted water, including typhoid, dysentery, hepatitis, different types of cancer, and cholera. The main causes of death are cardiovascular disease, respiratory disease, infectious diseases, parasitic diseases, and diseases of the digestive system. Reported cases of human immunodeficiency virus (HIV) increased after 2002, in large part because of drug abuse. Even though deaths from other diseases are common, cancer mortality is low, and has been steadily declining since 1986. Uzbekistan has the third-lowest rate in the region of mortality from cancer for those 0 to 64 years old, and the second-lowest rate of mortality from trachea/bronchus/lung cancer. As per World Health Organization (WHO) estimates, 15,000 people are afflicted by cancer annually in Uzbekistan. Of females with cancer, 40 percent have cervical and breast cancers. Among the male population in Uzbekistan, stomach, lung, and liver cancers cause the highest mortality. In the mid-20th century, a transition in disease burden occurred in the country: non-communicable diseases (NCDs) eclipsed infectious disease as the most widespread cause of premature death. Today, an estimated 80 percent of deaths are from NCDs. These diseases, including cancer, constitute the gravest threat to public health in Uzbekistan.

Since the mid-1990s, the International Atomic Energy Agency (IAEA) technical cooperation program has offered Uzbekistan sustained assistance in developing radiation medicine services. As a result of the program, there are now state-of-the-art radiotherapy services and the establishment of a single-photon emission computed tomography (SPECT) facility in Tashkent. As the threat of cancer diseases continues to increase with more cases, Uzbekistan’s Ministry of Health (MoH) has recently drafted a national plan to prevent and control cancer and other chronic NCDs. A delegation convened by the IAEA and commissioned by the MoH conducted a survey between March 31 and April 3, 2014, and noted that Uzbekistan’s radiotherapy and radiation medicine infrastructure faces challenges to meet national needs for diagnosis and treatment.

The findings by the delegation are substantiated by doctors in Uzbekistan, who say that their treatment solutions are not as strong as they should be because of poor diagnosis functions, lacking hospital facilities, and medicines that are either hard to find or far too expensive for general requirements. This challenge comes in the midst of increasing cancer incidences. A report by doctors in Uzbekistan showed that for the five-year period between 2003 and 2008, cancer incidences increased from 14 to 25 per 100,000 of the population. Statistics from the MoH indicate that in 2009, 90,000 cancers cases where recorded in the country. One of the areas where cancer cases are high is the Khorezm, which lies close to the Aral Sea that dried up over several decades. The high cancer cases have been linked with the Aral disaster because of harmful dust in the air from the dried up sea.

One environmental cause of cancer in Uzbekistan is the utilization of dangerous pesticides in cotton farms where children often work. According to experts in the health care system, even though this has been established, there are no mechanisms in place to prevent cancer or detect early signs among children, young women, and people who work with chemicals or other hazardous materials. This problem has been attributed to the lack of sufficient highly trained experts and inadequate state funding for cancer centers. In 2013, there were only 1,104 beds for cancer patients, so patients have to wait their turn for months on end.

Regardless of the challenges, the country has made considerable progress in the fight against cancer. The Republican Oncology Research Center, which is located in the MoH of Uzbekistan, has been in operation for more than 50 years, with the intention of studying radiology and oncology functions around the country. The facility is the head institution of oncology service of the Republic of Uzbekistan, incorporating 17 big institutions of oncology services (including city, regional, republican dispensaries), as well as 271 oncology cabinets at district and city polyclinics. Based on this program, the country has a total of 2,265 oncology beds, and 145 of them are for treating children. The aims of the institution’s activities are to offer strategically planned diagnostic, curative, and consultative treatment solutions for oncologic patients, to perform fundamental and practical research in oncology, to screen for and prevent malignant tumors, and to offer scientific-methodological supervisory assistance to regional oncologic dispensaries.

The facility also provides education and training for preparation of clinical residents, masters, trainee-researchers on oncology and clinical radiology specialties. The RORC is currently home to
18 fully registered doctors, six of whom are professors, and 55 Ph.D.s. based on these achievements, the facility is among the leading centers in the New Independent States in the area of diagnostics and treatment of oncologic diseases. Research in the RORC MoH UZB is quite wide, and includes theoretical, experimental, and clinical parts. Research is done using modern equipment and computers, and implemented by well-coordinated and highly competent groups, monitored by the Scientific Board, and under chairmanship of the director of the RORC MoH UZB, Professor S. N. Navruzov.

Michael Fox
Independent Scholar

See Also: Kazakhstan; Kyrgyzstan; Russia.

Further Readings
Vaccine Workers, HPV and HCV

Vaccine workers deliver vaccines that lessen rates of disease and death, often in conjunction with other health care professionals and community organizations (e.g., schools, community centers). Vaccines exist for human papilloma virus (HPV) under the commercial names of Gardasil (for HPV types 6, 11, 16 and 18; Food and Drug Administration (FDA)-approved in 2006) and Cervarix (for HPV types 16 and 18; FDA-approved in 2009). Currently, no vaccine exists for the Hepatitis C virus (HCV). Both HPV and HCV can be spread through sexual activity, and having the viruses increases one’s cancer risk. Vaccine workers must possess knowledge of HPV and HCV, vaccines, and treatment/risk prevention for the populations that they work with.

HCV and Hepatitis B virus (HBV) are top risk factors for cirrhosis and liver cancer. Liver cancer claims 600,000 lives each year and disproportionately affects Sub-Saharan Africa and southwest Asia. HCV screening tests, though relatively inexpensive in the West, are prohibitively expensive in the developing world. Women in developing countries die 85 percent more frequently from cervical cancer, a leading cause of which is HPV. HPV vaccine workers can reduce cervical cancer death and can direct their clients to screening and education about HCV that, like HPV, is spread through sexual activity. There is currently no HCV vaccine, though research is examining similarities between HCV and HPV to help find a vaccine. Vaccine workers might contract HCV by being accidentally stuck with needles. The Centers for Disease Control and Prevention (CDC) estimates that the risk of HCV infection with accidental needle sticks is 1.8 percent. To minimize the risk of infection, vaccine workers are recommended to practice proper hand hygiene, wear gloves, and practice care with used needles. Vaccine workers who are accidentally stuck need both immediate and follow-up testing to gauge their HCV exposure. It is recommended that vaccine workers receive the HBV vaccine (e.g., Heptavax-B; FDA approved in 1981) as a preventative measure.

Vaccine workers may come into contact with individuals with HCV in their work to vaccinate clients for HPV. Both viruses are spread by unprotected sexual contact and thus affect similar populations. A knowledgeable vaccine worker can advise HCV-infected individuals of effective health practices (e.g., avoiding alcohol and certain prescription and over-the-counter drugs that advance cirrhosis of the liver) and ways to avoid spreading the virus to others (e.g., through exposure to blood and bodily fluids).

HPV vaccinations prevent anal cancers and genital warts and require three inoculations over six months for females aged 11 to 26 and males aged 11 to 21. HPV vaccine workers face usual challenges
like vaccine resistance movements and reaching low-income clients, as well as specific challenges like religious/moral objection and misinformation. In Canada, Catholics initially objected to the HPV vaccine administration at publically funded Catholic schools in Ontario and Alberta; several schools have since allowed the vaccine though others have not. In the United States, Texas Governor Rick Perry faced religious and political opposition when he mandated the vaccine for all girls in 2007; the state legislature subsequently overturned this order. HPV vaccine workers have taken on a public advocacy and education role to overcome such cultural opposition. In the developing world, vaccine workers face the above-mentioned challenges in addition to the barriers posed by misinformation about HPV and its vaccines, even among health care workers, and the suspicion that Western medicine and vaccines actually cause the diseases they aim to guard against.

Vaccine workers in the developing world have developed strategies to overcome these barriers, such as using the media and distributing visual materials to those who may be illiterate and/or in remote areas. Vaccine workers also involve government, community, and educational leaders in their work to target the age groups appropriate for the HPV vaccines. Teachers help vaccine workers secure parental consent, keep vaccination records, and promote vaccination. Government officials, community leaders, and midwives help vaccination workers find young people who might not be reached through public school. This strategy would arguably be useful in the United States as well, where the approximately 3 percent of children who are homeschooled are considerably less likely to receive the HPV vaccination.

Vaccine workers working with populations susceptible to HPV and HCV face challenges, some of which might be experienced by vaccine workers (e.g., cost, ensuring participation) in other areas of health and some of which are unique (e.g., misinformation, social stigma). To overcome these challenges, vaccine workers require health information and communication skills. For those infected with HCV, for which there is no vaccine or cure, the vaccine worker may serve as a health information and screening resource.

See Also: Cervical Cancer; Developing Countries; Hepatitis B; Hepatitis C; Liver Cancer, Adult (Primary); Vaccines.

Further Readings

Vaccines
The formulation of the vaccine for smallpox by Edward Jenner in 1796 ultimately led to the eradication of smallpox as a disease from the face of the
Vaccines

planet (1979) and the formulation of thoroughly successful vaccine formulations for a variety of other diseases caused by bacteria or viruses such as tetanus and polio, respectively. The principle of these vaccines is to expose an individual to a killed or attenuated form of the pathogen in order to generate immune responses to “foreign” sequences known as antigens that subsequently protect the individual from infection with that specific pathogen. Despite the remarkable success of vaccines against many diseases, there are diseases where vaccines have proven to be thus far unsuccessful.

These include malaria, caused by a parasite, and cancer, a malignant disease that usually is not caused by a pathogen. There are examples where certain types of cancer are caused by viruses, such as cervical cancer, which is caused by the human papilloma virus (HPV), and indeed a prophylactic vaccine for HPV has resulted in a dramatic reduction in cervical cancer incidence worldwide. However, such a vaccine is only successful prophylactically, meaning that it must be administered prior to infection and development of the cancer in order to be protective. Since most cancers are not of viral origin, the use of a prophylactic vaccine is not considered practical, since there are over 100 different types of cancer and there is usually no predicting which of these cancers an individual may acquire. Therefore, cancer vaccines are currently recognized as having to be delivered therapeutically or, in other words, subsequent to diagnosis of a patient with cancer. The remainder of this essay will focus on cancer vaccines as potential therapies for cancer.

Cancer vaccines are a relatively new application in the field of clinical oncology, although their potential as a cancer therapy has been under investigation for many decades now. The idea that the immune system may be able to assist in the eradication of tumors was first seriously entertained through the clinical efforts of William B. Coley (1862–1936), a bone surgeon at New York Memorial Hospital, who noted that administration of bacterial products to cancer patients (with bone sarcoma) resulted in remarkable recoveries. Fuelled by his direct observations, as well as historical evidence, of tumor-burdened patients experiencing dramatic tumor regressions (or spontaneous regressions) while concomitantly experiencing febrile infection, Coley ultimately developed a therapeutic cancer therapy that comprised a combination of two killed bacterial species (Streptococcus pyogenes and Serratia marcescens), which was to become known as “Coley’s toxins.” The treatment involved daily (or every alternate day) intratumoral injections of increasing doses of Coley’s toxins for at least one month followed by weekly injections for at least six months. Although at the time Coley was unaware of how the treatment was achieving its therapeutic benefits, it has subsequently been shown that the immune system played an important role. It was noted that therapeutic efficacy strongly correlated with the patient experiencing fever. We now know that fever can be caused by a range of cytokines (hormone-like proteins) such as interleukin-1β, interleukin-6, and tumor necrosis factor-α that act as endogenous pyrogens but also play important roles in triggering downstream anti-tumor immune responses as well as having direct tumoricidal effects.

Therapeutic benefit was seen using Coley’s toxins in many patients with sarcomas and, later, with patients with carcinomas (cancers of epithelial origin); however, modern medicine, primarily in the form of chemotherapeutics, along with surgery and radiotherapy, attracted most of the attention of oncologists, and since the 1940s the promising results from Coley’s therapy were largely ignored for half a century. In 1999 a retrospective comparison of the therapeutic benefit of Coley’s toxins versus conventional therapy was published and suggested there was no difference in survival rates of patients treated with Coley’s toxins (between 1890 and 1960) and those treated with conventional therapy (post diagnosis in 1983). More recently, Coley’s toxins have been renamed Mixed Bacterial Vaccine, possibly to increase marketability since the word “toxin” may be off-putting for prospective patients. However, it is a moot issue as to whether one can consider Coley’s toxins a vaccine, as it is classically defined, since the therapeutic benefit appears to result from an immediate non-specific immune response in most cases.

Although the precise mechanism of action of Coley’s toxins remains unclear, it is likely that pathogen-associated molecular patterns (PAMPs), such as lipopolysaccharides (LPS) that constitute the outer membrane of gram-negative bacteria, play a critical role. PAMPs are conserved sequence motifs expressed by pathogens, such as bacteria, viruses, and fungi, which are recognized as “danger signals” by the host’s innate immune system. During
the 1990s it was recognized that certain cells of the innate immune system possessed a range of receptors, known as Toll-like receptors, capable of recognizing different PAMPs. For instance, Toll-like receptor-9 binds to bacterial DNA motifs, while Toll-like receptor-4 binds LPS. Cells of the innate immune system expressing these receptors can be triggered to release a range of cytokines upon encountering PAMPs, which in turn can lead to a range of downstream immune effects, not the least of which is the promotion of antigen-specific immune responses. The innate immune system is found in most multicellular organisms, from plants and insects to mammals, and is considered the first line of defense against pathogenic infection.

PAMPs trigger immediate responses from innate immune cells, such as phagocytes, which not only directly eliminate or destroy the invading pathogen, they also promote the influx of other immunocytes to the site of infection. The innate immune system per se has no immunological memory, but is a vital contributor to adaptive immune responses, possessed by animals in the phylum Chordata, which do have immunological memory. It has been shown that PAMPs can activate specialized antigen-presenting cells, known as dendritic cells, so as to favor an adaptive immune response over a suppressive immune response when delivered in association with "foreign" antigen. Tumors are known to express their endogenous version of "foreign" antigens, known as tumor antigens, which are aberrantly expressed proteins that are either not expressed by healthy adult tissues or have highly restricted tissue expression thereby making them potential targets for immune-mediated therapy.

To the uninitiated it may seem anti-intuitive that a patient with cancer could potentially mount an immune response against his or her own cancer since although it may be an unwanted malignant disease, the vast majority (more than 80 percent) are not caused by viruses and therefore do not actually express foreign proteins. However, accumulating evidence over the past 20 to 30 years lends strong support for the capacity of cancer patients to develop antitumor immune responses. The current paradigm amongst tumor immunologists is that tumors (or tumor cells) gain a distinct advantage within the host once they have eluded the surveillance by the host’s immune system, which scans the body for something “foreign.” Tumor cells that are either ignored by the immune system or actively suppress the immune system, either directly or indirectly, are the ones that progress.

If tumor cells have successfully evaded the immune system, then how can the immune system subsequently be manipulated for therapeutic effect? The aim of a cancer vaccine is to overcome the immunosuppressive elements of the tumor and make the tumor “visible” to the immune system through the recognition of the tumor antigen(s) that these tumors express. For example, the prostate gland in men contains cells that express a protein aptly named prostate-specific antigen (PSA) that is exclusively expressed by prostate cells. Prostate tumors develop from prostate cells and, therefore, express prostate proteins such as PSA.

Other than being expressed in larger quantities, PSA expressed by tumor cells is generally no different to the PSA expressed by normal cells. However, it turns out that the immune system possesses a small number of T lymphocytes (“T” because they undergo their development in the thymus) that are capable of recognizing PSA-expressing cells and, if appropriately activated, these T lymphocytes can become tumoricidal. It is the role of a cancer vaccine to stimulate those PSA-specific T cells into action. Such stimulation involves promoting their expansion or proliferation such that there is an increased number of these PSA-specific T cells. Aside from promoting their expansion, the cells must also become capable of killing the cell for which they are specific. There is now strong evidence that prostate cancer patients not only possess these tumor-specific T lymphocytes but that they can also be triggered into action. Other examples of tumor antigens include a group of proteins known as the cancer testis antigens. These proteins are variably expressed by a broad range of cancer types.

One particular example is NY-ESO-1 (so called because it was discovered in New York in a patient with esophageal cancer), discovered in 1996, and expressed by about one-quarter of patients with certain types of cancer such as prostate, melanoma, and lung cancer. NY-ESO-1 is considered an attractive tumor antigen for use in cancer vaccines for multiple reasons. These include (1) that NY-ESO-1 is highly immunogenic, being capable of triggering both cellular (T lymphocyte) and antibody (B lymphocyte) responses in situ; and (2) that NY-ESO-1 is expressed almost exclusively by cancer cells with
expression by healthy tissue being restricted to testis and placenta, which are immune-privileged tissues, meaning that immune responses tend to be suppressed within such tissues and, therefore, concerns of autoimmunity are alleviated. That the cancer patient harbors tumor antigen-specific immune cells (T lymphocytes and B lymphocytes) with the potential to mediate tumor cell killing is now well documented not only for NY-ESO-1 but for a wide range of other well-characterized tumor antigens.

The evidence that the immune system can play a role in protecting the host from the development and progression of tumors has been accumulating over recent decades. Of particular note have been a number of studies in animal models where removal (“knock-out”) of specific genes, intrinsic to the immune system, has been shown to have significant influence over tumor development. Specifically, it was shown that mice made incapable of responding to the cytokine, interferon-gamma (IFN-γ), had significantly more incidences of spontaneous tumors than wild type (normal) mice. IFN-γ, previously known as immune interferon and macrophage-activating factor, plays a vital role in both innate and adaptive immunity and protects the host from a variety of infections (e.g., viral, mycobacterial) that would otherwise prove lethal. It is thought that IFN-γ promotes immune-mediated eradication of tumor cells by directly acting on the tumor cell, upregulating tumor antigen expression (specifically major histocompatibility class I antigen in association with tumor antigen) and increasing the immunogenicity of the tumor cell, thereby increasing the tumor cells’ vulnerability to tumor-specific immune attack.

The types of cancer vaccines currently under preclinical and clinical investigation include whole-cell tumor vaccines, tumor-cell lysates, viral vectors (carrying tumor antigen gene[s]), dendritic cells (pulsed with tumor antigen[s]), and biodegradable microparticles encapsulating tumor antigen(s). While most of these vaccines may have inherent adjuvant properties, meaning that they help the immune system to recognize the tumor antigens being delivered as “foreign,” in the majority of cases co-administration of an adjuvant, such as a PAMP and/or GM-CSF (granulocyte-macrophage colony stimulating factor) is considered almost obligatory. These additional adjuvants are potent activators of dendritic cells that present tumor antigen to T lymphocytes and, upon appropriate activation, will promote the production and function of tumor-specific cytotoxic T lymphocytes. Thus far, the only therapeutic cancer vaccine that has received approval from the U.S. Food and Drug Administration has been the prostate cancer vaccine sipuleucel-T (also known as Provenge). Sipuleucel-T is a cancer vaccine that comprises the patient’s own dendritic cells pulsed ex vivo (out of the body) with a fusion protein comprising GM-CSF and the tumor antigen known as prostatic acid phosphatase.

Each of the vaccine formats has its own set of advantages and limitations. For instance, the sipuleucel-T involves extensive labor and cost in acquiring the end product, a scenario that would also apply to any autologous (i.e., patient-derived) whole-tumor-cell or cell-lysate-based vaccines. In addition, cancer vaccines using autologous tumors or dendritic cells will be limited with respect to cellular yields. Cancer vaccines carrying only one tumor antigen run the risk of immune evasion by the tumor through the

William B. Coley noted that administration of bacterial products to cancer patients resulted in remarkable recoveries. He developed a cancer therapy that became known as “Coley’s toxins.” (Wellcome Library, London)
selection of tumor cell clones that no longer express that particular tumor antigen. In addition, often only certain patients may be suitable candidates for single tumor antigen vaccines due to genetic factors that may compromise the ability of the patient to generate effective cytotoxic T lymphocyte responses. This is the reason that many researchers are working with whole-tumor cells and tumor-cell lysates as a source of multiple tumor antigens, many of which may be unknown, but reduce the capacity of tumor cells evading tumor antigen-specific T lymphocyte-mediated killing.

While the various cancer vaccine modalities have generally promoted impressive tumor regressions in animal models, their translation to clinical settings has met with more modest results. One key positive outcome thus far is that most cancer vaccines have proven to be well tolerated by cancer patients. Although the reasons for the lack of significant improvements in patient survival may be multifactorial, there is a general consensus that cancer vaccines per se are unlikely to overcome the immunosuppressive environment within the tumor itself and that additional therapeutic intervention is required. It has been observed that up to 20 percent of the cytotoxic T lymphocyte population within tumors from cancer patients can be tumor antigen-specific and yet fail to provide effective killing of tumor cells. Therefore, it is clear that some cancer patients possess tumor antigen-specific T lymphocytes capable of accumulating at the tumor site but, due to the hostile tumor microenvironment, these cells fail to unleash an effective antitumoral response. One major contributor to immunosuppression is a subset of T lymphocytes known as regulatory T lymphocytes that can also accumulate at tumor sites. As a result, there have been intensive preclinical and clinical investigations into the impact of dampening Treg function (Treg cells are regulatory T cells) in tumor-bearing individuals with promising outcomes. Currently, antibodies thought to significantly reduce regulatory T lymphocyte function are being used in clinical trials for cancers where there is no established effective therapy, such as melanoma and prostate cancer. Ultimately, it is hoped that cancer patients will benefit significantly from the combined treatment of a cancer vaccine and agents that can safely reduce the suppressive arm of the immune response.

In summary, while using conventional chemotherapy against cancer may prove to extend the survival of patients with certain types of cancer (particularly testicular cancer), it has proven to be insufficient for most other types of cancer as well as severely reducing the quality of life of those treated with high doses. Cancer vaccines offer a viable alternative that can be used in combination with other treatments with the potential to systemically eradicate a patient’s cancer without causing detrimental side effects. A range of cancer vaccines is being clinically trialed for a range of cancers considered susceptible to immune attack with the ultimate hope of not only extending survival for the patient but providing a cure.

Sean M. Geary
Aliasher K. Salem
College of Pharmacy/University of Iowa

See Also: Anticancer Drugs; Cervical Cancer; Drugs; Hepatocellular (Liver) Cancer, Adult (Primary); HPV Vaccination; Melanoma; Prostate Cancer; Young Adult Cancer Prevention.

Further Readings

Vaginal Cancer

Vaginal cancer is a rare gynecological malignancy representing 5 to 8 percent of all gynecological neoplasms. It was identified in 1952 by Graham and Meigs, who reported three patients with carcinoma of the vagina, one invasive and two intraepithelial, 10, six, and seven years after total hysterectomy for carcinoma in situ of the cervix. Due to the rarity, there is minimal data in the literature concerning this cancer, particularly with regard to therapy.
Historically, vaginal cancer has been a disease of older women, with the peak occurring during the sixth and seventh decades. Less than 50 percent of patients are diagnosed below the age of 50 years, and less than 10 percent of these tumors occur in patients under 40 years of age.

The vagina is a fibromuscular canal composed of stratified squamous epithelium, smooth muscle, and connective tissue. The vagina extends from the cervix to the vulva. It is H-shaped in its central portion; the sidewalls are suspended by their attachment to connective tissue in which they receive their blood supply. Additionally, the vagina is attached laterally to the pelvic sidewalls by condensations of connective tissue and smooth muscle.

Physical examinations and diagnostic procedures are the most common ways to detect and diagnose vaginal cancer. However, screening programs have only recently become routine in most physical assessments. A diagnostic workup includes a complete history and a physical and pelvic examination. A pelvic examination continues to be the most important tool for evaluating and diagnosing the extent of vaginal cancer. This consists of examining the vagina, cervix, uterus, fallopian tubes, ovaries, and rectum.

A Pap smear is a procedure in which cells are removed from the surface of the cervix and examined under a microscope. In early squamous cell lesions, the diagnosis is suggested by an abnormal Pap smear. Furthermore, abnormal Pap smears often result when patients have had previous hysterectomy or HPV-related invasive cervical disease; however this is not true for cell adenocarcinomas, which often are characterized by submucosal growth. Diagnosis of vaginal cancer can be easily accomplished by biopsying the gross lesion. If no gross lesions are present, then the evaluation of the vaginal tube as vaginal intraepithelial neoplasias (VAINs) is appropriate. A colposcopy can also be utilized to detect the signs of vaginal cancer. It is important to note that vaginal cancer often does not cause early symptomatology. Symptoms of vaginal cancer include, and are not limited to, painless vaginal bleeding and discharge, tumors, urinary retention, pain, constipation, pain during sexual intercourse, lump in the vagina, blood in stool, tenesmus, hematuria, and frequency of urination.

Vaginal cancer is staged based on clinical criteria. Stage I is defined as tumor limited to vaginal mucosa. In Stage II vaginal cancer, the neoplasia involves the sub-vaginal tissue but has not extended to the pelvic wall. Stage III is defined as a tumor extended to the pelvic wall. Stage IV vaginal cancer is extremely rare; in Stage IV, a tumor extends beyond the true pelvis or involves the mucosa of the bladder or rectum. In Stage IV A, disease has spread to adjacent organs; in Stage IV B, disease has spread to distant organs.

Traditionally, the primary plan to treat vaginal cancer is radiation therapy. Radiation therapy uses radioactive substances to destroy cancer cells and shrink tumors. Radiation therapy can be used in combination with other treatments to stop the growth of cancer cells and relieve symptoms of advanced cancer. Nearly 30 to 35 percent of women diagnosed with stages III or IV vaginal cancer will require radiation therapy. Radiation therapy can be delivered externally, internally, and systemically. External radiation (e.g., IMRT, Tomotherapy) is directed onto the cancerous cells from a machine outside of the body. Internal radiation therapy is placed inside the body via a catheter or some form of carrier and is directed near the tumor or cancerous cells. Systemic radiation therapy is a substance that is administered orally or either injected which destroys cancer cells by traveling through the bloodstream to locate the cancerous cells. Depending on the targeted area that is being treated, radiation can bring a variety of side effects. Some of the most common side effects associated with radiation are fatigue, nausea, and skin changes.

In conjunction with radiation therapy, or as an alternative, chemotherapy is another treatment option to destroy cancerous cells. Chemotherapy is the use of anticancer drugs that inhibits the advancement of rapidly dividing cancer cells. Chemotherapy could be administered in several delivery methods: orally as pills or liquid, intravenously by infusion into the vein, topically as a cream, injection, or direct placement via a lumbar puncture or device placed under the scalp. The direction of a chemotherapy drug could be systematic, in which it travels through the bloodstream to target the cells throughout the body or directed to a specific region or area of the body. Although chemotherapy targets cancer cells, it can also damage healthy cells and cause side effects such as vomiting, hair loss, fatigue, and mouth sores.

In addition to radiation and chemotherapy, there are surgical treatment methods for women
diagnosed with vaginal cancer. Surgical therapy eliminates the lesion, prevents the formation of invasive cancer, and preserves the autonomy and function of the vaginal region. Surgical therapy is the ideal form of therapy for women who are in stage I or II of vaginal cancer. However, surgery for women with more advanced disease is most often used for women who have recurrent disease after radiation therapy.

Most recurrences occur in the first two years after treatment. Alternatively, no established anticancer drug has proven clinical benefit, although patients are often treated with regimens used to treat cervical cancer. Generally, the prognosis and treatment options depend on stage of cancer, size of tumor, grade of tumor cells, location of cancer in vagina, symptoms of diagnosis site, occurrence, and patient’s age and general health.

The survival outcome of vaginal cancer is related to the stage of the disease. The five-year relative survival rate is approximately 95 percent for stage 0, 75 percent for stage I, 60 percent for stage II, 35 percent for stage III, 20 percent for stage IV A, and 0 percent for stage IV B disease. The outcome of survival rate also varies among women of different race and ethnicities. In gynecological cancer, there are disparities among treatment and survival rates between African Americans and whites, in which mortality rates for African Americans are substantially higher than their white counterparts. Moreover, African American women with vaginal cancer are more likely to present at a younger age and a more advanced stage and are less likely to receive surgical treatment compared to white women.

Vaginal cancer is one of the rarest forms of cancer in women. There is no single leading cause of vaginal cancer, and it can affect women of all age ranges. Risk factors for vaginal cancer include five or more sexual partners, first intercourse before 17 years of age, smoking, low socioeconomic status, a history of genital warts, prior abnormal cytology, exposure to diethylstilbestrol, and prior hysterectomy. A combination of age, socioeconomic status, smoking, and sexual intercourse before the age of 17 years is a risk factor associated with vaginal cancer. It is important to note that vaginal cancer often does not cause early symptomatology.

Although there are several treatment methods that could either monitor or alleviate vagina cancer, a pelvic examination continues to be the most important tool for evaluating and diagnosing the extent of vaginal cancer in women.

Christopher L. Edwards  
Duke University Medical Center  
Courtney Ward  
Tiarra Green  
North Carolina Central University

See Also: Cervical Cancer; HPV Vaccination; Women’s Cancers.

Further Readings

Vanderbilt-Ingram Cancer Center

Vanderbilt-Ingram Cancer Center (VICC) is the only National Cancer Institute (NCI)–designated Comprehensive Cancer Center in the state of Tennessee that provides pediatric and adult cancer treatment and conducts clinical, translational, and basic cancer research. VICC is a member of the National Comprehensive Cancer Network and is a leader in treatment, diagnosis, and prevention of cancer.

The center’s approach is patient-centered, integrated, and personalized. Support, education,
outreach are also key components of VICC. From diagnosis through survivorship, VICC provides a wide variety of wellness programs. VICC ranks in the top 10 in the nation for cancer research grant support and is one of the 41 institutions nationwide to be designated a Comprehensive Cancer Center by the NCI. VICC is organized and led by a director, a deputy director, a team of center directors, and a chief executive officer. They are also guided by the Cancer Clinical Enterprise Committee who oversees decision-making and strategy for clinical operations, a volunteer community Board of Overseers, and an external scientific advisory board.

VICC has been a designated cancer center since 1995 and achieved the Comprehensive Cancer Center designation in 2001. To achieve this designation, VICC had to be among national leaders in outreach, education, prevention, treatment, and all types of cancer research. Strength, depth, innovation, and commitment must be demonstrated in basic laboratory research, translational research, clinical research, clinical trials, prevention research and programs, cancer information services, community outreach and education, and training for nurses, researchers, physicians, and other cancer professionals. NCI reevaluates Comprehensive Cancer Centers every three to five years to ensure that strict standards are being met, and VICC must report progress and activities annually. Recently, VICC was invited to join the National Comprehensive Cancer Network (NCCN), which consists of 25 of the world's leading cancer centers. VICC research programs focus on the discovery of new approaches for the prevention, diagnosis, and treatment of cancer.

VICC has been ranked the number one cancer center in Tennessee and 28th in the nation by U.S. News & World Report. There are over 300 researchers in seven research programs, a comprehensive team of more than 100 physicians, and six community locations in addition to the primary clinic (Henry Joyce Clinic) at the VICC. They are currently ranked seventh in competitively awarded NCI grant funding, which is in excess of $65 million. The total research funding exceeds $155 million from public and private sources. VICC has affiliate relationships with Williamson Medical Center, NorthCrest Medical Center, Baptist Memorial Health Care, and Maury Regional Medical Center. VICC serves more than 6,200 new cancer patients each year while providing for more than 151,000 outpatient visits annually. At any given time, VICC has more than 150 clinical trials in process.

The mission of VICC is to pioneer research, patient-centered care, education, evidence-based prevention, and community programs that alleviate suffering and cancer deaths. VICC's vision is to be the recognized leader both nationally and globally in the effort to treat and prevent cancers. Values include: service, compassion, collaboration, translation, discovery, and innovation. VICC describes its commitment to reducing suffering and cancer death by: pioneering research, team science, team approach, evidence-based prevention, education, community activities, and comprehensive services (physical, emotional, psychological, and practical) regardless of type of cancer, where patients receive their care, or age at diagnosis.

VICC, with the support of NCI and the American Cancer Society, provides pilot funding for research by Vanderbilt faculty. Funds are primarily for collaborative projects with emphasis on innovative basic science and translational research, established faculty, or new faculty. Pilot projects in breast cancer, gastrointestinal cancer, and lung cancer are supported as well. Philanthropic support is provided by the Ayers Institute (early detection and prevention), Robert J. Kleberg, Jr. and Helen C. Kleberg Foundation (genetics), A.B. Hancock Jr. Memorial Laboratory for Cancer Research (early diagnosis and drug development), and Frances Williams Preston Laboratories (gene discovery, basic and translational research in breast, prostate, and lung cancer).

The VICC sponsors seminar programs, lectures, and mini symposia every year. Additionally, the Orrin Ingram Distinguished Lectureship series is offered annually and features four to five investigators who present discoveries that have been key to major advances in prevention, diagnosis, and treatment of cancers, and contribute to understanding tumors. The VICC also has an annual retreat that includes all of the laboratories, students, postdocs, fellows, and principal investigators for a poster session, shared resource displays, and mini symposium.

VICC advocates and provides an interdisciplinary team approach, as cancer is a collection of many types and subtypes of disease each with unique challenges. As appropriate, treatment teams include: surgeons, oncologists, hematologists, radiation oncologists, pathologists, nurses, psychologists, social workers, and other specialists.
are multiple team-specific groups that focus on: breast cancer, colon cancer, lung cancer, head and neck cancers, leukemias and lymphomas, bone and tissue cancers, gynecologic cancers, prostate and genitourinary cancers (bladder, kidney, etc.), brain and other neurologic cancers, melanoma, bone and tissue cancers, and childhood cancers.

VICC is involved in community outreach in a variety of ways. The Office of Patient and Community Education (OPACE) plans, implements, and evaluates community education programs every year to share expertise and offer resources. Programs are planned with national, state, and community organizations concerned with cancer. Priorities of OPACE include: prevention, early detection, and risk reduction that focus on high-risk populations and areas with the highest cancer and mortality rates in Tennessee. Some of the OPACE programs include: survivorship programs, health fairs, education/awareness, and screenings. The REACH for Survivorship program is the first dedicated survivor clinic in middle Tennessee. The program provides services to all survivors regardless of age, type of cancer, or treatment location for both pediatric and adult cancer populations. The Hope Connection brings together patients, families, and trained volunteers (who have personally experienced the challenges and issues of cancer) to offer support at any time, before, during, and after treatment.

Jessica Anne Hammer
Independent Scholar

See Also: University of Chicago Medicine Comprehensive Cancer Center; University of Hawaii Cancer Center; University of Minnesota Masonic Cancer Center; University of Pittsburgh Cancer Institute; University of Virginia Cancer Center.

Further Readings

Venezuela

Venezuela is the richest country of Latin America, with the world’s largest petroleum reserves. As a founding member of OPEC, its exports consist almost entirely from its oil production, while its imports are finished products. Due to economic instability under its current government, it has also turned to importing basic necessities and food. Prior to the development of its petroleum, it was self-sufficient in agriculture, and its exports were agricultural products. The development of Venezuela’s petroleum production was originally done under the influence of the United States, specifically the Rockefeller family. Eventually, this national resource was taxed, then nationalized in 1976 with the objective of subsidizing economic and social development. The substantial oil income has subsidized the nation’s development for decades in what President Romulo Betancourt called “siembra del petróleo” [planting petroleum]. Unanticipated consequences of this extractive economy have impacted all sectors of society, including the public health system. Over many decades, the proportion of Venezuelans living in poverty has steadily declined, but only by small increments until recently.

Under populist president Hugo Chávez, the income from oil exports reached levels much higher than under previous presidents, due to the high price levels sustained over this period. The Chávez administration devoted much of the export income toward projects and subsidies for Venezuela’s poor during his years in office, 1999 to 2013. The result has been a decrease of the proportion of the population living in poverty from 50 percent to 27 percent, but at the social cost of as many as 1 million middle class Venezuelans leaving the country due to opposition to the methods of the Chávez government. At this writing, the government has continued the Chávez approach under the administration of his successor, Nicolás Maduro. A byproduct of this social and economic path has been the acceptance of a Cuban model of public health along with friction with the United States over domestic human rights issues and foreign policy, while dependence on oil exports to the United States continues.

Venezuela’s cancer morbidity and mortality are directly related to its demographic profile and to the country’s level of social and economic development. A young population will be relatively cancer
free, while an aging population will have cancer as one of the most frequent causes of mortality. As the population of Venezuela ages, it will be joining the more-developed countries with an increasing concern about cancer diagnosis and treatment. The nation has a youthful population with the median age of 27 years, so the main public health concerns are with cancer prevention.

Historically, cancer has been considered to be a product of Western, industrialized countries and their rich diet, sedentary lifestyle, and other unhealthy practices. This orientation has been strengthened by the anti-American stance of the Venezuelan ruling party. When President Chávez was stricken with cancer, he traveled to Cuba for treatment there. He was not cured, and he died in office in 2013, shortly after having been reelected to the presidency. The assertions of his successor, Maduro, that Chávez was “infected” with cancer by agents of the U.S. government have furthered the impression among his followers that cancer is a product of Western society and can be transmitted from elsewhere.

While many social critics focus on the negative side of industrialization, the rise in cancer around the world is also coming to be recognized as a product of longer life spans in all countries, and it increases with educational level, income, and life expectancy. More recently, cancer has become understood as a worldwide cause of death, and it can be expected to increase as a byproduct of a nation’s social and economic development. Cancer now is seen as a rapidly growing threat to the world’s less wealthy countries undergoing development, although this forecast has been resisted for social and political reasons. The fact remains that developing countries are not well prepared for higher rates of cancer.

The World Health Organization forecasts cancer increasing considerably in Venezuela. This has been supported in Venezuela by such trends as urbanization. Venezuela has an urbanization rate of 93 percent, one of the highest in Latin America. Venezuelans are also protected by their proximity to health facilities, access to potable water and sanitation, and high levels of education. Rates of cancer in Venezuela have begun to follow the morbidity patterns of the United States and Europe. There is pressure to adapt the national health services to respond to this forecast increased risk of cancer, especially since about one-third of cancers
are preventable and others can be treated successfully if diagnosed early.

According to the Pan American Health Organization, Venezuela’s demographic profile is an aging population of 29,436,900 people, an average life expectancy of 75 years, with a youthful median age of 27 years. The leading causes of male cancer mortality are prostate, lung, and stomach cancers. For females, the leading cancers are breast, cervix, and lung. Cancer screening services, treatment facilities, and palliative care are generally available in Venezuela, but they are in transition under Cuban influence.

The rejection of Western medicine by the Chávez government led to exchanges with Cuba of Venezuelan oil for Cuban personnel, particularly in the fields of the military, education, and health. In this “oil for doctors” program, 31,000 Cuban doctors and dentists work in Venezuela in exchange for 100,000 barrels of oil supplied daily to Cuba. Prior to the current Chávez-style government, Venezuelan medical practice was most strongly influenced by the United States, with many medical doctors trained there.

The current situation has resulted in controversy among Venezuelan professionals, while Cuban medical practice has come to have a strong influence on the treatment of cancer in Venezuela. Nonetheless, as in Cuba itself, cancer treatment is the weakest part of Cuban medical practice, which is more successful at preventive care, public health measures, and, eventually, palliative care. There is a movement in Cuba toward more standard cancer treatments, alongside experimental cancer vaccines and homeopathic treatments. Given the uncertain political situation in Venezuela and its resolution for the future, it is difficult to forecast cancer treatment and mortality in coming decades.

Keith R. Johnson
Oakton Community College

See Also: Cuba; Developing Countries; Pollution, Air.

Further Readings

International Agency for Research on Cancer.

The Vermont Cancer Center (VCC) is a nonprofit clinical research and care center located in Burlington, Vermont. The VCC is operated by the University of Vermont (UVM) College of Medicine in partnership with Fletcher Allen Health Care. Founded in 1974, the VCC is the largest center of its kind in the state of Vermont. The VCC operates four multidisciplinary clinics (MDCs), including the Breast Care Center, Upper Gastrointestinal MDC, Lung MDC, and Melanoma MDC. Over 120 scientists and physicians make up the VCC’s constituency.

Members
VCC members must be full-time faculty at the University of Vermont and have served as principal investigators or co-principal investigators on a peer-reviewed cancer-relevant research grant or clinical trial. The VCC’s student members are comprised of current graduate students concentrating on cancer research as well as postdoctoral fellows.

The mission of the VCC is divided into three main programs: Mechanisms of Malignancy, Host Factors and Tumor Progression, and Cancer Control and Population Health Sciences. Each of the center’s three major programs fosters a transdisciplinary and collaborative approach to promoting discovery and advancing standards of care.

Facilities
Since July 2001, each of the VCC’s core laboratories has been centrally located at the Health Science Research Facility on the campus of the University of Vermont College of Medicine in Burlington. The center headquarters also includes an Ambulatory Care Center, Education and Conference Center, and the VCC’s clinical facility.

The VCC Core Facilities place an emphasis on delivering cancer screening and treatment to the state’s rural population as well as understanding the
impact of social and physical environments on the disease. The VCC’s major facilities and clinical center are comprised of four major facets, each of which works in concert by sharing research findings and patient assessments. The VCC’s Advanced Genome Technologies Core encompasses the facility’s DNA Analysis center and the Vermont Genetic Network Microarray group, each of which concentrates on research based on the genetic causes of the disease. The center’s Biostatistics facility is comprised of a program of research evaluating biostatistical trends in patient data and epidemiology. Researchers and students working in the VCC’s Flow Cytometry unit utilize advanced technologies for intercellular analysis. The VCC’s fourth core facility, the Microscopy Imaging core, consists of 10 microscopy-based imaging systems and an electron microscope for use in a myriad of research applications.

**Research Funding and Awards**

Each year, the VCC awards funding to members and UVM faculty for postdoctoral research related to the disease as well as other cancer-related research. The awards, determined by peer review, include the J. Walter Juckett Scholar Award, the Collaborative Cancer Translational Grant Program, and the VCC Program Grant Award. The J. Walter Juckett Scholar Award is given annually by the VCC in conjunction with the Lake Champlain Cancer Research Organization (LCCRO) and the National Institutes of Health. The grant has previously gone to extensive research trials in ovarian, lung, and breast cancers. The VCC’s biannually awarded Collaborative Cancer Transitional Grant was founded to promote and develop partnerships between cancer scientists and physician investigators in an effort to form multidiscipline research programs dedicated to prevention and early detection. The VCC Program Grant Award is a funds-matching program that also aims to foster collaborative, translational investigations throughout both the UVM College of Medicine and Fletcher Allen Health Care. Recent awards have helped fund work concentrating on the effects of genetic proteins in predicting breast cancer and the effects of chromosomal disorganization in the spread of cancer.

**Outreach Programs**

In addition to the VCC’s vast array of clinical and research efforts, the center also partners with Fletcher Allen Health Care to offer a comprehensive patient care and support network to patients in Vermont and northern New York. The VCC operates an ongoing affiliation with the UVM College of Medicine’s Program in Integrative Health, which was founded to examine and address the mind–body connection and spiritual health dimensions of the hospital’s patients.

The VCC also operates a variety of patient-oriented support groups to help patients and their family members endure their experience with cancer. Groups include the Children’s Support Group, Young Survivors Support Group, Patient Health Arts and Writing Group as the Rutland, Vermont-based Women-to-Women cancer support group. Other support groups provide help to specific groups of cancer sufferers, including those with pancreatic cancer, post thrombosis syndrome, and colorectal cancer.

The VCC is also a key partner in the annual Lake Champlain Dragon Boat Festival, the proceeds of which go to benefit a myriad of Vermont-based cancer charities. The event is comprised of time trials and head-to-head racing of large paddleboats on the Burlington, Vermont, waterfront. Over 1,600 participants take part in the festival each year across over 60 boating teams comprised of cancer survivors, local Vermont businesses, and Vermont-based non-profit groups.

**Accreditation and Future Development**

In February 2013, the VCC was awarded a three-year accreditation with commendation from the American College of Surgeons Commission on Cancer. The recognition lauded the VCC’s evaluations in quality and comprehensiveness of care, equipment, patient-treatment coordination, patient follow-up, and ongoing improvements to its facility.

Also in 2013, the University of Vermont College of Medicine and Fletcher Allen Health Care announced a $20 million dollar investment in the VCC’s basic science, clinical, and transitional research programs.

In July 2014, the VCC, in conjunction with the UVM College of Medicine and Fletcher Allen, joined the network of nationwide partners utilizing the PierianDx Network. The end-to-end informatics program offers rapid diagnosis and individualized treatment options for patients derived from its vast database of clinical interpretations of cancer cases throughout the United States. The system allows each hospital to share clinical interpretations and derives insights
into treatments, marking a next-generation approach to combatting cancer in its numerous forms. As of 2014, the VCC is helmed by co-directors Dr. Claire Verschraegen and Dr. Gary Stein.

John Pritchard III
Independent Scholar

See Also: Education; Psychosocial Care/Support; Screening, Access to.

Further Readings

Vietnam

Public health has become an issue of increasing concern to governments worldwide, particularly in Asia, the largest and most populous continent in the world. As in other countries around the world, however, Vietnam faces challenges from aging populations and health crises caused by noncommunicable diseases, such as cardiovascular disease, cancer, and others. There are many causes for these, such as environmental degradation, pollution, and lifestyle habits, among others. In the case of Vietnam, experts claim that health outcomes of years of warfare exposure to herbicide chemicals, such as Agent Orange during the Vietnam War, must be researched in more depth, particularly as pertains to cancer. Vietnamese doctors and scientists working to cure cancer face great resource and logistical roadblocks. Today, they work to forge local and international partnerships that will help bring modern protocols, technology, and knowledge to Vietnam in order to improve cancer treatment in the nation.

Background
Although previously one of the poorest nations, today Vietnam is categorized among the six favored emerging-market nations of the world. Statistics from the International Agency of Cancer Research (2012) show that out of Vietnam’s population of 89.7 million people, 125,000 are newly diagnosed with cancer each year. The risk of Vietnamese citizens developing cancer before age 75 is 14.5 percent. Approximately 94,700 Vietnamese die from cancer each year. A 1990 study estimated that the cancer incidence in Vietnam was about 133 per 100,000 in males and 91.7 per 100,000 in females, standardized to the world’s population.

Malnutrition and infectious diseases remain the top health problems. In comparison to these, cancer ranks relatively low in importance. The reason for this is in part due to scant reliable health statistics. The most prevalent types of cancer in the country are lung, liver, stomach, colorectal, and nasopharynx cancers in males. Among females, the leading cancers are breast, cervical, stomach, liver, colorectal, and lung. Compared with international data, statistics for Vietnam show a relatively high rate of nasopharynx, liver, and stomach cancer, and a low rate of breast and prostate cancer. There is a much higher rate of cervical and uterine cancers in south Vietnam than in the north. Liver cancer also shows a much higher incidence in the south.

Forms of cancer more prevalent in the north, although at less significant rates, are lung, stomach,
breast, and nasopharynx. Research has shown that cancer of the genital organs used to be frequent throughout the country as well, although scientists discovered important differences between the north and south. Cancer of the cervix showed higher incidence in the south, whereas cancer of the penis was more prevalent in the north. Nevertheless, the rates of genital tract cancer for both sexes have decreased notably, according to statistics gleaned from hospital records during the last two decades. Some experts ascribe the improvement to better health and hygiene conditions among the population, among other factors.

One of the most sensitive areas pertaining to cancer in Vietnam relates to children’s cancer. While the global average five-year survival rate for childhood cancer is 85 percent, Vietnamese children have a five-year survival rate of barely 10 percent.

Policy Making
The National Cancer Control Program in Vietnam has engaged in proactive government efforts in the areas of tobacco control, mass media education of the public, and improving cancer treatment. The latter includes the production of vaccine against the hepatitis B virus (HBV). Cancer control is still difficult to implement and assess because of scant data on cancer incidence, morbidity, and death rates. Vietnam also suffers from a dearth of resources for comprehensive cancer control and treatment, especially in peripheral areas. Despite its population density and relative poverty, however, Vietnam consistently achieves high scores in life expectancy, schooling level, and infant mortality rates, in comparison with other nations worldwide in the same stage of development.

Policies have also encouraged the development of registries. By 1990, cancer registries were introduced in Ho Chi Minh City and Hanoi. The reliable maintenance of these registries still faces serious challenges, due to shortages in resources, financial support, and general lack of quality in data and systems. By 1990, the country had opened two cancer centers, in Ho Chi Minh City and Hanoi. Since then, these cancer institutions have improved and expanded, but they remain inadequate to serve the health needs of the sizeable population of Vietnam.

One of the main problems, as related to the incidence of cancer, is the extremely elevated level of tobacco use. Vietnam produces large amounts of tobacco products. In the mid-1990s, the yearly consumption was approximately 600 cigarettes per capita. The tobacco industry plays a very important role in creating employment in both urban and rural areas. Education programs by way of mass media dissemination have been implemented in order to counteract the massive level of tobacco consumption. Another step forward occurred in the mid-1990s, when Vietnam began producing the vaccine against the Hepatitis B virus; liver cancer is one of the leading cancers in the nation. The primary goal of vaccination is the prevention of the disease.

Despite many challenges, efforts have been made to establish oncology training and research centers, as well as developing collaborative research agreements with institutions in other countries. Workshops and cancer control systems have been organized and implemented with the sponsorship of the World Health Organization, for example, and partnerships have been formed with research institutions and universities around the world.

Trudy Mercadal
Florida Atlantic University

See Also: Childhood Cancers; Environmental Tobacco Smoke; Global Health Issues and Cancer; Hepatitis B; Herbicide; War Gases and Chemicals.

Further Readings
Vinyl

Vinyl, the common name for polyvinyl chloride (PVC), is one of the most widespread polymer produced worldwide, next to polyethylene and polypropylene. Production of PVC involves the use of harsh toxic chemicals. The polymer is comprised of two monomers, ethylene and chlorine. When combined these two monomers combine they produce ethylene dichloride, which is then further processed into vinyl chloride, or PVC. There are two forms of PVC, rigid (RPVC) and flexible. More than half of the world’s production is in making plastics because it is relatively inexpensive to manufacture and can be used in rigid or flexible products. More than 30 billion pounds of PVC is produced every year by the vinyl industry. There is not an aspect of civilization that is exempt from the impact of PVC.

Both RPVC and flexible PVC are readily found in clothing, automotive, construction, household and kitchen items, medical and office supplies, garden furniture and other outdoor items, personal care, baby and children’s products, and much more. RPVC is used in piping, doors, windows, bottles, non-food packaging, luggage, car dashboards, strollers, and bank and membership cards. When organotins are added to RPVC products, wallpaper and flooring are produced.

Phthalates a type of plasticizer is added to the PVC polymer to make it flexible. Flexible PVC is as ubiquitous as RPVC and is found in shower curtains, plastic wrap, food containers, drinking straws, tablecloths, plumbing, electrical cables, imitation leather, inflatable products, baby teething rings, and products replacing rubber. The rubber replacing products have become common in medicine, due to the rise of allergies to Latex rubber. Some examples of PVC in medicine are blood bags, catheters, colostomy bags, tubing, draw sheets, gloves, shoe covers, and mattress covers. Diethyl hexyl phthalate (DEHP) can be found in PVC at a rate of up to 50 percent by weight.

Other additives are inserted to change the chemical structure of the polymer. Lead, mercury, and other heavy metals are added in some PVC products, such as in wire insulation. Adding the heavy metals are stabilizers or change agents giving other properties to the plastic, broadening its usage. The chemicals found in flexible PVC leach when coming in contact with moisture, such as the mucous membranes, contact with food, or in medical equipment. These chemicals have been linked to cancer formation.

PVCs emit toxins into the environment from production, through use, and when sitting in the landfill. Throughout the entire process it leaches pollutants. PVC products, for the most part, are not recyclable because of the additives and in fact, interfere with the recycling of other plastics. That “new car” smell is the off-gassing of the plastics found in car parts made from PVC.

Flexible PVC plasticizers are notorious for leaching chemicals with use. Not widely recycled, flexible PVC when burned releases hydrogen chloride gas and dioxin, one of the most toxic chemicals in modern world.

Health Effects
Learning disabilities are up 191 percent from 1977 to 1994. One in 100 American children have an autistic spectrum disorder. Eight thousand American children are diagnosed with cancer each year. Testicular cancer in young men is increased by 60 percent. Hypospadias doubled from 1968 to 1993. Breast cancer, childhood obesity, childhood asthma, autism, and attention deficit hyperactivity disorder in some studies have found links to exposure to vinyl and its components. People across the age continuum with PVC in the flooring have a much higher incidence of asthma and are twice as likely to have autism. High levels of phthalates are found in indoor dust and air, in human urine, breast milk, and blood. Organotins and phthalates are oestrogenic, or hormone mimickers, that disrupt the endocrine system leading to hormone dysregulation and obesity, and premature puberty. Premature breast development is linked to breast cancer. Reproductive issues are rising with each year: fertility treatments,
endometriosis, miscarriages, and premature births rates are up in women from 25 to 34 years of age. Sperm counts are decreasing and defect sperm rates are rising. Testosterone levels are decreasing, testes are smaller, and more undescended testes are noted.

Dioxins, 31 different chlorinated organic chemicals, are made during the production of PVC, such as when chlorine is made from salt and when plastic is made, and then during the incineration of wastes in the landfill. Because PVC is found throughout the environment, anything that contains PVC and will burn, releases dioxins into the atmosphere. Dioxins are a health threat, a known carcinogen since 1997, and classified as such in January 2001. Dioxins are also linked to diabetes.

Vinyl chloride is absorbed at a rate of 40 to 95 percent, depending on the route of exposure. Though the body excretes most of the substance within 24 hours, some of the other byproducts, such as dioxin, take much longer. Dioxins have a half-life, the rate it takes for half the original level to be decreased by half, of seven to 11 years. In addition to causing cancer, they are directly linked to reproductive, endocrine, and immune system conditions.

The Environmental Protection Agency (EPA) reports that most Americans have dioxin exposure more than 200 times above the known safe level.

Most vinyl chloride exposure occurs via the inhalation of contaminated air during production. The pollutant is expected to vaporize within hours of release, but since it does not bind to soil or biodegrade with the microorganisms found in the soil, the toxin ends up in the air and in the groundwater. Once in the groundwater it can remain a pollutant for years. Most groundwater contamination occurs through the solvents such as trichloroethene, tetrachloroethene, and 1, 1, 1-trichloroethane.

During manufacturing when workers are exposed to high levels, central nervous system depression occurs producing symptoms such as headaches, drowsiness, changes in vision and hearing, disorientation, euphoria, and dizziness.

Children appear to have more exposure than adults to the chemicals found in PVC. Young children put objects in their mouth. They spend more time on the floor or near the ground, breathing the off-gassing chemicals and ingesting the contaminated dust. People exposed to PVC dust have a 20 percent increase in lung cancer for each year...
of exposure. Phthalates levels are highest in children aged 6 to 11 and in women. One study found 100 percent of the girls aged 6 to 9 tested had toxic levels of phthalates. The plastics industry’s public relations data-sheets relate that humans are not exposed to toxic levels of chemicals in the making or disposal of PVC. The industry does agree that vinyl chloride is a carcinogen and causes liver cancer. They relate that mercury exposure, while having adverse effects of human health, is not readily used in the manufacturing of PVC, thus the levels persons are exposed to are low. The industry, though admitting dioxins are toxic to humans at low levels, claims to use less than 30 grams per year. All of the research provided to substantiate their claims is from the late 1980s to early 1990s.

Justina Higgins
Independent Scholar

See Also: Breast Cancer; Chemical Industry; Obesity.

Further Readings

Visual Pathway and Hypothalamic Glioma, Childhood

Childhood visual pathway glioma is a brain tumor originating from cells in the brain called astrocytes, which are the star-shaped cells that provide biochemical support to the cells of the blood–brain barrier and assist in the maintenance and support of the neurons. Astrocytes have an important role in the scarring process of the brain and spinal cord after traumatic brain injuries.

Generally, visual pathway glioma is classified as World Health Organization (WHO) grade I pilocytic astrocytoma, but in some younger patients it may show an aggressive clinical course and spread through the cerebrospinal fluid pathway. A visual pathway glioma occurs along the optic nerve, which carries messages from the eye to the brain. In some cases, the tumor may progress and invade neighboring structures, resulting in visual impairment or complete loss of vision; in other cases, the tumor may remain stable for several years, accompanied by a spontaneous improvement of associated symptoms. The prognosis for patients with optic nerve tumors is generally better than the prognosis for glioma of the chiasma and hypothalamus. Visual pathway gliomas account for approximately 5 percent of all brain tumors in children.

Cellular Classification
Childhood visual pathway and hypothalamic gliomas are usually low-grade (grades 1 and 2) astrocytomas,
according to the WHO classification system. The astrocytic tumors of the optic nerve, optic chiasm, and optic tract are all classified as visual pathway gliomas.

Malignant gliomas of the visual pathway are rare, and higher incidences of visual pathway gliomas have been reported in patients with neurofibromatosis type 1 (NF-1). NF-1 is a relatively common genetic condition with an incidence of 1 in every 3,000 births. Patients with a history of NF-1 have an increased risk of visual pathway glioma. The NF1 gene product neurofibromin acts as a tumor suppressor, and a lack of normal neurofibromin in NF-1 patients results in increased cell proliferation and the formation of gliomas.

NF-1 is also responsible for the development of brown spots, freckles, and tumors on the skin and nerves, accompanied by developmental changes in the nervous system, muscles, bone, and skin. Approximately 20 to 30 percent of all patients with NF-1 are at risk of developing a visual pathway glioma. Association with NF-1 is present in 50 to 70 percent of patients with isolated optical nerve tumors, while the association is present in 16 to 20 percent of patients with chiasmal or deeper optical tract tumors. Most children diagnosed with visual pathway glioma have NF-1, while the remaining cases are sporadic. In general, the tumors are observed to grow at a slower pace in patients with NF-1, and the presence of NF-1 has a positive effect on the prognosis.

The tumors may also arise in the hypothalamus in large infiltrating lesions, and the distinction between optic and hypothalamic tumors has little clinical significance. Infants and young children with visual pathway and hypothalamic glioma may exhibit the diencephalic syndrome characterized by macrocephaly, intermittent lethargy, and visual impairment, or may remain asymptomatic. Double vision is also a common associated symptom. Neurological signs and symptoms may also result from involvement of the hypothalamus with signs of precocious puberty and accelerated linear growth, as well as other symptoms associated with imbalance of the endocrine system.

Visual pathway and hypothalamic gliomas do not have a universally accepted classification system. They are generally classified as low-grade astrocytomas, characterized by slow growth, and may occur anywhere along the optic tract.

### Treatment Options

In the event of a complete loss of vision and considerable bulging of the eye, surgery is performed to remove the tumor while sparing the globe of the eye.

Radiation therapy has been shown to control gliomas in the long term for most children with chiasmatic and posterior pathway chiasmatic gliomas. However, radiation therapy may result in substantially compromised intellectual and endocrinologic functions in children, as well as damage to the cerebrovascular system in the form of Moyamoya disease symptoms. Radiation therapy also increases the risk of secondary tumor development.

Chemotherapy has been shown to result in tumor shrinkage and to delay the requirement for radiation therapy. In cases where vision is retained but the tumor has progressed, chemotherapy has been shown to be extremely effective, especially with the combination of carboplatin and vincristine (chemotherapy drugs) in cases with NF-1, and therefore it is the most widely used chemotherapy regimen in pediatric visual pathway gliomas. Other chemotherapy approaches based on multiagent platinum-based regimens have also been used to treat children with progressive optic pathway gliomas.

Radiotherapy is generally not recommended for children because of its long-term effects on their health and growth, including the development of secondary tumors and severe effects associated with cognitive function. However, radiation therapy may be recommended depending on the case and the type of glioma.

Poonam Balani
Independent Scholar

See Also: Brain Stem Glioma, Childhood; Visual Pathway and Hypothalamic Glioma, Childhood.

Further Readings
Vitamins

Vitamins are organic compounds that are essential to biological function. They are either not produced by the organism or only produced in limited quantities and thus must be obtained from the diet to sustain life. Vitamins are identified by a letter from A to K, but they also have a chemical structure name. The essential vitamins for humans are A, B, C, D, E, and K. While there is research available on the role of vitamins in the prevention and treatment of cancer, vitamin supplementation is not considered critical to either treatment or prevention by the American Cancer Society. Below is a review of each vitamin, its role in human physiology, and a summary of the cancer research from both supplementation and dietary sources. Often, studies use epidemiological data to show relationships. However, these relationships do not always match the findings of clinical trials.

Vitamin A is a fat-soluble vitamin found in meat products as well as in fruits and vegetables; it is also available as a dietary supplement. Carotenoids, compounds that give red, yellow, and orange coloration to many fruits and vegetables, can turn into a form of vitamin A. Vitamin A is important for growth and development, for immunity, and for good vision.

Some research has shown that vitamin A has been associated with a reduced risk of lung cancer. Supplementation with vitamin A has had little positive effect on reducing the risk of lung cancer. Humans can convert beta-carotene in food into vitamin A if a food source of fat or oil is present in the same meal. Conversion efficiency and absorption will depend on whether the food source is raw or cooked, the presence of fats and oils at the same time, current stores of both vitamin A and beta-carotene, and other factors such as the species of carotene, patient nutrient status, patient genetics and host specificity, and interactions with other dietary factors. In general, humans are not efficient converters of beta-carotene into vitamin A and only absorb 9 to 22 percent. Smokers should not consume vitamin A or beta-carotene supplements either on a regular basis or while undergoing chemotherapy and radiation therapy; consumption of vitamin A or beta-carotene supplements may actually increase tumor growth and lead to a poorer prognosis. Consuming food sources of beta-carotene and vitamin A is not contraindicated in smokers and may actually be beneficial. This apparent opposite effect may be due to the differences between natural and synthetic forms of these compounds. Cervical dysplasia is a pre-cancerous condition of the female cervix associated with several species of human papilloma virus. Consuming beta-carotene supplements and beta-carotene foods can reduce cervical dysplasia and may help with shedding of the virus.

Bladder cancer, for which smoking is the leading risk factor, has been studied with respect to vitamin A intake in diet and supplements. A recent meta-analysis of over 20 trials examined only studies that controlled for the effect of smoking as a possible causation of bladder cancer. They concluded that intake of dietary carotenoids with the potential to form vitamin A significantly reduced the risk of bladder cancer. Measurement of vitamin A in blood of the study subjects found an inverse relationship between the serum levels of vitamins A and the risk of bladder cancer.

Lycopene is a carotenoid without pro-vitamin A activity; it does not become vitamin A. While present in many fruits and vegetables, it is highest in tomatoes. Lycopenes are most absorbable when the tomato has been cooked and a fat is present in the same meal. Canned tomatoes, tomato paste, commercial tomato juice, and ketchup are common examples of cooked tomatoes. Epidemiological studies have found a lower risk of stomach, colon, rectal, and prostate cancers when the dietary daily intake of lycopenes exceeds 35 mg per day.

B vitamins are water-soluble and have an important role in cell metabolism, including a positive effect on metabolic rate, preservation of...
Vitamins

1291

muscle tone and skin quality, improvement of nervous and immune system function, and promotion of growth and cell division. By number and name they are B1 (thiamine), B2 (riboflavin), B3 (niacin or niacinamide), B5 (pantothenic acid), B6 (pyridoxine, pyridoxal, and pyridoxal-5-phosphate), B7 (biotin), B9 (folate), and B12 (cyanocobalamin, hydroxocobalamin, and methylcobalamin). All B vitamins, except B12, are available from plant sources. B12 is present in some bacteria and some nutritional yeasts, but it is most easily absorbed from red meat. Smaller amounts of B12 may be absorbed by consuming fish, eggs and dairy. A small amount of B12 is added to vegetarian foods such as tofu and tempeh since strict vegetarians do not consume foods containing B12. The remaining B vitamins are found in dark leafy greens, whole grains, legumes, and potatoes.

Epidemiological studies suggest that adequate folate, B6, and B12 can reduce the risk of developing breast cancer, especially in women with higher alcohol consumption. Alcohol consumption increases the need for B vitamins to metabolize ethanol and leads to the subsequent excretion of B1, B2, B3, biotin, and folic acid.

Recent studies of children with newly diagnosed leukemia found low plasma levels of pyridoxal-5-phosphate. Low levels of B12 have been found in rectal cancer and laryngeal cancer. Folate intake appears protective for colon cancer. However, taking supplemental folate once a tumor has been diagnosed may increase tumorgenesis, suggesting a dual-modulatory effect or a difference between food and synthetic sources of folic acid. Methylation influences gene expression, and folate is involved in the generation of methyl groups. Hypomethylation has been observed genetically in humans who have a deficiency of methylenetetrahydrofolate reductase and in humans who consume a low folate diet. About 10 percent of Asians and Caucasians have 70 percent less activity of this enzyme, and another 40 percent can only convert a limited amount of folic acid. The ingestion of methyltetrahydrofolate may assist those with this deficiency.

Riboflavin deficiency can disrupt the integrity of the esophagus epithelium. The best food sources of riboflavin are spinach, tempeh, yogurt, mushrooms, and eggs. Some studies show a relationship between diets low in riboflavin and esophageal cancer. Riboflavin deficiency has also been identified as a risk factor for cervical dysplasia, the precursor to cervical cancer. Low B2 and B6 levels have been found in patients with non–small cell lung cancer. B2 seems to have an important role in breast cancer. Niacin has moderate scavenging effects on invasive liver cancer in rats. A similar mechanism has been suggested for humans.

Inositol is a member of the B vitamin complex and can be produced from glucose. It is involved in biological processes such as insulin signal transduction, cell membrane maintenance, breakdown of fats, and gene expression. Inositol is found in fruit, legumes, grains, and nuts. Inositol hexaphosphate (IP6) helps the body in the use and metabolism of calcium and other minerals. Animal research has shown that it can prevent tumors from forming and slow the growth of existing tumors. Human trials using very large doses have shown that it can reduce the side effects of chemotherapy, improve quality of life, and increase survival time in breast and lung cancer patients.

B10, or para-aminobenzoic acid (PABA), is found in liver, brewer’s yeast, kidney, molasses, and whole grains. Because humans can metabolize it, it is not considered an essential vitamin. Humans cannot
metabolize it into folate, although some bacteria such as *E. coli* can. PABA can prevent ultraviolet-B damage to the skin, but taken internally it may increase the risk of ultraviolet damage and cause an allergic reaction. Its popularity as a topical and oral sunscreen to prevent skin cancers fell, but now a water-insoluble PABA derivative, padimate O, is used in some products.

B17, or amygdalin, is a glycoside isolated from the seeds of bitter almonds. When properly metabolized, one gram of amygdalin may yield 68 mg of hydrogen cyanide. Amygdalin has been confused with laevomandelonitrile, or laetrile for short. Laetrile is a semi-synthetic molecule sharing a portion of the amygdalin structure. It was popularized in the 1960s and 1970s as a cancer treatment, but it was derived from apricot pits or neo-amygdalin. Human trials have not shown laetrile to decrease tumor size or enhance survival.

Vitamin C is water-soluble, and humans, unlike most mammals, cannot synthesize it. Vitamin C is available as the reduced ascorbic acid and the oxidized dehydroascorbic acid. The latter is the most common form in the human body, but the former is the best method of ingesting it orally. Vitamin C is highest in cantaloupe, citrus fruits, kiwi, and vegetables such as broccoli, peppers, and spinach. Cooking and storage reduces the amount of vitamin C present, so these foods are best ingested fresh.

Vitamin C is important for the growth and repair of body tissue. It helps form collagen to make skin, tendons, ligaments, and blood vessels. It aids in the healing of cuts and surgical incisions and repairs and maintains bones, cartilage, and teeth. Deficiency of vitamin C is associated with anemia, bleeding gums, decreased wound healing, and ability to fight infections, nosebleeds, dry scaly skin, and swollen, painful joints. This medical condition is known as scurvy.

Vitamin C has two important and opposite roles in the human body. Ascorbic acid is a potent antioxidant that quenches free radicals produced from extracellular and intracellular processes. Free radicals protect people from smoke, radiation, and pollution, and they increase with the aging process. As a pro-oxidant, ascorbic acid promotes the formation of reactive oxygen species such as hydrogen peroxide in the presence of pro-oxidant vitamin C. In the presence of high concentration of ascorbic acid in the extracellular fluid, the absence of tumor cell catalase, and the presence of iron and/or copper, vitamin C can have a cytotoxic effect on tumor cells.

In the 1970s, Ewan Cameron, Linus Pauling, and Allan Campbell gave cancer patients high doses of intravenous vitamin C. They found longer survival times in the intravenous patients compared to controls and patients given oral vitamin C. Research that followed demonstrated that in plasma, intravenous vitamin C could exceed the concentration of oral vitamin C by 100 to 200 fold. It was these higher intravenous concentrations, not the oral doses, that led to the observed clinical effect. It has also been demonstrated that vitamin C will kill some cancer cells but not normal cells. Tumor cells selectively take up more vitamin C compared to normal cells through facilitated transport by glucose transporters. This is because tumor cells have an increased metabolic need for glucose. Intravenous ascorbic acid acts as a prodrug leading to the formation of the ascorbate radical and hydrogen peroxide in the extracellular spaces. Oral ascorbic acid acts as an antioxidant to prevent reactive oxygen species formation.

A study of patients with advanced cancerous tumors and hematological malignancy found antitumor activity. Studies have been done using intravenous vitamin C in ovarian, pancreatic, hematological, colorectal, breast, liver, lung, and prostate cancer. Tumor markers were reduced in the intravenous vitamin C group. Intravenous vitamin C has also been used in combination with paclitaxel, carboplatin, and gemcitabine with a reduction in adverse treatment effects from chemotherapy and no reduction of the clinical effects of the chemotherapeutic agent. Studies of high concentrations of vitamin C have shown it to have an additive effect on cisplatin, cyclophosphamide, doxorubicin, etopoide, fluorouracil, gemcitabine, irinotecan, paclitaxel, tamoxifen, vincristine, and FOLRIFI and FOLFOX regimens. Intravenous vitamin C may interfere with bortezomib and methotrexate. Patients with a G6PD deficiency who receive intravenous vitamin C above 15 grams are at risk for red blood cell lysis. G6PD deficiency is considered the most common enzyme deficiency in humans.
Vitamin D is a fat-soluble vitamin formed after ultraviolet radiation of the skin converts 7-dehydrocholesterol to vitamin D or 1,25 cholecalciferol.

Vitamin D can also be obtained from some foods, including fatty fish, fish liver oil and eggs, and dietary supplements. It helps the body use calcium and phosphorous to make strong bones and teeth, and a deficiency of vitamin D may weaken the bones, leading to a disease called rickets (when it occurs in children) or osteomalacia (when it occurs in adults). Two types of vitamin D important to humans are D$_2$ or ergocalciferol, which is made naturally by plants, and D$_3$ or cholecalciferol, which is made when the skin is exposed to ultraviolet radiation. The Institute of Medicine (IOM) recommends that persons between 1 and 70 years of age consume 15 micrograms (μg) per day, which is the same as 600 international units (IU) per day. For those age 71 or older, the IOM recommendation is 20 μg (800 IU) per day. D$_3$ is recommended for supplements because D$_2$ is poorly converted to the active form of the vitamin.

Initial interest in studying the relationship between vitamin D and cancer was motivated by the observation that the incidence and death rates for some cancers were lower among individuals living in the southern latitudes, where they were likely to receive more sun exposure than people living in the northern latitudes. Experimental evidence from animal studies has also suggested that vitamin D might lower cancer risk by several means, including decreasing cellular growth, stimulating apoptosis (cell death), promoting cellular differentiation, and reducing angiogenesis (tumor blood vessel formation).

Some epidemiologic studies with humans have also found associations between vitamin D and the risk of certain cancers, but results are inconsistent and based on observation rather than experimental designs. This means that observed associations might be due to reasons other than vitamin D consumption or blood levels. For instance, people who consume high levels of vitamin D might differ in other ways (such as healthier behaviors) from those with low levels of consumption, and those other differences might explain the observed relationships. Vitamin D has been included as a variable in some experimental studies, but none of those trials was designed to study cancer specifically, so further research is needed before conclusions can be drawn.

Multiple epidemiologic studies have found an association between high vitamin D intake and high bloodstream levels of vitamin D are associated with a lower risk of colorectal cancer, but these studies are all observational and thus cannot demonstrate causality for the reasons noted above. The Women's Health Initiative, a randomized trial, found no relationship between taking vitamin D and calcium supplement and reduced risk of colorectal cancer, but the results from that study have been criticized on several grounds, including the low level of vitamin D in the supplements (10 μg/100 IU daily), the short period of follow-up, and the fact that participants could have taken vitamin D on their own. There is insufficient evidence to draw any conclusions about the relationship between vitamin D and any other types of cancer at this time.

Vitamin E is a fat-soluble vitamin absorbed in the small intestine. Vitamin E is found in raw nuts and seeds, avocados, fish, and olive oil. It requires bile and pancreatic esterase for absorption, and then enters circulation via the lymphatic system where it is transported to the liver. Vitamin E is essential for cell membranes, gene expression and signaling, cell proliferation, and reproduction. Vitamin E consists of four tocopherols, alpha, beta, delta, and gamma, and four tocotrienols, alpha, beta, delta, and gamma. Research findings debate the importance of alpha-tocopherol versus the other three forms; but, in nature, the four are often found together, and gamma has been found to have clinical importance in some conditions. The synthetic or commonly supplemented form is all-racemic alpha-tocopherol, while the natural form is d-alpha-tocopherol.

The natural form has twice the biological activity of the synthetic form. A deficiency of vitamin E leads to increased peroxidation of red blood cells and fatty acids, neurological symptoms such as difficulty walking and speaking, lipoprotein abnormalities, and poor fat absorption syndrome. At high doses, vitamin E inhibits protein kinase C and tumor promotion. Protein kinase C is important in the signaling of apoptosis or normal cell death, a process absent in most cancer cells. Vitamin E at sufficient doses can reduce cell proliferation in lung cancer. Vitamin E has been shown to suppress telomerase activity in ovarian cancer cells. Thus, it could be a useful therapeutic adjuvant. In a large prostate cancer study, vitamin E and selenium
alone and together did not prevent prostate cancer in a generally healthy group of men. Many of these studies have used synthetic alpha-tocopherol rather than the natural vitamin E with its multiple forms. The natural form may have more clinical activity than synthetic alpha-tocopherol.

Many patients with cancer will develop a hypercoagulability state. The formation of clots can lead to cardiovascular accidents and strokes that complicate the lives of patients dealing with cancer. The natural mixed tocotrienols have been shown to reduce increased coagulation states, with the gamma portion appearing to be the most active. Their mechanism is different than that of aspirin, coumadin, and fish oil. Tocotrienols have been shown to inhibit the inflammatory nuclear factor kappa B when it is activated by tumor necrosis factor alpha, cigarette smoke, interleukin 1-beta, and epidermal growth factor, all of which promote cancer cell growth. Tocotrienols can also inhibit the growth of breast cancer cells—both estrogen positive and estrogen negative—and this is not via an estrogen receptor mediated pathway. In addition, they do not inhibit breast cancer cell growth by interfering with the insulin growth factor pathway or increased binding of its proteins. Similar results have also been shown for human prostate cancer cells. These findings further suggest an important role for the natural form of vitamin E.

Vitamin K consists of vitamin K1 (phyloquinone), vitamin K2 (menaquinone), and vitamin K3 (menadione). Vitamin K1 is found in green leafy vegetables and controls one of the mechanisms by which blood clots. Vitamin K2 is synthesized in the gut by intestinal flora and is involved in bone metabolism. Vitamin K3 is a synthetic analogue derived from K1, K2, and a provitamin.

Vitamin K1 has been studied for anticancer properties since 1947. It has shown activity against liver, colon, lung, stomach, nasopharyngeal, and breast cancer as well as leukemia. In a trial of hepatocellular carcinoma patients, a 20 percent tumor-response rate was observed, and several patients survived longer than one year. In a second trial with the same cancer, 20 percent of patients’ disease stabilized, and lab values normalized in half of the patients. K1 induces cancer cell apoptosis via production of a reactive oxygen species and modulation of transcription factors of cell reproduction. Epidemiological studies have found that individuals with the highest levels of K1 in the diet had a much lower risk of developing Non-Hodgkin lymphoma.

Vitamin K2 has shown to have an effect against liver, colon, stomach, lung, lymphocyte, nasopharyngeal, and breast cancer as well as leukemia. In leukemia it has been shown to induce apoptosis in leukemic blast cells. K2 may induce cell apoptosis through a nonoxidative mechanism involving transcription factors and cell cycle arrest. It also modifies growth factors and receptor molecules and freezes cell cycles, making growth and replication of tumor cells more difficult or impossible. Its activity is known as oncosis, or stress activated ischemic cell death. Tumor cells are particularly susceptible to oncosis. In patients with viral liver cirrhosis and a high risk of liver cancer, ingestion of K2 over several years reduced the development of liver cancer in the K2 group compared to control patients. In myelodysplastic syndrome, K2 has been shown to increase survival and delay onset of hematological cancers. In prostate cancer, when supplementing with vitamin C and K2 serum, cancer markers were decreased and prostate cancer cells were destroyed. Vitamin K2 may be depleted by extended use of warfarin, antibiotic use that significantly alters intestinal flora, and medications that reduce fat absorption.

K3 combined with vitamin C has been shown to cause cancer cell death. This mechanism is called autoschizis and differs from apoptosis and oxidative stress. K3 has also been shown to be effective when combined with 5-fluorouracil, bleomycin, cisplatin, and dacarbazine.

Conclusion
The field of vitamin research and cancer includes many more cell line and animal studies than it does human clinical trials. Most of the human trials are small in number. These trials have shown whether there is a clinical effect against various types of tumor cells, interactions with various chemotherapeutic agents and radiotherapy, and patient quality of life under vitamin therapy versus conventional chemotherapy and radiotherapy. More clinical trials are needed before the use of vitamins will become a part of conventional treatment of patients with cancer.

Paul Richard Saunders
Canadian College of Naturopathic Medicine
Vulvar Cancer

Vulvar cancer is a disease that affects the vulva, the external part of the female genital area. This area consists of the mons pubis (a fat pad that grows hair during puberty), the clitoris (the area that becomes erect when aroused), the labia minora and labia majora (coverings over the vaginal opening), and the vulvar vestibule (the opening to the vagina).

Vulvar cancer is a rare cancer, accounting for about four percent of cancers affecting the female genital tract. Most cases of vulvar cancer appear in postmenopausal women. However, some cases have been reported in younger women. Four main types of vulvar cancer include the following:

- **Squamous Cell Carcinoma:** The most common type of vulvar cancer (accounting for about 90 percent of cases), it starts in the squamous cells and is usually located on the labia.
- **Adenocarcinoma:** This cancer begins in the vulvar glands. About eight percent of vulvar cancers are adenocarcinomas.
- **Vulvar Melanoma:** This cancer is rare, representing about five percent of vulvar cancers.
- **Sarcoma:** This is another rare form of vulvar cancer, making up about two percent of vulvar cancers. This cancer forms in the connective tissue.

When the cancer begins in the vulva, it is referred to as primary vulvar cancer. However, if the cancer begins in another part of the body and then is found in the vulva, this condition is referred to as secondary vulvar cancer.

**Risk Factors**

Despite the fact that vulvar cancer is not as common as other cancers, there are factors that can predispose someone or be risk factors for developing this type of cancer. There are many factors that can put an individual at risk for developing vulvar cancer, including the following:

- Contraction of the human papilloma-virus (HPV) or genital warts in women younger than the age of 50
- Women who have had cervical or vaginal cancer
- Pronounced changes on the skin such as lichen sclerosis or squamous hyperplasia
- Contracting a sexually transmitted disease or infection increases the risk. Developing antibodies to fight off the herpes simplex virus 2 has been determined to be a predisposing risk factor for developing vulvar cancer.
- Having systemic lupus erythematosus has been reported to carry a three-fold risk of developing vulvar cancer.
- Women who have had a kidney transplant are put in a higher risk category to develop vulvar cancer.
- Women with psoriasis have a higher risk of developing vulvar cancer.
- Having vulvar intraepithelial neoplasia (VIN)

**Symptoms of Vulvar Cancer**

There are instances when women do not have any symptoms in the early stages of cancer or are embarrassed to report any symptoms, but a medical professional may notice some changes in the vulvar region during an examination. Women are encouraged to report changes that may occur to a doctor before the condition becomes serious and needs immediate medical treatment. If a woman...
does experience symptoms of vulvar cancer, these may include the following:

- Bleeding
- Dyspareunia (painful sexual intercourse)
- Burning during urination (dysuria) or pain only in the vulvar or genital region
- Intense itching
- Rash in the vulvar region
- Vulvar region becomes red and raw
- Strong smell coming from the vulva

Since the skin of the vulva is extremely sensitive, changes or deformities of the skin can occur in vulvar cancer. Women should be aware of any changes and report them to a medical professional. Changes or deformities to the skin may include the appearance of red, white, pink, or gray mole or freckle; the skin around the vulva may appear like a lump or begin to thicken abnormally; or an ulcer may form that can bleed and become painful and sensitive to touch.

**Diagnostic Testing for Vulvar Cancer**

Once there is a suspicion of vulvar cancer, a patient will undergo diagnostic testing. These tests are important to rule out the disease or help with determining a treatment. A medical professional will conduct a thorough pelvic examination to detect skin changes or any other problems with the genital region. Tests may include swabbing of the area, and using an ultraviolet light can aid in the detection of skin changes or the appearance of abnormal squamous epithelial cells. A biopsy of the vulva will be performed to detect the presence of abnormal cells. If a medical professional feels that there should be more testing done, a CT scan or MRI of the pelvis will be ordered. Medical professionals may consider performing a cystoscopy or proctoscopy to aid in the diagnoses of vulvar diseases or conditions that could have spread to other areas of the body. A cystoscopy is a diagnostic tool that examines the bladder, and a proctoscopy is used to examine the rectum.

**Stages of Vulvar Cancer**

As with all types of cancers, medical professionals use staging to describe the severity of the cancer as well as how to treat the patient. There are five stages of classifying vulvar cancer:

- **Stage 0:** Cancer is confined to the surface of the skin. This stage is referred to as carcinoma in situ.
- **Stage 1:** The cancer is confined in the perineum and vulvar region and has not spread to the lymph nodes.
- **Stage 2:** The cancer has spread into the lower part of the urethra, the lower part of the vagina, or the anus.
- **Stage 3:** Cancer has spread into the lymph nodes.
- **Stage 4:** Cancer has spread into the upper part of the urethra, the upper part of the vagina, or other parts of the body.

**Treatment of Vulvar Cancer**

Depending on the staging, there are several treatment options available when treating vulvar cancer. Laser surgery is a great option if the cancer is detected early. Sometimes a surgeon is able to clear out diseased tissue, but patients may have to consider a complete removal of the vulvar region in order to remove the cancer cells. Radiation and chemotherapy are other options used in treating vulvar cancer.

*Cindy Ferraino*

*Independent Scholar*

**See Also:** Cervical Cancer; Vaginal Cancer; Women’s Cancers.

**Further Readings**


Waldenström's Macroglobulinemia

Waldenström's macroglobulinemia (WM) is a rare blood cancer. The Swedish physician Jan Waldenstrom first described the disease in 1944. The name macroglobulinemia refers to an excess of large proteins in the blood. Known as immunoglobulin M, or IgM, molecules, these are the largest type of antibodies produced in the body. WM shares characteristics with both lymphoma as well as multiple myeloma. The WM tumor cells are actually a mix of lymphocytes (the white cells causing lymphoma), plasma cells (the white cells causing multiple myeloma), and cells looking somewhat in between both of these, known as lymphoplasmacytic cells.

The categories of blood cancers encompassing WM are referred to as plasma cell dyscrasias, or monoclonal gammopathies. In this regard, the tumor cells arise from the same type of white cells, which make antibodies; however, WM tumor cells multiply as clones and all produce identical IgM antibody proteins. Monoclonal IgM proteins are known collectively as the m-spike, and this is a crucial component in the diagnosis of WM. These monoclonal antibodies can be visualized as a narrow band when blood proteins are sorted by weight and charged by electrophoresis (SPEP), as opposed to a wide band from normal diverse antibodies. This technique can also identify an m-spike excreted in the urine. The type of protein making up the m-spike can be characterized as IgM by immunofixation electrophoresis (IFE). Because antibodies are all composed of both heavy and light chains, another test detects excessive monoclonal free light chains in the blood (serum free light chain testing). The diagnosis of WM is made by two components: a documented m-spike and a bone marrow biopsy showing the specific characteristics described above, known as lymphoplasmacytic lymphoma.

There are 1,000 to 1,500 new cases diagnosed in the United States each year. The average age at diagnosis is 60 to 70 years. WM is more common in men than women. A benign, precursor state, known as monoclonal gammopathy of undetermined significance, can progress into WM or other blood disorders. There are no known environmental risk factors for developing WM. However, there is a familial variant in about 20 percent of patients and Ashkenazi ethnicity in 20 to 25 percent of patients. Patients may initially present with a wide variety of symptoms. Presenting symptoms may be constitutional, such as fatigue, fevers, night sweats, or weight loss. Symptoms may be related to loss of normal blood cells from overcrowding tumor cells in the bone marrow, including low red cells, white cells, or platelets. These low counts can lead to fatigue, increased infections, and bleeding.
WM patients often have other immune system dysfunction, including decreased production of normal antibodies, which further increases their risk of infection. A variety of additional symptoms may be caused by the excessive IgM protein itself, including autoimmune disorders, painful and often-debilitating nerve damage (peripheral neuropathy), or thick blood (hyperviscosity), which can lead to occlusion of small blood vessels.

The treatment of WM shares many therapies that are also utilized in either lymphomas or myelomas. WM is often an indolent disease and progresses slowly. As such, patients are observed closely and not treated until they become symptomatic. If a patient develops hyperviscosity, plasmapheresis is an acute and temporary treatment that reduces the number of IgM proteins in the blood. The mainstay of treatment is a combination of the biological therapy rituximab and single/combination chemotherapy or another anticancer medication. Active therapies include steroids, fludarabine, cyclophosphamide, bortezomib, and ibrutinib. One of the latest discoveries, by Treon et al, is a somatic mutation in over 90 percent of WM patients, known as L265P. This may pave the way to new and more effective treatments for this disease.

Andrew Branagan
Yale School of Medicine

See Also: Lymphoma, Non-Hodgkin’s, Adult; Myeloma, Multiple.

Further Readings

Chemical agents have been used as weapons of war throughout human history. It was during World War I, however, that chemical weaponry came of age. Highly toxic war gases, primarily mustard gas and phosgene, were used with devastating effectiveness on the bodies and minds of troops on both sides of the conflict. The tragedy of approximately 90,000 soldiers dying a comparatively slow and miserable death on the killing fields of the World War I, with nearly 1 million others permanently injured, generated a universal repugnance to chemical weapons. To this day, with the field of military weapons greatly expanded, when single bombs can kill millions, and ever-more-ingenious killing devices are invented, chemical weapons remain the only military hardware banned from the battlefield.

In 1925, the first international agreement banning chemical weapons from warfare, the Geneva Protocol, was drafted. Some limited use of war gases did occur thereafter (e.g., invasions of Ethiopia by Italy and China by Japan in the 1930s; Saddam Hussein on Iran in the Iraq–Iran War and against Kurdish Iraqi citizens; and in 2013 by Syria against its own citizens), but war gases were not used in World War II. The Nazis did employ poisonous gases (hydrocyanic acid) as an important method for the systematic murder of concentration camp inmates, mostly Jews, but these gases are not technically considered to be war gases since they were not used as weapons of war.
The precise definition of chemical weapons can be contentious. The Chemical Weapons Convention (CWC), introduced to the United Nations in 1992 and entered into force in 1997, defines a chemical weapon as an armament using a toxic substance in a delivery system such as a bomb or artillery shell to cause permanent harm to humans or animals. The CWC is administered by the Organisation for the Prohibition of Chemical Weapons, an independent, autonomous international organization. As of 2014, 190 countries were Member States of the Organisation. The World Health Organization (WHO) has a broader definition of chemical agents of warfare: “all substances employed for their toxic effects on man, animals or plants.” The WHO definition is not considered in establishing international law.

In general, chemicals like napalm, magnesium, and white phosphorus smoke that act as incendiary substances to create physical force, smoke, or fire are not considered chemical weapons. Riot control agents are specifically prohibited from warfare by the CWC, but they are not outlawed for use by domestic police forces in crowd control. The United States sprayed about 20 million gallons of military herbicides on the Republic of Vietnam, its ally, during the Vietnam War, but such herbicide spray missions are not classified as chemical warfare under the CWC. The reasoning is that the chemicals were used as tactical weapons to destroy foliage and “unfriendly” crops that fed the enemy forces and were not designed to inflict harm on human beings or animals. For purposes of discussion here, the herbicides will be included as war chemicals because of their potential human health effects, regardless of the stated military reason for their having been employed.

Biological agents are often classified with chemical agents, and there is a narrow borderline between the two weapons types because many biological agents exert their toxic effect with poisonous chemicals. For example, botulism is caused by a toxic chemical released by *Clostridium botulinum*, the microorganism associated with the disease. This article does not include biological agents.

The CWC classifies chemical weapons into the following types:

- Choking agents
- Blister agents
- Blood agents
- Nerve agents
- Riot control agents
- Mustard agents

The chemicals are generally used in warfare as “lethal agents” designed to kill or injure an enemy severely enough to necessitate evacuation and medical treatment; as “incapacitating agents” to put the enemy out of action for hours or days, but to allow recovery without medical intervention; or as “harassing agents” to incapacitate an enemy for as long as he or she remains exposed.

Many chemicals, like mustard gas and the arsenical vesicants, can be absorbed percutaneously (i.e., enter the body by skin absorption), thus making respirators ineffective, and also increasing their toxic potency. Nerve gases known as G-agents are both much more toxic and quicker acting than agents like the lung gas phosgene. Nerve gases can penetrate eyes and skin, as well as poison the victim through inhalation. Tabun (or GA) is an example of a G-agent. It was discovered by the Germans in 1936 and is a nerve gas that acts as a cholinesterase inhibitor. Many nerve gases, and organophosphate pesticides, share this toxic pathway. Cholinesterase is an enzyme that breaks down acetylcholine, a compound formed at nerve junctions to transmit nervous signals. Cholinesterase inhibition does not permit the nerve cells to return to their resting state and leads to serious—even fatal—neurological dysfunction.

Soman and sarin also belong to this family. Sarin was the chemical used in 1995 by the Japanese cult Aum Shinrikyo for an attack in the Tokyo subway system that killed 12 people and injured about 1,000 commuters. By the beginning of World War II, massive quantities of tabun had been manufactured and stockpiled, but sarin became the G-agent of choice after the manufacturing processes were improved. Sarin is 50 times more lethal than phosgene.

The alphabetical code names for the chemicals were assigned to them by U.S. military authorities. In the United States, the committees of scientists assembled by the National Academy of Sciences to aid the government during World War II followed this alphabetic naming tradition. The first committee was called the ABC Committee, followed by the DEF Committee. Records of meetings and reports are now declassified and open for public inspection in Washington, D.C., at the Academy.

In 1955, another class of nerve gases, V-agents, was discovered. V-agents are 10 times more lethal
Table 1  Major chemical warfare agents classified by typology of the Chemical Weapons Convention

<table>
<thead>
<tr>
<th>Agent</th>
<th>Comments</th>
<th>Acute Effects</th>
<th>Chronic Diseases Associated With Exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Choking Agents</td>
<td></td>
<td></td>
<td>Sublethal doses cause chronic lung disease; pneumonitis</td>
</tr>
<tr>
<td>• Chlorine [Cl]</td>
<td></td>
<td>Acute lung irritant slowly burns lung tissue, causing fluids to accumulate,</td>
<td></td>
</tr>
<tr>
<td>• Phosgene (carbonyl chloride)</td>
<td></td>
<td>leading to “dry land” drowning of victim. Effects are delayed after initial</td>
<td></td>
</tr>
<tr>
<td>• Diphosgene [DP]</td>
<td></td>
<td>exposure.</td>
<td></td>
</tr>
<tr>
<td>• Chloropicrin [PS]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Acute lung irritant slowly burns lung tissue, causing fluids to accumulate,</td>
<td>Sublethal doses cause chronic lung disease; pneumonitis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>leading to “dry land” drowning of victim. Effects are delayed after initial</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>exposure.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Oily substances that act as irritants and then as cell poisons. Causes</td>
<td>All agents can cause permanent lung injury and blindness in survivors. Mustard gas is a known human</td>
</tr>
<tr>
<td></td>
<td></td>
<td>blistering. Effects are delayed after initial exposure.</td>
<td>carcinogen, associated with cancers at several sites, particularly upper respiratory tract and lung cancer.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Nitrogen mustards can cause bone marrow suppression and lead to blood disease. Causes cancer in laboratory</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>animals. Cancer potential of lewisite and phosgene oxime not known.</td>
</tr>
<tr>
<td>Blood Agents</td>
<td></td>
<td>A form of hydrogen cyanide (Zyklon B) was used in Nazi concentration camp</td>
<td>Hydrogen cyanide is not considered a carcinogen, teratogen, or mutagen.</td>
</tr>
<tr>
<td>• Hydrogen cyanide (hydrocyanic</td>
<td></td>
<td>gas chambers.</td>
<td></td>
</tr>
<tr>
<td>(hydrocyanic acid in aqueous</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>solution) [AC]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Cyanogen chloride [CK]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Arsine (lewisite, 2-chlorovinyl</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>dichloroarsine ) [SA]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nerve Agents</td>
<td></td>
<td>In general, inhibit ability of blood to carry oxygen, fatally interfering</td>
<td>Hydrogen cyanide is not considered a carcinogen, teratogen, or mutagen.</td>
</tr>
<tr>
<td>• Tabun [GA]</td>
<td></td>
<td>with respiration.</td>
<td></td>
</tr>
<tr>
<td>• Sarin (isopropyl methylphosphonyl</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>fluoridate) [GB]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Soman [GD] [GF]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• VX (O-ethyl S-[2-</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(diisopropylamino) ethyl]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>methylphosphonothioate)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Riot Control Agents</td>
<td></td>
<td></td>
<td>Recovery from sublethal dose may require a long period. Cancer-causing potential not known.</td>
</tr>
<tr>
<td>• 2-chlorobenzalmalononitrile [CS]</td>
<td>Banned from warfare but permissible for</td>
<td>Very irritating to the eyes; causes tearing and possible vomiting and</td>
<td></td>
</tr>
<tr>
<td></td>
<td>police control of riots.</td>
<td>prostration.</td>
<td></td>
</tr>
<tr>
<td>Defoliating and Crop-</td>
<td></td>
<td></td>
<td>Permanent damage to the eyes and respiratory system can occur if contact persists. Other long-term</td>
</tr>
<tr>
<td>Destroying Agents</td>
<td></td>
<td></td>
<td>health effects not observed.</td>
</tr>
<tr>
<td>• 2,4,5-T/2,4-D mixtures</td>
<td>Not considered chemical weapon under the</td>
<td>Acute effects not observed at typical exposure.</td>
<td>2,4,5-T herbicides contaminated with dioxin (2,3,7,8-tetrachlorodibenzodioxin) to varying degrees. Soft</td>
</tr>
<tr>
<td>(Agent Orange)</td>
<td>Chemical Weapons Convention.</td>
<td></td>
<td>tissue sarcomas and non-Hodgkin lymphoma associated with exposure to Agent Orange. Suggestive evidence on</td>
</tr>
<tr>
<td>• 2,4-D / picloram mixtures</td>
<td></td>
<td></td>
<td>multiple myeloma. Studies of farmers exposed to 2,4-D indicate association with non-Hodgkin lymphoma.</td>
</tr>
<tr>
<td>(Agent White)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Dimethylarsinic acid (Agent Blue)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
than sarin and are more readily absorbed percutaneously. The WHO estimates a human lethal dose of mustard gas, via skin absorption, to be 5,000 mg; sarin to be 1,000 to 2,000 mg; and V-agent to be as low as about five mg. V-agents are remarkably effective in penetrating skin and causing death. These agents are also persistent, so that their use requires effective decontamination procedures following a military assault to prevent further poisoning.

Table 1 provides chemical and health data on a number of important war gases and chemicals.

Public Health Considerations

In the 1970s, the WHO produced a document on chemical warfare agents that is still relevant today because of the limited research and development of war gases and chemicals that has taken place since then. The WHO summarizes characteristics of chemical weapons relevant to public health as follows.

Chemical weapons differ from conventional weapons in their potential for unintended consequences on civilian populations, both those living within the target area and those living at considerable distances from the target, and “pose a special threat to civilians.”

Very small quantities of chemical weapons may have devastating ecological and public health consequences on the populations and environments in targeted areas, as well as distant from the battlefield.

There may be unintended long-term consequences of exposure to chemical gases and sprays, sometimes decades after hostilities have ended. Some war gases and sprays are associated with the development of chronic diseases, like cancer, which may take years to manifest after the initial exposure. This is particularly true of highly bioreactive alkylating chemicals like the mustard gases used during World War I.

Chemical weapons can pose grave dangers to large populations and ecologies through sabotage and non-conventional warfare terrorist attacks that do not require large scale sophisticated weapons for their launching.

The WHO considers that for those who survive a chemical attack, “the long-term effects of the military use of agents that are not directly lethal may be considered more important than their immediate effects.” The lethality of chemical weapons and their ability to cause long-term chronic diseases, like cancer, is related to their innate chemical activity and to the dose of exposure. It has, however, proven difficult to identify precisely the long-term effects, except for a few agents such as mustard gas. Standard epidemiological methods require that the at-risk population be accurately identified (i.e., the true denominator for a risk calculation); that the exposure be quantified (i.e., the doses of toxins delivered); and that relevant diseases and causes of death be accurately diagnosed and recorded. For substances for which a good deal of either clinical or epidemiological data exist on civilian or occupational cohorts, the dissimilarity of scenarios between wartime exposures and non-combat exposure make it difficult to extrapolate potential effects among combatants or exposed civilians.

Exposure dose is particularly problematic. The amount of the chemicals delivered to the target will vary with weather conditions. The same weapon may deliver different effective doses at different times. War gases and chemicals may persist in the environment and their rate of decay will vary with the environmental characteristics of the terrain, making calculation of an exposure rate problematic. The chemical agents may spread over large, poorly defined areas. Accurate data on the at-risk population and its health status may also be difficult to ascertain. People who live in war zones are apt to be very mobile, and recordkeeping of transient populations is poor.

With regard to health effects in military personnel who may have been exposed to the agents, few countries maintain records of the environmental exposures that troops may have encountered. In the United States, it is extraordinarily difficult to even identify the names of individual soldiers at risk.

Jeanne Mager Stellman
Columbia University

See Also: Chemical Industry; Lymphoma, Non-Hodgkin’s, Adult; Myeloma, Multiple; Skipper, Howard E.

Further Readings


Water Treatment

Concerns over drinking water contaminants and human health date back centuries. However, it was only beginning in the 1970s that contaminant sampling became more common and extensive. Since that time, scientists have discovered that hundreds of manufactured chemicals can be found in various drinking water supplies, such as groundwater and rivers. Many of these substances are known or suspected human carcinogens.

History

Although treating water for consumption dates back as far as 4000 B.C.E., treatments initially focused on improving the aesthetic qualities of drinking water, such as taste and odor. It was not until the 19th century that scientists began to understand the health effects of drinking water and the sources of health problems due to microscopic organisms and other invisible constituents. Water treatment systems in the United States created in the early 20th century focused on reducing turbidity to remove microbial contaminants that could cause epidemics such as typhoid, dysentery, and cholera.

Although water filtration methods could reduce turbidity, disinfectants ultimately proved to be more effective in reducing waterborne-disease outbreaks. Chlorine was first used as a water disinfectant in 1908 in a water treatment plant in Jersey, New Jersey. Federal regulations concerning drinking water began in 1911 with bacteriological quality standards set by the U.S. Public Health Service (PHS). Standards have been revised and expanded over the years.

Concern over drinking water supplies grew in the late 1960s as the PHS began to investigate the presence of man-made chemicals in drinking water. These chemicals were from sources such as factory discharges, runoff from farms and streets, and underground storage and disposal tank leaks. In 1960, a PHS water system survey found that only 60 percent of water treatment systems produced water that met all PHS standards.

In 1973, the U.S. Congress began to debate issues regarding water treatment and supply safety. These debates led to passage of the Safe Drinking Water Act of 1974 to regulate public water supplies. Amendments were added to the act in 1986 and 1996. The act addressed threats to the drinking water supply, including chemicals, animal wastes, pesticides, naturally occurring contaminants, and other threats to human health. The act also addressed health risks from water that is not properly treated or travels through a distribution system that is improperly maintained.

In 2009, a New York Times analysis of federal data found that key provisions of the Safe Drinking Water Act had been violated by 20 percent of water treatment systems in the United States. These violations had occurred over the previous five years beginning in 2004. Among the violations found were increased concentrations of arsenic, radioactive substances such as uranium, and the solvent tetrachloroethylene. All have been linked to increased risk for cancer.

Contaminants

Chemical contaminants in drinking water come from various sources, from the improper disposal of household products and cleaning solvents to increased pesticide use in the last half of the 20th century. The U.S. Environmental Protection Agency (EPA) regulates more than 40 contaminants known carcinogens. For some scientists, no level of carcinogens in drinking water is thought to be safe. Over the years, the EPA has regulated many of these carcinogens in drinking water by limiting allowable concentrations of these substances.

The EPA’s list of contaminants in drinking water includes microorganisms, disinfectants, disinfection
Water Treatment

400 cases of the disease are diagnosed in the United States each year in children and teenagers. Several epidemiological studies have found a connection between nitrate in drinking water and an increased risk for colon cancer. A 2010 study conducted in Iowa studied nitrogen leaching in drinking water and found an increased risk for colon cancer in people exposed to drinking water exceeding 25 mg/L of nitrate for more than 10 years and who were above average meat consumers. Another study, the Iowa Women's Health Study, found an increased risk for bladder cancer in older women in Iowa due to exposure to nitrate in drinking water.

In 2010, a study published in *Environmental Science & Technology* reported that dishwashing detergents and shampoos found in drinking water supplies might be a precursor of harmful nitrosamines. Furthermore, neither ozone nor chlorine treatments reduce nitrosamines. Of particular concern is the nitrosamine, N-nitrosodimethylamine (NDMA) because it is suspected as a human carcinogen. Concerns focus on particularly high levels due to large consumer use. In general, a variety of detergents also contain benzene, which is associated with blood cell cancers such as leukemia, and 1,4 dioxane and acetaldehyde, which has been found to cause cancer in animal studies.

U.S. Geological Survey (USGS) and EPA researchers conducted an analysis of 25 U.S. water utilities and found 18 unregulated chemicals in the water supplies. One of the perfluorinated compounds found was linked to several health problems. An increased risk for cancer was found in a West Virginia water supply contaminated by a chemical plant.

Wastewater Workers

Studies have also shown that wastewater workers are at a higher risk for developing cancer than the general population. A retrospective study conducted in 1991 of sewer authority workers employed between 1950 and 1979 found that workers exposed to chemicals in sewage effluent, sludge, or wastewater had an increased cancer risk. This risk included mortality from lung, larynx, and liver cancer. Another study in Copenhagen, Denmark, found that wastewater workers experienced a small increase in cancer incidence, as well as a rare but strong increase of primary liver cancer.

Another later study in Sweden found no overall increase in the cancer risk in wastewater workers but did find a slight increase in prostate cancers. A study byproducts, inorganic chemicals, organic chemicals, and radionuclides. Disinfectant byproducts found in drinking water that increase risk for cancer include bromate, haloacetic acids, and trihalomethanes (THMs), which enter the water supply via the use of chlorine treatment. More than 20 organic chemicals in water supplies are associated with increased cancer risk, including benzene, chlorobenzene, dioxin, polychlorinated biphenals (PCBs), and tetrachloroethylene. Arsenic is an inorganic chemical and carcinogen found in water supplies. Radionuclides found in some water drinking supplies include radium and uranium.

Oral exposure to radium increases the risk for tumors in the bones, head, and nasal passages of humans. Uranium has been associated with lung cancer and tumors of the lymphatic and hematopoietic tissues. According to the American Cancer Institute, arsenic exposure can lead to several types of cancers in humans, including bladder, lung, skin, stomach, kidney, and prostate cancer, as well as leukemia and lymphomas.

The addition of chlorine to water leads to the formation of disinfection byproducts, such as THMs, which have been associated with an increase in several cancers, including anal, bladder, and liver cancer. Disinfectants in swimming pools have been found to react with other water contaminants, such as sunscreen. These interactions are associated with several health risks, including a higher incidence of bladder cancer.

A 2013 report released by the Environmental Protection Group stated that chemicals used in water treatment plants could raise the risk of cancer. As a result, the group has petitioned the EPA to consider reevaluating certain standards associated with the byproducts resulting from disinfecting water with chlorine and other substances. Although some dangerous compounds that are used in or result from water treatment are regulated, an estimated 600 disinfection byproducts have still not been identified.

Fluoridation of drinking water to help prevent cavities began in the United States in the early 1960s following a 1962 recommendation by the Public Health Service. A 1990 report by the U.S. National Toxicology Program found fluoridated drinking water increased cancer in male rats, particularly osteosarcoma (a type of bone cancer). Most studies, however, have not found a strong link between fluoridation and cancer. Furthermore, osteosarcoma, which is the cancer of most concern connected with fluoridation, is extremely rare. Only about one in 400 cases of the disease are diagnosed in the United States each year in children and teenagers.
published in 2011 in *Environmental Health* found that when workplace air concentrations of polycyclic aromatic hydrocarbons and volatile organic compounds (VOCs) were elevated, it translated into an increased lifetime cancer risk. Nevertheless, because of the still relatively small number of studies in this area, the general scientific consensus is that more studies have to be performed on this population to determine if there is an increased risk for cancer among wastewater workers.

**Protection**

One dilemma in solving the problem of cancer and other health risks associated with drinking water is that many of the substances used in water treatment protects people’s health in other ways, such as fluoridation. Researchers have noted that there is a risk trade-off. For example, chlorination of drinking water protects against serious waterborne microbial diseases.

Reducing the risk of protecting against a potential higher risk for cancer in the long term because of chlorination is counterbalanced by the potential for higher incidence of waterborne diseases. Such diseases can immediately affect human health, including death in severe cases. Several approaches are being researched to seek alternatives to chlorination, including alternative disinfectants such as chloramines, chlorine dioxide, and ozone.

Despite advanced water treatment technologies, some have suggested that, depending on the data for specific water supplies, individuals may want to take further measures to protect their health. For example, individuals can install home water treatment systems. According to Cornell University’s Program on Breast Cancer and Environmental Risk Factors in New York State, the first step is to have the drinking water tested for its contents and levels of detectable contaminants.

The Cornell University program notes that activated carbon filters help remove radon and some organic chemicals, including VOCs, pesticides, and THMs, which are used in some industries. Reverse osmosis is recommended for removing carcinogens such as suspended asbestos particles and some pesticides. Aeration is also an option for removing high levels of VOCs and radon.

Treating water through distillation is connected with the removal of arsenic, certain pesticides, and some organic chemicals. Anion exchange devices remove negatively charged compounds, such as nitrate and some forms of arsenic, from drinking water. Methods for reducing fluoride exposure in water include boiling and home fluoride water filtration systems.

David Petechuk
*Independent Scholar*

**See Also:** Bladder Cancer; Chlorine; Detergents; Kidney (Renal Cell) Cancer; Lung Cancer, Non–Small Cell; Lung Cancer, Small Cell; Prostate Cancer.

**Further Readings**


**Western Diet**

The Western diet (WD) has been described as the eating pattern typical of developed nations and industrialized societies. In populations consuming the WD, substantial amounts of total nutrient intake are often provided by sweets, fried foods, high-sodium processed foods, red and processed meats, and refined forms of grains, sugars, and
vegetable oils. The WD pattern does not include recommended amounts of fruits, vegetables, whole grains, and healthful fat sources such as nuts, seeds, and fish. Excessive energy intake is common among populations consuming the WD, since low-calorie nutrient sources such as fruits and vegetables comprise a suboptimal proportion of total food consumption. Some researchers have proposed that chronic diseases, including cancer, have emerged as a major public health problem in conjunction with the adoption of the WD over the past century by large populations in developed nations.

There is no standard definition of the WD, although the diet has been described in the scholarly literature. Epidemiological studies have indicated that individuals from traditional societies who enter industrialized nations quickly begin developing Western-style chronic diseases including cardiovascular disease and cancer, suggesting a dietary connection. Some experts advise that rejecting the WD in favor of a diet pattern providing a substantial proportion of total intake in the form of fruits, vegetables, legumes, fish, poultry, nuts, seeds, and whole grains may play a role in the prevention of chronic diseases. Research indicates that diet is a key factor in the pathogenesis of chronic diseases, although associations among specific foods, dietary patterns, and chronic diseases remain unclear.

**Development of the Western Diet Pattern**

The development and industrialization of agriculture following the Neolithic period and the Industrial Revolution resulted in significant dietary changes for which the human genome may be poorly adapted. Hunter-gatherer populations prior to the Neolithic age subsisted on diets consisting of meat, nuts, seeds, and gathered fruits and vegetables. Epidemiological studies suggest that when individuals from contemporary hunter-gatherer societies are subjected to a WD, chronic diseases appear in previously disease-free people. Thus, it appears that human phenotypes may be highly dependent on environmental, including dietary, factors.

Prior to the Industrial Revolution, there was a lack of food processing technology and economic systems to facilitate the efficient distribution of staple foods across population groups. To a large extent, access to food was dependent on locality and season. Food was minimally processed. Meats, sugar, sweets, and refined grains such as white flour were expensive and often difficult to obtain. Low-technology food preservation methods such as drying and salting were common and were important for survival. The lack of large factory-type facilities for food processing meant that food preparation and preservation took place in the context of family homes or local communities. The labor and expense involved in growing, obtaining, processing, and preserving food tended toward self-limitation of energy intake. The Industrial Revolution stimulated the mass production of cheap, easily available, highly processed foods with stable shelf life. Such foods became the basis of the WD. As food processing became more industrialized, overall consumption of fruits and vegetables as a proportion of total diet declined.

**The Western Diet and Chronic Diseases of Westernized Populations**

During the past 100 years, obesity, cardiovascular disease, certain types of cancer, diabetes, and hypertension have been identified as chronic diseases of developed countries. A majority of older adults in industrialized nations are afflicted with multiple chronic diseases, and Westernized young adults often exhibit subclinical manifestations of chronic disease. Epidemiological studies report increased risk of cardiovascular and non-cardiovascular mortality in older adults who follow a WD pattern and decreased risk in older adults who consume diets rich in fruits, vegetables, and fish. Relationships among chronic disease, diet, genotype, phenotype, and environmental factors are complex and poorly understood; however, it appears that on a population-wide basis, the WD pattern is positively associated with the development of chronic diseases.

**The Western Diet and Cancer Risk**

Based on observational studies, it is thought that about 30 percent of overall cancer risk in developed countries can be explained by dietary factors. Obesity related to overconsumption of energy typical of the WD is associated with increased risk of a number of cancers. Consumption of particular foods common in the WD may be associated with higher rates of certain cancers; for example, colorectal cancer has been linked with intake of processed and red meat. The WD pattern has been associated with increased recurrence and reduced survival in colorectal cancer treated with surgery and chemotherapy.

Substantial evidence indicates that in contrast to the WD, a diet rich in plant-based foods reduces the risk of some types of cancer. Fruit and vegetable
consumption appears to be inversely related to population risk of certain cancers, including esophageal, oral, and colorectal cancers. The specific nutrients or food components responsible for reduction of cancer risk are not well understood, although researchers speculate that fiber, vitamin D, calcium, and antioxidants may play important roles in cancer prevention. Studies investigating the effects of nutrient supplementation for cancer prevention have been disappointing. It is recommended that most individuals should obtain adequate but not excessive amounts of nutrients from food sources rather than supplements.

Alternatives to the Western Diet
It remains unknown if there is any one superior dietary pattern for humans. However, it is likely that any of the following dietary patterns will result in improved health outcomes when compared to the typical WD. All healthful dietary patterns are characterized by moderation or avoidance of alcohol.

The prudent diet, represented by dietary guidance tools such as MyPlate and the now-obsolete Food Guide Pyramid, encourages liberal consumption of fruits, vegetables, and whole grains while recommending moderate consumption of healthful fats and proteins. Limiting intake of foods high in added sugars and solid fats is characteristic of the prudent diet pattern.

The American Institute for Cancer Research has developed the “New American Plate” as a research-based dietary guidance tool for healthful eating and cancer prevention. The New American Plate is similar to the prudent diet, but it places a greater emphasis on consumption of fruits, vegetables, and legumes while limiting intake of animal protein.

The Mediterranean diet includes fruits, vegetables, legumes, grains, fish and poultry, and red wine in moderation. Red meat consumption is minimal, and fat sources include olive oil, nuts, and seeds. The Mediterranean diet has been associated with health benefits including reduced incidences of cardiovascular disease, type II diabetes, and some cancers.

Hunter-Gatherer Diet
Chronic diseases, including cancer, are not often seen in persons from hunter-gatherer populations that have reached or exceeded 60 years of age. A hunter-gatherer diet, sometimes called the Paleolithic diet, encourages consumption of eggs, meat, shellfish, fish, roots, seeds, nuts, and fruits and vegetables, and de-emphasizes grains, added sugar, dairy, and vegetable oils. Some studies have shown favorable outcomes for a hunter-gatherer diet pattern in regards to glucose tolerance, blood pressure, and inflammation. However, because evidence links red meat consumption to risk for some cancers, further research is needed to determine any effects of the hunter-gatherer diet pattern in regards to cancer.

Contrasting Opinions
It has been suggested that a return to pre-industrial diets ignores the positive aspects of the industrialization of agriculture, which include the attainment of the safest, most abundant food supply in human history. The development of public sanitation, food safety innovations, population-wide vaccination programs, and new medical treatments has greatly lengthened the human life span. Longer life, rather than the WD, may be responsible for increased rates of chronic illness, since chronic diseases are associated with aging. Future developments in nutrition are likely to include dietary recommendations and nutraceuticals specifically tailored to maximize each individual’s genetic potential for avoidance of chronic diseases including cancer.

Conclusion
Relationships among dietary patterns, cancer risk, and human genetics are complex and poorly understood overall. The WD pattern appears to be associated with increased risk for chronic diseases including cancer. Risk for particular cancers may be reduced by shifting from a WD pattern to a more healthful diet based on moderation in the use of alcohol, routine consumption of a variety of fruits, vegetables, whole grains, and legumes, and reduced consumption of processed/red meats and refined carbohydrates.

Kyle Thompson
Appalachian State University

See Also: Alcohol; Alternative Therapy: Diet and Nutrition; American Association for Cancer Research; Meat Processing; Obesity.

Further Readings


---

**Wilms’ Tumor**

Renal tumors account for approximately 7 percent of all malignancies in children under 15 years of age in the United States. Wilms’ tumor in particular accounts for the overwhelming majority of childhood renal tumors. In many cases, Wilms’ tumor exists as part of a congenital syndrome, presenting with several other extra-renal findings. Nearly all cases of Wilms’ tumor arise sporadically, making new cases of this rare malignancy difficult to predict. Given the excellent response to treatment, the prognosis is largely dependent on early detection, making familiarity with the presentation and index of suspicion of utmost importance for clinicians.

Wilms’ tumor, or nephroblastoma, is a malignant tumor that arises from the primitive tissue of the kidney during fetal development. It accounts for 95 percent of all childhood renal cancers and nearly six percent of all childhood cancers. There are approximately 500 newly diagnosed cases per year in the United States, with 75 percent occurring in children less than 5 years of age, and a peak incidence of 2 to 3 years of age. Wilms’ tumor is exceedingly rare in the adult population. There is also ethnic disparity, with greatest incidence among African Americans and the least among Asians. Genetic analysis has linked Wilms’ tumor with loss of function of several tumor-suppressor genes including WT1, p53, FWT1, and FWT2. Familial Wilms’ tumor occurs in less than five percent of cases and is associated with mutations in BRCA2 or p53.

Furthermore, there are several congenital syndromes associated with Wilms’ tumor. WAGR syndrome is associated with a mutation of the WT1 gene and is named for the presence of Wilms’ tumor, aniridia (absence of iris of the eye), genitourinary abnormalities, and mental retardation. Beckwith-Wiedemann is another rare syndrome associated with mutations of chromosome 11 and is characterized by Wilms’ tumor, macroglossia (enlarged tongue), macrosomia (large body), hypoglycemia (low blood sugar), and other anomalies. Denys-Drash syndrome involves a different mutation of the WT1 gene and is characterized by the triad of male pseudohermaphroditism (genitalia do not match genotype), progressive kidney disease, and Wilms’ tumor.

There are classically three types of cells found on histologic analysis of these tumors: blastema cells (undifferentiated), stromal cells (often consisting of skeletal muscle, cartilage, and bone), and epithelial cells (cells that line the renal tubules). Examination of the mass often reveals hemorrhage, cysts, and large amounts of dead cells. Most Wilms’ tumors exist as solitary renal masses; however, there can be bilateral renal involvement (five to seven percent) and multiple tumors within one kidney (10 percent).

The most common presentation of Wilms’ tumor is an asymptomatic abdominal mass, often found incidentally by a parent. Patients may also present with abdominal pain, hematuria (bloody urine), hypertension, fatigue, and fever. Rupture of the tumor by trauma may additionally result in a rapidly expanding abdominal mass and anemia. Physical examination yields a large, firm, and non-tender mass on the child’s flank. If occurring as part of a congenital syndrome, often times the other findings associated with the syndrome will be discovered first. The most common location of Wilms’ tumor metastasis is the lungs; however, children rarely present with respiratory symptoms. Metastatic disease is present in up to 12 percent of patients at the time of diagnosis. When index of suspicion is high, diagnostic workup typically begins with an ultrasound of the abdomen and kidneys to confirm the presence of a renal mass. This is often followed by an abdominal CT scan to confirm the presence of a solid mass in the kidney. Once confirmed, a chest CT should be performed to determine the presence of lung metastases. Due to the ability of these tumors to invade nearby blood vessels, a Doppler ultrasound of the renal vein and inferior vena cava should also be performed. A definitive diagnosis of
Wilms’ tumor can only be made by biopsy, typically after the tumor is surgically removed. At the time of diagnosis, patients should be screened for von Willebrand’s disease (in which patients have difficulty forming blood clots to stop bleeding), found in approximately eight percent of patients.

The prognosis of Wilms’ tumor is a testament to the achievements of modern medicine. Five-year survival rates have increased from 30 percent in the 1930s to nearly 90 percent today. Prognosis is based on several factors including tumor histology, stage, age, and genetic markers. Tumor histology is the strongest predictor of survival. The presence of anaplasia, or cells that are highly undifferentiated, is associated with poorer outcomes. Tumor staging is based on the extent of gross anatomic involvement and is assigned after imaging and surgical resection. Higher stages indicate more extensive disease involvement and are associated with more adverse outcomes. Multiple studies have shown that a younger patient age at diagnosis is associated with improved outcomes, particularly those diagnosed before the age of two. Recent studies indicate that adults with Wilms’ tumor have similar outcomes to pediatric patients, although adults generally experience greater toxicity from chemotherapy. The most well-defined genetic marker associated with recurrence and mortality is a loss of heterozygosity of chromosomes 1p and 16q.

Surgical resection, chemotherapy, and radiation are the mainstays of treatment of Wilms’ tumor. Initial therapy typically involves surgical resection followed by chemotherapy; however, similar outcomes can be achieved by initiating treatment with chemotherapy to shrink the tumor, followed by surgery. Patient groups that benefit from preoperative chemotherapy include those with bilateral renal tumors, involvement of the inferior vena cava, and tumors too large to be safely resected. Surgery involves removal of the affected kidney, although care must be taken not to rupture the tumor or leave tumor fragments behind, as these are associated with a higher rate of recurrence. Radiation therapy is generally reserved for higher stages. The most effective chemotherapy regimens involve different combinations of vincristine, dactinomycin, and doxorubicin. Even with adequate treatment, tumors will recur in 15 percent of patients with favorable histology and nearly 50 percent of patients with anaplastic histology. Survival rate with recurrence declines to less than 60 percent. Screening for recurrent disease involves interval chest CT scans and abdominal ultrasonography.

Alan Yaghoubian
Nima Nassiri
David Geffen School of Medicine at UCLA

See Also: Childhood Cancer; Kidney Cancer, Childhood; Ureter and Renal Pelvis, Transitional Cell Cancer.

Further Readings

Wistar Institute
Now considered among the elite biomedical research centers dedicated specifically to cancer research, one of only seven such institutes nationwide designated and funded by the National Cancer Institute, Philadelphia’s Wistar Institute Cancer Center began as a teaching facility dedicated to advancing anatomical studies among medical students in post–Revolutionary War America. Indeed, the Wistar Institute began actually as a kind of museum for wax-preserved human body parts that Dr. Caspar Wistar (1761–1818) had collected and catalogued.

Wistar considered himself not merely a physician and certainly not a researcher but rather a philosopher of science (he was a good friend of Thomas Jefferson who held a similar view about the appropriate public role of doctors). Wistar took the broad view of research and formulated several treatises on the importance of observation and diligent note-taking in the sciences. Not surprisingly, Wistar’s Institute also served as a medical school, the first institution in America independent of any university that focused on medical research and teaching. The institute would be led for more than two decades by Wistar, himself known as America’s first anatominist (his textbook on human anatomy, published in
1787, the first such textbook in America, remained the standard text in the field for nearly a century). His students found Wistar a mesmerizing, even inspirational, lecturer who used the specimen collection (as well as papier-mâché models of anatomical parts) to give his students, among the best and brightest of the era, the opportunity to actually see and handle body parts—at the time a revolutionary teaching methodology.

By the late 1880s, however, the institute, which had since added animal bones and fossils, had become something of a natural history museum and was still a major attraction not only for premed students but also for the general public curious about such eccentric objets d’art. The building had been loosely made into a de facto adjunct facility to the University of Pennsylvania. But the collection, despite careful management, had started to deteriorate to the point that Penn administrators began an effort to close it. After a fire destroyed nearly one-third of the collection, the university rethought its position and began a massive citywide fundraiser to reestablish the institute as a teaching and research facility that would be entirely independent of the university.

The two-year campaign came to be spearheaded by Wistar’s great-nephew, Isaac, a prominent attorney who had made a fortune as chief executive officer of Pennsylvania Canal Company, which shipped the state’s abundant coal resources nationwide. Officially reopened in 1894, the Wistar Institute of Anatomy and Biology was dedicated to fulfilling the vision of Caspar Wistar: promoting original research in the fight against a variety of diseases and teaching promising medical students through hands-on instruction. Among its earliest achievements, in 1906, was focusing on the problem with inconsistent data because scientists and researchers worldwide used a wide variety of rats as experimental subjects. Wistar’s researchers developed a single specialized strain of rat, which came to be known as the Wistarat, that would, in turn, help to standardize research. Today, close to 60 percent of all lab rats in the world are genetic descendants of the original Wistarat. In post-World War II America, following the heroic narrative of the polio vaccine that had riveted the nation throughout the 1950s, immunology became a global campaign. The institute quickly established a name for itself through its wide-ranging research into immunology, including vaccines licensed during the 1950s and the 1960s to treat, among other feared conditions, rabies, rubella, hepatitis C, malaria, and influenza. Indeed, its rubella vaccine is largely credited with eradicating German measles, relatively mild in children but a real fear for pregnant women. Today, Wistar has maintained that interest and has pioneered research into a vaccine against AIDS.

In the 1970s, given the growing national awareness of the potential to fight cancer, the Wistar Institute opted to convert nearly all of its laboratories specifically to cancer research thanks largely to a significant endowment awarded to the institute in 1975 that went to creating the wing of the research facility now known as the Wistar Institute Cancer Center. Over the next three decades, the institute developed three primary research programs: the study of genetics and the mechanics of genes, the changes in genetic makeup that caused cancers to develop, and how they might be manipulated in the earliest stages of development; the study of the molecular and cellular changes involved in the process of the creation of tumors and specifically the critical process of metastasis; and the study of tumor growth, tumor environment, and tumor spread, specifically the roles of cells in that process and the possibility of introducing cellular counterattacks that might halt the development by changing the cellular environment itself. These were ambitious, cutting-edge research divisions—genetics, molecular biology, and cellular structures—and Wistar established itself as a premiere research facility with more than 30 laboratories, able to attract a cadre of some of the world’s most respected oncology researchers and to recruit the most promising postdoctoral biomedical technicians.

At a time when a national debate raged over the medical ethics of stem cell research, Wistar pioneered cancer research using stem cells harvested from unwanted, discarded, or damaged embryos—part of the facility’s dedication to tracing how genetic malfunctions or misdirection led to the first stages of cancers. As a natural extension of its long history into anatomy and medical research, Wistar’s laboratories became far more involved with early cancer detection than with either prevention or treatment. Indeed, one of its earliest successes was a simple blood test that could detect lung cancer earlier than ever before—a critical element in lung cancer treatment, as it remains the most deadly form of cancer and is often mistaken for much milder conditions in patients reluctant to acknowledge the implications of
persistent coughing, thus rendering treatment virtually useless by the time the diagnosis is made.

Wistar research teams also investigated the cancer with the widest patient population: melanomas associated with skin cancer. Again, the research teams attempted to trace the development of the melanomas, the stages of the process through which UV rays alter the cell structures and begin the furious business of metastasizing. Perhaps its signature achievement was the introduction of a monoclonal antibody capable of tracking down and actually destroying cancer cells. Although its research accomplishments have been significant, the institute plays up its role in the Philadelphia community, promoting science in high schools, offering a variety of prestigious internships for college students, and developing a program for post-doctoral candidates who show promise in the field of biomedical research.

Joseph Dewey
Broward College

See Also: Lung Cancer, Non–Small Cell; Lung Cancer, Small Cell; National Cancer Institute; Vaccines.

Further Readings


Women’s Cancers

The American Cancer Society’s two main characterizations of cancer—as abnormal cell growth and the ability to spread to other parts of the body—offer guidance to a discussion of women’s cancers. Viewed from the point of location, several cancers are indeed women’s cancers. The National Cancer Institute identifies the following as women’s cancers: breast, cervical, endometrial, gestational trophoblastic disease, ovarian, uterine, vaginal, and vulvar. Notably, these cancers are location-specific. While women’s susceptibility to other cancers—lung, skin, bone, and brain, etc.—is not greater or less than men’s, cancer’s ability to spread to other sites raises the risk of metastases.

Sylvia Estrada-Claudio in Gender Issues in Cancer Care discussed the long history of bias against women. She asserted that the medical profession’s antipathy toward women and their reproductive organs dates back to beginnings of the discipline, and was shared by some most illustrious members: Barker-Benfield, Ehrenreich and English, and Scully, to name a few. In Spanish-speaking countries, medical students use the term pudenda to indicate the female vulva. The term pudenda is derived from the Latin pudendus meaning “something to be ashamed of.” Similarly, the term hysteria comes from the Greek hystér meaning the womb. From Hippocrates to Freud, hysteria has been associated with women’s reproductive organs: ovaries and the uterus. These examples of the early perspectives held by medical practitioners have influenced the research, care, and treatment of women’s cancers.

Healthy People 2020 identifies “health disparity” as a concern which refers to differences between groups of people and how frequently the group is affected. Women’s health disparities are embedded in Healthy People 2020 health disparities lists of (1) racial and ethnic minorities; (2) residents of rural areas; (3) women, children, the elderly; and (4) persons with disabilities.

An example of the concerns of women’s cancer is highlighted in the case of Henrietta Lacks, an African-American woman who was diagnosed with terminal cervical cancer in 1951. She was treated at Johns Hopkins University, where cells were removed from her cervix without her knowledge. Her cells—known as HeLa—have been used in medical research for the past 60 years. Only in the recent past was her family informed. The Immortal Life of Henrietta Lacks evokes questions concerning research and medical care, ethics and morality, and marginalized members of society.

The definitions and data used in this article were gleaned from the American Cancer Society, the Mayo Clinic, the National Cancer Institute, and Healthy People 2020. Some of the technical terms are used multiple times. It is useful to recall that cancer is abnormal cell growth that can spread: the
notion of cancer as first in situ (site-specific) and second as metastatic (having spread) is helpful to the discussion.

In 2014, the American Cancer Society reported adjusted death rates (per 100,000) for women for the years 1930 and 2010 as the following: breast cancer deaths declined from 30.1 to 29.1; ovarian cancer death rates doubled from 4.4 to 8.1; and uterine cancer death rates declined from 36.3 to 6.7. Since 2001, women's cancers have risen from the fourth to the second leading cause of death for all females in the United States.

The National Institutes of Health (NIH) reported the most common type of breast cancer as ductal carcinoma (70 percent of cases). Ductal carcinoma begins in the lining of the milk ducts (thin tubes that carry milk from the lobules of the breast to the nipple). A second type of breast cancer is lobular carcinoma (15 percent of cases), which, as the names suggest, begins in the lobules (milk glands) of the breast. Both ductal and lobular are location-specific.

There are other rare types of breast cancers, including medullary carcinoma, Paget's disease (which affects the nipple and areola), tubular carcinoma, inflammatory breast cancer, and phyllodes tumors. When a doctor speaks of invasive breast cancer, it means that the cancer has spread, or metastasized, to surrounding tissue.

Advances in breast cancer research have led to the identification of BRCA1 and BRCA2 as the most common genes involved in hereditary breast and ovarian cancers. Genetic testing is a simple procedure involving collecting a blood or cheek swab sample. Results can indicate whether or not the patient carries one of the genes. It is important to note that tests for BRCA1 and BRCA2 can neither diagnose the presence of cancer nor predict future development of either breast or ovarian cancer.

Breast cancer management has evolved from radical mastectomies to a triad of management approaches, including surgery, medication, and radiation. Jerome Urban (1914–1991) practiced the super-radical mastectomy until 1963 when he became convinced that less-mutilating procedures resulted in survival rates equal to the super-radical approach. Current approaches of breast cancer management include the following methods. One is mastectomy (removal of the whole breast and some of the surrounding tissue), or a quadrantectomy (removal of one-quarter of the breast), or a lumpectomy (removal of a small part of the breast); removal of (some) nodes is used as a sentinel (indicator) node removal. A second method is adjuvant chemotherapy, which has been practiced with success for the past 30 years. It is administered solely or in combination.

The following are more commonly prescribed chemotherapy drugs: cyclophosphamide, methotrexate, fluorouracil, doxorubicin, docetaxel, and epirubicin. In some cases, patients receive neoadjuvant therapy (before surgery) to reduce the tumor's size. Depending upon the cancer staging, some patients will receive hormone-blocking therapies to reduce estrogen production, including tamoxifen, anastrozole, and letrozole. The third method is radiation, which can be delivered as an external beam radiotherapy or brachytherapy (internal radiotherapy). It is intended to eradicate microscopic cancer cells that remain after surgery.

Researchers observe two notable health outcomes of breast cancer: first, that white women have a higher incidence of breast cancer than
that in the United States in 2104, about 52,630 new cases of cancer the uterus will be diagnosed and that some 8,590 women will die from cancers of the uterine body. These estimates include endometrial and uterine cancers. Generally speaking, endometrial cancer in women under the age of 45 is rare. And, as with breast cancer, endometrial cancer is slightly more common in white women, but African American women are more likely to die from it.

Ovarian, fallopian tube, uterine, vaginal, and vulvar cancers are localized in the highly vascularized and hormone-rich environment of the pelvis. While each is a different cancer, it is appropriate to introduce the following three because of their location.

According to the Mayo Clinic, ovarian cancer is a type of cancer that begins in the tissues of the ovaries: epithelial cells (covering of the ovary), germ cells (develop into the egg, or ovum, produced monthly), and stromal cells (the supporting tissue) of the ovary. Ovarian cancer often goes undetected until it has spread within the pelvis and abdomen. Late stage ovarian cancer is difficult to treat and often is fatal. Fallopian tube cancer is often connected to ovarian cancer. Researchers have identified fallopian tube tissue-specific cancers of the fimbrias (fingers) of the tube, the smooth muscle of the fallopian tube (which moves the ovum trough the tube), and supporting tissue involvement. Often due to the interconnectedness of these cancers, the term ovarian cancer is used to describe cancer that begins in the fallopian tube and travels to the ovary.

Uterine cancer, which forms in tissues of the uterus (small, hollow, pear-shaped organ in a woman's pelvis), is identified as endometrial cancer (cancer that begins in cells lining the uterus) and uterine sarcoma (a rare cancer that begins in muscle or other tissues in the uterus). Endometrial cancer usually occurs post-menopause, but not always.

Vaginal cancer forms in the tissues of the vagina (also known as the birth canal). The vagina leads from the cervix (the opening of the uterus) to the outside of the body. The most common type of vaginal cancer is squamous cell carcinoma, which starts in the thin, flat cells lining the vagina. Another type of vaginal cancer is adenocarcinoma, cancer that begins in glandular cells in the lining of the vagina.

Vulvar cancer is cancer of part or all of the external female genitalia, including the clitoris, labia (vaginal lips), and the opening to the vagina. Vulvar cancer usually forms slowly over a number of years and is mostly asymptomatic. However, when
Wood Dust

In 1981, the International Agency for Research on Cancer (IARC) found strong evidence of a causal relationship between sino-nasal adenocarcinoma and occupations in woodworking industries, particularly furniture and cabinetmaking. It did not, however, find at the time sufficient causal evidence of a link between specific types of cancer and working in sawmills, carpentry, and joinery, and in the pulp and paper industries. Adenocarcinoma of the nasal cavities is a rare type of tumor. It constitutes about three percent of tumors in the upper respiratory tract. The sinus is the most common location for adenocarcinomas related to wood dust. The proximity of adenocarcinoma tumors of the sinus to organs of vital importance such as the brain, optic nerves, and carotid arteries poses significant risks. Initially, gleaned from information available in the late 1960s and early 1970s when studies were first initiated, the average annual incidence reported in people older than age 15 was approximately zero to eight per million in men and zero to four per million in women. The disease today is more common in people between 45 and 85 years of age, and after many studies, continues to be linked to wood dust. Other causes for sinus tumors are viral infections, such as the human papillomavirus, which can produce a benign tumor.

The first study on adenocarcinoma of the nasal cavity, published in Britain in the early 1970s, showed evidence of the relationship between working in the furniture industry and adenocarcinoma. Follow-up studies sought to find out if the increased risk for this tumor, associated with the woodworking industry, occurred in other parts of the country. After that, similar studies were performed in other regions of Europe, all showing similar results.

In 1981, IARC considered the woodworking and related industries in the category of occupational and cancer hazards. In the beginning, scientists at the IARC considered the possibility that
carcinogens in wood were the culprits for cancers, rather than chemicals used in processing wood. Despite some deficiencies in the research results, which left some questions unanswered, the IARC scientists established that their finding that nasal adenocarcinoma is caused by breathing wood dust—especially hardwood dust—was reasonable. They also found that there was no indication that dust wood caused other forms of cancer.

In 1987, the IARC classified cabinetmaking as Group 1, that is, establishing that sufficient evidence had been found of carcinogenicity, largely on sino-nasal adenocarcinoma, in humans related to this occupation. Other related woodworking occupations, such as carpentry and joinery, were classified as Group 2B, that is, of possible carcinogenicity to humans. Lumber, sawmill, and the pulp and paper industries were classified as Group 3, that is, not classifiable as to its carcinogenicity to humans. In general, carcinogenic risks to humans in the woodworking industries are related to exposure to wood dust, and other related forms of cancer can be linked to chemicals used in woodworking, such as formaldehyde. Workers may be exposed to formaldehyde in the manufacture of plywood particleboard and furniture, and during wood floor sanding and varnishing. Cancer risks linked to chemicals used in woodworking affect areas such as the oral cavity, larynx, pharynx and respiratory tract. However, studies have proven inconclusive.

The most common exposure to wood dust occurs in the manufacture of furniture and cabinetmaking, in particular during machine sanding. In plywood and particleboard mills, the highest level of exposure occurs in the finishing occupations, and in sawmills, in the workshop air, especially near saws, planers, and related equipment.

Symptoms for early nasal cancer are the same as for noncancerous conditions, and include: nosebleeds from one nostril, blockage of a nostril, and runny nose on one side. Tumor advances can cause persistent headaches and double vision or other changes in vision.

Background
Death and disease from occupational cancers usually take place several years, even decades, after initial exposure to the carcinogenic agents. Therefore, many scientists state that it is important to consider the pattern of particular industries at least two decades before beginning a study period. In the 1950s, furniture manufacturers in London hired large numbers of workers. Based on previous anecdotal evidence, it was not unexpected to find an association between nasal cancer and trades related to woodworking. The first link between cancer and woodworking occupations was found in 1965 among male British woodworkers. Many other studies since then have shown that high exposure to wood dust is related to the highest risk for nasal adenocarcinoma, particularly in Europe. Other types of cancer, such as nasopharynx, larynx, and lung cancers and Hodgkin's disease, have also been associated with exposure to wood dust; most of the evidence for these other types of cancer, however, is still inconclusive.

The prevalence of nasal cancer has been linked to the type of wood dust to which individuals are exposed. Wood dust falls into two general categories: softwood and hardwood. Softwoods, such as pine, are inexpensive and easier to work with. Hardwoods are heavy, harder woods and come mostly from deciduous trees. Wood dust is created during the cutting, sanding, and shaping of wood materials, and the type of dust generated varies according to tree species. The most deleterious effects for sinonasal cancer among woodworkers have been observed in those who work with oak and beech wood. In 2001, a European study titled “Risk Assessment of Wood Dust: Assessment of Exposure, Health Effects and Biological Mechanisms” was launched in Europe with the aim of measuring exposure to wood dust. An occupational exposure database—WOODEX—was developed, providing information on wood dust exposure in 24 European Union states. The database offers estimates of exposure to inhalable wood dust classified by state and industry, as well as level of exposure and type of wood. The European Union, which recognizes hardwood dust as a carcinogen, has set the occupational exposure limit to five mg of inhalable dust per cubic meter of workroom air. The WOODEX database estimates that approximately five million workers in the European Union are possibly exposed to dust levels exceeding five mg.

Cancer related to wood dust is rare. Studies have been performed to find out if, besides exposure to hardwood dust, cancer may also be related to the textile, leather, and other industries that produce chemicals and dust. Other supposed factors for nasal cancer are exposure to formaldehyde, nickel compounds, and chromates, although the evidence remains limited. Wood dust may also cause or exacerbate non-cancer diseases, such as asthma.
Millions of workers are exposed at work to inhalable wood dust, the majority of them woodworkers who must often use machinery indoors with no general ventilation or exhaust systems. Carpenters are believed to be the largest group of workers with significant exposure to wood dust, although the duration and level of exposure is still not clearly known. The concentration of wood dust is higher in the furniture and cabinetmaking industries than in other areas, such as in sawmills. Sawmills probably also offer a different level of exposure, because they tend to work with green softwoods. Furniture plants tend to use dried hardwoods.

In the United States, 25 states abide by the Occupational Safety and Health Administration (OSHA) federal standards, which support the five-mg-per-cubic-meter airborne particle standard established by the European Union. In other states, the industries have adopted their own standards and enforcement policies; these, however, tend to be similar to federal OSHA standards.

Research
A study performed in Denmark found double the risk for sino-nasal cancer in male workers in wood-related occupations than for those who had never worked in a wood-related job. No such excess risk was observed among workers in forestry, logging, and pulp and paper mills. A series of studies in Britain up to 1986 reiterated that a surge of male mortality in London in the 1960s and 1970s was related to excessive exposure to wood dust. Bladder cancer was also associated with occupations in road transport driving, as well in leather-working, and a consistent relative risk was also found for woodworkers, machinists, plumbers, and mechanics. These findings not only reinforce, directly or peripherally, the role of wood dust in occupational-related nasal cancer, but also the role of occupational factors in cancer causation. According to a number of studies, overall, the only occupational category with a significantly increased risk for nasal cancer was woodworking. The studies controlled for other possible cancer-causing factors and activities, such as smoking. No evidence was found in this type of cancer linked to other dusty trades, such as textile and clothes manufacturing.

By the mid-1990s, wood dust had been classified as carcinogenic to humans, and evidence with nasal cancer had been observed in a large number of studies. Besides confirming previous findings, some suggested further research into other occupational sectors possibly at risk, such as shipbuilding and repairing.

In general, wood dust is the most frequent carcinogen found in occupational exposures reported not only by the IARC but also by Italian Information System on Occupational Exposure to Carcinogens (SIREP), which confirmed the results of distinct European studies that found this widespread risk exposure in all of the European Union member states. The SIREP database, which is available for research, contains records from 1,822 companies and 11,322 workers exposed to wood dust, collected from 1996 to 2006.

Following the publication of the SIREP study, a 2006 research project performed among sawmill workers in Finland found an excess of pharyngeal cancer but just a slight excess of nasal cancer. This study is of interest because Finnish woodworking industries rely mostly on softwood, such as pine and spruce. According to scientists, the small risk for nasal cancers produced by wood dust represented among workers in this study seems to corroborate that softwood pine dust presents fewer risks than hardwood for sino-nasal cancer. However, the same study found a higher rate of lung cancer linked to dust in paper mills.

Studies have also been made in several other countries. They all corroborate that risk for
adenocarcinoma from wood dust increases with duration of exposure. These studies also shed light on different types of cancer possibly related to wood dust. An increased risk of squamous cell carcinoma, for example, was found solely among workers employed for 39 or more years in jobs with exposure to fresh wood. The results of different studies strongly support the association of the exposure to wood dust in a variety of wood-related occupations and specific types of nasal cancer. The magnitude of risk, however, has varied across different studies.

Trudy Mercadal
Florida Atlantic University

See also: International Agency for Research on Cancer; Laryngeal Cancer; Nasopharyngeal Cancer; Nickel Compounds; Paper Industry; Paranasal Sinus and Nasal Cavity Cancer; Wood Preserver; Workplace Wellness Programs.

Further Readings


Wood Preserver

There are many types of wood preservers available on the market, for use in a variety of settings, from industrial and commercial to residential. Agencies in the United States, such as the Occupational Safety and Health Administration (OSHA) and the Environmental Protection Agency (EPA), Australian Department of Agriculture, and the International Agency for Research on Cancer (IARC) have determined that many wood preservatives are carcinogenic and are causal agents in many acute and chronic health conditions. Wood preservatives frequently contain arsenicals, copper, chromium, creosote, formaldehyde, naphthenate, and penta compounds. Exposure to these compounds cause impaired immune systems, cancer, infertility, birth defects, fetal death, genetic mutations, hormone dysregulation, and peripheral nerve degeneration, making them an environmental concern.

Creosote is the most common oil-type preservative, used industrially, commercially, medicinally, and residentially. As a wood preservative, creosote is now only approved for commercial applications. Creosote is and has been used medicinally in many cultures. In the United States, the Native Americans living in the southwest used larrea tridentate, the creosote bush, to treat tuberculosis. It was also used as an antibacterial, an antiseptic poultice, and a caustic agent for wounds and sores, for joint and limb stiffness, snake bites, menstrual cramps, intestinal complaints, and as an emetic. In the Caribbean, it was used to treat tropical diseases and syphilis.

Farther back in history, substances such as pitch and resins were used for toothaches, to kill parasites, and to treat phthiriasis, porrigo, elephantiasis, and ulcers. Medical books written in the 1800s recommend using creosote to treat dyspepsia, induce vomiting, improve wound healing, and decrease tumors. During the 1900s, it was sold in pharmacies as aqua creosoti. Physicians believed that it was an effective treatment for gastrointestinal complaints, detoxification, to kill entozoa parasites, treat ulcer and abscess, epilepsy, neuralgias, diabetes, and glanders, and stimulate throat mucosal tissue. Livestock was dipped in a solution of creosote to kill external parasites. McDougall’s Powder was sold as a sewer deodorant.

Despite wood preservatives being listed as a toxic agent, including creosote and its chemical byproducts, it can be found in medications such as guaifenesin, an over-the-counter expectorant found in cough syrups. In Japan, seirogan, a popular Kampo medicine prescribed as an antidiarrheal, is made from
133 milligrams of creosote from beech, pine, maple, and oak trees. Forms such as kreosotum, chaparral, or kreosote are found in herbal supplements.

From the 1830s on, wood preservatives have been used in food processing. Liquid smoke is a commercially available additive designed to add a smoky flavor to meats. This product is primarily comprised of creosote. In 1987, the United States restricted the use of pentachlorophenol (PCP) as a pesticide. However, PCP is still used in restricted applications, such as utility poles, railroad ties, and wharf pilings. It is a toxic substance that is labeled a human carcinogen, and is linked to other serious health risks. Other oil-based wood preservatives are copper naphthenate, oxine copper (copper-8-quinolinolate), and 3-lodo-2-propynyl butylcarbamate (IPBC).

**Formaldehyde**

Waterborne preservatives are compounds that are water soluble or readily mix with water. One of the most common water-soluble wood preservatives is formaldehyde. This chemical is pervasive in the environment. It is classified as a preservative and a disinfectant. One will find formaldehyde in drinking water, cosmetics, plastics, fungicides, resin glues, embalming fluid, carpets, clothing, tobacco, and combustion appliances. In construction, pressed woods that are glued together with adhesives are made of urea-formaldehyde (UF) or glued together using resin glues have the highest concentrations. Some examples of pressed wood are particle board, paneling, hardwood plywood, and medium-density fiberboard.

UF is measured in parts per million (ppm), and reactions in adults are seen in as little as 0.1 ppm. The elderly, children, and those with allergies and respiratory problems are even more susceptible to reactions at lower doses than 0.1 ppm. At levels of 1,000 ppm or higher, or with chronic exposure, it can be carcinogenic. In most settings, levels are well below the recommended 0.1 ppm, but levels can be higher in mobile homes, manufactured homes, and newer construction because of the large amount of pressed wood or UF foam insulation used in the construction. Off gassing of the UF occurs within the enclosed space, so proper ventilation is necessary. When UF foam insulation is used, holes and cracks should be filled with spackle or caulk, and walls painted or wallpapered with vinyl to reduce gas exposure.

**Copper**

Comprised of chromium, copper, and arsenic, chromated copper arsenate (CCA) was once heavily used in residential settings. Because of its tendency to leach into the surrounding environment and transfer through dermal contact with the treated wood, it is no longer approved for residential uses, but it is still used. When an individual comes into contact with the treated wood, and then eats, smokes, or has any hand to mucous membrane contact, ingestion of CCA can occur. Long-term exposure to the arsenic found in this compound increases the risk of cancer. Acid copper chromate (ACC) is only used in industrial and commercial settings. Treated wood contains hexavalent chromium, also called chromium VI. This substance has the highest EPA toxicity rating for oral, dermal, and inhalation toxicity. Chromuim VI has been shown to cause cancers in the lungs, nasopharynx, oropharynx, and nasal passages, liver damage, leukcytosis, leukopenia, eosinophilia, chronic obstructive airways diseases (COPD), dermatitis, ulcerations, and kidney disease.

Alkaline copper quaternary (ACQ) compounds have four classifications: A, B, C, and D. All classes are made using various percentages of copper oxide (62–71 percent) and aquaternary ammonia (29–38 percent). This chemical is listed as an insecticide and a fungicide. As a water-based preservative, ACQ leaves the surface dry and paintable. Because this compound does not contain arsenic or chromium, it is found in residential settings such as lumber, fence posts, decking, landscape ties, wooden play structures, utility poles, sea walls, wood shingles, pilings (land, freshwater, and marine), and other wooden structures. When exposures remain below toxicity levels, there are minimal health risks. Bis-(N-cyclohexyldiazeniumdioxy)-copper (Cu-HDO) is composed of copper and N-cyclohexyldiazeniumdioxy (HDO). Pressure-treated lumber, poles, millwork, and pilings are oftentimes coated with this preservative. It does not readily leach into the soil, but it is highly toxic in aquatic environments. If used in the packaging of food, livestock feed, or construction of beehives, toxicity can arise.

Copper azoles (CA) comes in two forms: Type A known as CBA-A because it contains copper, boric acid, and tebuconazole, and Type B, called CA-B, which lacks boric acid, but has higher concentrations of copper and tebuconazole. This substance is approved as a wood preservative in above and
belowground and fresh and saltwater applications. Micronized copper is a newer form of ACQ and CA. The difference in micronized copper is the presence of tiny particles of solid copper carbonate, instead of the soluble copper found in ACQ and CA. Because the copper is still in a solid state, there is some likelihood the particles will leach from the treated wood, leading to health and environmental risks.

**Borates, Azoles, and Fire Retardants**

Disodium octoborate tetrahydrate are naturally occurring minerals that comprise borate wood preservatives. These are used to protect wood from fungus, termites, and other wood-boring organisms. Because of the low toxicity of borates, they are used on interior applications such as joists, sheathing, and sill plates. Cyproconazole is used on above-ground wood products and as a fungicide on crops. Currently, cyproconazole is approved by the EPA for surface application of siding, plywood, millwood, lumbar, and shingles. The antimicrobial didecyldimethylammonium chloride (DDAC) is found in some of the cyproconazole products. Propiconazole is an antifungus designed to prevent wood decay. It is used to treat above-ground wood. It is also a fungicide for turf, ornamental plants, and food and livestock feed crops, and as an antimicrobial preservative. The Food and Drug Administration (FDA) approved this compound for surface application and pressure treatment of siding, plywood, millwork, shingles and, and above-ground timber and lumber. Other water-soluble wood preservatives include copper sulfate, sodium fluoride, mercuric chloride, arsenic compounds containing fluorine, chromium, ammoniacal copper zinc arsenate (ACZA), and phenol.

In laboratory tests, wood treated with fire retardant chemicals (FRT), including formaldehyde phosphoric acid, amine-aldehyde-phosphorus, and phospho-ammonium boron compounds, are highly effective in suppressing the spread of flames and decreasing smoke, and will withstand combustion for approximately 30 minutes when directly exposed to flames. They are used for the interior of structures requiring fire retardant construction materials, and when required by building codes. FRT can be found on trusses, plywood sheathing, decking, rafters, studs, walls, subfloors, joists, beams, stairways, and paneling. Classified as a Group 1 human carcinogen and a skin and lung irritant, FRT wood should not be burned nor used as chips, mulch, or sawdust. Occupational exposure can cause adenocarcinomas of the nasal cavities and paranasal sinuses. The OSHA considers the dust to be a potential explosive hazard when combined with air and an ignition source.

**Health Risks and Protection**

The health risks associated with wood preservatives vary by compound. Statistically, there is a significant increase in the incidence of adenomas, carcinomas, adrenal medulla pheochromocytomas, malignant pheochromocytomas, hemangiosarcomas, and hemangiomas when exposed to pentachlorophenols in wood preservatives. Creosote has a high likelihood of causing cancer, and arsenicals have been proven to cause cancer in humans. In animals studies, cresols, a component in creosote, intensifies the effect of some carcinogenic chemicals. Arsenic, either ingested or inhaled, increases the risk of liver, bladder, kidney, and lung cancers. Occupational exposures to wood products containing penta have a direct link with acute leukemias, Hodgkin’s and non-Hodgkin’s lymphoma, and multiple myelomas. The hexachlorobenzene and hexachlorodibenzo-p-dioxins, penta components, cause soft-tissue sarcoma and non-Hodgkin’s and Hodgkin’s lymphoma.

When working with any wood treated with preservatives, personal protective equipment should be used. This type of equipment includes leather gloves, safety glasses, or chemical goggles, a NIOSH approved P95 or P100 particulate filter respirator, and a long-sleeved shirt, pants, and steel-toed boots. Hands should be thoroughly washed prior to any mucosal membrane contact. Disposal of all wood treated with preservatives or its byproducts fall under municipal, state, and federal guidelines, and may be considered hazardous waste. In order to avoid environmental contamination, all unused materials, residues, and containers must be properly disposed of.

Justina Higgins
Independent Scholar

**See Also:** Chemical Industry; Leukemia, Acute Lymphoblastic, Adult; Lymphoma, Hodgkin’s, Adult; Lymphoma, Non-Hodgkin’s, Adult; Myeloma, Multiple; Pheochromocytoma.
Further Readings

Workplace Wellness Programs

Workplace wellness can be defined as a program or set of programs organized and supported by firms and other organizations, designed to lend support to employees (and sometimes their families), as they adopt and maintain lifestyle and personal behaviors aimed at reducing health risks and increasing personal quality of life. These benefits are understood to transcend the individual and benefit the organization at large. In other words, healthy employees cost less and produce more.

Modern firms today understand that human capital is their most important resource. Therefore, having employees who are healthy in mind and body is important for the long-term survival and competitiveness of most organizations. Cutting-edge firms often increase the quality of their labor resources by way of corporate wellness programs, which results in increased productivity, creativity, and commitment from employees and other stakeholders or interested parties. Evidence-based research shows that wellness programs also reduce levels of stress and absenteeism, as well as medical expenses. According to the World Economic Forum (2008), businesses that implement wellness and health programs obtain the following rates of return upon investment: 30 percent increase in productivity; 35 percent increase in creativity and innovation; 40 percent decrease in employee turnover; and 60 percent increase in employee sense of ownership.

Wellness Program Implementation
According to published Harvard studies in the area of workplace wellness, providing medical personnel in the workplace—a doctor or nurse—achieved a decrease of up to 80 percent in absenteeism for a period of six years. The authors of one study (2010) explained that providing access to a gym and to nutritional information in the workplace is simply not enough. A firm must invest more in developing an effective and sustainable workplace wellness program. Experts also recommend these six pillars for an effective workplace wellness program: (1) multilevel leadership, (2) alignment, (3) scope, relevance and quality, (4) accessibility, (5) partnerships, and (6) communication.

Leadership works to create and integrate a health culture in the organization. This requires, at all levels, leadership that is dedicated, persuasive, and persistent. It requires commitment and strategizing from upper-level management, and also that middle management act in order to integrate wellness goals into organizational strategies and goals. Alignment refers to actions and strategies that reinforce the natural extension of the firm’s identity and its goals. These should include wellness programs. It is important to bear in mind that cultural changes—including wellness program integration—take some time to develop properly and to produce outcomes.

Scope, relevance, and quality refer to designing wellness programs that are holistic or comprehensive and attractive. Otherwise, employees will not feel engaged, and the program will lack participation. Accessibility refers to services that are either low cost or free of charge. Making it as accessible and as user-friendly as possible should be a priority. Partnerships refer to active and constant collaboration with internal and external associates, including providers and vendors. These partnerships can help provide some of the essential components to a wellness program and many enhancements as well.

Finally, communication is a very important component of the wellness program strategy. Wellness is not just a goal; it is also a culture, and communication is key. The delivery of the message can
produce a marked difference in how it is received by the target audience. It is important to create messages that are not only informative but also creative, attractive, and sensitive to diversity. It is also important to consider a wide variety of media options for the dissemination of the message.

Research has also shown the following outcomes:

1. Lower costs. Savings in health services, just by themselves, show significant rates of returns on investments.
2. Higher rates of productivity. Participants in wellness programs show reduced levels of absenteeism and higher workplace performance than employees in organizations that do not participate in wellness programs.
3. Higher levels of morale. Pride, trust, and commitment among employees have been shown to grow.

A wellness program, then, is not just about workers’ health. It also includes organizational actions that serve to increase workplace safety, productivity, organizational culture, and work-family integration.

**Research Outcomes.**

Workers today are increasingly at risk for noncommunicable diseases related to aging and lifestyle. These include diabetes, cancer, cardiovascular and chronic pulmonary diseases, and mental health issues as well. The World Economic Forum’s Workplace Wellness Alliance estimates that as rising economies grow, talent gaps for up to 45 million workers in Western Europe are forecasted for 2030. This trend must be considered in light of the growing risks for aging and disease, which decrease productivity in the workplace. In fact, it is estimated that noncommunicable diseases will cost about $47 million over the next two decades. Studies done in 2010 show that workplace absenteeism and underperformance had already caused productivity losses worth up to $16.8 trillion, mostly related to cardiovascular disease and mental illness combined. These numbers, according to experts, could double by 2030.

In 2008, the World Health Organization estimated that 36 million of the 57 million global deaths were due to noncommunicable diseases, mainly cardiovascular disease, cancer, chronic respiratory disease, and diabetes. The United Nations noted with considerable concern that these noncommunicable diseases were among the leading causes of preventable mortality. In 2011, the United Nations’s Political Declaration on the Prevention and Control of Non-Communicable Diseases convened a General Assembly in order to address the prevention and control of noncommunicable diseases worldwide, focusing on developmental and other challenges at the social and economic levels, especially for developing nations. It also issued a call for the private sector to lead workplace wellness initiatives as part of the solution to these worldwide challenges. The Workplace Wellness Alliance was born in 2010 as a response to this call for action. Currently, it numbers 150 members from across industries and aims to improve health and productivity in the workplace.

Today, there is a growing understanding that government and workplace policies and alliances are of crucial importance in reducing levels of exposure to modifiable risk factors for noncommunicable diseases, such as smoking and exposure to secondhand smoke, unhealthy dietary habits, low levels of physical activity, abuse of intoxicants, and others. They are also of critical importance in encouraging and supporting healthy lifestyle habits, so that individuals and groups may make healthier informed choices and follow healthful lifestyles. This would not only result in tangible and intangible benefits for firms, but enhance the quality of life in society at large.

Trudy Mercadal
Florida Atlantic University

**See Also:** Health Advocacy; Healthy People; Sedentary Occupations; World Health Organization.

**Further Readings**


World Health Organization

The World Health Organization (WHO) is an agency within the United Nations (UN) responsible for directing and coordinating health for the UN. The responsibilities of the WHO include: establishing health policies for the UN, providing leadership in health issues worldwide, setting the international health research agenda, monitoring and assessing health throughout the world, and providing assistance to individual regions that may require aid. Member states have agreed upon a set of categories of work for the WHO to focus their attention on communicable diseases, noncommunicable diseases, promoting health through the life course, healthy systems, and preparedness, surveillance, and response. These categories help to determine the WHO’s priorities and agenda. The overall WHO agenda consists of six points of response to global public health: promoting development, fostering health security, strengthening health systems, harnessing research information and evidence, enhancing partnerships, and improving performance.

All countries that are members of the UN may become members of the WHO simply by accepting the WHO constitution. To date, all UN member states have accepted the WHO constitution and are therefore also a part of the WHO. Countries that are not members of the UN may also be admitted as members of the WHO by a majority vote of the World Health Assembly. Territories may also apply to be Associate Members through the country that is responsible for their international relations. There are 194 member states of the WHO. The headquarters of the WHO are located in Geneva, Switzerland, with regional offices found around the globe. The regions of the WHO are the African region, region of the Americas, European region, eastern Mediterranean region, and the western Pacific region.

World Health Organization and Cancer

The WHO reports that cancer accounted for 8.2 million deaths worldwide in 2012. The leading types of cancer worldwide are: lung, liver, stomach, colorectal, breast, and esophageal cancers, accounting for 4.673 million cancers. More than 60 percent of the world’s new annual cases of cancer occur in Africa, Asia, and Central and South America, with those regions accounting for 70 percent of the world’s cancer deaths.

The WHO supports many countries in all facets of health, with one such targeted area being cancer. This disease is addressed in the WHO Cancer Control Programme. The WHO Cancer Control Programme’s mission is to promote national cancer control policies, plans, and programmes. The WHO Cancer Control Programme’s core tenets are to encourage evidence-based prevention, early detection, treatment, and palliative care tailored to different regions of the WHO member states.

Contrary to the belief that cancer is a disease that mainly occurs in industrialized countries, it is estimated that half of all cancer patients are in developing countries. However, unlike industrialized countries, developing countries lack the resources for systemic cancer control. In low- to middle-income countries, people tend to develop chronic diseases like cancer at a younger age and suffer longer, often from preventable complications, and die younger than those in high-income countries.

The WHO clusters member countries together by region. Each region has different foci for cancer intervention strategies based on what is most relevant to that area.

Fifty-five percent of the member states report having capable health system response and capacity to address and respond to noncommunicable diseases as well as having an operational policy/strategy/action plan for chronic cancer. Thirty-eight percent of member countries report not having a clear operational policy/strategy/action plan for chronic cancer. The member countries without these plans are most often low- to middle-income countries.
While the WHO does not create national action plans on cancer for every member country, it does offer insights into what each of the tenets of the WHO Cancer Control Programme entails. The WHO has created an overarching plan to help guide member countries as to what a successful detailed plan of action would look like.

At the core of the WHO Cancer Control Programme lies the cancer priority ladder. This ladder is what the WHO believes to be the most pressing issues when it comes to cancer control in a country. The ladder includes the steps of tobacco control, a curable cancer program, a healthy eating program, effective pain control, referral guidelines, clinical care guidelines, nurse education, national cancer networks, clinical evaluation, basic and clinical research programs, and an international aid program. By focusing on each of these aspects of the cancer priority ladder, countries are better equipped to handle cancer epidemics. More broadly based, the WHO Cancer Control Programme includes the four main tenets of prevention, early detection, treatment, and palliative care.

**Prevention**
The first and largest step to cancer control is preventing cancer from developing. The WHO highlights tobacco, obesity and physical inactiveness, alcohol use, infections, environmental pollution, occupational carcinogens, and radiation as preventable causes to cancer. One-third of all cancers stem from a preventable cause, and by reducing incidence of these things, a country can lower its incident rate of cancer. While each of these preventable causes can be found across the world, certain causes are more prevalent among higher-income countries versus lower-income countries. Low-income countries are more prone to cancer from infections such as HBV/HCV and HPV, and environmental pollutants such as indoor coal use for cooking than high-income countries. Obesity and physical inactiveness is more often a cause of cancer in high-income countries, especially those with high-processed-food diets.

**Early Detection**
Detecting cancer in early stages greatly increases the chances of survivability and successful treatment. Early detection comes in two parts: educating the population about cancer signs and symptoms as well as screening for cancer. It is important to note that screening may be used as an early diagnostic tool, but that is not the sole purpose of screening for cancer. Screening healthy populations can trace the risk factors of a population as a whole. Screening campaigns are often initiated by governments, public health entities, or health service providers, and not by the individuals being screened. Therein lies the difference between true diagnostic tools and screening campaigns.

Screening is an aspect that many countries even with health action plans lack due to limited resources and funds. Screening is only effective if it can be broadly employed in nearly the entire targeted group without causing resource depletion. Screening facilities and tools can often be expensive and unsustainable for remote low-resource areas. Early detection screening should only be concerned with detecting diseases and disorders that cause significant suffering, disability, or death, not in detecting trivial or untreatable conditions. Detecting these trivial conditions can cause unwarranted anxiety and waste resources, especially in low-resources regions.

The WHO only recommends undertaking screening programs if they can be fully supported by the community. Not only does the implementation and execution of screening processes need to be supported, but also the evaluation of the data collected. Communities may have the resources to carry out screening measures, but they must also have the resources to understand and apply the data collected. The WHO looks to studies on low-cost screening to inform the low resource countries as to how to best offer screening programs to their region’s populations.

**Treatment**
The WHO offers less advice for how countries should implement treatment in their action plans, as this is a highly subjective part of the cancer experience. Initial diagnosis is integral in the treatment of cancer, regardless of the cancer or the region. However, the next steps are subjective to the type of cancer, the stage of cancer, and the resources available to the population. The most effective treatment plans are often those that (1) are sustained and equitable, (2) are linked to early detection, and (3) follow evidence-based standards of care and utilize a multidisciplinary approach.
Typical treatment options include surgery, radiotherapy, and chemotherapy. These treatment methods are used independently or in conjunction with one another. All of these options may not be available to lower-resource communities that will need to adapt different strategies to cancer eradication. The ultimate goal of cancer treatment is either to cure or prolong the life of patients and provide the best quality of life to survivors.

**Palliative Care**

Palliative care is an interdisciplinary approach to improving the life of patients and families facing life-threatening diseases. Palliative care provides pain and symptom relief, as well as spiritual and psychosocial support. Using a team approach to dealing with cancer offers support to both patients as well as their families. Palliative care is an integral part of coping with cancer for patients and their families as it is intended to provide relief from the burden of cancer. In most of the world, cancer is not detected and diagnosed until late stages of the disease. This means that palliative care is mostly focused on end-of-life care, and how to cope with pain management, death, and bereavement for patients and their surviving families.

The WHO offers a cancer pain ladder to those patients in end-of-life palliative care. This ladder is a means to make patients feel more comfortable and explains how medication should be administered to provide the greatest relief from pain.

**WHO Cancer Research**

The WHO offers specialized guidance to low- and middle-income countries. In addition to the WHO Cancer Control Programme as a guide, the WHO also offers a guide directed at those countries with lower socioeconomic standing. This guide offers six modules that provide practical advice to policy makers and programme implementers. The guide follows the four main tenets of the Cancer Control Programme, with the two additional modules of planning and policy/advocacy. These two extra modules are especially important in low-income countries, as there may be little experience with forming national programmes and a potentially difficult bureaucracy to go through. This guide is of great importance to the WHO, as 70 percent of world-reported deaths from cancer come from low-to middle-income countries.

Not only does the WHO offer guidance to its member states as to how to handle cancer incidence on the individual level, but it also conducts its own research on a broader level. The WHO traces epidemiology on different types of cancers and also does in-depth research on factors that may cause different cancers.

The main WHO research center for cancer is located in Lyon, France, at the International Agency for Research on Cancer (IARC). The IARC’s main objectives in cancer research are: monitoring global cancer occurrence, identifying the causes of cancer, explaining mechanisms of carcinogens, and developing scientific strategies for cancer control.

The WHO has offered in-depth looks at the histories of most major cancers including lung cancer, cervical cancer, and breast cancer among others. The WHO has also researched specific environmental causes to cancer such as air pollution and cell phone use as well as world events such as environmental carcinogens from the meltdown at the Japanese nuclear power plant in 2011 that was caused by a tsunami triggered by an earthquake.

The WHO is a multidimensional organization that uses all facets of public health to eradicate suffering caused by cancer. With the global cancer epidemic on the rise, the WHO uses every resource available to aid in the reduction of cancer worldwide and to help countries take the cancer epidemic into their own hands through program and policy implementation as well as general education about the deadly disease.

Courtney Vail Fletcher
Chelsea Halstead
*University of Portland*

See Also: International Agency for Research on Cancer; Pain and Pain Management.

Further Readings


World Health Organization Framework Convention on Tobacco Control

The idea for the World Health Organization's Framework Convention on Tobacco Control, or WHO FTCT, was born in 1993, with a recommendation by Ruth Roemer and Allyn Taylor. They proposed that the World Health Organization (WHO) use its standing in order to develop international conventions to promote public health at the international level. Roemer and Taylor also proposed the concept of the framework convention and protocol, which they designed to develop international coordination to fight against the tobacco epidemic. After some initial resistance, the idea was gradually accepted by the WHO; after negotiations with member states, it was discussed at the World Health Assembly in May 2003 so that it could be formally voted upon. The WHO Framework was adopted by consensus that same year, and was enacted in 2005.

The WHO FTCT was the first treaty negotiated by the WHO. The treaty is based on empirical evidence and takes a new angle to the traditional way of addressing addictive products. As opposed to other treaties on addictive substances, the WHO FTCT focuses not only on supply issues, but also on ways to reduce demand. The objective of the convention and its protocols is to protect people from the catastrophic consequences of consuming tobacco and exposure to secondhand tobacco smoke. These consequences cover the areas of health, social, and environmental damage. In order to achieve this, the WHO FTCT provides a framework for tobacco control measures to be implemented by the convention signatories at all levels—national, regional, and international—so that the prevalence of tobacco use, consumption, and exposure to its smoke can be significantly reduced.

The trigger for the inception of the WHO FTCT was the growing worldwide expansion of the tobacco epidemic. The global increase of tobacco occurs due to a wide range of social and economic factors, including the prevalence of lifting trade regulations. Other contributing elements are global tobacco marketing, sponsorships, advertising, and promotion, and the increasing illegal trade of tobacco products. The latter includes contraband and counterfeiting of tobacco products.

The FTCT provides a global coordinated action meant to combat the tobacco epidemic, setting distinct steps for states to use in developing policies related to tobacco use. To summarize, the provisions of the WHO FTCT that aim to reduce tobacco use and its effects are listed in articles 6 to 14 of the published document: protection from exposure to tobacco smoke; regulation of contents of tobacco products; regulation of tobacco product disclosures; packaging and labeling of tobacco products; education and other measures of public awareness; issues of tobacco advertising, promotion, and sponsorship; and demand of reduction measures concerning tobacco dependence and quitting. It also
includes price and taxation measures in order to decrease the demand for tobacco.

The principal reduction provisions in the WHO FCTC are published in articles 15 to 17 and include illicit trade in tobacco products, sales to and by minors, and support for economically viable alternative activities.

The Convention
A treaty or convention is an agreement enacted between nations and international entities that have been given treaty-creating rights. Treaties are meant to fall within the framework of international law, and nations that become signatories commit to following its rules. Treaties may take many forms and become known under other denominations, such as conventions, protocols, charters, acts, statutes, and others. Conventional international law requires treaties to be ratified by all signatory parties. Therefore, additions such as amendments and protocols must be unanimously agreed upon by all signatories to the main treaty.

The WHO FCTC, the first international treaty created under the WHO, was opened for signature in June 2003 in Geneva, Switzerland. From then until June 2004, the institution in charge of the treaty was the United Nations. The treaty has 168 signatories, making it one of the mostly widely accepted treaties in the history of the United Nations. Signatory states commit to working to ratify, accept, and approve the treaty. Although the document has been closed for signatures, states that wish to sign on may do so by way of a process called accession, which is equivalent to ratification of the treaty. The convention was enacted on February 27, 2005, after being approved or ratified by 40 nations. It provides a new stepping-stone for broader dimensions of international cooperation for public health. It was signed by 168 of the 192 WHO member states.

The Protocols
Humanitarian treaties are often followed by protocols, which are annexed or adopted to provide tools and procedures for a treaty or convention, or to a specific part of a treaty. These protocols are considered treaties by themselves. As with the original treaty for which they provide support, they are opened for signature and ratification by states that are parties to the main treaty. The first protocol to the WHO FCTC was accepted in November 2012 at the Conference of the Parties in Seoul, South Korea. The protocol was opened for signature from January 2013 to January 2014. The protocol counts 53 signatory states as well as the European Union. The Protocol has been opened for ratification and approval by all WHO FCTC parties. As with the treaty, it will be enacted as soon as it is ratified by 40 states.

The purpose of the Protocol is to eliminate all forms of illegal trade in tobacco products. It offers resources for the prevention and fight against illegal trade, including licensing for the manufacture, import, and export of tobacco products and related manufacturing equipment, as well as a tracking system for all tobacco products made in a specific area or region.

Summary of Core Areas
The convention is fact-based; it relies on scientific evidence that establishes that exposure to tobacco is directly linked to death, disease, and disability. It is also concerned with the deleterious consequences of tobacco use worldwide. Therefore, it urges all signatories to commit to the adoption and implementation in their respective national jurisdictions, of legislative, executive, economic, and other measures that protect the public from the use of tobacco, and the exposure to secondhand tobacco smoke in the environment. It encourages the formation of policies that will provide protection from exposure to tobacco smoke in indoor public places, public transportation, and other public places deemed appropriate.

The convention document is divided into 11 parts and two annexes. The core issues are laid out in Parts II (articles 3–5), III (articles 6–14), IV (articles 15–7), and V (article 18). Part II provides the objective, guiding principles, and general obligations; Part III lists the measures relating to the reduction of demand for tobacco; Part IV refers to measures relating to the reduction of supply of tobacco; and Part V deals with environment protection. Among the strategies for the reduction of tobacco demand, for example, are price and tax measures, which are expected to deter consumption particularly among young people. It also incorporates financial and nonfinancial measures to reduce consumption.

Other important articles list the scientific and technical cooperation measures that will be
undertaken to develop, promote, and coordinate tobacco control-related research programs at the regional and international levels. The signatories commit to create scientific programs that will establish surveillance of patterns, factors, and consequences of tobacco consumption and exposure to tobacco smoke; to establish national systems for epidemiological surveillance of tobacco; to cooperate with government and nongovernment international health efforts in the development of procedures and guidelines; and to share and publish any relevant findings. It also establishes that, within the framework of national laws, the parties will promote the exchange of scientific, socioeconomic, legal, and commercial information, including information regarding the practices of the tobacco industry. Finally, the WHO FCTC provides for taking legal action, either by supporting existing laws or creating them when necessary, in order to address judicial liability, including compensation, in reference to tobacco control.

Trudy Mercadal
Florida Atlantic University

See Also: American Lung Association; Health Advocacy; International Association for the Study of Lung Cancer; Lung Cancer, Non–Small Cell; Lung Cancer, Small Cell; Smoking in Society; Smokeless Tobacco; World Health Organization.

Further Readings

Wynder, Ernst

Ernst Wynder was a pioneer cancer researcher with notable achievements in tobacco and nutrition epidemiology that began in medical school, when he co-authored a seminal paper on smoking and lung cancer. He had a strong interest in prevention-oriented health education, especially for schoolchildren. Wynder began his career in an era when there was little scientific basis for prevention of chronic diseases like cancer and heart disease, and he played a significant role in developing the principles and practice of cancer control that still guide the field today. He was a tireless advocate of policies that integrated the roles of government, medical institutions, and individuals in using studies of disease causes to develop prevention and control strategies. He was an influential adviser on cancer policy to many U.S. government and international organizations, and he was founder and editor-in-chief of a major medical journal, Preventive Medicine, one of the first academic journals in the field. He died of thyroid cancer in 1999.

Early Years
Born in Herford, Germany, he immigrated with his family to the United States in 1938 to escape Nazi persecution. He received a B.A. from New York University (1943), served as a U.S. Army Intelligence officer in World War II, and received an M.D. at Washington University in St. Louis (1950). In 1948, while still a medical student, he began collecting case histories of lung cancer victims. He eventually convinced Dr. Evarts Graham, a prominent surgeon at Washington University who was also a smoker and strongly skeptical, to allow him to interview
patients there and, importantly, to support a successful application for funding from the American Cancer Society. Their data became the basis for a landmark paper in the *Journal of the American Medical Association* linking lung cancer to cigarette smoking that was noteworthy for unusually rigorous attention to methodological detail, such as pathological confirmation of diagnoses, distinguishing different lung cancer types, and handling potential biases.

Although cancer had been caused experimentally in animals using chemicals found in tobacco smoke as early as 1918, by the 1950s lifestyle and environmental causes of cancer were still poorly understood, and the pervasiveness of smoking, along with aggressive support of medical research by the tobacco industry, left many researchers unconvinced that the statistical associations represented disease causation. Wynder believed that these questions could not be answered by epidemiology alone, but required a coordinated approach involving experimental biology and chemistry, and, above all public education. He continued studies of cancer patients beginning in 1951, as a medical resident at Memorial Hospital and researcher at the Sloan-Kettering Institute for Cancer Research, where he and chemist Dietrich Hoffmann (1924–2011) began a collaboration on experimental studies on tobacco chemistry and air pollution that would become one of the most enduring partnerships in cancer research.

More than 20 of their studies were cited in the cancer chapter of the first “Surgeon-General’s Report on Smoking and Health” (1964). At Memorial, Wynder carried out definitive studies of cancers of the mouth, larynx, breast, and other sites. However, his unrelenting focus on harmful effects of tobacco at an institution that was receiving substantial support from tobacco company Philip Morris made him the target of threats to censor or suppress his studies, thwarted only by the intercession of board member and Nobel laureate Peyton Rous. Although Wynder maintained an affiliation at Memorial Sloan-Kettering until his death (the two institutions merged in 1960), he eventually decided to strike out on his own.

**American Health Foundation**

In 1969, Wynder founded the American Health Foundation (AHF), serving as its president and medical director for almost 30 years. The foundation’s epidemiology and health behavior divisions were headquartered in the Ford Foundation building in Manhattan, near Memorial Sloan-Kettering and other hospitals where epidemiological studies could be done. Its basic science divisions were housed in a specially designed building in Valhalla, New York, also known as the Naylor Dana Institute after the Eleanor Naylor Dana Foundation, which, with the National Cancer Institute (NCI), provided major construction support. The AHF, supported largely by competitive grants from the NCI, the American Cancer Society, and other agencies, was built on extensive multidisciplinary research programs in epidemiology, tobacco and chemical carcinogenesis, nutrition, pathology, and health behavior and promotion, and was the only NCI-designated cancer center devoted exclusively to prevention. At its peak, it employed over 200 scientists and technicians, with sophisticated state-of-the-art instrumentation and animal research facilities and a scientific library.

In 1972, Wynder recruited John Weisburger (1921–2014), then director of the NCI’s bioassay program, to be vice president and director of research. Hoffmann served as associate director and chief of the Division of Environmental Carcinogenesis, where he made numerous contributions including identification (along with Dr. Stephen Hecht) of an important class of carcinogens—nitrosamines—in tobacco smoke. Other major epidemiological initiatives included studies of the impact of dietary change on both breast and prostate cancer, with special emphasis on the possible impact of dietary fat on survival from both cancers.

Concerned about the fragmented state of school health education, Wynder directed substantial foundation efforts toward developing, implementing, and evaluating K–12 curricula and materials in a program called “Know Your Body” (KYB) in at least eight countries. A central prop of KYB was a health passport for each child that was intended to track key health measurements. This concept was eventually adopted by many organizations as a useful record-keeping device.

**Preventive Medicine**

In 1972, Wynder founded *Preventive Medicine*, the first academic journal devoted to the topic, and served as its editor-in-chief for 25 years during
which he oversaw publication of hundreds of influential articles. In his opening editorial, he quoted a Greek adage: “It is the function of medicine to help people to die young as late as possible,” an epigram that he often repeated in writings and speeches.

**Awards and Publications**

**Personal**
Wynder was a noted international traveler who frequented elite social circles, often with research funding in mind. The American Health Foundation Board of Directors at times included representatives of Norton Simon, Inc., Merrill Lynch, Perrier, the Miami Dolphins, and various entertainment industry figures. He was once linked romantically with actress Kim Novak. He eventually married Sandra Miller, his companion of 25 years.

Steven D. Stellman
*Columbia University*

**See Also:** Tobacco in History; Tobacco Smoking; Tobacco-Related Exposures.

**Further Readings**
Half of the male population and one-third of the female population in the United States will develop cancer in their lifetimes. X-rays are an indispensable tool in both the diagnosis and treatment of cancer. Computed tomography (CT) is the most widely used diagnostic tool for the localization and planning procedures necessary in the cancer treatment process. Megavolt X-ray photons are generated by an accelerator for the actual treatment of the cancer site and can be combined with CT to verify the treatment site. This type of X-ray treatment is called external beam radiation therapy (EBRT).

History
Wilhelm Conrad Roentgen discovered X-rays in November 1895. A mere 17 days later, on January 12, 1896, Emil Grubbe supposedly used X-rays to treat breast cancer for palliation. Since he did not publish this event until much later, claims that he was the first to use X-rays for radiotherapy purposes is highly disputed. A more reliable first record of radiotherapy treatment is that of French physician Victor Despeignes, who treated a male with stomach cancer in July 1896. In 1903, two physicians, Drs. Senn and Pusey, reported on the effects of radiation on the lymph nodes. From then, X-rays had forever changed the face of cancer treatment.

The treatment given at the time was less than ideal with high morbidity and mortality rates. The doses given were extremely high, with single exposures typically lasting up to an hour. The energy of the X-rays was not sufficient to reach deep-seated tumors.

In 1914, an Austrian physician mentioned that radiotherapy side effects could be reduced if the dose was given in smaller portions. The medical profession was divided on the topic until Claudius Regaud, employed by the Curie Institute, proved in 1922 that fractionated radiation therapy delivered the same positive outcome with less severe side effects.

Linear Accelerators
Linear accelerators (LINACs) are used to generate high-energy X-ray photon beams used in EBRT. The first concept for a linear accelerator was conceived by Rolf Wideroe in 1930. The first LINAC, installed at Stanford University in 1950, could generate deep-penetrating megavoltage X-rays.

Since then, the greatest advancements made in X-ray treatment were the invention of the CT scan, the perfecting of the LINAC with the addition of multileaf collimators (MLCs), and, more recently, image-guided radiation therapy (IGRT) and intensity-modulated radiation therapy (IMRT).

A LINAC consists of a negatively charged cathode and a positively charged anode. The cathode
is an electron beam gun that emits electrons. A potential difference is applied between the cathode and the anode, which moves electrons from the cathode to the anode. The electrons pass through a waveguide where they are accelerated by radio-frequency electromagnetic waves. A bending magnet bends the electron beam just before they impact on the anode. When the electrons collide with a tungsten anode, an X-ray beam is emitted. This X-ray beam is shaped by an MLC, which consists of multiple separate lead strips. Each lead strip is driven by its own individual motor to a pre-specified position. The MLC can also move during the treatment process, as seen in more dynamic types of treatment like IMRT.

A gantry head aims the emitted X-ray beam at the patient. The gantry can move 360 degrees around the patient. The patient is positioned on a couch, which can also move 180 degrees to ensure that the X-ray beam can enter the patient at any angle.

**Computerized Axial Tomography (CAT)/Computed Tomography (CT)**

Before the invention of the CT scan, cancer was diagnosed by two-dimensional X-ray imaging. As a result of superimposition, the margins of the lesions were not well defined. There was also no way of knowing how large the tumors were. This left a lot of room for uncertainties.

In 1930, the Italian radiologist Alessandro Vallecbona invented X-ray tomography. He overcame the problem by creating multiple virtual cross sections of a certain body part. By simultaneously moving both the X-ray tube and the radiographic film, he recorded a sharper image of the specified area, while the rest of the unnecessary image was blurred due to the motion. With the development of computers and their incorporation into the medical discipline, CT as we know it today became a reality.

In 1967, Sir Godfrey Hounsfield, who was working as an electrical engineer at Electric and Musical Industries (EMI), wondered if it was possible to determine what a box contained by collecting X-ray readings at multiple angles through the box. He soon realized that it would be possible in a medical setting, using finely collimated X-ray beams. The first prototype of a head scanner, called Mark 1, was built in 1972 at the Atkinson Morley's Hospital in Wimbledon. A cystic brain tumor was the first image ever obtained by the scanner. In 1975, a general scanner was available which could create three-dimensional images of most parts of the human body.

At the time that Hounsfield and EMI were developing the CT scanner, the Beatles were EMI's greatest success story. It is believed by some that it was due to the band's success that EMI could help fund Hounsfield's research on the scanner.

In addition to its three-dimensional imaging ability, the CT scan can also provide electron density information of examined human tissue. This is important because it can demonstrate how different tissues will react to an X-ray beam passing through them. The name used to describe the electron density of various types of tissue is the Hounsfield unit. This electron density information is at the heart of every computerized radiation planning algorithm.

A CT scanner uses a cone-shaped X-ray beam that rotates on the inside of a round opening. Multiple detectors are positioned opposite the cone-shaped beam to acquire the data necessary to produce an image. A patient is positioned on a mobile couch that enters the opening of the scanner while the beam rotates around the patient. The size of the incident X-ray beam can range from 1 mm to 10 mm. Each rotation takes approximately one second. Ten to 50 rotations may be necessary to acquire enough data. The recorded data is sent to a computer where it is used to reconstruct an axial slice of the patient's internal anatomy.

Spiral CT scanners acquire data in a continuous mode without the couch needing to stop for
each slice increment. A major advantage is that the acquisition time is greatly reduced.

**Image Guided Radiotherapy**

Accurate patient setup is crucial to ensure that the tumor receives the maximum possible radiation dose while the surrounding normal tissue is spared. To achieve this, the patient's position should be easily reproducible for every fraction of treatment. There are radiotherapy treatments that require as many as 35 fractions. The patient’s position needs to be exactly the same for all 35 treatments. Internal organ movement is another challenge to the reproducibility of patient setup.

A CT scanner placed in the same room as the LINAC is the newest form of IGRT. The patient’s position, as well as the internal organ position, can be verified right before treatment commences.

**Ionization**

X-rays cause ionization by interacting with the electrons in the atoms of tissue. Compton scattering occurs when an incident X-ray photon transfers some of its energy to an electron, but undergoes a change in direction as a result of the collision. A recoiling electron is released.

X-ray photons with adequate energy can eject an electron from its orbit. This is termed the photoelectric effect. The ejected electrons act as free radicals to further damage surrounding atoms.

Very-high-energy photons can interact with an atom’s nucleus, resulting in an electron and positron pair. This process is called pair production.

The change in the cells’ atomic structures causes DNA damage. If the cells do not repair the DNA damage before they enter their next cell cycle, the cells will die.

**X-Rays and Society**

X-rays have the ability to both cure and cause cancer. Of all the imaging modalities, the CT scan delivers the highest dose to the patient. There has been a drastic increase in the use of CT scanning for medical diagnostic purposes.

According to the U.S. Food and Drug Administration, the radiation dose per individual has risen approximately 500 percent since 1982. According to one study, it is estimated that 29,000 future cancers could be as a result of CT scans done in the United States during 2007.

The average effective dose for an adult undergoing a CT examination is 2 to 16 millisievert. This dose is equivalent to that of 100 to 800 chest X-rays.

The accumulated radiation dose increases as a person undergoes more and more X-ray examinations, increasing lifetime risk for cancer. The younger a person is when receiving an X-ray dose, the higher the risk of developing cancer. Female patients are at a higher risk of developing cancer from the same radiation exposure at the same age as men.

X-rays are essential for the diagnosis and treatment of many conditions, especially cancer. The benefits of using X-rays, either for diagnosis or treatment, should always outweigh the risks. Approximately half of all patients diagnosed with cancer will need radiotherapy as part of their treatment regime.

René Julyan
Independent Scholar

**See Also:** Neutrons; Radiation; Radiation, Ionizing.

**Further Readings**


Yale Cancer Center

Yale Cancer Center (YCC) was founded in 1974 as a result of an act of congress in 1971, which declared the nation’s “war on cancer.” Combining the tradition of innovative cancer treatment and quality care, YCC strives to provide exceptional patient-centered care. YCC brings together the resources of the Yale School of Medicine (YSM), Yale-New Haven Hospital (YNHH), the Yale School of Public Health (YSPH), and Yale University. For over 40 years, YCC has been a National Cancer Institute (NCI)-designated comprehensive cancer center, one of only 41 throughout the country and the only one in southern New England. These comprehensive cancer centers play a vital role in the advancement of the NCI’s goal of reducing morbidity and mortality from cancer through scientific research, cancer prevention, and innovative cancer treatment. The National Comprehensive Cancer Network (NCCN), an alliance of the world’s leading cancer centers dedicated to improving the quality, effectiveness, and efficiency of care provided to patients with cancer, recognized YCC/Smilow Cancer Hospital at Yale-New Haven, New Haven, Connecticut, as an NCCN member institution in March 2014.

History

YSM pioneered the modern concept of chemotherapy over 60 years ago with the efforts of faculty by administering the very first anticancer agent, nitrogen mustard, to a patient with cancer. Scientists and clinicians at YCC today are collaborating to design and develop the latest cancer therapeutics and combination therapy for patients in Phase I, II, and III clinical trials. The National Cancer Act of 1971, from its inception, has mandated that comprehensive cancer centers like Yale develop fundamental basic science that translates into innovative cancer therapies.

Mission Statement

YCC and Smilow Cancer Hospital aim to prevent and cure cancer through groundbreaking research, scientific discovery, and compassionate patient care. The collaboration of over 450 scientists and physicians focused on cancer research at YCC provides a strong foundation for breakthroughs in cancer prevention, diagnosis, and treatment.

YCC seeks to capitalize on the scientific strengths of Yale University to benefit cancer patients throughout the world, while providing the very best in clinical cancer care to the patients at Smilow Cancer Hospital at Yale-New Haven. Smilow Cancer Hospital at Yale-New Haven is part of the nationally recognized Yale-New Haven Hospital and is affiliated with YCC. Smilow Cancer Hospital, the most comprehensive cancer facility in New England, is a 14-story, 500,000-square-foot cancer hospital, which includes 168 private inpatient rooms,
outpatient multidisciplinary treatment centers, 12 operating rooms, infusion suites, diagnostic imaging services, a floor for children with cancer, a specialized women’s cancer center, and diagnostic and therapeutic radiology services for children and adults. YNHH’s York Street campus and associated ambulatory sites are magnet-designated by the American Nurses Credentialing Center.

Strategic Goals

1. Remain committed to developing a cure for all cancers.
2. Become a leader in personalized cancer care through innovative tumor-profiling techniques used to analyze every patient’s cancer.
3. Ensure every patient has an outstanding and positive cancer care experience at Smilow Cancer Hospital at Yale-New Haven, with a steadfast focus on patient- and family-centered care.
4. Build on the scientific traditions of Yale University, with continued investment in interdisciplinary cancer research in basic science, translational research, and prevention and control.
5. Maintain and support the expertise of the physicians, nurses, and clinical staff at Smilow Cancer Hospital and YCC.

Research

Yale School of Medicine was home to the nation’s first university-based Medical Oncology Section. Its faculty has since pioneered many breakthrough cancer treatments. Today, there are seven research programs at YCC, including: developmental therapeutics, genetics and genomics, cancer immunology, molecular virology, cancer prevention and control, radiobiology and radiotherapy, and signal transduction. Cancer research at Yale began decades before the center was founded. The first research program in developmental therapeutics began in 1974, representing the foundation of the clinical translational research efforts at YCC. Laboratory/research-based discoveries are taken into the clinical setting and observations. These are returned to the laboratories for further refinement into improved cancer treatments.

Basic research in cancer is a hallmark of YCC, drawing approximately $140 million in cancer research funding to Yale annually. Yale is home to some of the leading international investigators in cancer research, who have provided a steady stream of advances in a number of disciplines, contributing to the basic understanding of cancer and to the development of new therapies and diagnostic strategies.

YCC’s Developmental Therapeutics Research Program has been successful in discovering a wide range of novel therapeutics, many of which are now undergoing preclinical and clinical testing. The recent initiative of the Developmental Therapeutics Program, a Phase I research team, focuses on the application of promising laboratory discoveries in the design and conduct of clinical trials at YCC.

Clinical Care

YCC brings the convergence of science and medicine as the latest research directly applicable to patient care. Led by Roy S. Herbst, M.D., Chief of Medical Oncology and Associate Director for Translational Research, Yale medical oncologists care for patients in Smilow Cancer Hospital at Yale-New Haven. Twelve multidisciplinary programs have been developed at YCC and Smilow Cancer Hospital to organize patient care. These provide physicians and specialists at YCC with the opportunity to focus their expertise on specific types of cancers.

Clinical trials and research studies are available for appropriate patients with early or late-stage diseases who are under the care of the YCC’s oncology staff. Currently 64 clinical trials are available for patients in over 15 different disease areas.

Other services provided at the center include access to clinical trials covering the majority of cancer types as well as assistance for cancer survivors. On completion of their treatment, patients are offered services through the Connecticut Challenge Survivorship Clinic. The clinic provides medical care, nutritional and lifestyle guidance, and support for cancer survivors throughout the state.

Rakesh Verma
Andrew Branagan
Yale School of Medicine

See Also: Chemotherapy; Chemoprevention; Clinical Trials; National Cancer Institute.
Yemen

While Yemen has sought to improve its health care system over the past 10 years, its system is still substantially lacking. Yemen only has 3 doctors for every 10,000 people. For people living in rural areas, emergency services are nonexistent. A quarter of the people living in rural areas have access to health services, whereas 80 percent of the urban population has access. The mortality rate in childhood is largely from diseases for which there is a vaccine or that would have been preventable if there had been adequate health services available. In 2003, it was estimated that 12,000 people were living with human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS). Per capita, Yemen's total health expenditure is one of the lowest in the world. It spends $40 per person on health care needs each year.

According to the National Anti-Cancer Corporation (NACC), more than 12,000 cases of cancer emerged in Sana'a in 2012. Logistics, lack of infrastructure, and lack of funding are obstacles preventing Yemen from taking action to help alleviate this large number of cases. Yemen has among the highest cancer rates of any Middle Eastern or north African country, up to 10 times higher than most Arabic countries. This burden has become so out of control that vice president Abduh Raboh Mansor Hadi has asked about the practicality of using a portion of funds from mobile phone revenue to fund the fight against cancer. The high cancer rates in Yemen are attributable to lifestyle choices and farming practices. Consumers smoke more tobacco, and Yemeni farmers use more herbicides and pesticides than before. The NACC reports that 25 to 30 cases are discovered each day, and this only accounts for the cases that have been reported to the corporation. It is likely that many more cases are not reported.

The NACC has attempted to arrange free access to pharmaceuticals and health services for cancer patients who otherwise would not be able to afford treatment. In addition to this, it intends to provide between 30 and 50 percent of the cost of medication and health services for those who are able to contribute partially to their treatment. The corporation also intends to sponsor awareness campaigns and other cultural projects for the Yemeni people. Because of a lack of infrastructure and health services, more than half of all new cases are fatal. Because there are no adequate early detection screenings available, many cancer cases are discovered in the late stages, when treatment options are severely limited. People are also unaware of the signs and symptoms of cancer, so they do not know when or if they should seek treatment. For those who are treated, many stop taking medications when their symptoms have improved, against the recommendation of physicians. For cancer patients who seek treatment in hospitals, they are provided medical treatment and lab tests to determine the cause of their illness and its progression. In addition to medical support, emotional and psychological support is available.

Yemen is composed of 555,000 square kilometers, but it only has 2,000 reproductive health centers, with 60 percent providing different services such as labor and pregnancy, care after delivery, and family planning assistance. There are 520 centers that provide people with emergency services, and 69 hospitals for other purposes, according to the national Yemeni Ministry of Health. According to international standards, there should be a comprehensive emergency delivery hospital for every 500,000 persons, and four basic health centers. However, Yemen is an exception because the majority of its population lives in inaccessible rural areas. Yemen has about 130,000 residential areas, but many are in nearly impassable locations. Some places barely have roads. These locations are so far from medical facilities that the Yemeni people only go to health centers when they are having emergencies. Unfortunately, the long trip and time spent before arriving at the health center means that individuals come in too late for most treatment.

The patient mortality rate is very high in rural Yemen, especially for individuals who make their
homes near the Saudi Arabian and Omani borders. As of December 2014, according to the United Nations Office for the Coordination of Humanitarian Care, an estimated 8.4 million people in Yemen lack access to basic health care, a 1 percent increase from 2013. While the Ministry of Health is seeking to resolve the problems faced by the health care services in Yemen, geographic and cultural difficulties in rural areas present an extremely difficult challenge. Currently, the government is aiming to build facilities so that one comprehensive emergency center and four basic emergency centers exist for every 250,000 people. Other obstacles in the way of an effective health care system include lack of funding, scarcity of medicine, lack of equipment, and lack of medical professionals. All of these difficulties together form a large impediment to extending health care services to rural Yemen. Because most of the health care centers in Yemen have a shortage of doctors, one general practitioner may have to take on the responsibility as physician, pharmacist, and labor and delivery doctor.

There are extreme difficulties when it comes to recruiting staff. There are not enough doctors to facilitate shift rotations, and there are very few physicians in Yemen altogether. With only one doctor on staff, it becomes extremely difficult to attend regular patient visits as well as emergencies. Severe lack of funding is largely to blame for the rarity of doctors. The immense problems facing health services are known to local politicians and councils, but no substantial steps have been taken to fund them. Even with what financial aid local communities could muster, the health centers would not be fully supported. However, committees have been formed to investigate the health service needs in these areas. The Ministry of Health has made mothers and children a high priority. They are endorsing midwives to make house calls, especially where there are insufficient facilities to care for these patients. This is an attempt to combat the lack of facilities and personnel. There are also mobile teams who make the difficult trek into rural Yemen in order to provide health care services several times each year. In 2013, the Ministry of Health donated funds to support 10 governorates. This action had the effect of adding 24 new medical facilities in the area.

Michael Fox
Independent Scholar

See Also: Developing Countries; Disparities Within Nations (Elimination of Cancer); Saudi Arabia.

Further Readings

Young Adult Cancer Prevention

Cancer is often thought of as something that develops later in life. Many people think that cancer is a health issue that only affects older people. Unfortunately, this type of thinking leads many young people to neglect focusing on their own health in terms of cancer prevention and screening. Some cancers that develop in young adults have no known cause, but others are linked to certain lifestyle risk factors and can be prevented. Because of this, researchers and educators have increasingly devoted effort to cancer education and prevention in the young adult population.

The Myth That Young Adults Are Impervious to Cancer
Young adulthood (approximately 15 to 39 years old) is usually characterized by good overall health, as many of the diseases and conditions that people face do not manifest until later in life. In fact, young adults are sometimes referred to as “young invincibles,” illustrating the fact that many believe they are impervious to diseases and health issues that older adults face. In addition, young adulthood is often characterized by engaging in risky health behaviors; people this age often want to explore their
Young Adult Cancer Prevention

Independence and experiment with different life experiences (e.g., drinking, drugs, sex). However, in believing that they are invincible at this age, many young adults do not think about some of the short- and long-term effects of these risky behaviors. Specifically, many of these risky health behaviors have direct links to cancer. The following are some examples:

- Young adults are not only engaging in more sexual activity than older or younger age groups, but they are also more likely to have more than one sexual partner; both of these behaviors increase their risk for contracting genital human papillomavirus (HPV). Genital HPV infections are the most common sexually transmitted diseases in the United States, specifically among young adults. Persistent genital HPV infections have been shown to lead to the development of cervical and other cancers (e.g., anal, penile, head, and neck).

- Many people start smoking during late adolescence and early adulthood. Research shows that the more years a person smokes (i.e., the younger they start) and the more frequently they smoke, the higher their chances are for developing lung cancer later in life.

- Exposure to high levels of ultraviolet (UV) radiation, whether from the sun or a tanning bed, significantly increases one's risk for developing skin cancer. The risk of getting skin cancer from UV radiation increases for young adults, as their skin is particularly susceptible to the damage caused by the radiation. Young, adult, white (Caucasian) women report frequent sunbathing and tanning bed use, which significantly increases their chances of developing skin cancer. Much like smoking and lung cancer, the frequency (i.e., repetitive exposure) and timing (i.e., earlier exposure) of excessive UV radiation exposure is related to a higher risk of developing skin cancer.

- Having a low-fiber/high-fat diet as well as a sedentary lifestyle are both factors that increase one's risk for developing colon cancer. These diet and activity habits are often developed early in adulthood, and years of poor diet and exercise significantly increases one's risk for colon cancer later in life.

- Substantial and repetitive exposure to any form of radiation earlier in life can increase the risk for many different kinds of cancer. Ironically, many people are exposed to increased amounts of radiation because of medical procedures like positron emission tomography (PET) scans, computed tomography (CT) scans, fluoroscopies, and X-rays.

In addition to engaging in these risky behaviors that can lead to certain types of cancer, research also shows that young adults are significantly less likely to seek out and use preventive health services compared to other age groups. This includes being less likely to follow the recommended guidelines for cancer screening or clinical preventive measures (e.g., Pap testing, HPV vaccination for cervical cancer, skin cancer counseling, etc.).

On the other hand, there are many types of cancers that occur in young adults that have no known cause and therefore cannot really be prevented. In other words, they develop spontaneously, usually due to some type of gene mutation within the body.

Preventing and Screening to Reduce Cancer Risks

Drawing attention to the risk factors that can lead to cancer and the ways that young adults can prevent cancer are important at two levels. First, when young adults engage in risky behaviors and fail to focus on preventive health, this can lead to cancer developing later in life. In fact, for all of the cancer examples listed above, it is often noted that the cause or root of the cancer stems from unhealthy or risky behaviors enacted during early adulthood. Second, while most of these preventable cancers do not develop until later in life, it does not mean that they will not develop in early adulthood.

For example, the American Academy of Dermatology notes that melanoma skin cancer is the most common form of cancer for young adults ages 25 to 29, and rates among young adult women (those under 44 years old) have been increasing 6.1 percent annually. Another example is cervical cancer; the
National Cancer Institute reports that HPV-associated cervical cancer is most frequently diagnosed among women 35 to 44 years old. Other HPV-associated cancers, lung cancer, and colon cancer are less commonly diagnosed among young adults.

Therefore, research and education focusing on preventing (and screening) for these types of cancers in young adulthood is not only important for the “now,” but also for the long-term health of individuals.

**Education and Promotion in This Population**

One of the best tools to fight cancer is education. People face barriers to preventing cancer if they do not think they are at risk for a certain cancer, if they are ignorant that their behavior or lifestyle choices could lead to cancer, or if they do not know about the preventive measures and early screening tools available to them. Recently, there has been increased research on cancer prevention in young adults. Many medical researchers as well as social scientists have devoted time and attention to not only understanding young adults’ cancer knowledge, attitudes, and behaviors, but also to developing cancer prevention interventions to reduce young adults’ chances of developing cancer. One organization that is a leader in this area is the Prevent Cancer Foundation. It generates public discussions about cancer prevention, promotes research on the topic, increases access to knowledge and early detection services (particularly in underserved communities), and collaborates with others working in this area. An infographic developed by the Prevent Cancer Foundation sums up seven important lifestyle behaviors related to reducing the risk for cancer. Obviously, the earlier that people adopt these behaviors, the lower their risks for developing cancers even more.

In addition to increasing general education about cancer prevention among young adults, some organizations and researchers have focused on places that young adults frequent in order to better address young adult cancer prevention. One such place is college campuses. For example, many college campuses have focused on tobacco use prevention and tobacco cessation. Because of this, the Tobacco Technical Assistance Consortium, which focuses on assisting organizations developing their own tobacco control programs, created a page called the College Tobacco Prevention Resource (http://www.ttac.org/services/college/index.html); this Web site serves as a clearinghouse for resources about tobacco-related programs at colleges and tips for colleges that want to develop their own programs.

**Conclusion**

Young adult cancer prevention is an important topic. Not only do young adults often engage in risky behaviors that can lead to cancer, some young adults also do not believe that they are susceptible to cancer. Educating young adults on the importance of life choices made now can help to reduce their cancer burden both earlier and later in life.

Katharine J. Head  
*Indiana University–Purdue University Indianapolis*  
Elisia L. Cohen  
*University of Kentucky*

**See Also:** Cervical Cancer; Colon Cancer; Diet and Nutrition; Education; Exercise; Melanoma.

**Further Readings**


---

**Yul Brynner Head and Neck Cancer Foundation (Head and Neck Cancer Alliance)**

The Yul Brynner Head and Neck Cancer Foundation was incorporated in 1984 by actor Yul Brynner and medical specialist Dr. George Sisson (1920–2006). Its primary purpose was to educate the public about the dangers of tobacco use in relation to incidences of throat and mouth cancers.
Today, the foundation is referred to as the Head and Neck Cancer Alliance.

Yul Brynner, who had over 40 movie roles and was best known for his role in the Rodgers and Hammerstein musical, *The King and I*, developed lung cancer and died on October 10, 1985. Before he had lung cancer, he was diagnosed with a precancerous growth of his vocal cord (larynx). By all accounts, Brynner always recognized that smoking could cause him to develop lung cancer, but he had not realized that it could cause symptoms and that treatment would affect his voice. While he kept his vocal cord lesion secret since he was best known for his singing and acting, the radiation therapy needed to treat his lung cancer greatly affected his voice. He eventually dedicated monies for the development of the foundation that bore his name.

Before Yul Brynner died, he recorded a public service announcement sponsored by the American Cancer Society and extracted from a *Good Morning America* interview in which Brynner warned the audience not to smoke in a hoarse and harsh voice. He had quit smoking in 1971, knowing all too well that despite stopping smoking, his risk of lung cancer was still high. The finalized public service announcement aired after his death.

Initially, the foundation developed educational programs and secured funding from numerous research grants in head and neck cancer. It went through a period of inactivity in the late 1980s and early 1990s. The Association for Head and Neck Cancer Awareness and the Yul Brynner Foundation combined in 1997, to be called the Head and Neck Cancer Alliance, and was directed by Dr. Terry Day, the current president. The Head and Neck Cancer Alliance is a nonprofit organization mainly dependent on donations. In 1998, the alliance organized and directed the first annual Head and Neck Cancer Awareness Week, officially changed to Oral, Head, and Neck Cancer Awareness Week® (OHANCAW®), to communicate awareness about oral cancer, the most common of head and neck cancers. The Head and Neck Cancer Alliance plans to continue to sponsor this awareness week until these types of cancer are no longer detectable. As of 2014, several organizations and educational institutions have sponsored awareness events including the University of Florida College of Dentistry 5K Awareness Walk, Johns Hopkins Education Day, and Anchorage Alaska’s Mission of Mercy.

Presently, the overall mission of the Head and Neck Cancer Alliance is to support and educate oral, head, and neck cancer patients and their families; sponsor new and groundbreaking research; and educate children and adults in the preventative measures of head and neck cancer. The foundation encourages people to become involved in the organization. It posts cancer resources to its Web site (including news articles, clinical trials, events, and conferences) and provides information for hosting a head and neck cancer screening day. In fact, the main focus of Oral, Head, and Neck Cancer Awareness Week is to encourage preventative screenings of the head and neck areas. Head and neck cancers are defined as cancers that occur in the head and neck region, including the nasal cavity, sinuses, lips, tongue, mouth, salivary glands, throat, and vocal regions.

The Head and Neck Cancer Alliance National Board member, and the author of *My Voice: A Physician’s Personal Experience With Throat Cancer*, Dr. Itzhak Brook offered his book about his own laryngectomy at no cost to many professionals in the United States through a generous grant from the Head and Neck Cancer Alliance. His book focuses on his complete journey as a throat cancer patient, with the added knowledge of that of a physician. Readers of the book are taken through his journey from cancer discovery, to removal of his voice box, to learning how to speak again with an assistive speech device. Details about the experience, the professionals he met, and the lessons he learned along the way are carefully detailed. Awareness is the key of the alliance, and this book brings the experience of throat cancer to professionals and the public alike. Kathy Brynner-Hifl er, the widow of Yul Brynner, has always been and continues to be active with the foundation as chair, emeritus, of the Advisory Board.

Yul Brynner’s lung cancer diagnosis and his own discovery of a lump on his vocal cords resulted in the development of the Head and Neck Cancer Alliance (formerly known as the Yul Brynner Head and Neck Cancer Foundation). At a time when little emphasis was placed on oral, head, and neck cancers, Yul Brynner’s experience shaped this foundation to shed light on an often less-discussed cancer.

Diane Ferrero-Paluzzi
Iona College
**See Also:** Head and Neck Cancer; Oral Cancer, Childhood; Oral Cavity Cancer, Lip and; Salivary Gland Cancer; Thyroid Cancer; Tobacco Smoking.

**Further Readings**


Zambia

The Republic of Zambia is a landlocked country in southern Africa that is surrounded by the Democratic Republic of the Congo to the north; Tanzania to the northeast; Malawi to the east; Mozambique, Zimbabwe, Botswana, and Namibia to the south; and Angola to the west. It is part of what is known as sub-Saharan Africa. Zambia became a British colony known as Northern Rhodesia in 1911, and in 1953 it became part of the Federation of Rhodesia and Nyasaland until 1963. The country gained its independence in 1964 as Zambia. Zambia’s population, as of July 2014, is estimated at 14.6 million, with a life expectancy at birth of 51.8 years. For every 100,000 citizens, there are 10 doctors, 80 nurses, and 30 community health workers.

As with most African countries, access to quality or adequate health care was reserved for Europeans during the time of colonization and occupation, with few indigenous people having access to medicine and quality health care. Folk remedies and herbal cures still compete with modern medicine, particularly in remote regions of Zambia, to treat all manner of illness. This includes cancer.

Zambia has some of the highest rates of cancer in Africa, and cancer incidence is on the rise. Estimates suggest there are more than 7,000 new cases a year, the most common being cervical cancer. Zambia has one of the highest cervical cancer rates in the world, with 90 out of every 100,000 women contracting cervical cancer. The World Health Organization ranks Zambia as having the third highest mortality rate from cervical cancer, a preventable disease.

Cervical cancer in Zambia is closely linked to the human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) and the human-papilloma virus (HPV). It has been reported that women infected with HIV are thought to be three to five times more likely to develop cervical lesions that can become cancerous. The increased attention of the incidence of cervical cancer among Zambian women has brought awareness to the causal link between cervical cancer, HPV, and male circumcision. Some are skeptical that this can be a contributing factor to cervical cancer’s being more common in Zambian women than in women from other countries, while others consider this a significant factor, as the vast majority of Zambian men are not circumcised. The Center for Infectious Disease Research is home to one of the largest cervical cancer screening initiatives in the world as well as to Zambia’s HPV vaccination campaign, which began in 2013 to reduce incidence of cervical cancer, including public education and outreach.

A growing cancer burden in Zambia is the increasing rate of childhood cancers. Lymphomas have been the most reported, followed by retinoblastoma, kaposi, and sarcomas. Many cancers
are presented and diagnosed at an advanced stage while others are left undetected, adding to the poor survival rates and high mortality. With early detection, children diagnosed with cancer have a 70 to 85 percent chance of being cured.

The Kayula Childhood Cancer Foundation was established in March 2012. It is a Non-Governmental Organization established in memory of Kayula Zina Sata who passed away in 2009 at the age of 4 from neuroblastoma, a rare form of cancer. The foundation was created to support the University Teaching Hospital’s Pediatric Cancer Ward. The University Teaching Hospital in Lusaka is the only hospital in the country that has a pediatric oncology department. Patients come from all ten provinces of Zambia to seek treatment, sometimes spending more than a year. One of the main contributions of the foundation is the Parent House, where parents stay while their children undergo treatment. Children who are well enough are able to stay at the Parent House in between their chemotherapy and other treatments. This is beneficial to the family and helps the parents feel at home and also give the children a “home away from home” feeling, as a majority of the patients come from far beyond Lusaka. The Cancer Diseases Hospital (CDH) also treats some children’s cancer cases but only on an outpatient basis.

Organizations and Institutions
The National Council for Scientific Research in Lusaka and the School of Medicine at the University of Zambia coordinate cancer research in Zambia. The Zambia Cancer Foundation, operating from the University Teaching Hospital in Lusaka, is involved in raising money for cancer treatment and caring for patients and their families. The University Teaching Hospital is the biggest hospital in Zambia.

In July 2007, the CDH opened in Zambia. The CDH marked a milestone in cancer treatment, as it was the first of its kind in Zambia and was designed to house facilities to treat patients who previously had to travel great distances to South Africa for cancer treatment. The hospital houses five scanners, the largest of which is a linear accelerator. The rooms where the majority of scanners are kept were constructed with reinforced concrete walls up to 700 mm thick. The walls of the room that house the linear accelerator range from 1,200 mm to 2,500 mm. Thicker walls contain radiation more effectively. However, thicker walls produce more heat, increasing the tendency for walls to crack and allow radiation to escape. The health risks for the hospital staff and the general public are great. As such, the International Atomic Energy Agency frequently visited the site to monitor the design and construction of the rooms.

The International Atomic Energy Agency supports cancer care and treatment through a variety of initiatives and partnerships. The Technical Cooperation Program is the key mechanism for planning and delivery of radiotherapy assistance to Africa and other regions. The Program of Action for Cancer Therapy (PACT) is a broad-based global partnership that aims to help developing countries build a comprehensive, sustainable cancer control program.

Other organizations provide support to cancer patients and their families. The Zambian Cancer Society (ZCS), founded in 2007, seeks to provide access to and disseminate information on cancer, offer psychosocial support to cancer patients and their families, and increase awareness of the programs, products, and services provided by the ZCS and other resources. The Zambian Childhood Cancer Foundation was established to provide holistic care for children with cancer and life-threatening blood disorders (such as hemophilia and sickle cell disease) and also provide assistance to their families through practical and psychosocial support programs.

Many countries in the developing world are facing a cancer crisis; with few resources to fight the increasing cancer burden, many individuals and organizations work together to fill a variety of needs.

Annette Madlock Gatison
Southern Connecticut State University

See Also: AIDS-Related Cancers; HPV Vaccination; South Africa; Zimbabwe.

Further Readings
Zimbabwe

The Republic of Zimbabwe is a southern African country located between the Zambezi and Limpopo rivers. It is bordered by South Africa to the south, Botswana to the southwest, Zambia to the northwest, and Mozambique to the east. Zimbabwe has 16 official languages, with English, Shona, and Ndebele being the most common. The history of Zimbabwe is one of European colonization and contemporary political turmoil. The United Kingdom annexed Southern Rhodesia from the British South Africa Company in 1923. A 1961 constitution was formulated that favored whites in power. In 1965, the government unilaterally declared its independence, but the United Kingdom did not recognize the act and demanded more complete voting rights for the black African majority in the country then called Rhodesia. UN sanctions and a guerrilla uprising finally led to free elections in 1979 and independence as Zimbabwe in 1980.

Robert Mugabe, the nation’s first prime minister, has been in power since 1987 as president and has dominated the country’s political system since independence with devastating effects. His chaotic land redistribution campaign, which began in 1997 and intensified after 2000, caused an exodus of white farmers, crippled the economy and ushered in widespread shortages of basic commodities. Ignoring international condemnation, President Mugabe rigged the 2002 presidential election to ensure his win. In April 2005, the capital city of Harare embarked on Operation Restore Order, which destroyed the homes or businesses of 700,000 mostly poor supporters of the opposition. President Mugabe in June 2007 instituted price controls on all basic commodities, which caused panic buying and left store shelves empty for months; a period of increasing hyperinflation ensued. General elections held in March 2008 contained irregularities but still amounted to a censure of the Zimbabwe African National Union Patriotic Front-led government, with the opposition winning a majority of seats in parliament. Opposition leader Morgan Tsvangirai won the most votes in the presidential polls. In the lead up to a runoff election in late June 2008, considerable violence took place against opposition party members, which led to the withdrawal of Tsvangirai from the ballot. There was evidence of violence and intimidation, resulting in international condemnation of the election process. Difficult negotiations ensued over sharing power, control, and creating a truly unified government in which Mugabe remained president and Tsvangirai became prime minister. A settlement was reached in February 2009, although both men failed to agree upon several key governmental issues. Mugabe was reelected president in June 2013 in balloting that was severely flawed and once again internationally condemned.

Politics influence the human services provided in a country with a growing cancer burden, as government support is needed to provide the necessary resources. The population of Zimbabwe is estimated at approximately 14 million, with a life expectancy of 56 years. For every 100,000 people, there are 10 doctors and 130 nurses and midwives. These numbers decrease when medical specialization is factored in.

The Zimbabwe National Cancer Registry (ZNCR) was established in 1985 as a result of a collaborative agreement between the Zimbabwean Ministry of Health and the International Agency for Research on Cancer (IARC). Operations began in Harare in 1986, with complete coverage of the population of the city by 1990. Recognized as one of the few well-established registries in Africa, the ZNCR provides technical support to other registries in the region at the request of the IARC, the World Health Organization’s African Regional Office (WHO/AFRO), and the International Network for Cancer Treatment and Research (INCTR).

The registry is strategically located in the Parirenyatwa Group of Hospitals complex, a large government referral center that provides most of the specialized cancer management services for the country and is also one of the two teaching hospitals used by the University of Zimbabwe College of Health Sciences. The Ministry of Health and Child Welfare, the IARC, the INCTR, and other organizations support the registry.

Eric Chokunonga, the registrar of the ZNCR, along with other researchers completed a study that
examined the incidence rates of different cancers in the black population of Harare over a 20-year period (1991 to 2010), along with social and lifestyle changes and the peak and subsequent wane of the HIV/AIDS epidemic. The results indicate that the overall risk of cancer increased in both sexes during the period, with rates of cervical and prostate cancers showing dramatic increases of 3.3 percent and 6.4 percent annually, respectively. By 2004, prostate cancer had become the most common cancer of men. The incidence of cancer of the esophagus, formerly the most common cancer of men, remained relatively constant, whereas rates of breast and cervical cancers, the most common malignancies of women, showed significant increases at 4.9 percent and 3.3 percent annually, respectively.

The incidence of Kaposi's sarcoma increased to a maximum around 1998 to 2000 and then declined in all age groups and in both sexes. The incidence of squamous cell cancers of the conjunctiva (eye) is relatively high, with temporal trends similar to those of Kaposi's sarcoma. Non-Hodgkin's lymphoma, the fifth most common cancer of men and fourth of women, showed a steady increase in incidence throughout the period (6.7 percent to 6.9 percent annually), although rates in young adults (aged 15 to 39) have decreased since 2001. Cancer control in Zimbabwe, as elsewhere in sub-Saharan Africa, involves meeting the challenge of emerging cancers associated with Westernization of lifestyles (large bowel, breast, and prostate), while the incidence of cancers associated with poverty and infection (liver, cervix, and esophagus) shows little decline, and the residual burden of the AIDS-associated cancers remains significant.

The National Cancer Prevention and Control Strategy for Zimbabwe 2013–2017 recognizes that cancer is a major cause of morbidity and mortality in Zimbabwe, with over 5,000 new diagnoses being made and over 1,000 deaths per year. The number of people developing cancer is expected to increase due to an increasingly aging population, HIV and AIDS, a Westernized diet, and other unhealthy lifestyle choices in the population. The Ministry of Health and Child Welfare and its partners in cancer control are prioritizing cancer policy and implementation of relevant advances, with the vision that Zimbabwe will have a system for cancer control that will reduce cancer incidence, morbidity, and mortality rates. The goal is for the people of Zimbabwe to practice health-promoting and cancer-prevention behaviors and have access to early cancer detection. This strategy ultimately seeks to enhance the range, capacity, and quality of cancer services comprising prevention, early detection, diagnosis, treatment, palliative care, rehabilitation, surveillance, and research.

Annette Madlock Gatison
Southern Connecticut State University

See Also: AIDS-Related Cancers; South Africa; Zambia.

Further Readings
Abdomen: The part of the body that contains the pancreas, stomach, intestines, liver, gallbladder, and other organs.

Accelerated phase: Refers to chronic myelogenous leukemia that is progressing. The number of immature, abnormal white blood cells in the bone marrow and blood is higher than in the chronic phase, but not as high as in the blast phase.

Achlorhydria: A lack of hydrochloric acid in the digestive juices in the stomach. Hydrochloric acid helps digest food.

Actinic keratosis: A precancerous condition of thick, scaly patches of skin; also called solar or senile keratosis.

Acute leukemia: Leukemia that progresses rapidly.

Adenocarcinoma: Cancer that begins in cells that line certain internal organs.

Adenoma: A noncancerous tumor.

Adjuvant therapy: Treatment given in addition to the primary treatment to enhance the effectiveness of the primary treatment.

Adrenal glands: A pair of small glands, one located on top of each kidney. The adrenal glands produce hormones that help control heart rate, blood pressure, the way the body uses food, and other vital functions.

Aflatoxin: A substance made by a mold that is often found on poorly stored grains and nuts. Aflatoxins are known to cause cancer in animals.

Agranulocyte: A type of white blood cell; monocytes and lymphocytes are agranulocytes.

Allogeneic bone marrow transplantation: A procedure in which a patient receives bone marrow from a compatible, though not genetically identical, donor.

Alpha-fetoprotein: A protein often found in abnormal amounts in the blood of patients with liver cancer.

Alveoli: Tiny air sacs at the end of the bronchioles.

Anal cancer: Anal cancer, an uncommon cancer, is a disease in which cancer (malignant) cells are found in the anus. The anus is the opening at the end of the rectum (the end part of the large intestine) through which body waste passes.
Anaplastic: A term used to describe cancer cells that divide rapidly and bear little or no resemblance to normal cells.

Anastomosis: A procedure to connect healthy sections of the colon or rectum after the diseased portion has been surgically removed.

Androgen: A hormone that promotes the development and maintenance of male sex characteristics.

Anemia: A decrease in the normal amounts of red blood cells.

Anesthesia: Loss of feeling or awareness. A local anesthetic causes loss of feeling in a part of the body. A general anesthetic puts the person to sleep.

Anesthetic: A substance that causes loss of feeling or awareness. A local anesthetic causes loss of feeling in a part of the body. A general anesthetic puts the person to sleep.

Angiogenesis: Blood vessel formation, which usually accompanies the growth of malignant tissue.

Angiogram: An X-ray of blood vessels; the patient receives an injection of dye to outline the vessels on the X-ray.

Angiography: A procedure to X-ray blood vessels. The blood vessels can be seen because of an injection of a dye that shows up in the X-ray pictures.

Angiosarcoma: A type of cancer that begins in the lining of blood vessels.

Antiandrogen: A drug that blocks the action of male sex hormones.

Antibiotics: Drugs used to treat infection.

Antibody: A protein produced by certain white blood cells in response to a foreign substance (antigen). Each antibody can bind only to a specific antigen. The purpose of this binding is to help destroy the antigen. Antibodies can work in several ways, depending on the nature of the antigen. Some antibodies disable antigens directly. Others make the antigen more vulnerable to destruction by white blood cells.

Anticonvulsant: Medicine to stop, prevent, or control seizures (convulsions).

Antigen: Any foreign or “non-self” substance that, when introduced into the body, causes the immune system to create an antibody.

Antithymocyte globulin: A protein preparation used to prevent and treat graft-versus-host disease.

Aplastic anemia: A deficiency of certain parts of the blood caused by a failure of the bone marrow’s ability to generate cells.

Apoptosis: A normal cellular process involving a genetically programmed series of events leading to the death of a cell.

Arterial embolization: Blocking an artery so that blood cannot flow to the tumor.

Arteriogram: An X-ray of blood vessels, which can be seen after an injection of a dye that shows up in the X-ray pictures.

Asbestos: A natural material that is made up of tiny fibers. If the fibers are inhaled, they can lodge in the lungs and lead to cancer.

Ascites: Abnormal buildup of fluid in the abdomen.

Aspiration: Removal of fluid from a lump, often a cyst, with a needle and a syringe.

Astrocytoma: A type of brain tumor that begins in the brain or spinal chord in small, star-shaped cells called astrocytes.

Ataxic gait: Awkward, uncoordinated walking.

Atypical hyperplasia: A benign (noncancerous) condition in which tissue has certain abnormal features.

Autologous bone marrow transplantation: A procedure in which bone marrow is removed from a patient and then is given back to the patient following intensive treatment.
Axilla: The underarm.

Axillary: Pertaining to the lymph nodes under the arm.

Axillary dissection: Surgery to remove lymph nodes under the arm.

B cells: White blood cells that develop in the bone marrow and are the source of antibodies. Also known as B lymphocytes.

Barium enema: A series of X-rays of the lower intestine. The X-rays are taken after the patient is given an enema with a white, chalky solution that contains barium. The barium outlines the intestines on the X-rays.

Barium solution: A liquid containing barium sulfate that is used in X-rays to highlight parts of the digestive system.

Barrett’s esophagus: A change in the cells of the tissue that lines the bottom of the esophagus. The esophagus may become irritated when the contents of the stomach back up (reflux). Reflux that happens often over a long period of time can lead to Barrett’s esophagus.

Basal cell carcinoma: A type of skin cancer that arises from the basal cells.

Basal cells: Small, round cells found in the lower part, or base, of the epidermis, the outer layer of the skin.

Basophil: A type of white blood cell. Basophils are granulocytes.

BCG (Bacillus Calmette-Guerin): A substance that activates the immune system. Filling the bladder with a solution of BCG is a form of biological therapy for superficial bladder cancer.

Benign: Not cancerous; does not invade nearby tissue or spread to other parts of the body.

Benign prostatic hyperplasia: A noncancerous condition in which an overgrowth of prostate tissue pushes against the urethra and the bladder, blocking the flow of urine. Also called benign prostatic hypertrophy or BPH.

Benign tumor: A noncancerous growth that does not spread to other parts of the body.

Beta-carotene: A substance from which vitamin A is formed; a precursor of vitamin A.

Bilateral: Affecting both the right and left side of body.

Bile: A yellow or orange fluid made by the liver. Bile is stored in the gallbladder. It passes through the common bile duct into the duodenum, where it helps digest fat.

Bioimmunotherapy: Treatment to stimulate or restore the ability of the immune system to fight infection and disease.

Biological response modifiers: Substances that stimulate the body’s response to infection and disease. The body naturally produces small amounts of these substances. Scientists can produce some of them in the laboratory in large amounts and use them in cancer treatment.

Biological therapy: The use of the body’s immune system, either directly or indirectly, to fight cancer or to lessen side effects that may be caused by some cancer treatments. Also known as immunotherapy, biotherapy, or biological response modifier therapy.

Biopsy: The removal of a sample of tissue, which is then examined under a microscope to check for cancer cells.

Bladder: The hollow organ that stores urine.

Bladder cancer: Bladder cancer is a disease in which cancer (malignant) cells are found in the bladder. The bladder, a hollow organ in the lower part of the abdomen, stores urine.

Blast phase: Refers to advanced chronic myelogenous leukemia. In this phase, the number of immature, abnormal white blood cells in the bone marrow and blood is extremely high. Also called blast crisis.
**Blasts:** Immature blood cells.

**Blood-brain barrier:** A network of blood vessels with closely spaced cells that makes it difficult for potentially toxic substances (such as anticancer drugs) to penetrate the blood vessel walls and to enter the brain.

**Bone marrow:** The soft, spongy tissue in the center of large bones that produces white blood cells, red blood cells, and platelets.

**Bone marrow aspiration or biopsy:** The removal of a small sample of bone marrow (usually from the hip) through a needle for examination under a microscope to see whether cancer cells are present.

**Bone marrow biopsy:** The removal of a sample of tissue from the bone marrow with a large needle. The cells are checked to see whether they are cancerous. If cancerous plasma cells are found, the pathologist estimates how much of the bone marrow is affected. Bone marrow biopsy is usually done at the same time as bone marrow aspiration.

**Bone marrow transplantation:** A procedure in which doctors replace marrow destroyed by treatment with high doses of anticancer drugs or radiation. The replacement marrow may be taken from the patient before treatment or may be donated by another person.

**Bone scan:** A technique to create images of bones on a computer screen or on film. A small amount of radioactive material is injected and travels through the bloodstream. It collects in the bones, especially in abnormal areas of the bones, and is detected by a scanner.

**Bowel:** Another name for the intestine. There is both a small and a large bowel.

**Brachytherapy:** Internal radiation therapy using an implant of radioactive material placed directly into or near the tumor.

**Brain stem:** The stemlike part of the brain that is connected to the spinal cord.

**Brain stem glioma:** A type of brain tumor that occurs in the lowest, stemlike part of the brain.

**Brain tumor—astrocytoma:** Astrocytomas are tumors that start in brain cells called astrocytes. There are different kinds of astrocytomas, which are defined by how the cancer cells look under a microscope.

**Brain tumor—ependymoma:** Ependymal tumors are tumors that begin in the ependyma, the cells that line the passageways in the brain where special fluid that protects the brain and spinal cord (called cerebrospinal fluid) is made and stored. There are different kinds of ependymal tumors, which are defined by how the cells look under a microscope.

**Brain tumor—glioblastoma:** Glioblastoma multiformes are tumors that grow very quickly and have cells that look very different from normal cells. Glioblastoma multiforme is also called grade IV astrocytoma.

**Brain tumor—medulloblastoma:** Medulloblastomas are brain tumors that begin in the lower part of the brain. They are almost always found in children or young adults. This type of cancer may spread from the brain to the spine.

**BRCA1:** A gene located on chromosome 17 that normally helps to restrain cell growth. Inheriting an altered version of BRCA1 predisposes an individual to breast, ovary, and prostate cancer.

**Breast reconstruction:** Surgery to rebuild a breast’s shape after a mastectomy.

**Bronchi:** Air passage that leads from the windpipe to the lungs.

**Bronchioles:** The tiny branches of air tubes in the lungs.

**Bronchitis:** Inflammation (swelling and reddening) of the bronchi.

**Bronchoscope:** A flexible, lighted instrument used to examine the trachea and bronchi, the air passages that lead into the lungs.
**Bronchoscopy:** A test that permits the doctor to see the breathing passages through a lighted tube.

**Buccal mucosa:** The inner lining of the cheeks and lips.

**Burkitt’s lymphoma:** A type of non-Hodgkin’s lymphoma that most often occurs in young people between the ages of 12 and 30. The disease usually causes a rapidly growing tumor in the abdomen.

**Bypass:** A surgical procedure in which the doctor creates a new pathway for the flow of body fluids.

**Cancer:** A term for diseases in which abnormal cells divide without control. Cancer cells can invade nearby tissues and can spread through the bloodstream and lymphatic system to other parts of the body.

**Cancer screening:** Different tests may show whether a person has a higher than normal risk for getting certain types of cancer. The person’s family history and medical history are also key parts of the cancer screening process.

**Carcinogen:** Any substance that is known to cause cancer.

**Carcinogenesis:** The process by which normal cells are transformed into cancer cells.

**Carcinoma:** Cancer that begins in the lining or covering of an organ.

**Carcinoma in situ:** Cancer that involves only the cells in which it began and has not spread to other tissues.

**Cartilage:** Firm, rubbery tissue that cushions bones at joints. A more flexible kind of cartilage connects muscles with bones and makes up other parts of the body, such as the larynx and the outside of the ears.

**Cauterization:** The use of heat to destroy abnormal cells.

**CEA assay:** A laboratory test to measure the level of carcinoembryonic antigen (CEA), a substance that is sometimes found in an increased amount in the blood of patients with certain cancers.

**Cell:** The basic unit of any living organism.

**Cell differentiation:** The process during which young, immature (unspecialized) cells take on individual characteristics and reach their mature (specialized) form and function.

**Cell motility:** The ability of a cell to move.

**Cell proliferation:** An increase in the number of cells as a result of cell growth and cell division.

**Cellular adhesion:** The close adherence (bonding) to adjoining cell surfaces.

**Central nervous system:** The brain and spinal cord.

**Cerebellum:** The portion of the brain in the back of the head between the cerebrum and the brain stem.

**Cerebral hemispheres:** The two halves of the cerebrum.

**Cerebrospinal fluid:** Watery fluid flowing around the brain and spinal cord.

**Cerebrum:** The largest part of the brain. It is divided into two hemispheres, or halves.

**Cervical cancer:** Cancer of the cervix, a common kind of cancer in women, is a disease in which cancer (malignant) cells are found in the tissues of the cervix. The cervix is the opening of the uterus (womb).

**Cervical intraepithelial neoplasia:** A general term for the growth of abnormal cells on the surface of the cervix. Numbers from 1 to 3 may be used to describe how extensive the abnormal cells are and how deeply they penetrate through the epithelium. Also called CIN.

**Cervix:** The lower, narrow end of the uterus that forms a canal between the uterus and vagina.

**Chemoprevention:** The use of natural or laboratory made substances to prevent cancer.
Chemotherapy: Treatment with anticancer drugs.

Cholangiosarcoma: A type of cancer that begins in the bile ducts.

Chondrosarcoma: A cancer that forms in cartilage, occurring mainly in the pelvis, femur, and shoulder areas.

Chordoma: A form of bone cancer that usually starts in the lower spinal column.

Chromosome: Part of a cell that contains genetic information. Normally, human cells contain 46 chromosomes that appear as a long thread inside the cell.

Chronic leukemia: Leukemia that progresses slowly.

Chronic phase: Refers to the early stages of chronic myelogenous leukemia or chronic lymphocytic leukemia. The number of immature, abnormal white blood cells in the bone marrow and blood is higher than normal, but lower than in the accelerated or blast phase.

Clinical trials: Research studies that involve patients. Each study is designed to find better ways to prevent, detect, diagnose, or treat cancer and to answer scientific questions.

CNS (central nervous system): The brain and the spinal cord.

CNS prophylaxis: Chemotherapy or radiation therapy to the central nervous system (CNS). This is preventive treatment. It is given to kill cancer cells that may be in the brain and spinal cord, even though no cancer has been detected there.

Colectomy: An operation to remove all or part of the colon. In a partial colectomy, the surgeon removes only the cancerous part of the colon and a small amount (called a margin) of surrounding healthy tissue.

Colon: The long, coiled, tubelike organ that removes water from digested food. The remaining material, solid waste called stool, moves through the colon to the rectum and leaves the body through the anus.

Colon cancer: Cancer of the colon, a common form of cancer, is a disease in which cancer (malignant) cells are found in the tissues of the colon. The colon is part of the body's digestive system. The last six feet of intestine is called the large bowel or colon.

Colonoscope: A flexible, lighted instrument used to view the inside of the colon.

Colonoscopy: An examination in which the doctor looks at the colon through a flexible, lighted instrument called a colonoscope.

Colony-stimulating factors: Substances that stimulate the production of blood cells. Treatment with colony-stimulating factors (CSF) can help the blood-forming tissue recover from the effects of chemotherapy and radiation therapy.

Cryosurgery: Treatment performed with an instrument that freezes and destroys abnormal tissues.

Cryptorchidism: A condition in which one or both testicles fail to move from the abdomen, where they develop before birth, into the scrotum; also called undescended testicles.

CT (or CAT) scan: A series of detailed pictures of areas inside the body; the pictures are created by a computer linked to an X-ray machine. Also called computed tomography scan or computed axial tomography scan.

Curettage: Removal of tissue with a curette.

Curette: A spoon-shaped instrument with a sharp edge.

Cutaneous: Related to the skin.

Cutaneous T-cell lymphoma: Cutaneous T-cell lymphoma is a disease in which certain cells of the lymph system (called T lymphocytes) become cancer (malignant) and affect the skin. Lymphocytes are infection-fighting white blood cells that are made in the bone marrow and by other organs of the lymph system. T-cells are special lymphocytes that help the body's immune system kill bacteria and other harmful things in the body.
Cyst: A sac or capsule filled with fluid.

Cystectomy: Surgery to remove the bladder.

Cystoscope: An instrument that allows the doctor to see inside the bladder and remove tissue samples or small tumors.

Cystoscopy: A procedure in which the doctor inserts a lighted instrument into the urethra (the tube leading from the bladder to the outside of the body) to look at the bladder.

Dermis: The lower or inner layer of the two main layers of cells that make up the skin.

Diabetes: A disease in which the body does not use sugar properly. (Many foods are converted into sugar, a source of energy for cells.) As a result, the level of sugar in the blood is too high. This disease occurs when the body does not produce enough insulin or does not use it properly.

Dialysis: The process of cleansing the blood by passing it through a special machine. Dialysis is necessary when the kidneys are not able to filter the blood.

Diaphanography: An exam that involves shining a bright light through the breast to reveal features of the tissues inside. This technique is under study; its value in detecting breast cancer has not been proven. Also called transillumination.

Diaphragm: The thin muscle below the lungs and heart that separates the chest from the abdomen.

Diathermy: The use of heat to destroy abnormal cells. Also called cauterization or electrodiathermy.

Diethylstilbestrol: A drug that was once widely prescribed to prevent miscarriage. Also called DES.

Differentiation: In cancer, refers to how mature (developed) the cancer cells are in a tumor. Differentiated tumor cells resemble normal cells and grow at a slower rate than undifferentiated tumor cells, which lack the structure and function of normal cells and grow uncontrollably.

Digestive system: The organs that take in food and turn it into products that the body can use to stay healthy. Waste products the body cannot use leave the body through bowel movements. The digestive system includes the salivary glands, mouth, esophagus, stomach, liver, pancreas, gall-bladder, intestines, and rectum.

Dilation and curettage: A minor operation in which the cervix is expanded enough (dilation) to permit the cervical canal and uterine lining to be scraped with a spoon-shaped instrument called a curette (curettage). This procedure also is called D and C.

Dilator: A device used to stretch or enlarge an opening.

DNA: The protein that carries genetic information; every cell contains a strand of DNA (deoxyribonucleic acid).

Ductal carcinoma in situ: Abnormal cells that involve only the lining of a duct. The cells have not spread outside the duct to other tissues in the breast. About 15 to 20 percent of breast cancers are sometimes called carcinoma in situ. They may be either ductal carcinoma in situ (sometimes called intraductal carcinoma) or lobular carcinoma in situ. Even though it is referred to as a cancer, it is not actually cancer. However, patients with this condition have a 25 percent chance of developing breast cancer in either breast in the next 25 years. Also called DCIS or intraductal carcinoma.

Dumping syndrome: A group of symptoms that occur when food or liquid enters the small intestine too rapidly. These symptoms include cramps, nausea, diarrhea, and dizziness.

Duodenum: The first part of the small intestine.

Dysplasia: Abnormal cells that are not cancer.

Dysplastic nevi: Atypical moles; moles whose appearance is different from that of common moles. Dysplastic nevi are generally larger than ordinary moles and have irregular and indistinct borders. Their color often is not uniform, and ranges from pink or even white to dark brown...
or black; they usually are flat, but parts may be raised above the skin surface.

**Edema:** Swelling; an abnormal buildup of fluid.

**Electrodesiccation:** Use of an electric current to destroy cancerous tissue and control bleeding.

**Electrolarynx:** A battery-operated instrument that makes a humming sound to help laryngectomees talk.

**Embolization:** Blocking an artery so that blood cannot flow to the tumor.

**Encapsulated:** Confined to a specific area; the tumor remains in a compact form.

**Endocervical curettage:** The removal of tissue from the inside of the cervix using a spoon-shaped instrument called a curette.

**Endometrial cancer:** Cancer of the endometrium, a common kind of cancer in women, is a disease in which cancer (malignant) cells are found in the lining of the uterus (endometrium). The uterus is the hollow, pear-shaped organ where a baby grows. Cancer of the endometrium is different from cancer of the muscle of the uterus, which is called sarcoma of the uterus.

**Endometriosis:** A benign condition in which tissue that looks like endometrial tissue grows in the abdomen.

**Endometrium:** The layer of tissue that lines the uterus.

**Endoscope:** A thin, lighted tube through which a doctor can look at tissues inside the body.

**Endoscopic retrograde cholangiopancreatography:** A procedure to X-ray the common bile duct. Also called ERCP.

**Endoscopy:** An examination of the esophagus and stomach using a thin, lighted instrument called an endoscope.

**Ependymoma:** A type of brain tumor that usually develops in the lining of the ventricles but may also occur in the spinal chord.

**Enterostomal therapist:** A health professional trained in the care of urostomies and other stomas.

**Environmental tobacco smoke:** Smoke that comes from the burning end of a cigarette and smoke that is exhaled by smokers. Also called ETS or second-hand smoke. Inhaling ETS is called involuntary or passive smoking.

**Enzyme:** A substance that affects the rate at which chemical changes take place in the body.

**Ependymoma:** Ependymal tumors are tumors that begin in the ependyma, the cells that line the passageways in the brain where special fluid that protects the brain and spinal cord (called cerebrospinal fluid) is made and stored. There are different kinds of ependymal tumors, which are defined by how the cells look under a microscope.

**Epidermis:** The upper or outer layer of the two main layers of cells that make up the skin.

**Epidermoid carcinoma:** A type of lung cancer in which the cells are flat and look like fish scales. Also called squamous cell carcinoma.

**Epiglottis:** The flap that covers the trachea during swallowing so that food does not enter the lungs.

**Epithelial carcinoma:** Cancer that begins in the cells that line an organ.

**Epithelium:** A thin layer of tissue that covers organs, glands, and other structures in the body.

**ERCP (endoscopic retrograde cholangiopancreatography):** A procedure to X-ray the common bile duct.

**Erythrocytes:** Cells that carry oxygen to all parts of the body. Also called red blood cells (RBCs).

**Erythroleukemia:** Leukemia that develops in erythrocytes. In this rare disease, the body produces large numbers of abnormal red blood cells.

**Erythroplakia:** A reddened patch with a velvety surface found in the mouth.
Glossary

**Esophageal cancer:** Cancer of the esophagus is a disease in which cancer (malignant) cells are found in the tissues of the esophagus. The esophagus is the hollow tube that carries food and liquid from the throat to the stomach.

**Esophageal speech:** Speech produced with air trapped in the esophagus and forced out again.

**Esophagectomy:** An operation to remove a portion of the esophagus.

**Esophagoscopy:** Examination of the esophagus using a thin, lighted instrument.

**Esophagram:** A series of X-rays of the esophagus. The X-ray pictures are taken after the patient drinks a solution that coats and outlines the walls of the esophagus. Also called a barium swallow.

**Esophagus:** The muscular tube through which food passes from the throat to the stomach.

**Estrogen:** A female hormone.

**Ewing's sarcoma:** Ewing's sarcoma/primitive neuroepithelial tumor is a rare disease in which cancer (malignant) cells are found in the bone. The most common areas in which it occurs are the pelvis, the thigh bone (femur), the upper arm bone (humerus), and the ribs. Ewing's sarcoma/primitive neuroepithelial tumor most frequently occurs in teenagers.

**External radiation:** Radiation therapy that uses a machine to aim high-energy rays at the cancer from outside of the body.

**Fallopian tubes:** Tubes on each side of the uterus through which an egg moves from the ovaries to the uterus.

**Familial polyposis:** An inherited condition in which several hundred polyps develop in the colon and rectum.

**Fecal occult blood test:** A test to check for hidden blood in stool. (Fecal refers to stool. Occult means hidden.)

**Fibroid:** A benign uterine tumor made up of fibrous and muscular tissue.

**Fibrosarcoma:** A type of soft tissue sarcoma that begins in fibrous tissue, which holds bones, muscles, and other organs in place.

**Fluoroscope:** An X-ray machine used to view internal organs in motion.

**Fluoroscopy:** An X-ray procedure that makes it possible to see internal organs in motion.

**Fluorouracil:** An anticancer drug. Its chemical name is 5-fluorouracil, commonly called 5-FU.

**Fractionation:** Dividing the total dose of radiation therapy into several smaller, equal doses delivered over a period of several days.

**Fulguration:** Destroying tissue using an electric current.

**Gallbladder:** The pear-shaped organ where bile from the liver is stored. The gallbladder is located beneath the liver.

**Gamma knife:** Radiation therapy in which high-energy rays are aimed at a tumor from many angles in a single treatment session.

**Gastrectomy:** An operation to remove all or part of the stomach.

**Gastric:** Having to do with the stomach.

**Gastric atrophy:** A condition in which the stomach muscles shrink and become weak. It results in a lack of digestive juices.

**Gastric cancer:** Cancer of the stomach, also called gastric cancer, is a disease in which cancer (malignant) cells are found in the tissues of the stomach.

**Gastrointestinal tract:** The part of the digestive tract where the body processes food and eliminates waste. It includes the esophagus, stomach, liver, small and large intestines, and rectum.
Gastroscope: A thin, lighted instrument to view the inside of the stomach.

Gastroscopy: An examination of the stomach with a gastroscope, an instrument to view the inside of the stomach.

Gene: The biological or basic unit of heredity found in all cells in the body.

Gene deletion: The total loss or absence of a gene.

Gene therapy: Treatment that alters genes (the basic units of heredity found in all cells in the body). In studies of gene therapy for cancer, researchers are trying to improve the body’s natural ability to fight the disease or to make the tumor more sensitive to other kinds of therapy.

Genetic: Inherited; having to do with information that is passed from parents to children through DNA in the genes.

Genetic testing: Specific tests can be done to see whether a person has changes in certain genes that are known to be associated with cancer.

Genitourinary system: The parts of the body that play a role in reproduction, in getting rid of waste products in the form of urine, or in both.

Germ cells: The reproductive cells of the body, specifically, either egg or sperm cells.

Germ cell tumors: A type of brain tumor that arises from primitive (developing) sex cells, or germ cells.

Germinoma: The most frequent type of germ cell tumor in the brain.

Germline mutation: See hereditary mutation.

Gestational trophoblastic disease: Gestational trophoblastic tumor, a rare cancer in women, is a disease in which cancer (malignant) cells grow in the tissues that are formed following conception (the joining of sperm and egg). Gestational trophoblastic tumors start inside the uterus, the hollow, muscular, pear-shaped organ where a baby grows. This type of cancer occurs in women during the years when they are able to have children.

Gland: An organ that produces and releases one or more substances for use in the body. Some glands produce fluids that affect tissues or organs. Others produce hormones or participate in blood production.

Glioblastoma multiforme: A type of brain tumor that forms in the nervous (glial) tissue of the brain. They grow very quickly and have cells that look very different from normal cells. Glioblastoma multiforme is also called grade IV astrocytoma.

Glioma: A name for brain tumors that begin in the glial cells, or supportive cells, in the brain. “Glia” is the Greek word for glue.

Glottis: The middle part of the larynx; the area where the vocal cords are located.

Grade: Describes how closely a cancer resembles normal tissue of its same type, and the cancer’s probable rate of growth.

Grading: A system for classifying cancer cells in terms of how malignant or aggressive they appear microscopically. The grading of a tumor indicates how quickly cancer cells are likely to spread and plays a role in treatment decisions.

Graft: Healthy skin, bone, or other tissue taken from one part of the body to replace diseased or injured tissue removed from another part of the body.

Graft-versus-host disease: A reaction of donated bone marrow against a patient’s own tissue. Also called GVHD.

Granulocyte: A type of white blood cell. Neutrophils, eosinophils, and basophils are granulocytes.

Hairy cell leukemia: A rare type of chronic leukemia in which the abnormal white blood cells appear to be covered with tiny hairs.

Helicobacter pylori: Bacteria that cause inflammation and ulcers in the stomach.
Hematogenous: Originating in the blood, or disseminated by the circulation or through the bloodstream.

Hepatitis: Inflammation of the liver.

Hepatitis B: A type of hepatitis that is carried and passed on through the blood. It can be passed on through sexual contact or through the use of “dirty” (bloody) needles.

Hepatoblastoma: A type of liver tumor that occurs in infants and children.

Hepatocellular carcinoma: The most common type of primary liver cancer.

Hepatocyte: A liver cell.

Hepatoma: A liver tumor.

Hereditary mutation: A gene change in the body’s reproductive cells (egg or sperm) that becomes incorporated into the DNA of every cell in the body of offspring; hereditary mutations are passed on from parents to offspring.

Herpes virus: A member of the herpes family of viruses. One type of herpes virus is sexually transmitted and causes genital sores.

HER-2/neu: Oncogene found in some breast and ovarian cancer patients that is associated with a poor prognosis.

Hodgkin’s disease: Hodgkin’s disease is a type of lymphoma. Lymphomas are cancers that develop in the lymph system, part of the body’s immune system.

Hormonal therapy: Treatment of cancer by removing, blocking, or adding hormones.

Hormone receptor test: A test to measure the amount of certain proteins, called hormone receptors, in breast cancer tissue. Hormones can attach to these proteins. A high level of hormone receptors means hormones probably help the cancer grow.

Hormone therapy: Treatment that prevents certain cancer cells from getting the hormones they need to grow.

Hormones: Chemicals produced by glands in the body and circulated in the bloodstream. Hormones control the actions of certain cells or organs.

Human papillomaviruses: Viruses that generally cause warts. Some papillomaviruses are sexually transmitted. Some of these sexually transmitted viruses cause wart-like growths on the genitals, and some are thought to cause abnormal changes in cells of the cervix.

Hydrocephalus: The abnormal buildup of cerebrospinal fluid in the ventricles of the brain.

Hypercalcemia: A higher-than-normal level of calcium in the blood. This condition can cause a number of symptoms, including loss of appetite, nausea, thirst, fatigue, muscle weakness, restlessness, and confusion.

Hyperfractionation: Giving radiation therapy in smaller-than-usual doses two or three times a day.

Hyperplasia: A precancerous condition in which there is an increase in the number of normal cells lining the uterus.

Hypertermia: Treatment that involves heating a tumor.

Hypothalamus: The area of the brain that controls body temperature, hunger, and thirst.

Hysterectomy: An operation in which the uterus and cervix are removed.

Ileostomy: An opening created by a surgeon into the ileum, part of the small intestine, from the outside of the body. An ileostomy provides a new path for waste material to leave the body after part of the intestine has been removed.

Imaging: Tests that produce pictures of areas inside the body.

Immune system: The complex group of organs and cells that defends the body against infection or disease.

Immunodeficiency: A lowering of the body’s ability to fight off infection and disease.
**Immunology:** A science that deals with the study of the body’s immune system.

**Immunosuppression:** The use of drugs or techniques to suppress or interfere with the body’s immune system and its ability to fight infections or disease. Immunosuppression may be deliberate, such as in preparation for bone marrow or other organ transplantation to prevent rejection by the host of the donor tissue, or incidental, such as often results from chemotherapy for the treatment of cancer.

**Immunotherapy:** Treatment that uses the body’s natural defenses to fight cancer. Also called biological therapy.

**Implant radiation:** Radiation therapy that places radioactive materials in or close to the cancer.

**Infiltrating cancer:** See invasive cancer.

**Inflammatory breast cancer:** A rare type of breast cancer in which cancer cells block the lymph vessels in the skin of the breast. The breast becomes red, swollen, and warm, and the skin of the breast may appear pitted or have ridges.

**Inguinal orchiectomy:** Surgery to remove the testicle through the groin.

**Insulin:** A hormone made by the islet cells of the pancreas. Insulin controls the amount of sugar in the blood.

**Interferon:** A type of biological response modifier (a substance that can improve the body’s natural response to disease). It stimulates the growth of certain disease-fighting blood cells in the immune system.

**Interleukin:** A substance used in biological therapy. Interleukins stimulate the growth and activities of certain kinds of white blood cells.

**Interleukin 2:** A type of biological response modifier (a substance that can improve the body’s natural response to disease). It stimulates the growth of certain blood cells in the immune system that can fight cancer. Also called IL-2.

**Internal radiation:** Radiation therapy that uses radioactive materials placed in or near the tumor.

**Intestine:** The long, tube-shaped organ in the abdomen that completes the process of digestion. It consists of the small and large intestines.

**Intraepithelial:** Within the layer of cells that forms the surface or lining of an organ.

**Intrahepatic:** Within the liver.

**Intrahepatic bile duct:** The bile duct that drains bile from the liver.

**Intraoperative radiation therapy:** Radiation treatment given during surgery. Also called IORT.

**Intraperitoneal chemotherapy:** Treatment in which anticancer drugs are put directly into the abdomen through a thin tube.

**Intrathecal chemotherapy:** Chemotherapy drugs infused into the thin space between the lining of the spinal cord and brain to treat or prevent cancers in the brain and spinal cord.

**Intravenous:** Injected in a vein. Also called IV.

**Intravenous pyelogram:** A series of X-rays of the kidneys and bladder. The X-rays are taken after a dye that shows up on X-ray film in injected into a vein. Also called IVP.

**Intravenous pyelography:** X-ray study of the kidneys and urinary tract. Structures are made visible by the injection of a substance that blocks X-rays. Also called IVP.

**Invasion:** As related to cancer, the spread of cancer cells into healthy tissue adjacent to the tumor.

**Invasive cancer:** Cancer that has spread beyond the layer of tissue in which it developed. Invasive breast cancer is also called infiltrating cancer or infiltrating carcinoma.

**Invasive cervical cancer:** Cancer that has spread from the surface of the cervix to tissue deeper in the cervix or to other parts of the body.

**Islet cell cancer:** Cancer arising from cells in the islets of Langerhans.
Islets of Langerhans: Hormone-producing cells in the pancreas.

IV (intravenous): Injected in a vein.

Jaundice: A condition in which the skin and the whites of the eyes become yellow and the urine darkens. Jaundice occurs when the liver is not working properly or when a bile duct is blocked.

Kaposi's sarcoma: A relatively rare type of cancer that develops on the skin of some elderly persons or those with a weak immune system, including those with acquired immune deficiency syndrome (AIDS).

Kidney cancer: Renal cell cancer (also called cancer of the kidney or renal adenocarcinoma) is a disease in which cancer (malignant) cells are found in certain tissues of the kidney. Renal cell cancer is one of the less common kinds of cancer. It occurs more often in men than in women.

Kidneys: A pair or organs in the abdomen that remove waste from the blood. The waste leaves the blood as urine.

Krukenberg tumor: A tumor of the ovary caused by the spread of stomach cancer.

Laparoscopy: A surgical procedure in which a lighted instrument shaped like a thin tube is inserted through a small incision in the abdomen. The doctor can look through the instrument and see inside the abdomen.

Laparotomy: An operation that allows the doctor to inspect the organs in the abdomen.

Large cell carcinomas: A group of lung cancers in which the cells are large and look abnormal.

Laryngectomy: A person who has had his or her voice box removed.

Laryngectomy: An operation to remove all or part of the larynx.

Laryngoscope: A flexible lighted tube used to examine the larynx.

Laryngoscopy: Examination of the larynx with a mirror (indirect laryngoscopy) or with a laryngoscope (direct laryngoscopy).

Larynx: An organ in the throat used in breathing, swallowing, and talking. It is made of cartilage and is lined by a mucous membrane similar to the lining of the mouth. Also called the voice box.

Larynx cancer: Cancer of the larynx (or voice box) is a disease in which cancer (malignant) cells are found in the tissues of the larynx. Your larynx is a short passageway shaped like a triangle that is just below the pharynx in the neck. The pharynx is a hollow tube about five inches long that starts behind the nose and goes down to the neck to become part of the tube that goes to the stomach (the esophagus).

Leiomyosarcoma: Leiomyosarcoma is a tumor of smooth muscle tissue. This cancer affects the uterus, lower abdomen, and extremities (hands and feet) most often.

Lesion: An area of abnormal tissue change.

Leukemia: Cancer of the blood cells.

Leukemia—Acute lymphoblastic: Acute lymphocytic leukemia (also called acute lymphoblastic leukemia or ALL) is a disease in which too many infection-fighting white blood cells called lymphocytes are found in the blood and bone marrow.

Leukemia—Acute myeloblastic: Acute myeloid leukemia (AML) is a disease in which cancer (malignant) cells are found in the blood and bone marrow. Normally, the bone marrow makes cells called blasts that develop (mature) into several different types of blood cells that have specific jobs to do in the body. AML affects the blasts that are developing into white blood cells called granulocytes. In AML, the blasts do not mature and become too numerous.

Leukemia—Chronic myelogenous: Chronic myelogenous leukemia (also called CML or chronic granulocytic leukemia) is a disease in which too many white blood cells are made in
the bone marrow. CML affects the blasts that are developing into white blood cells called granulocytes.

**Leukocytes:** Cells that help the body fight infections and other diseases. Also called white blood cells (WBCs).

**Leukoplakia:** A white spot or patch in the mouth.

**Li-Fraumeni Syndrome:** A rare family predisposition to multiple cancers, caused by an alteration in the p53 tumor suppressor gene.

**Ligation:** The process of tying off blood vessels so that blood cannot flow to a part of the body or to a tumor.

**Limb perfusion:** A chemotherapy technique that may be used when melanoma occurs on an arm or leg. The flow of blood to and from the limb is stopped for a while with a tourniquet, and anticancer drugs are put directly into the blood of the limb. This allows the patient to receive a high dose of drugs in the area where the melanoma occurred.

**Liver:** A large, glandular organ located in the upper abdomen that cleanses the blood and aids in digestion by secreting bile.

**Liver cancer:** Liver cancer is a disease in which cancer (malignant) cells start to grow in the tissues of the liver. The liver is one of the largest organs in the body, filling the upper right side of the abdomen and protected by the rib cage.

**Liver scan:** An image of the liver created on a computer screen or on film. For a liver scan, a radioactive substance is injected into a vein and travels through the bloodstream. It collects in the liver, especially in abnormal areas, and can be detected by the scanner.

**Lobe:** A portion of the liver, lung, breast, or brain.

**Lobectomy:** The removal of a lobe.

**Lobular carcinoma in situ:** Abnormal cells in the lobules of the breast. This condition seldom becomes invasive cancer. However, having lobular carcinoma in situ is a sign that the woman has an increased risk of developing breast cancer. Also called LCIS.

**Lobule:** A small lobe.

**Local:** Reaching and affecting only the cells in a specific area.

**Local therapy:** Treatment that affects cells in the tumor and the area close to it.

**Lower GI series:** A series of X-rays of the colon and rectum that is taken after the patient is given a barium enema. (Barium is a white substance that outlines the colon and rectum on the X-ray.)

**Lumbar puncture:** The insertion of a needle into the lower part of the spinal column to collect cerebrospinal fluid or to give intrathecal chemotherapy. Also called a spinal tap.

**Lumpectomy:** Surgery to remove only the cancerous breast lump; usually followed by radiation therapy.

**Luteinizing hormone-releasing hormone (LHRH) agonist:** A substance that closely resembles LHRH, which controls the production of sex hormones. However, LHRH agonists affect the body differently than does LHRH. LHRH agonists keep the testicles from producing hormones.

**Lymph:** The almost colorless fluid that travels through the lymphatic system and carries cells that help fight infection and disease.

**Lymph nodes:** Small, bean-shaped organs located along the channels of the lymphatic system. The lymph nodes store special cells that can trap bacteria or cancer cells traveling through the body in lymph. Clusters of lymph nodes are found in the underarms, groin, neck, chest, and abdomen.

**Lymphangiogram:** An X-ray of the lymphatic system. A dye is injected to outline the lymphatic vessels and organs.
**Lymphangiography:** X-ray study of lymph nodes and lymph vessels made visible by the injection of a special dye.

**Lymphatic system:** The tissues and organs that produce, store, and carry white blood cells that fight infection and disease. This system includes the bone marrow, spleen, thymus, and lymph nodes and a network of thin tubes that carry lymph and white blood cells. These tubes branch, like blood vessels, into all the tissues of the body.

**Lymphedema:** A condition in which excess fluid collects in tissue and causes swelling. It may occur in the arm or leg after lymph vessels or lymph nodes in the underarm or groin are removed.

**Lymphoma:** Cancer that arises in cells of the lymphatic system.

**Lymphocytes:** White blood cells that fight infection and disease.

**Lymphocytic:** Referring to lymphocytes, a type of white blood cell.

**Lymphoid:** Referring to lymphocytes, a type of white blood cell. Also refers to tissue in which lymphocytes develop.

**M proteins:** Antibodies or parts of antibodies found in unusually large amounts in the blood or urine of multiple myeloma patients.

**Magnetic resonance imaging:** A procedure in which a magnet linked to a computer is used to create detailed pictures of areas inside the body. Also called MRI.

**Maintenance therapy:** Chemotherapy that is given to leukemia patients in remission to prevent a relapse.

**Malignant:** Cancerous; can invade nearby tissue and spread to other parts of the body.

**Mammogram:** An X-ray of the breast.

**Mammography:** The use of X-rays to create a picture of the breast.

**Mastectomy:** Surgery to remove the breast (or as much of the breast as possible).

**Mediastinoscopy:** A procedure in which the doctor inserts a tube into the chest to view the organs in the mediastinum. The tube is inserted through an incision above the breastbone.

**Mediastinotomy:** A surgical procedure in which a small opening is made in the upper chest in order to allow examination of the lungs and chest.

**Mediastinum:** The area between the lungs. The organs in this area include the heart and its large veins and arteries, the trachea, the esophagus, the bronchi, and lymph nodes.

**Medical oncologist:** A doctor who specializes in treating cancer. Some oncologists specialize in a particular type of cancer treatment. For example, a radiation oncologist specializes in treating cancer with radiation.

**Medulloblastoma:** A type of brain tumor that recent research suggests develops from primitive (developing) nerve cells that normally do not remain in the body after birth. Medulloblastomas are sometimes called primitive neuroectodermal tumors. They are almost always found in children or young adults.

**Melanin:** A skin pigment (substance that gives the skin its color). Dark-skinned people have more melanin than light-skinned people.

**Melanocytes:** Cells in the skin that produce and contain the pigment called melanin.

**Melanoma:** Cancer of the cells that produce pigment in the skin. Melanoma usually begins in a mole.

**Membrane:** A thin layer of tissue that covers a surface.

**Meninges:** The three membranes that cover the brain and spinal cord.

**Meningioma:** A type of brain tumor that develops in the meninges. Because these tumors grow very slowly, the brain may be able to adjust to their
presence; meningiomas often grow quite large before they cause symptoms.

**Mesothelioma**: Malignant mesothelioma, a rare form of cancer, is a disease in which cancer (malignant) cells are found in the sac lining the chest (the pleura) or abdomen (the peritoneum). Most people with malignant mesothelioma have worked on jobs where they breathed asbestos.

**Metastasize**: To spread from one part of the body to another. When cancer cells metastasize and form secondary tumors, the cells in the metastatic tumor are like those in the original (primary) tumor.

**Microcalcifications**: Tiny deposits of calcium in the breast that cannot be felt but can be detected on a mammogram. A cluster of these very small specks of calcium may indicate that cancer is present.

**Mole**: An area on the skin (usually dark in color) that contains a cluster of melanocytes.

**Monoclonal antibodies**: Substances that can locate and bind to cancer cells wherever they are in the body. They can be used alone, or they can be used to deliver drugs, toxins, or radioactive material directly to tumor cells.

**Monocyte**: A type of white blood cell.

**Morphology**: The science of the form and structure of organisms (plants, animals, and other forms of life).

**MRI (magnetic resonance imaging)**: A procedure in which a magnet linked to a computer is used to create detailed pictures of areas inside the body.

**Mucus**: A thick fluid produced by the lining of some organs of the body.

**Multiple myeloma**: Cancer that affects plasma cells. The disease causes the growth of tumors in many bones, which can lead to bone pain and fractures. In addition, the disease often causes kidney problems and lowered resistance to infection.

**Mutations**: Changes in the way cells function or develop, caused by an inherited genetic defect or an environmental exposure. Such changes may lead to cancer.

**Mycosis fungoides**: A type of non-Hodgkin’s lymphoma that first appears on the skin. Also called cutaneous T-cell lymphoma.

**Myeloid**: Referring to myelocytes, a type of white blood cell. Also called myelogenous.

**Myelogram**: An X-ray of the spinal cord and the bones of the spine.

**Myelogenous**: Referring to myelocytes, a type of white blood cell. Also called myeloid.

**Myelodysplastic syndrome**: Myelodysplastic syndromes, also called pre-leukemia or “smoldering” leukemia, are diseases in which the bone marrow does not function normally and not enough normal blood cells are made. (See Preleukemia)

**Myometrium**: The muscular outer layer of the uterus.

**Nasopharynx cancer**: Cancer of the nasopharynx is a disease in which cancer (malignant) cells are found in the tissues of the nasopharynx. The nasopharynx is behind the nose and is the upper part of the throat (also called the pharynx). The pharynx is a hollow tube about five inches long that starts behind the nose and goes down to the neck to become part of the tube that goes to the stomach (the esophagus).

**Nephrectomy**: Surgery to remove the kidney. Radical nephrectomy removes the kidney, the adrenal
gland, nearby lymph nodes, and other surrounding tissue. Simple nephrectomy removes just the affected kidney. Partial nephrectomy removes the tumor, but not the entire kidney.

**Nephrotomogram:** A series of special X-rays of the kidneys. The X-rays are taken from different angles. They show the kidneys clearly, without the shadows of the organs around them.

**Neuroblastoma:** Neuroblastoma is a disease in which cancer (malignant) cells are found in certain nerve cells in the body. Neuroblastoma most commonly starts in the abdomen, either in the adrenal glands (located just above the kidney in back of the upper abdomen) or around the spinal cord. Neuroblastoma can also start around the spinal cord in the chest, neck, or pelvis.

**Neuroma:** A tumor that arises in nerve cells.

**Neurosurgeon:** A doctor who specializes in surgery on the brain and other parts of the nervous system.

**Neutrophil:** A type of white blood cell.

**Nevus:** The medical term for a spot on the skin, such as a mole. A mole is a cluster of melanocytes that usually appears as a dark spot on the skin. The plural of nevus is nevi (NEE-vye).

**Nitrosoureas:** A group of anticancer drugs that can cross the blood–brain barrier. Carmustine (BCNU) and lomustine (CCNU) are nitrosoureas.

**Non-Hodgkin’s lymphoma:** Adult non-Hodgkin’s lymphoma is a disease in which cancer (malignant) cells are found in the lymph system. There are many types of non-Hodgkin’s lymphomas. Some types spread more quickly than others. The type is determined by how the cancer cells look under a microscope.

**Nonmelanoma skin cancer:** Skin cancer that does not involve melanocytes. Basal cell cancer and squamous cell cancer are nonmelanoma skin cancers.

**Nonseminoma:** A classification of testicular cancers that arise in specialized sex cells called germ cells. Nonseminomas include embryonal carcinoma, teratoma, choriocarcinoma, and yolk sac tumor.

**Non-small cell lung cancer:** A form of lung cancer associated with smoking, exposure to environmental tobacco smoke, or exposure to radon. Non-small cell lung cancer is classified as squamous cell carcinoma, adenocarcinoma, and large cell carcinoma depending on what type of cells are in the cancer.

**Oat cell cancer:** A type of lung cancer in which the cells look like oats. Also called small cell lung cancer.

**Oligodendrogloma:** A rare, slow-growing type of brain tumor that occurs in the cells that produce myelin, the fatty covering that protects nerves.

**Ommaya reservoir:** A device implanted under the scalp and used to deliver anticancer drugs to the fluid surrounding the brain and spinal cord.

**Oncogene:** The part of the cell that normally directs cell growth, but which can also promote or allow the uncontrolled growth of cancer if damaged (mutated) by an environmental exposure to carcinogens, or damaged or missing because of an inherited defect.

**Oncologist:** A doctor who specializes in treating cancer. Some oncologists specialize in a particular type of cancer treatment.

**Oncology:** The study of tumors encompassing the physical, chemical, and biologic properties.

**Oophorectomy:** The removal of one or both ovaries.

**Ophthalmoscope:** A lighted instrument used to examine the inside of the eye, including the retina and the optic nerve.

**Optic nerve:** The nerve that carries messages from the retina to the brain.

**Oral cavity cancer:** Cancer of the oral cavity is a disease in which cancer (malignant) cells are
found in the tissues of the lip or mouth. The oral cavity includes the front two-thirds of the tongue, the upper and lower gums (the gingiva), the lining of the inside of the cheeks and lips (the buccal mucosa), the bottom (floor) of the mouth under the tongue, the bony top of the mouth (the hard palate), and the small area behind the wisdom teeth (the retromolar trigone).

**Orchiectomy:** Surgery to remove the testicles.

**Organisms:** Plants, animals, and other forms of life that are made up of complex and interconnected systems of cells and tissue.

**Oropharynx:** The area of the throat at the back of the mouth.

**Osteosarcoma:** A cancer of the bone that is most common in children. Also called osteogenic sarcoma. It is the most common type of bone cancer.

**Ostomy:** An operation to create an opening from an area inside the body to the outside. See Colostomy.

**Ovarian cancer:** Cancer of the ovary is a disease in which cancer (malignant) cells are found in the ovary. Approximately 25,000 women in the United States are diagnosed with this disease each year. The ovary is a small organ in the pelvis that makes female hormones and holds egg cells that, when fertilized, can develop into a baby.

**Ovaries:** The pair of female reproductive glands in which the ova, or eggs, are formed. The ovaries are located in the lower abdomen, one on each side of the uterus.

**p53:** A gene in the cell that normally inhibits the growth of tumors, which can prevent or slow the spread of cancer.

**Palate:** The roof of the mouth. The front portion is bony (hard palate), and the back portion is muscular (soft palate).

**Palliative treatment:** Treatment that does not alter the course of a disease but improves the quality of life.

**Palpation:** A technique in which a doctor presses on the surface of the body to feel the organs or tissues underneath.

**Pancreas:** A gland located in the abdomen. It makes pancreatic juices, and it produces several hormones, including insulin. The pancreas is surrounded by the stomach, intestines, and other organs.

**Pancreatic cancer:** Cancer of the pancreas is a disease in which cancer (malignant) cells are found in the tissues of the pancreas. The pancreas is about six inches long and is shaped something like a thin pear, wider at one end and narrowing at the other. The pancreas lies behind the stomach, inside a loop formed by part of the small intestine.

**Pancreatectomy:** Surgery to remove the pancreas. In a total pancreatectomy, the duodenum, common bile duct, gallbladder, spleen, and nearby lymph nodes also are removed.

**Pancreatic juices:** Fluids made by the pancreas. Pancreatic juices contain proteins called enzymes that aid in digestion.

**Papillary tumor:** A tumor shaped like a small mushroom with its stem attached to the inner lining of the bladder.

**Papilledema:** Swelling around the optic nerve, usually caused by pressure on the nerve by a tumor.

**Pap test:** Microscopic examination of cells collected from the cervix. It is used to detect changes that may be cancer or may lead to cancer, and it can show noncancerous conditions, such as infection or inflammation. Also called Pap smear.

**Paraneoplastic syndrome:** A group of symptoms that may develop when substances released by some cancer cells disrupt the normal function of surrounding cells and tissue. Such symptoms do not necessarily mean that the cancer has spread beyond the original site.

**Parotid cancer:** Cancer of the salivary gland is a disease in which cancer (malignant) cells are found
in the tissues of the salivary glands. Your salivary glands make saliva, the fluid that is released into your mouth to keep it moist and to help dissolve your food. Major clusters of salivary glands are found below your tongue (sublingual glands), on the sides of your face just in front of your ears (parotid glands), and under your jawbone (submaxillary glands).

**Pathologist:** A doctor who identifies diseases by studying cells and tissues under a microscope.

**Pelvis:** The lower part of the abdomen, located between the hip bones.

**Penile cancer:** Cancer of the penis, a rare kind of cancer in the United States, is a disease in which cancer (malignant) cells are found on the skin and in the tissues of the penis.

**Percutaneous transhepatic cholangiography:** A test sometimes used to help diagnose cancer of the pancreas. During this test, a thin needle is put into the liver. Dye is injected into the bile ducts in the liver so that blockages can be seen on X-rays.

**Perfusion:** The process of flooding fluid through the artery to saturate the surrounding tissue. In regional perfusion, a specific area of the body (usually an arm or a leg) is targeted, and high doses of anticancer drugs are flooded through the artery to reach the surrounding tissue and kill as many cancer cells as possible. Such a procedure is performed in cases in which the cancer is not thought to have spread past a localized area.

**Perineal prostatectomy:** Surgery to remove the prostate through an incision made between the scrotum and the anus.

**Peripheral blood stem cell transplantation:** A procedure that is similar to bone marrow transplantation. Doctors remove healthy immature cells (stem cells) from a patient's blood and store them before the patient receives high-dose chemotherapy and possibly radiation therapy to destroy the leukemia cells. The stem cells are then returned to the patient, where they can produce new blood cells to replace cells destroyed by the treatment.

**Peripheral stem cell support:** A method of replacing blood-forming cells destroyed by cancer treatment. Certain cells (stem cells) in the blood that are similar to those in the bone marrow are removed from the patient’s blood before treatment. The cells are given back to the patient after treatment.

**Peristalsis:** The rippling motion of muscles in the digestive tract. In the stomach, this motion mixes food with gastric juices, turning it into a thin liquid.

**Peritoneal cavity:** The lower part of the abdomen that contains the intestines (the last part of the digestive tract), the stomach, and the liver. It is bound by thin membranes.

**Peritoneum:** The large membrane that lines the abdominal cavity.

**Pernicious anemia:** A blood disorder caused by a lack of vitamin B12. Patients who have this disorder do not produce the substance in the stomach that allows the body to absorb vitamin B12.

**Petechiae:** Tiny red spots under the skin; often a symptom of leukemia.

**Pharynx:** The hollow tube about five inches long that starts behind the nose and ends at the top of the trachea (windpipe) and esophagus (the tube that goes to the stomach).

**Photodynamic therapy:** Treatment that destroys cancer cells with lasers and drugs that become active when exposed to light.

**Pigment:** A substance that gives color to tissue. Pigments are responsible for the color of skin, eyes, and hair.

**Pineal gland:** A small gland located in the cerebrum.

**Pineal region tumors:** Types of brain tumors that occur in or around the pineal gland, a tiny organ near the center of the brain. The pineal region is very difficult to reach, therefore these tumors often cannot be removed.
Pineoblastoma: A fast-growing type of brain tumor that occurs in or around the pineal gland, a tiny organ near the center of the brain.

Pineocytoma: A slow-growing type of brain tumor that occurs in or around the pineal gland, a tiny organ near the center of the brain.

Pituitary cancer: Pituitary tumors found in the pituitary gland, a small organ about the size of a pea in the center of the brain just above the back of the nose. Your pituitary gland makes hormones that affect your growth and the functions of other glands in your body. Most pituitary tumors are benign. This means that they grow very slowly and do not spread to other parts of the body.

Pituitary gland: The main endocrine gland; it produces hormones that control other glands and many body functions, especially growth.

Plasma: The liquid part of the blood.

Plasma cells: Special white blood cells that produce antibodies.

Plasmacytoma: A tumor that is made up of cancerous plasma cells.

Plasmapheresis: The process of removing certain proteins from the blood. Plasmapheresis can be used to remove excess antibodies from the blood of multiple myeloma patients.

Platelets: Blood cells that help clots form to help control bleeding. Also called thrombocytes.

Pleura: The thin covering that protects and cushions the lungs. The pleura is made of two layers of tissue separated by a small amount of fluid.

Pleural cavity: A space enclosed by the pleura, thin tissue covering the lungs and lining the interior wall of the chest cavity. It is bound by serous membranes.

Pneumatic larynx: A device that uses air to produce sound to help a laryngectomee talk.

Pneumonectomy: An operation to remove an entire lung.

Polyp: A mass of tissue that projects into the colon.

Positron emission tomography scan: For this type of scan, a person is given a substance that reacts with tissues in the body to release protons (parts of an atom). Through measuring the different amounts of protons released by healthy and cancerous tissues, a computer creates a picture of the inside of the body. Also called PET scan.

Postremission therapy: Chemotherapy to kill leukemia cells that survive after remission induction therapy.

Precancerous: A term used to describe a condition that may or is likely to become cancer.

Precancerous polyps: Growths in the colon that often become cancerous.

Prednisone: A drug often given to multiple myeloma patients along with one or more anticancer drugs. Prednisone appears to act together with anticancer drugs in helping to control the effects of the disease on the body.

Preleukemia: A condition in which the bone marrow does not function normally. It does not produce enough blood cells. This condition may progress and become acute leukemia. Preleukemia also is called myelodysplastic syndrome or smoldering leukemia.

Primitive neuroectodermal tumors: A type of brain tumor that recent research suggests develops from primitive (developing) nerve cells that normally do not remain in the body after birth. Primitive neuroectodermal tumors are often called medulloblastomas.

Proctoscopy: An examination of the rectum and the lower end of the colon using a thin, lighted instrument called a sigmoidoscope.

Proctosigmoidoscopy: An examination of the rectum and the lower colon using a thin, lighted instrument called a sigmoidoscope.

Progesterone: A female hormone.
**Prognosis:** The probable outcome or course of a disease; the chance of recovery.

**Prophylactic cranial irradiation:** Radiation therapy to the head to prevent cancer from spreading to the brain.

**Prostatectomy:** An operation to remove all or part of the prostate.

**Prostate cancer:** Cancer of the prostate, a common form of cancer, is a disease in which cancer (malignant) cells are found in the prostate. The prostate is one of the male sex glands and is located just below the bladder (the organ that collects and empties urine) and in front of the rectum (the lower part of the intestine). It surrounds part of the urethra, the tube that carries urine from the bladder to the outside of the body. The prostate makes fluid that becomes part of the semen, the white fluid that contains sperm.

**Prostate gland:** A gland in the male reproductive system just below the bladder. It surrounds part of the urethra, the canal that empties the bladder. It produces a fluid that forms part of semen.

**Prostate-specific antigen:** A protein whose level in the blood goes up in some men who have prostate cancer or benign prostatic hyperplasia.

**Prostatic acid phosphatase:** An enzyme produced by the prostate. Its level in the blood goes up in some men who have prostate cancer. Also called PAP.

**Proteins:** Substances that are essential to the body’s structure and proper functioning.

**PTC (percutaneous transhepatic cholangiography):** A test sometimes used to help diagnose cancer of the pancreas. During this test, a thin needle is put into the liver. Dye is injected into the bile ducts in the liver so that blockages can be seen on X-rays.

**Radiation fibrosis:** The formation of scar tissue as a result of radiation therapy to the lung.

**Radiation oncologist:** A doctor who specializes in using radiation to treat cancer.

**Radiation therapy:** Treatment with high-energy rays (such as X-rays) to kill cancer cells. The radiation may come from outside the body (external radiation) or from radioactive materials placed directly in the tumor (implant radiation). Also called radiotherapy.

**Radical cystectomy:** Surgery to remove the bladder as well as nearby tissues and organs.

**Radical prostatectomy:** Surgery to remove the entire prostate. The two types of radical prostatectomy are retropubic prostatectomy and perineal prostatectomy.

**Radionuclide scanning:** An exam that produces pictures (scans) of internal parts of the body. The patient is given an injection or swallows a small amount of radioactive material. A scanner then measures the radioactivity in certain organs.

**Radiosensitizers:** Drugs that make cells more sensitive to radiation.

**Rectal cancer:** Cancer of the rectum, a common form of cancer, is a disease in which cancer (malignant) cells are found in the tissues of the rectum. The rectum is part of the body’s digestive system. The last six feet of intestine is called the large bowel or colon. The last eight to 10 inches of the colon is the rectum.

**Rectum:** The last 8 to 10 inches of the large intestine. The rectum stores solid waste until it leaves the body through the anus.

**Red blood cells:** Cells that carry oxygen to all parts of the body. Also called erythrocytes.

**Reed-Sternberg cell:** A type of cell that appears in patients with Hodgkin’s disease. The number of these cells increases as the disease advances.

**Reflex:** The term used when liquid backs up into the esophagus from the stomach.

**Regional chemotherapy:** Treatment with anticancer drugs that affects mainly the cells in the treated area.
Relapse: The return of signs and symptoms of a disease after a period of improvement.

Remission: Disappearance of the signs and symptoms of cancer. When this happens, the disease is said to be “in remission.” A remission can be temporary or permanent.

Remission induction therapy: The initial chemotherapy a patient with acute leukemia receives to bring about a remission.

Renal capsule: The fibrous connective tissue that surrounds each kidney.

Renal cell cancer: Cancer that develops in the lining of the renal tubules, which filter the blood and produce urine.

Renal pelvis: The area at the center of the kidney. Urine collects here and is funneled into the ureter.

Respiratory system: The organs that are involved in breathing. These include the nose, throat, larynx, trachea, bronchi, and lungs.

Respiratory therapy: Exercises and treatments that help patients recover lung function after surgery.

Retinoblastoma: An eye cancer caused by the loss of both gene copies of the tumor-suppressor gene RB; the inherited form typically occurs in childhood, because one gene is missing at birth.

Retropubic prostatectomy: Surgical removal of the prostate through an incision in the abdomen.

Rhabdomyosarcoma: Rhabdomyosarcoma is a disease in which cancer (malignant) cells begin growing in muscle tissue somewhere in the body. Rhabdomyosarcoma is a type of sarcoma, which means a cancer of the bone, soft tissues, or connective tissue (e.g., tendon or cartilage). Rhabdomyosarcoma begins in the soft tissues in a type of muscle called striated muscle. It can occur anywhere in the body.

RNA (ribonucleic acid): One of the two nucleic acids found in all cells. The other is DNA (deoxyribonucleic acid). RNA transfers genetic information from DNA to proteins produced by the cell.

Salivary glands: Glands in the mouth that produce saliva.

Salpingo-oophorectomy: Surgical removal of the fallopian tubes and ovaries.

Sarcoma: A malignant tumor that begins in connective and supportive tissue.

Scans: Images of the organs or other parts of the body. Scans are often used in diagnosing, staging, and monitoring patients include liver scans, bone scans, and computed tomography (CT) or computed axial tomography (CAT) scans. In liver scanning and bone scanning, radioactive substances that are injected into the bloodstream collect in these organs. A scanner that detects the radiation is used to create pictures. In CT scanning, an X-ray machine linked to a computer is used to produce detailed pictures of organs inside the body.

Schiller test: A test in which iodine is applied to the cervix. The iodine colors healthy cells brown; abnormal cells remain unstained, usually appearing white or yellow.

Schwannoma: A type of benign brain tumor that begins in the Schwann cells, which produce the myelin that protects the acoustic nerve the nerve of hearing.

Seminal vesicles: Glands that help produce semen.

Seminoma: A type of testicular cancer that arises from sex cells, or germ cells, at a very early stage in their development.

Shunt: A catheter (tube) that carries cerebrospinal fluid from a ventricle in the brain to another area of the body.

Sigmoidoscope: An instrument used to view the inside of the colon.

Sigmoidoscopy: A procedure in which the doctor looks inside the rectum and the lower part of the colon (sigmoid colon) through a lighted tube. The
doctor may collect samples of tissue or cells for closer examination. Also called proctosigmoidoscopy.

**Sinus cancer**: Sinus cancer is a disease in which cancer (malignant) cells are found in the tissues of the paranasal sinuses or nasal cavity. Your paranasal sinuses are small hollow spaces around your nose. The sinuses are lined with cells that make mucus, which keeps the nose from drying out; the sinuses are also a space through which your voice can echo to make sounds when you talk or sing.

**Skin cancer**: Skin cancer is a disease in which cancer (malignant) cells are found in the outer layers of your skin. The skin has two main layers and several kinds of cells. The top layer of skin is called the epidermis. It contains three kinds of cells: flat, scaly cells on the surface called squamous cells; round cells called basal cells; and cells called melanocytes, which give your skin its color.

**Skin graft**: Skin that is moved from one part of the body to another.

**Small cell lung cancer**: A type of lung cancer in which the cells are small and round. Also called oat cell lung cancer.

**Small intestine**: The part of the digestive tract that is located between the stomach and the large intestine.

**Smoldering leukemia**: See Preleukemia.

**Soft tissue sarcoma**: A sarcoma that begins in the muscle, fat, fibrous tissue, blood vessels, or other supporting tissue of the body.

**Somatic cells**: All the body cells except the reproductive cells.

**Somatic mutations**: See mutation.

**Sperm banking**: Freezing sperm before cancer treatment for use in the future. This procedure can allow men to father children after loss of fertility.

**SPF (sun protection factor)**: A scale for rating sunscreens. Sunscreens with an SPF of 15 or higher provide the best protection from the sun’s harmful rays.

**Spinal tap**: A test in which a fluid sample is removed from the spinal column with a thin needle. Also called a lumbar puncture.

**Spleen**: An organ that produces lymphocytes, filters the blood, stores blood cells, and destroys those that are aging. It is located on the left side of the abdomen near the stomach.

**Splenectomy**: An operation to remove the spleen.

**Sputum**: Mucus from the lungs.

**Squamous cell carcinoma**: Cancer that begins in squamous cells, which are thin, flat cells resembling fish scales. Squamous cells are found in the tissue that forms the surface of the skin, the lining of the hollow organs of the body, and the passages of the respiratory and digestive tracts.

**Squamous cells**: Flat cells that look like fish scales; they make up most of the epidermis, the outer layer of the skin.

**Squamous intraepithelial lesion**: A general term for the abnormal growth of squamous cells on the surface of the cervix. The changes in the cells are described as low grade or high grade, depending on how much of the cervix is affected and how abnormal the cells are. Also called SIL.

**Stage**: The extent of a cancer, especially whether the disease has spread to other parts of the body.

**Staging**: Doing exams and tests to learn the extent of the cancer, especially whether it has spread from its original site to other parts of the body.

**Stem cells**: The cells from which all blood cells develop.

**Stereotaxis**: Use of a computer and scanning devices to create three-dimensional pictures. This method can be used to direct a biopsy, external radiation, or the insertion of radiation implants.

**Steroids**: Drugs used to relieve swelling and inflammation.
Stoma: An opening in the abdominal wall; also called an ostomy or urostomy.

Stool test: A test to check for hidden blood in the bowel movement.

Subglottis: The lowest part of the larynx; the area from just below the vocal cords down to the top of the trachea.

Supportive care: Treatment given to prevent, control, or relieve complications and side effects and to improve the patient’s comfort and quality of life.

Supraglottis: The upper part of the larynx, including the epiglottis; the area above the vocal cords.

Systemic: Reaching and affecting cells all over the body.

Systemic therapy: Treatment that uses substances that travel through the bloodstream, reaching and affecting cancer cells all over the body.

Systemic treatment: Treatment using substances that travel through the bloodstream, reaching and affecting cancer cells all over the body.

T-cell lymphoma: A cancer of the immune system that appears in the skin; also called mycosis fungoides.

Testicular cancer: Cancer of the testicle (also called the testis), a rare kind of cancer in men, is a disease in which cancer (malignant) cells are found in the tissues of one or both testicles. The testicles are round and a little smaller than golf balls. Sperm (the male germ cells that can join with a female egg to develop into a baby) and male hormones are made in the testicles. There are two testicles located inside of the scrotum (a sac of loose skin that lies directly under the penis).

Testosterone: A male sex hormone.

Thermography: A test to measure and display heat patterns of tissues near the surface of the breast. Abnormal tissue generally is warmer than healthy tissue. This technique is under study; its value in detecting breast cancer has not been proven.

Thoracentesis: Removal of fluid in the pleura through a needle.

Thoracic: Pertaining to the chest.

Thoracotomy: An operation to open the chest.

Thrombocytes: See Platelets.

Thrombophlebitis: Inflammation of a vein that occurs when a blood clot forms.

Thymoma: Malignant thymoma is a disease in which cancer (malignant) cells are found in the tissues of the thymus. The thymus is a small organ that lies under the breastbone. It makes white blood cells called lymphocytes, which travel through your body and fight infection. People with malignant thymoma often have other diseases of their immune system. The most common disease in people with thymoma is one in which the muscles are weak, called myasthenia gravis.

Thymus: An organ in which lymphocytes mature and multiply. It lies behind the breastbone.

Thyroid cancer: Cancer of the thyroid is a disease in which cancer (malignant) cells are found in the tissues of the thyroid gland. Your thyroid gland is at the base of your throat. It has two lobes, one on the right side and one on the left. Your thyroid gland makes important hormones that help your body to function normally.

Tissue: A group or layer of cells that together perform specific functions.

Tonsils: Small masses of lymphatic tissue on either side of the throat.

Topical chemotherapy: Treatment with anticancer drugs in a lotion or cream.

Total pancreatectomy: Surgery to remove the entire pancreas.
Toxins: Poisons produced by certain animals, plants, or bacteria.

Trachea: The airway that leads from the larynx to the lungs. Also called the windpipe.

Tracheoesophageal puncture: A small opening made by a surgeon between the esophagus and the trachea. A valve keeps food out of the trachea but lets air into the esophagus for esophageal speech.

Tracheostomy: Surgery to create an opening (stoma) into the windpipe. The opening itself may also be called a tracheostomy.

Tracheostomy button: A small plastic tube placed in the stoma to keep it open.

Tracheostomy tube: A two- to three-inch-long metal or plastic tube that keeps the stoma and trachea open. Also called a trach (“trake”) tube.

Transformation: The change that a normal cell undergoes as it becomes malignant.

Transfusion: The transfer of blood or blood products from one person to another.

Transitional cell carcinoma: Cancer that develops in the lining of the renal pelvis. This type of cancer also occurs in the ureter and the bladder.

Transitional cells: Cells lining some organs.

Transplantation: The replacement of an organ with one from another person.

Transrectal ultrasound: The use of sound waves to detect cancer. An instrument is inserted into the rectum. Waves bounce off the prostate and the pattern of the echoes produced is converted into a picture by a computer.

Transurethral resection: Surgery performed with a special instrument inserted through the urethra. Also called TUR.

Transurethral resection of the prostate: The use of an instrument inserted through the penis to remove tissue from the prostate. Also called TUR or TURP.

Tumor: An abnormal mass of tissue that results from excessive cell division. Tumors perform no useful body function. They may either be benign (not cancerous) or malignant (cancerous).

Tumor debulking: Surgically removing as much of the tumor as possible.

Tumor marker: A substance in blood or other body fluids that may suggest that a person has cancer.

Tumor necrosis factor: A type of biological response modifier (a substance that can improve the body’s natural response to disease).

Tumors of unknown primary origin: This is a disease in which cancer (malignant) cells are found somewhere in the body, but the place where they first started growing (the origin or primary site) cannot be found.

Tumor-suppressor gene: Genes in the body that can suppress or block the development of cancer.

Ulcerative colitis: A disease that causes long-term inflammation of the lining of the colon.

Ultrasound: A test that bounces sound waves off tissues and internal organs and changes the echoes into pictures (sonograms). Tissues of different densities reflect sound waves differently.

Ultrasonicography: A test in which sound waves (called ultrasound) are bounced off tissues and the echoes are converted into a picture (sonogram).

Ultraviolet (UV) radiation: Invisible rays that are part of the energy that comes from the sun. UV radiation can burn the skin and cause melanoma and other types of skin cancer. UV radiation that reaches the Earth’s surface is made up of two types of rays, called UVA and UVB rays. UVB rays are more likely than UVA rays to cause sunburn, but UVA rays pass further into the skin. Scientists have long thought that UVB radiation can cause melanoma and other types of skin cancer. They now think that UVA radiation also may add to skin damage that can lead to cancer. For this reason, skin specialists recommend that people use...
sunscreen that block or absorb both kinds of UV radiation.

**Upper GI series**: A series of X-rays of the upper digestive system that are taken after a person drinks a barium solution, which outlines the digestive organs on the X-rays.

**Ureter**: The tube that carries urine from the kidney to the bladder.

**Urethra**: The tube that empties urine from the bladder.

**Urinalysis**: A test that determines the content of the urine.

**Urinary tract**: The organs of the body that produce and discharge urine. These include the kidneys, ureters, bladder, and urethra.

**Urostomy**: An operation to create an opening from inside the body to the outside, making a new way to pass urine.

**Uterine cancer**: Cancer of the endometrium, a common kind of cancer in women, is a disease in which cancer (malignant) cells are found in the lining of the uterus (endometrium). The uterus is the hollow, pear-shaped organ where a baby grows. Cancer of the endometrium is different from cancer of the muscle of the uterus, which is called sarcoma of the uterus. Sarcoma of the uterus, a very rare kind of cancer in women, is a disease in which cancer (malignant) cells start growing in the muscles or other supporting tissues of the uterus.

**Vaginal cancer**: Cancer of the vagina, a rare kind of cancer in women, is a disease in which cancer (malignant) cells are found in the tissues of the vagina. The vagina is the passageway through which fluid passes out of the body during menstrual periods and through which a woman has babies. It is also called the birth canal.

**Ventricles**: Hollow chambers within the body; the heart has two ventricles, and the brain has four ventricles.

**Vinyl chloride**: A substance used in manufacturing plastics. It is linked to liver cancer.

**Viruses**: Small living particles that can infect cells and change how the cells function. Infection with a virus can cause a person to develop symptoms. The disease and symptoms that are caused depend on the type of virus and the type of cells that are infected.

**Vocal cords**: Two small bands of muscle within the larynx. They close to prevent food from getting into the lungs, and they vibrate to produce the voice.

**Waldenstrom’s macroglobulinemia**: This is a rare, chronic cancer that affects white blood cells called B lymphocytes, or B cells. These cells form in the lymph nodes and the bone marrow, the soft, spongy tissue inside bones, and are an important part of the body’s immune (defense) system. Some B cells become plasma cells, which make, store, and release antibodies. Antibodies help the body fight viruses, bacteria, and other foreign substances. In Waldenstrom’s macroglobulinemia, abnormal B cells multiply out of control. They invade the bone marrow, lymph nodes, and spleen and produce excessive amounts of an antibody called IgM.

**Wart**: A raised growth on the surface of the skin or other organ.

**Whipple procedure**: A type of surgery used to treat pancreatic cancer. The surgeon removes the head of the pancreas, the duodenum, a portion of the stomach, and other nearby tissues.

**White blood cells**: Cells that help the body fight infection and disease. These cells begin their development in the bone marrow and then travel to other parts of the body.

**Wilms’ tumor**: Wilms’ tumor is a disease in which cancer (malignant) cells are found in certain parts of the kidney. The kidneys are a “matched” pair of organs found on either side of the backbone. Inside each kidney are tiny tubes that filter and clean the blood, taking out unneeded products, and making urine. Wilms’ tumor occurs most commonly in children under the age of 15 and is curable in the majority of affected children.

**Xerogram**: An X-ray of soft tissue.
Xeroradiography: A type of mammography in which a picture of the breast is recorded on paper rather than on film.

X-ray: High-energy radiation used in low doses to diagnose diseases and in high doses to treat cancer.

Source: Adapted from the National Cancer Institute online glossary by the University of Texas MD Anderson Cancer Center
Resource Guide

Books


**Journals**

*American Journal of Clinical Pathology*  
*American Journal of Medicine*  
*American Journal of Preventive Medicine*  
*Angiogenesis*  
*Annals of Cancer Research and Therapy*  
*BMC Cancer*  
*British Journal of Cancer*  
*British Medical Journal*  
*CA: A Cancer Journal for Clinicians*  
*Cancer & Metabolism*  
*Cancer and Metastasis Reviews*  
*Cancer Biology & Medicine*  
*Cancer Biology & Therapy*  
*Cancer Biotherapy*  
*Cancer Causes and Control*  
*Cancer Cell*  
*Cancer Chemotherapy and Pharmacology*  
*Cancer Control*  
*Cancer Detection and Prevention*  
*Cancer Epidemiology*  
*Cancer Epidemiology, Biomarkers & Prevention*  
*Cancer Gene Therapy*  
*Cancer Genetics*  
*Cancer Genomics & Proteomics*  
*Cancer Imaging*  
*Cancer Immunology, Immunotherapy*
Cancer Immunology Research
Cancer Investigation
Cancer Journal
Cancer Letters
Cancer Medicine
Cancer Microenvironment
Cancer Nursing
Cancer Prevention Research
Cancer Research Carcinogenesis
Cancer Reviews Online
Cancer Science
Cancer Treatment and Research
Cancer Treatment Communications
Carotenoids in Health and Disease
Cell
Clinical Cancer Research
Clinical Medicine Insights: Oncology
Current Treatment Options in Oncology
Environmental Health Perspective
European Journal of Cancer Prevention
Evidence-Based Oncology
Frontiers in Oncology
Journal of Cancer Education
Journal of Cancer Research and Clinical Oncology
Journal of Clinical Investigation
Journal of Clinical Medicine and Research
Journal of Clinical Oncology
Journal of Mammary Gland Biology and Neoplasia
Journal of Medical Sciences Monitor
Journal of Molecular Diagnostics
Journal of Nutrition
Journal of Oncology Pharmacy Practice
Journal of Physical Anthropology
Journal of the American Medical Association
Journal of the National Cancer Institute
Lancet Oncology
Molecular Aspects of Medicine
Molecular Cancer Research
Nature Clinical Practice. Oncology
Nature Reviews. Cancer
Nature Reviews. Clinical Oncology
New England Journal of Medicine
Nucleic Acids Research
Nutrition and Cancer Oncology
Oncology Reports
Oncology Research
Perspectives in Biology and Medicine
Pharmacogenetics
Reports of Practical Oncology and Radiotherapy
Science and Medicine
Seminars in Cancer Biology
Statistics in Medicine
Toxicology Science
Internet
Agency for Healthcare Research and Quality
http://www.ahrq.gov
American Cancer Society
http://www.cancer.org
Canadian Cancer Society
http://www.cancer.ca
Cancer Genome Atlas (NCI)
http://cancergenome.nih.gov
Cancer Research UK
http://www.cancerresearchuk.org
Centers for Disease Control and Prevention:
Cancer Prevention and Control
http://www.cdc.gov/cancer
CRN Cancer Communication Research Center
http://www.crn-ccrc.org
European Association for Cancer Research
http://www.eacr.org
International Agency for Research on Cancer
http://www.iarc.fr
International Cancer Genome Consortium
https://icgc.org
Mayo Clinic: Cancer
http://www.mayoclinic.org/diseases-conditions/cancer/basics/definition/con-20032378
National Cancer Institute
http://www.cancer.gov
National Institutes of Health Database of Clinical Trials
http://www.clinicaltrials.gov
Proceedings of the National Academy of Sciences
http://www.pnas.org
SEER: Surveillance, Epidemiology, and End Results Program
http://seer.cancer.gov
Sitemann Cancer Center, Washington University
School of Medicine
http://www.yourdiseaserisk.wustl.edu
World Health Organization
http://www.who.int

Sarah E. Boslaugh
Kennesaw State University
Appendix

National Cancer Institute, Surveillance, Epidemiology, and End Results Program

CANCER STATISTICS REVIEW 1975-2011: INTRODUCTION

The annual SEER Cancer Statistics Review (CSR) contains incidence, mortality, prevalence, and survival statistics from 1975 through the most recent year for which data are available. This report is published by the Surveillance Research Program of the National Cancer Institute, which manages the Surveillance, Epidemiology, and End Results (SEER) Program. The scope and purpose of the CSR follow a report to the Senate Appropriations Committee (Breslow, 1988), which recommended that a broad profile of cancer be presented regularly to the American public.

The SEER program is an authoritative source of information on cancer incidence and survival in the United States. SEER collects and publishes these statistics from population-based registries covering 28% of the US population. The 18 SEER registries routinely collect data on patient demographics, primary tumor site, tumor morphology, extent of disease, first course of treatment, and active follow-up for vital status. Detailed information describing these fields can be found at http://seer.cancer.gov/resources/.

This report presents statistics on 29 primary sites and subsites, organized into site-specific chapters. Detailed statistics on cancer incidence, mortality, survival, and prevalence are reported by sex, race and ethnicity, age, stage at diagnosis, and geographic area. Information on tumor morphology is also presented. In addition, the CSR features a chapter on adolescent and young adult cancers and a chapter on childhood cancers. Information on some rare cancers can be found in the summary tables of section I. For a detailed list of primary sites, the summary tables provide incidence and death rates for the most recent 5-year period, trends from 1975 to the most recent year, median age at diagnosis, median age at death, and survival rates.

Delay-adjusted cancer incidence rates are a distinctive feature of the CSR. Delay-adjustment corrects the current case count to account for underreporting and corrections to the data. The final delay-adjusted rates are valuable in more precisely estimating trends.

New features added to the CSR include:
- Statistics for lung and bronchus cancer are shown by new histology groupings in Chapter 15 (Lewis DR, et al., 2014).
- Confidence intervals for state ranks in mortality were added (Zhang S, et al., 2014).

Changes in methodology to CSR include:
- New standard error calculation for delay-adjusted incidence rates was used. See http://surveillance.cancer.gov/reports/tech2014.01.pdf for more information.
- The default censoring age for survival calculations has changed from 199 to 99 years when using newly available expected survival tables. For most survival calculations there are no changes. Minimal changes may occur in survival for older age groups. See http://seer.cancer.gov/expsurvival/ for more information.
The CSR files are provided in both PDF and HTML formats. The HTML format is provided as an alternative and accessible version of the SEER Cancer Statistics Review. The current edition of the CSR is available on the web at http://seer.cancer.gov/csr/. Statistics from SEER may also be obtained via FastStats (http://seer.cancer.gov/faststats/) or Cancer Query Systems (http://seer.cancer.gov/canques/), which allow the user to access over 10,000,000 cancer statistics. The SEER Research Data file (http://seer.cancer.gov/data/) may be accessed by the public, either through SEER*Stat software or in an ASCII text format that can be analyzed with standard statistical software.

While most of the rates in this publication have been age-adjusted to the 2000 US standard population, some previous SEER publications have used the 1970 US standard million population. Therefore, rates given in this publication cannot be compared to rates given in those publications. This change conforms to a federal policy for reporting disease rates; it allows for the age-adjusted rate to more accurately reflect the current age distribution and burden of cancer.

**INTERPRETATION OF CANCER STATISTICS**

A number of factors may affect the interpretation of cancer incidence, mortality, and survival statistics provided in this report.

**Survival rates for all cancers combined:** The mix of cancers changes over time as the incidence of some cancers increases and the incidence of others decreases. The overall cancer survival rate can fluctuate even when the survival rates for site-specific cancers remain unchanged. (While it is possible to adjust the survival rate for all cancers combined on the basis of the relative frequencies of the component cancers, rates adjusted in this manner differ by only a small amount from unadjusted rates. In the future, such an adjustment may become more important if there are substantial changes in the incidence of various cancers.)

**Early detection/screening:** The improved earlier detection and diagnosis of cancers caused by new screening procedures may produce an increase in both incidence rates and survival rates. These increases can occur as a result of the introduction of a new procedure to screen subgroups of the population for a specific cancer; they need not be related to whether use of the screening test results in a decrease in mortality from that cancer. As the proportion of cancers detected at screening increases, presumably as a result of increased screening of the population, patient survival rates will increase, because they are based on survival time after diagnosis. The interval between the time a cancer is diagnosed by a screening procedure and the time when the cancer would have been diagnosed in the absence of screening is called lead-time (Zelen, 1976). (Screening for breast cancer has been demonstrated to result in increased survival over and above that resulting from lead-time alone and to reduce breast cancer mortality. The benefit of screening is being studied for some other cancers.)
If a new screening procedure consistently detects cancer in a preinvasive phase, it may result in a decrease in survival rates for invasive cancer. In this case, length-biased sampling (Zelen, 1976) may be operating. Length-biased sampling would result in the preferential detection—in a preinvasive phase—of those cancers that would have had a relatively good prognosis had they progressed to invasive disease; these potentially invasive cancers would be systematically eliminated. If this occurs, the mix of cancers that are not detected at screening and then progress to invasive behavior may become less prognostically favorable, resulting in a decrease in survival rates for patients with invasive cancers. (Length-biased sampling may at least partially explain survival trends for cervical cancer. Other cancers possibly affected include breast, colon, rectum, and prostate.)

Changes in diagnostic criteria: Early detection of cancer resulting from either screening or earlier response to symptoms may result in the increasing diagnosis of small tumors that are not yet life-threatening. This may have the effect of raising the incidence rates and survival estimates without changing the mortality rates. Breast, colon, prostate, cervix uteri, bladder, and skin (melanoma) are the cancer sites most likely to be affected.

Technological advances in diagnostic procedures: In this report, trends in survival by stage at diagnosis for specific cancers are not presented; trends in stage distributions are presented rarely. However, it is possible to compare survival by stage.

The assignment of a given stage to a particular cancer may change over time due to advances in diagnostic technology. Introduction of new technology can give rise to a phenomenon known as stage migration. Stage migration occurs when diagnostic procedures change over time, resulting in an increase in the probability that a given cancer will be diagnosed in a more advanced stage. For example, certain distant metastases that would have been undetectable a few years ago can now be diagnosed by a computer tomography (CT) scan or by magnetic resonance imaging (MRI). Therefore, some patients who would have been diagnosed previously as having cancer in a localized or regional stage are now diagnosed as having cancer in a distant stage. The likely result would be to remove the worst survivors, those with previously undetected distant metastases, from the localized and regional categories and put them into the distant category. As a result, the stage-at-diagnosis distribution for a cancer may become less favorable over time, but the survival for each stage may improve: The early stage will lose cases that will survive shorter than those remaining in that category, while the advanced stage will gain cases that will survive longer than those already in that category. However, overall survival would not change (Feinstein et al., 1985). Stage migration is an important concept to understand when examining temporal trends in survival by stage at diagnosis as well as temporal trends in stage distributions; it could affect the analysis of virtually all solid tumors.

Evolution of stage classifications: Every few years, the American Joint Committee on Cancer produces a new cancer-staging manual; the seventh edition is the most recent (Edge et al., 2010). The evolution of such classifications reflects the identification of new prognostic factors that may influence choice of treatment. Historically, the SEER Program has only collected data
on extent of disease (EOD), rather than stage. EOD is more specific than stage and usually determines stage, even when stage definitions change. Thus, SEER easily adapts to changes in stage definitions; moreover, trends in a newly redefined stage can usually be calculated. Recently the SEER Program has begun collecting Collaborative Stage. Collaborative Stage has the advantage of being a consolidated data collection system of three main staging systems (TNM, EOD, and Summary Stage) and allows combined pathological and clinical stage to be captured. New prognostic variables are introduced into staging for some cancers and so previously collected EOD data cannot determine new stage categories. There can be problems in assessing trends in stage of disease for these cancers. Only by reviewing the evolution of staging for a given cancer is it possible to determine what effects changes in stage definitions have had on stage-specific survival and on stage-at-diagnosis distributions. Stage migration (mentioned above) and EOD migration need also be taken into account. For some sites, the historic stage (localized, regional, or distant) is not shown, either because of inconsistencies in its definition over time or because stage is not appropriate (such as for leukemias, which are all considered to be distant at diagnosis).

Interpreting relative survival: The relative survival estimate is the ratio of observed survival to expected survival for a given patient cohort. Expected survival is based on mortality rates for the entire population, taking into account, as appropriate, the age, sex, race, and year of diagnosis of the patients. Assuming that the presence of cancer is the only factor that distinguishes the cancer patient cohort from the general population, relative survival estimates the probability that a patient will not die of the diagnosed cancer within the given time interval. This is the same as the probability that the patient will either survive the interval or die of a different cause.

A factor related to the risk of a cancer may also be related to the risk of dying from causes unrelated to the cancer. An example of such a factor is smoking. Smoking is a major risk factor for lung cancer; therefore, a cohort of lung cancer patients will contain a much higher proportion of smokers than the general population. However, smoking is also a risk factor for other diseases so smokers have a shorter life expectancy than nonsmokers. For this reason, expected survival estimates for lung cancer patients based on life tables for the general population will be unrealistically high; since relative survival = observed / expected, this will result in relative-survival estimates that are lower than they would be if the population consisted only of smokers. The problem cannot be easily corrected because separate life tables for smokers and nonsmokers are not available. Moreover, amount of smoking (usually measured in pack-years) is an important variable and cannot be easily quantified. In addition, expected survival may not be appropriate for patients with cancers of the cervix uteri or breast because the risk of these cancers has been associated with socioeconomic status (Baquet et al., 1991) which may be related to life expectancy. This should be considered when interpreting relative survival for these cancers.

Previous to the CSR for 1973–1996, the expected survival tables used were for 1970 and 1980; there were separate tables for whites, blacks, American Indians, Chinese, Japanese, Filipinos, white Hispanics, and Hawaiians. In updating the tables for 1990, several problems emerged.
The US life tables are based on age, race, and sex information from death certificates. The information on race on the death certificate may not be accurate (Rosenberg et al., 1999). One reason is that funeral directors may inaccurately report race on a death certificate. Also, reported age at death, especially for those older than 85, may not be accurate because birth certificates were not issued with as much regularity in the early 1900s as they are today. Although race misclassification and age-at-death misreporting exist across all races, they may be more problematic for races other than white or black because of those races' smaller population sizes. Therefore, life tables were generated for 1970, 1980, 1990, and 2000 only for white, black, and other; these life tables were used to produce the relative survival estimates in this review. There may be small variations among survival estimates calculated in this CSR and those in CSRs prior to 1973–1996.

Comparison with other databases: The SEER data are obtained from population-based cancer registries covering about 28 percent of the US population. It is sometimes of interest to compare cancer statistics for SEER areas with those from other registries both in the US and worldwide. In making such comparisons, one must carefully consider the factors mentioned above for both data sources. In addition, one should assess all of the following: (1) completeness of case ascertainment, (2) rules used to determine multiple primaries, (3) follow-up, (4) rules used in assigning and coding cause of death, and (5) the sources and procedures used in obtaining population estimates. Depending on the rates being compared, there could be other confounding factors which should be considered. The same standard or standard million population should be used for the age-adjustment of each group being compared; most statistics from outside the US are based on the 2000 world standard million population. Examples of other databases are US Cancer Statistics (http://apps.nccd.cdc.gov/uscs) and CINA+ Online (http://www.cancer-rates.info/naaccr/).

It is sometimes of interest to compare survival for cancer patients in SEER areas with data from clinical trials. This must be done with great caution. Survival data from clinical trials may have been obtained from a patient population that differs from that of SEER patients in prognostic factors for the given cancer; any survival comparisons would have to adjust for such differences. Also, it is necessary to verify that the methodology used in computing survival is the same for both data sources. Furthermore, patients on clinical trials may differ from SEER patients in characteristics that may be related to survival but are not recorded in either database. If this were true for a given cancer, it would not be possible to make valid comparisons of this type.

Errors in data collection: In the process of registering cancer patients, errors may be made in abstracting and coding the data, which include demographic information, cancer site, histology, extent of disease, treatment, and patient survival. Quality control studies are periodically carried out to detect and correct this type of error, but no attempt is made to incorporate this source of error into the variance estimates of cancer rates reported here.

Comparison of this report with previous reports: The cancer registries that participate in the SEER Program submit data on all cancers diagnosed in their coverage areas to the NCI each
Because of the dynamic nature of the registries' databases, the reported number of new cancer cases in a particular race, sex, age, cancer category in a given calendar year may change from that which has been reported in a previous publication. For a given diagnosis year, additional cancer cases that were previously overlooked may have been found and reported to the central registry. There may have been follow-back of cancers diagnosed by death certificate only; successful efforts to establish the dates of diagnosis for such patients will change the number of patients reported for a given diagnosis year. Code changes may occur when a patient dies; for example, information on race is generally available on the death certificate and may be used to update a previously unknown value. There may have been elimination of duplicate records for the same patient, often due to name changes or misspellings.

Thus, a recent report may have a different number of cases for a given diagnosis year than an earlier report, with resulting effects on incidence and possibly survival. Population estimates may also change from one report to another for some calendar years. This occurs because the NCI receives population estimates that are regularly revised and updated by the Bureau of the Census (BOC). Such changes may result in some differences between incidence and mortality rates for a given calendar period as published in different reports. See our website for the most current information about the population estimates (http://seer.cancer.gov/popdata/).

REFERENCES


TECHNICAL NOTES

There are four measures commonly used to assess the impact of a cancer in the general population and are reported in this review. The incidence rate is the number of new cases per year per 100,000 persons. The death (or mortality) rate is the number of deaths per year per 100,000 persons. The survival estimate is the proportion of patients alive at some point subsequent to the diagnosis of their cancer. The prevalence count is the number of people alive that have ever been diagnosed with a cancer. The Surveillance, Epidemiology, and End Results (SEER) Program (http://seer.cancer.gov) (based within the Surveillance Research Program (SRP) at the National Cancer Institute (NCI) collects incidence and survival data for all areas that participate in the Program. The National Center for Health Statistics (NCHS) provides mortality data for the entire United States (US). All incidence and mortality rates in this report are age-adjusted (see below) to the 2000 US standard population (see Appendix) unless otherwise specified. Age-adjustment minimizes the effect of a difference in age distributions when comparing rates.

THE SEER PROGRAM

The National Cancer Act of 1971 mandated the collection, analysis, and dissemination of data useful in the prevention, diagnosis, and treatment of cancer. This mandate led to the establishment of the SEER Program. The population-based cancer registries participating in NCI’s SEER Program routinely collect data on all cancers occurring in residents of the participating areas. Trends in cancer incidence and patient survival in the US are derived from this database. See the SEER Research Data (http://seer.cancer.gov/data/) for more information.

The SEER Program is a sequel to two earlier NCI programs—the End Results Program and the Third National Cancer Survey. The initial SEER reporting areas were the States of Connecticut, Iowa, New Mexico, Utah, and Hawaii; the metropolitan areas of Detroit, Michigan, and San Francisco-Oakland, California; and the Commonwealth of Puerto Rico. Case ascertainment began with January 1, 1973, diagnoses.

In 1974-1975, the program was expanded to include the metropolitan area of New Orleans, Louisiana, the thirteen-county Seattle-Puget Sound area in the State of Washington, and the metropolitan area of Atlanta, Georgia. New Orleans participated in the program only through the 1977 data collection year. In 1978, ten predominantly African-American counties in rural Georgia were added. American Indian residents of Arizona were added in 1980. In 1983, four counties in New Jersey were added with coverage retrospective to 1979. New Jersey and Puerto Rico participated in the program until the end of the 1989 reporting year. The National Cancer Institute also began funding a cancer registry that, with technical assistance from SEER, collects information on cancer cases among Alaska Native populations residing in Alaska. In 1992, the SEER Program was expanded to increase coverage of minority populations, especially Hispanics, by adding Los Angeles County and four counties in the San Jose-Monterey area south of San Francisco. In 2001, the SEER Program expanded coverage to
include Kentucky, Greater California (the counties of California that were not already covered by SEER), New Jersey, and Louisiana. In 2012, Greater Georgia (the parts of Georgia not included in Atlanta and Rural Georgia) was added to the SEER Program, with data retroactive to 2000.

The long-term incidence trends and survival data for this report are from five states (Connecticut, Hawaii, Iowa, New Mexico, and Utah) and four metropolitan areas (Detroit, Atlanta, San Francisco-Oakland, and Seattle-Puget Sound) (Fig. I-1); this set of registries is called the SEER 9. Additional tables show more recent incidence trends for the SEER 13 areas (the 9 areas above plus Los Angeles, San Jose-Monterey, Alaska Native Registry, and rural Georgia) since 1992 and additional information on race and ethnicity. Other tables give statistics for the SEER 18 areas; these are the SEER 13 plus Kentucky, Greater California, New Jersey, Louisiana, and Greater Georgia.

The participating regions were selected principally for their ability to operate and maintain a population-based cancer reporting system and for their epidemiologically significant population subgroups. With respect to selected demographic and epidemiologic factors, they are when combined a reasonably representative subset of the US population. Data from the 9, 13, or 18 SEER geographic areas are used in this report; the given groups contain, respectively, approximately 9, 14, or 28 percent of the US population. By the end of the 2011 diagnosis year, the database of the 18 SEER registries (plus Arizona Indians) contained information on over 7 million cases diagnosed since 1973. New cases added in the most recent data year numbered over 449,000.

The goals of the SEER Program are:
1) to assemble and report, on a periodic basis, estimates of cancer incidence, mortality, survival, and prevalence in the US;
2) to monitor annual cancer incidence trends to identify unusual changes in specific forms of cancer occurring in population subgroups defined by geographic and demographic characteristics;
3) to provide continuing information on trends over time in the extent of disease at diagnosis, trends in therapy, and associated changes in patient survival; and
4) to promote studies designed to identify factors amenable to cancer control interventions, such as: (a) environmental, occupational, socioeconomic, dietary, and health-related exposures; (b) screening practices, early detection and treatment; and (c) determinants of the length and quality of patient survival.

DATA SOURCES

INCIDENCE AND SURVIVAL DATA

The SEER Program contracts with nonprofit, medically-oriented organizations having statutory responsibility for registering diagnoses of cancer among residents of their respective geographic coverage areas. Each SEER contractor:
1) maintains a cancer information reporting system;
2) abstracts records for resident cancer patients seen in every hospital both inside and outside the coverage area;
3) abstracts all death certificates of residents (dying both inside and outside the coverage area) on which cancer is listed as a cause of death;
4) strives for complete ascertainment of cases by searching records of private laboratories, radiotherapy units, nursing homes, and other health services units that provide diagnostic service;
5) registers all in situ and malignant neoplasms (with the exceptions of certain histologies for cancer of the skin and—beginning in 1996—in situ neoplasms of the cervix uteri);
6) records data on all newly diagnosed cancers, including selected patient demographics, primary site, morphology, diagnostic confirmation, extent of disease, and first course of cancer-directed therapy;
7) provides active follow-up on all living patients (except for those with in situ cancer of the cervix uteri);
8) maintains confidentiality of patient records;
9) at least annually submits electronically to NCI data on all reportable diagnoses of cancer made in residents of the coverage area.

For 1992 to 2000 diagnoses, the SEER program codes site and histology by the International Classification of Diseases for Oncology, second edition (ICD-O-2) (Percy et al., 1990). All cases before 1992 were machine-converted to ICD-O-2. Cases diagnosed 2001-2009 have been coded according to the third edition (ICD-O-3) (Fritz et al., 2000). Starting with patients diagnosed in 2007, the new multiple primary and histology coding rules may impact their incidence data for some cancer sites (e.g., female breast). However, the impact of the new rule on observed incidence is negligible for a majority of the cancer sites. To learn more about the multiple primary rules, visit: http://seer.cancer.gov/tools/mphrules/. Beginning with 2010 diagnoses, cases are coded based on ICD-O-3 updated for hematopoietic codes based on WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues (2008). The primary site groupings used for incidence are found in the Appendix. Changes were made to the site recode for ICD-O-2 for comparability with cases coded to ICD-O-3. Follow-up rates are also in the Appendix.

Underreporting Adjustment for Veterans Affairs Cases: A CSR section on Department of Veterans Affairs (VA) underreporting (Howlader et al., 2009) was included in recent versions of the CSR. As of the current CSR this section was removed since available evidence indicates that VA underreporting is resolved as of diagnosis year 2010. The section of the CSR introduction about the reporting delay describes measures to address any backlog of VA cases reported after the initial reporting year.

Excluded cancers: Some cancers were excluded from most of the analyses. Myelodysplastic syndrome (MDS), for example, was reclassified in ICD-O-3 (effective diagnosis year 2001) from nonmalignant to malignant; other cancers so reclassified include endometrial stromal sarcoma (low grade), papillary ependymoma, papillary meningioma, polycythemia vera, chronic myeloproliferative disease (NOS), myelosclerosis with myeloid metaplasia,
essential thrombocythemia, refractory anemia, refractory anemia with sideroblasts, refractory anemia with excess blasts, and refractory anemia with excess blasts in transformation. In contrast, borderline tumors of the ovary were reclassified from malignant to nonmalignant at the same time. In addition, benign brain/CNS tumors were collected beginning for 2004 diagnoses. All of these cancers were excluded from most of the analyses, especially time trends. Pilocytic astrocytoma, although reclassified in ICD-O-3, was not excluded. Separate tables for MDS and benign brain/CNS are shown.

MORTALITY DATA

The SEER Program annually obtains from the National Center for Health Statistics (NCHS) a file containing information on all deaths occurring in the US by calendar year. Information on each death includes age at death, sex, geographic area of residence, and underlying and contributing causes of death. For this publication, only the underlying cause of death is used in the calculation of death rates. Cause of death for 1969-1978 was coded according to ICD-8; for 1979-1998, ICD-9 was used; beginning with deaths in 1999, ICD-10 was used. Mortality rates for the SEER geographic areas, for each state, and for the entire US are obtained from these data. A list of the mortality site groupings used in this publication is in the Appendix and reflects updates made in 2004.

POPULATION DATA

The population estimates used in the SEER*Stat software to calculate cancer incidence and mortality rates for this report are a modified version of the intercensal and Vintage 2011 annual time series of July 1 county population estimates by age, sex, race, and Hispanic origin that are produced by the Population Estimates Program of the US Census Bureau (http://www.census.gov/popest/) with support from the NCI through an interagency agreement. Descriptions of the methodologies employed by the Census Bureau for various sets of estimates may be found on the same website. Vintage 2011 population estimates were used; these estimates were developed from the actual 2010 census results.

County population estimates for 2000 and later years must be bridged from 31 race categories used in Census 2000 to the four race categories specified under the 1997 OMB standards in order to report long-term cancer trends. The bridging methodology was developed by the National Center for Health Statistics and is described in a report (Ingram et al., 2003) and on their website http://www.cdc.gov/nchs/nvss/bridged_race.htm

Modifications made by the NCI to the population estimates are documented in “Population Estimates Used in NCI’s SEER*Stat Software” (http://seer.cancer.gov/popdata/methods.html) and the population data files are available for download (see “Download US Population Data” from http://seer.cancer.gov/popdata/download.html). Several of the modifications pertaining to the grouping of specific counties needed to assure the compatibility of all incidence, mortality and population datasets. Another modification affects only population estimates for the State of Hawaii. The Epidemiology Program of the Hawaii Cancer Research Center has developed its own set of population estimates, based on sample survey data collected by the Hawaii
Department of Health. This effort grew out of a concern that the native Hawaiian population has been vastly undercounted in previous censuses. The "Hawaii adjustment" to the Census Bureau's estimates has the net result of reducing the estimated white population and increasing the estimated Asian and Pacific Islander population for the state. The estimates for the total population, black population, and American Indian and Alaska Native populations in Hawaii are not modified.

The cancer incidence and mortality rates for American Indians and Alaska Natives (AI/AN) are based on the geographic areas (counties) included in the Indian Health Service's Contract Health Service Delivery Area (CHSDA). This reflects a concern that previously reported AI/AN rates were underestimated due to racial/ethnic misclassification of American Indian cases in geographic areas outside of CHSDA. This change has the net effect of higher, and more accurate, incidence and mortality rates for this population. Beginning in 2013, CSR reporting diagnoses 1975-2010, CHSDA counties were updated with 9 new counties designated as CHSDA. Four of these are in SEER areas. This addition was made to better reflect AI/AN populations that had been living in these counties.

Usually the use of a population estimate for July 1 of a particular year reflects the average population of that area for the year. Both Hurricane Katrina and Hurricane Rita struck the Gulf Coast area of the United States in 2005. This had the effect of displacing large populations. Since there weren't any population estimates by age, race, sex, and county for time periods just after the hurricanes, it is very difficult to estimate the actual population at risk for certain areas along the Gulf Coast for 2005. For Louisiana, only the first six months of incidence data for 2005 coupled with ½ of the population estimate for July 1, 2005, were used to calculate cancer incidence. For death rate calculations, no adjustments were made to the total US population, but for the Gulf area, an adjustment for displaced populations was made for 2005 state rates. For more details, see http://seer.cancer.gov/popdata/methods.html.

2000 US STANDARD POPULATION

Starting with the November 2004 SEER submission of data (diagnoses through 2002), the SEER Program age-adjusts using the 2000 US standard population based on single years of age from the Census P25-1130 series estimates of the 2000 US population (Day, 1996). For the CSR, 19 age groupings were used for age-adjustment: <1, 1–4, 5–9, … , 80–84, 85+.

STATISTICAL METHODS

ESTIMATED CANCER CASES AND DEATHS IN 2014

The American Cancer Society (ACS) projects the numbers of new cancer cases and cancer deaths in the US in 2014 (American Cancer Society, 2012). The ACS projects incidence in 2014 based on incidence rates for 1995-2009 from 49 states and the District of Columbia, representing about 98% of the US population. These high-quality incidence data were submitted to the North American Association of Central Cancer Registries (NAACCR) by 49 states (and District of Columbia) belonging to the SEER Program and/or the National Program of Cancer
Registries (NPCR). For additional details please refer to
http://www.cancer.org/docroot/STT/STT_0.asp

LONG-TERM TRENDS, 1950-2011

Trends in cancer mortality from 1950 to 2011 are summarized by age both for all cancers combined and for lung cancer (Table 1-2). These cancer mortality trends are based on the mortality experience in the entire US. Summaries of long-term trends back to 1950 in cancer survival are also shown for whites.

Use caution when interpreting these statistics. Evaluating trends over a long period of time may hide recent changes in the trends.

YEARS OF LIFE LOST DUE TO PREMATURE DEATH FROM VARIOUS CAUSES

Death rates alone give an incomplete picture of the burden that deaths impose on the population. Another measure is the years of life lost due to premature death. This shows the extent to which life is cut short by a particular cause or disease.

This measure is estimated by linking life table data to each death of a person of a given age and sex. The life table permits a determination of the number of additional years an average person of that age, race, and sex would be expected to live. In this report, the age groups used in the calculation were 1-year intervals. These remaining years of life left are summed over all deaths due to a particular cause, yielding the estimate of the number of person-years of life lost (PYLL). The average years of life lost (AYLL) is obtained by dividing the PYLL by the number of deaths. Both of these measures can be calculated for any cause of death.

RELATIVE SURVIVAL

Relative survival (Ederer, 1961) was developed to provide an objective measure of the probability of survival of cancer in the absence of other causes of death. It is a measure that is not influenced by changes in mortality from other causes and, therefore, provides a useful measure for both tracking survival across time and comparisons between racial/ethnic groups or between registries. For most cancer registries, cause-of-death information obtained from death certificates is either unavailable or unreliable due to misclassification error. Therefore, instead of calculating the probability of surviving cancer in the usual (cause-specific) way, considering deaths from other causes as censoring events, relative survival compares the observed survival proportion of a group of cancer patients with the survival of a “similar” theoretical cancer-free group. Relative survival is formally defined as the ratio of the observed survival (all causes of death) of a cohort of cancer patients to the expected survival of a comparable set of cancer-free individuals. Since a cohort of cancer-free individuals is difficult to obtain, life tables representing survival of the general population are used instead. The underlying assumption is that the cancer deaths are a negligible proportion of all deaths. To learn more on this topic, visit:
Expected survival can be calculated using different methods which vary with respect to the definition of the matching group. The three most common methods are: Ederer I (Ederer, et al., 1961), Ederer II (Ederer and Heise, 1959) and Hakulinen (Hakulinen, 1982). In previous versions of SEER*Stat, relative survival has been calculated using Ederer I and Hakulinen methods, Ederer I being the default for calculations in the Cancer Statistics Review. In the Ederer I and Hakulinen methods, theoretical individuals are matched to each patient and are considered to be at risk for the entire follow-up. Hakulinen adjusts for potential follow-up times. Relative survival using expected rates derived via these two methods are very similar. However, recent research on relative survival has resuscitated the initial method to estimate expected rate: the Ederer II method. Although none of the three methods can be considered a gold standard, the Ederer II method has been shown to be in better alignment with the concept of net cancer survival. For that reason, as of 2011, we have switched to Ederer II as our default choice for calculating expected rate in SEER*Stat and the CSR. For more detail regarding this topic, read Cho et al., 2011 at: http://surveillance.cancer.gov/reports/. As of 2013, Survival time was calculated using pre-calculated months based on the exact day information. See http://seer.cancer.gov/survivaltime/. As of 2014, the default censoring age for survival calculations has changed from 199 to 99 year when using newly available expected survival tables. Minimal changes may occur in survival for older age groups. See http://seer.cancer.gov/expsurvival/ for more information.

CAUSE-SPECIFIC SURVIVAL

Cause-specific survival is a net-survival measure representing survival of a specified cause of death in the (theoretical) absence of other causes of death. Estimates are calculated by specifying the cause of death. Individuals who die of causes other than the specified cause are censored. This requires a cause-of-death variable that accurately captures all causes related to the specific cause. Cancer registries use algorithms to process causes of death from death certificates in order to identify a single, disease-specific, underlying cause of death. In some cases, attribution of a single cause of death may be difficult and misattribution may occur. For example, a death may be attributed to the site of metastasis instead of the primary site (Percy et al., 1981).

To capture deaths related to the specific cancer but not coded as such, the SEER cause-specific death classification variable is defined by taking into account causes of deaths in conjunction with tumor sequence (i.e., only one tumor or the first of subsequent tumors), site of the original cancer diagnosis, and comorbidities (e.g., AIDS and/or site-related diseases). To learn more on this topic, please read the recent article published at the Journal of National Cancer Institute (Howlader et al., 2010) or visit: http://seer.cancer.gov/causespecific/.

CANCER PREVALENCE

Methods: In this report prevalence is calculated at 1/1/2011. Limited-duration prevalence is calculated using the counting method implemented in the SEER*Stat software. This method calculates the number or proportion of people alive at the prevalence date who had a diagnosis of the disease within the past x years (e.g., x = 5, 10, 20, or the full history of the registry).
Because SEER has available information for the various racial/ethnic groups for different numbers of years, different years and registries were used to estimate limited-duration prevalence. Prevalence estimates for all races combined, for whites, and for blacks use cases from 1975 through 2010 from the SEER 9 registries; prevalence estimates for Asian Pacific Islanders and Hispanics use cases diagnosed from 1990 through 2011 from the SEER 11 areas and rural Georgia.

The limited-duration prevalence method includes a correction for people lost to follow-up. For each individual lost to follow-up, a probability of being alive at the prevalence date is estimated from an appropriate survival function stratified by age at diagnosis (0–59, 60–69, 70+), sex, cancer site, year of diagnosis, and race, conditional on being alive at the time of loss to follow-up. Year of diagnosis is stratified into 5-year groups from the prevalence date, with the least recent interval being of varying length (4-8 years), depending on the length of years used to calculate prevalence. Race is stratified into white, black, other (American Indian/Alaska Native, Asian/Pacific Islander), and unknown/other-unspecified. When we use the SEER 11 registries, the same stratification as before is used, with American Indian/Alaska Native separated from Asian/Pacific Islander. Prevalence calculations for Hispanics use race stratified into: white, non-white, and unknown.

Different methods can be used to determine which tumors are to be included for people diagnosed with multiple tumors. Unless otherwise specified, prevalence calculations include only the first malignant tumor per person; that is, in situ cancers and second-or-later primary cancers were not included. Thus, if a woman had a melanoma prior to a breast cancer diagnosis, her melanoma would contribute to the prevalence of melanoma and to the prevalence of all sites, but the breast cancer would not contribute to the prevalence of breast cancer. Counting only one cancer per individual avoids some ambiguity in prevalence counts, and allows the counts for individual sites to sum to the all sites total. Prevalence using different selection criteria is compared in a table in the overview chapter. For more information on tumor selection criteria refer to http://surveillance.cancer.gov/prevalence/methods.html.

Complete prevalence is an estimate of the number of persons (or the proportion of population) alive on a specified date who had been diagnosed with the given cancer, no matter how long ago that diagnosis was. It was estimated for all races, whites, and blacks by applying the completeness index method (Capocaccia & De Angelis, 1997; Merrill et al., 2000; Mariotto et al., 2002) to limited-duration prevalence. The completeness index method is implemented in the COMPREV software, which can be found at http://surveillance.cancer.gov/comprev/. Validation of the completeness index for all races and for whites was made by using data from the Connecticut Tumor Registry (CTR) beginning with 1940. For blacks, SEER 9 data beginning with 1975 were used; identification of blacks is not possible in the CTR data prior to 1970. To validate the completeness index for blacks, we have compared the performance of the method to obtain 24-year prevalence from 10-year limited-duration prevalence. For all races combined and for whites, in cases where the validation indicated some lack of fit of the model, an approximation to the completeness index was derived from the CTR data. If there was a lack of
fit for blacks, no estimate of complete prevalence was reported. Complete prevalence for Asian/Pacific Islanders and Hispanics is not available at this time. Complete prevalence by age for all races combined was validated by comparing estimated 10-year complete prevalence with observed prevalence from the CTR data. Prevalence by age is reported for the sites that validated well.

The US cancer prevalence counts at 1/1/2011 were estimated by multiplying the SEER age- and race-specific prevalence proportions by the corresponding US population estimates based on the average of 2010 and 2011 population estimates from the US Census Bureau. US cancer prevalence counts for all races were estimated by summing the US estimated counts for whites/unknown, blacks, and other races. For Hispanics, the estimates for Hispanics of white or unknown race and for Hispanics of other races were summed.

Complete prevalence estimates of the number of individuals in the US diagnosed with cancer as children (ages 0-19), including those surviving for more than 36 years, is calculated using a statistical method that estimates the number of childhood survivors diagnosed before 1975 (Simonetti et al., 2008; Mariotto et al., 2009). Limited-duration prevalence proportions by age at prevalence are not shown for childhood cancers (age at diagnosis 0-19) since many of these estimates are not informative. For example, the number of people diagnosed with childhood cancers in the last 25 years and who are currently age 50-59 is zero by definition. For more details on available prevalence estimates, see http://surveillance.cancer.gov/prevalence/.

The overview chapter contains two prevalence tables. The first table reports US complete prevalence counts by age at prevalence and sex for some main cancer sites. The second table reports US prevalence counts for people diagnosed in the 5 years and 36 years prior to the prevalence date using different tumor inclusion criteria. Each site-specific chapter contains a prevalence table that reports limited-duration US prevalence counts by time since diagnosis for different racial/ethnic groups. US complete prevalence estimates are also reported when available. The second part of the site-specific tables displays the percent of the population in the SEER 11 areas diagnosed in the previous 19 years with the specific cancer by 10-year age groups for the different racial/ethnic groups.

**PROBABILITY OF BEING DIAGNOSED WITH OR DYING FROM CANCER**

*Lifetime and interval risks of being diagnosed with cancer:* The probability of being diagnosed with cancer is computed by applying cross-sectional age-specific 2008-2011 incidence rates from the SEER 17 areas and death rates from those same areas to a hypothetical cohort of 10,000,000 live births. This cohort is considered to be at risk for two mutually exclusive events: (1) developing the specified cancer, and (2) dying of other causes without developing the specified cancer. Using these two types of events, a standard multiple decrement life table (with 20 age groups from 0-4 to 90-94 and 95+) is derived. For each age interval, the number alive and free of the specified cancer at the beginning of the interval is decremented by the number who develop the specified cancer and the number who die of other causes. The lifetime
risk of being diagnosed with the specified cancer is derived by summing all cancer cases from age 0-4 through age 95+ and dividing by 10,000,000. This calculation does not assume that an individual lives to any particular age; rather, it is the sum over all age intervals of the probability of living to the beginning of that interval without developing the given cancer times the probability of developing the cancer in that interval. The probability of developing cancer during any time period (e.g., between age 50 and age 60) is calculated by adding up all the cancers in the life table over the specified age range and dividing by the number of individuals alive and free of the specified cancer at the beginning of the period. The methodology is described in detail in (Fay et al., 2003) and (Fay, 2004). To improve the precision of the calculations, rates were calculated beyond the usual last open ended age interval (i.e. 85+) for the age groups 85-89, 90-94, and 95+.

**Lifetime risk of dying from cancer:** The lifetime risk of dying from a specified cancer is derived using a standard multiple decrement life table (Elandt-Johnson & Johnson, 1980). For each age, the risks of dying of the specified cancer and of all other causes are calculated, based on mortality data from the entire United States.

**Detailed methodology and software:** The estimates of developing and dying from cancer are implemented in DevCan (Probability of DEVeloping or dying from CANcer software). More details on the software, various databases, and the methodology can be found at [http://surveillance.cancer.gov/devcan/](http://surveillance.cancer.gov/devcan/).

**US CANCER DEATH RATES BY STATE**

Each cancer-site-specific section presents the death rate for the given cancer for each state and the District of Columbia, specifying the five highest and the five lowest death rates by state for the most recent 5-year period for all persons, males only, and females only. The rates are per 100,000 persons; they are age-adjusted to the 2000 US standard population. (In some previous editions of the CSR, the 1970 US standard million population was used; death rates standardized to the 2000 US standard million population cannot be compared to death rates standardized to the 1970 US standard million population.)

The **percent difference (PD)** between a state rate and the rate for the total US is given by the formula:

\[
PD = \frac{\text{(State Rate} - \text{Total US Rate})}{\text{Total US Rate}} \times 100
\]

The **standard error** for each age-adjusted state death rate is calculated, based on the assumptions that (1) for each age-specific rate, the number of deaths is a Poisson random variable (Keyfitz, 1966) and (2) the variance of the age-adjusted rate is a linear combination of the variances of the age-specific rates (Snedecor & Cochran, 1980; pp. 188-9).

The **standard error of the difference (SEd)** between a state rate and the total US rate is given
Appendix 1397

by the formula

\[ SE_d = \text{Square Root of} \left( SE_s^2 + SE_U^2 - 2 \times \text{Cov}_{s,U} \right) \]

where \( SE_s \) and \( SE_U \) are the standard errors of a state rate and of the total US rate, respectively, and \( \text{Cov}_{s,U} \) is the covariance between the two rates. The variance of each rate (i.e., the square of the standard error) and the covariance between the two rates are based on the Poisson assumption. The standard error does not represent the total error that may be present in the age-adjusted rate; it is merely the square root of the variance associated with the rates. In addition to this variance, there also exist potential biases and errors in the measurement of the rate that are difficult to assess accurately and probably impact differently on the error calculations for different states.

The difference between each age-adjusted state rate and the age-adjusted US rate is tested for statistical significance (see below) by calculating a \( Z \) (standard normal) statistic from the formula:

\[ Z = \frac{\text{State rate} - \text{Total US rate}}{SE_d} \]

Although the rates being compared are not independent because each state is part of the US, the statistical test may not be substantially affected if the state represents a small proportion of the total US. There is also an adjustment for multiple comparisons; see below under Statistical Significance.

JOINPOINT REGRESSION ANALYSIS OF CANCER TRENDS

An advance in the presentation of cancer trends is the use of joinpoint models (Kim et al., 2000). In some past issues of the Cancer Statistics Review, certain time intervals (e.g., 1973–1996) were specified and the annual percent changes (APC) were computed over those intervals. The choices of where to start and where to end an interval were arbitrary and sometimes did not give an accurate picture of the trend for a given cancer site. For example, the rates might be increasing and decreasing in different parts of the same interval. For some sites, increases occurred in the earlier years, followed by declines in more recent years.

To achieve greater descriptive accuracy, a statistical algorithm finds the optimal number and location of places where a trend changes. The point (in time) when a trend changes is called a joinpoint. Trends may change in different ways at a joinpoint: from up to down, from down to up, from up to up at a different rate, or from down to down at a different rate. A joinpoint regression model describes the trends by a continuous, piecewise-exponential function. Adjacent segments are connected at a joinpoint. The segments are connected because we assume that rates generally change smoothly, rather than “jump” abruptly. In each segment, the rates are assumed to grow or decay exponentially \((y = e^{mx+b})\), i.e., to change by a constant percentage each year. Thus the “slope” \(m\) in each segment can be associated with a fixed annual percent change (APC) by \( APC = 100(e^m - 1) \).

Joinpoint analysis first assumes no joinpoints are needed to describe the data accurately, i.e.,
the trend over the entire interval 1975-2011 does not change. Joinpoints are added in turn if they are statistically significant. Thus, in the final model, each joinpoint represents a significant change in trend. Smoother polynomial models may provide a good fit overall, but are less sensitive to what is occurring at the ends of the data.

In running the Joinpoint program, we set the program parameters as follows:

1. Joinpoints occur only at exact years; the joinpoint is not necessarily the same as the data point for that year;
2. The minimum time interval between consecutive joinpoints is three years;
3. The first joinpoint is not earlier than two years after the first year of data;
4. The last joinpoint is not later than two years before the last year of data;
5. The maximum number of joinpoints is five for 1975-2011 (SEER 9) data and three for 1992-2011 (SEER 13) data.

These restrictions provide some added stability to the resultant models. Different values for these parameters may yield a different joinpoint model. Since the test statistic to determine if additional joinpoints are necessary cannot be compared against any known standard distribution to determine significance (e.g., the normal, t, or f), a permutation test is used which simulates the distribution of the test statistic under the null hypothesis. Thus an element of randomness is introduced by the random number stream used. However, for greater consistency in the p-values obtained if one were to change the random seed for each run, we run the program for 4499 permutations.

A Windows-based program, Joinpoint, is freely available at http://surveillance.cancer.gov/joinpoint; it accepts data from the SEER*Stat program, as well as user-defined data. Further details on joinpoint regression may be found at the website. Starting with the 2011 edition of CSR, we have generated all our cancer trend statistics using a Linux-based Joinpoint program as opposed to the downloadable Windows-based program. As a result of using a different platform, in rare instances the results (e.g., # of joinpoints) may differ.

Average Annual Percent Change (AAPC) is a summary measure of a trend over a pre-specified fixed interval based on an underlying joinpoint model. It allows us to use a single number to describe the average trend over a period of multiple years. It can be estimated even if the joinpoint model indicates that there were changes in trends during those years, since it is estimated as a geometric weighted average of the joinpoint APCs, with the weights equal to the lengths of each segment over the pre-specified fixed interval. In this report, we have included AAPCs as an addendum to the underlying joinpoint trends, and as a summary measure to compare fixed interval trends by race/ethnicity. For more information on how the AAPC is calculated and the advantages of reporting an AAPC over APCs, see http://surveillance.cancer.gov/joinpoint/aapc.html.

REPORTING DELAY

Timely and accurate calculation of cancer incidence rates is hampered by reporting delay,
time lapse before a diagnosed cancer case is reported to the NCI or the delay in receiving updated information for an existing case. Currently, the NCI allows a standard delay of 22 months between the end of the diagnosis year and the time the cancers are reported to the NCI in November, almost two years later. The data are released to the public in the spring of the following year. For example, cases diagnosed in 2011 were first reported to the NCI in November 2013 and released to the public in April 2014. However, in each subsequent release of the SEER data, records from all prior diagnosis years (e.g., diagnosis years 2010 and earlier in the 2013 submission to the NCI) are updated as either new cases are found or new information is received about previously submitted cases.

The submissions for the most recent diagnosis year are, in general, about two percent below the total number of cancers that will eventually be submitted for that year, although this varies by cancer site and other factors.

The idea behind modeling reporting delay is to adjust the recent rates to anticipate future corrections (additions, changes, and deletions) to the data. These adjusted rates and the associated delay model are valuable in more precisely determining current cancer trends, as well as in monitoring the timeliness of data collection—an important aspect of quality control (Clegg et al., 2002). Reporting delay models have been previously used in the reporting of AIDS cases (Brookmeyer & Damiano, 1989; Pagano et al., 1994; Harris, 1990).

In this report, we show SEER age-adjusted incidence rates and trends, along with their calculated delay adjustments for SEER 9 and SEER 13 areas. The adjusted rates, factors, and trends are available for all cancers combined (malignant only except for urinary bladder), for female breast in situ, for urinary bladder (in situ and malignant combined), and for 22 malignant cancer sites: melanoma (for all races combined and whites only), lung/bronchus, colon/rectum, prostate, female breast, liver and intrahepatic bile duct, pancreas, cervix uteri, corpus and uterus, ovary, testis, kidney and renal pelvis, brain and other nervous system, Hodgkin lymphoma, non-Hodgkin lymphoma, all leukemias, esophagus, larynx, myeloma, oral cavity and pharynx, thyroid, and stomach.

For more information on cancer incidence rates adjusted for reporting delay, see http://surveillance.cancer.gov/delay/. Estimates of observed incidence rates, delay-adjusted incidence rates, and delay-adjustments factors may be found in the Cancer Query Systems at http://seer.cancer.gov/canques/.

Adjustment for VA Case Backlog, Submission Year 2011

A policy change of the Department of Veterans Affairs (VA) regarding data sharing on VA cancer cases resulted in underreporting on VA hospital cases for submission years 2007-2011. Some special adjustments to case counts are necessary to fit the delay adjustment model. Beginning with the 2009 submission of SEER data, some SEER registries began accounting for the backlog of VA cases that would have been reported in 2006-2008. This upsurge in cases could cause perturbation in the delay model if fit in the usual manner.
As with the 2009 to 2011 submissions, to take account of the effect of the VA backlog in the 2012 submission on the delay adjustment model, the counts are adjusted by re-distributing VA cases to previous submission years according to the expected counts from the delay distribution conditional on the current submission. Specifically, for each of the diagnosis years 2004-2009, given the total cancer count in submission year 2012, the proportion of cumulative cancer count in each subsequent submission year is calculated based on the estimated parameters from previous year’s reporting delay model. The VA cases in the 2012 submission are re-distributed to each of the prior submission years according to this proportion. The adjusted total cancer count in that submission year was then calculated by combining the non-VA cases and the re-distributed VA counts.

Delay-adjusted incidence rates and trends are reported for all cancers combined (malignant only except for urinary bladder), for female breast in situ, for urinary bladder (in situ and malignant combined), and for 22 malignant cancer sites: melanoma (for all races combined and whites only), lung/bronchus, colon/rectum, prostate, female breast, liver and intrahepatic bile duct, pancreas, cervix uteri, corpus and uterus, ovary, testis, kidney and renal pelvis, brain and other nervous system, Hodgkin lymphoma, non-Hodgkin lymphoma, all leukemias, esophagus, larynx, myeloma, oral cavity and pharynx, thyroid, and stomach.

**STATISTICAL SIGNIFICANCE**

Errors may be made in the estimation of a given statistic. In order to test whether two groups (such as the populations of a state and the entire US) have the same or different actual rates, the observed rates for the groups are compared. Statisticians consider that a difference in observed rates can be explained by one of two hypotheses: (H₀) The actual rates are really the same, but the observed rates are different because of some combination of error-causing factors, or (H₁) the actual rates of the groups are really different. H₀ is called the null hypothesis (because it says there is no real difference); H₁ is called the alternate hypothesis. Typically, H₀ is rejected only if there is strong evidence in favor of H₁. (Thus, if the observed rates are equal, we cannot reject H₀.)

Using statistical theory, one can determine the distribution of the rate difference under the assumption that H₀ is true. Then values of the rate difference that are very unlikely to occur if H₀ is true are identified. More specifically, a small positive number, called alpha (α), is chosen; usually, α is 0.05 or 0.01. (Alpha is called the significance level of the hypothesis test.) One can then identify limits for the difference in rates such that, if H₀ is true, the probability of the difference being outside of those limits is α. If the observed difference is outside of these limits, then the observed result is very unlikely to happen if H₀ is true, so H₀ is rejected.

Another way of looking at the same process is to calculate, assuming H₀ is true, the probability that the observed difference or any greater difference would occur; this number is called the P-value of the observed result. If the P-value of a comparison is less than α (that is, the observed difference is very unlikely to happen if the null hypothesis is true), H₀ will be rejected. If the P-value of a test is greater than the significance level α, H₀ will not be rejected. When a difference
in rates is sufficiently large to cause the null hypothesis to be rejected for a given value of \( \alpha \) (usually 0.05), it is called a **statistically significant** difference.

When a null hypothesis is rejected, there remains a small chance that a wrong decision has been made. If many statistical comparisons are done, even with \( \alpha = 0.01 \), the chance of making at least one wrong decision becomes a concern. In testing the differences between the total US rate and the rate for each state (or for the District of Columbia) for a given cancer, 51 statistical comparisons of the type described above are performed. Based on one of Bonferroni's inequalities (if there are \( n \) events and \( p_i \) is the probability of success in event \( i \), then \( P(\text{at least 1 success}) < p_1 + \ldots + p_n \) (Snedecor & Cochran, 1980; p. 115-117), the significance level \( \alpha \) for each individual comparison was set equal to \( 0.01/51 \approx 0.0002 \). Thus, only individual-state-to-total-US comparisons with an associated \( P \)-value less than 0.0002 are considered to be statistically significant. That is, a **very small** significance level \( \alpha \) (0.0002) is used in order to minimize the total risk (0.01) of falsely deciding that some pair of equal rates are unequal.

*Use caution in assessing statistically significant differences.* Population size has an important role in any calculation of statistical significance. Some states may have estimated rates that are very close to the estimated total US rate, but because of their large population, the difference between their estimated rate and the estimated total US rate is found to be statistically significant. In this case, the true state rate and the true US rate are almost certainly different, because the observed difference, though small, is nearly impossible if the null hypothesis (equal rates) is true. A small difference in rates, however, may have no practical importance. On the other hand, some smaller states may have estimated rates that differ substantially from the estimated total US rate, but because of their relatively small population, the differences are found to be statistically nonsignificant. When this happens, if the true state rate and the true US rate were equal, the probability of obtaining a difference at least as large as what has been observed is greater than \( \alpha \approx 0.0002 \). Therefore, *because the evidence against it isn't strong enough, the null hypothesis (equal rates) is not rejected.*

If the percent difference (PD) between the two rates is small, there may be some question about the importance of the difference. It is difficult to specify a minimally significant absolute PD, below which the difference would always be unimportant, because the observed PD will depend on the populations of the areas involved. It may be of value to consider the size of the PD between a state rate and the US rate in assessing the importance of a statistically significant difference.

Comparing individual state rates with the US rate and assessing statistical significance is not an appropriate procedure for assessing geographic clustering of state rates. Identification of states which may represent regional clusters of high or low rates would require additional statistical and graphical analyses.

For a number of cancers, the District of Columbia has the highest death rates. *Use caution when comparing cancer rates for the District with those from the 50 states.* The District is an entirely urban area, whereas a state includes urban, suburban, and rural areas. Mortality rates
for many cancers are higher in urban areas. Also, the District has a higher percentage of blacks—51% of the total population in 2010 (US Census Bureau, 2013)—than any state. In addition, their higher mortality rates for several types of cancer elevate the overall rate for the District.

**STANDARD ERRORS OF RATES**

**Survival rates:** In the tables presenting survival estimates, the magnitude of the standard error is given as a measure of the reliability of a given rate: the greater the standard error, the more uncertainty associated with the estimated rate. In addition, if there were fewer than 25 diagnoses in the first interval of the life table constructed to calculate survival, or if all cases became lost to follow-up within an interval, a valid survival estimate could not be calculated, as is noted in the table footnotes.

The **standard error (SE)** of a relative survival estimate is obtained as follows (Ederer et al., 1961):

\[
SE(CR_t) = CR_t \times \text{square root of } \left[ \frac{q_1}{e_1-d_1} + \frac{q_2}{e_2-d_2} + \ldots + \frac{q_t}{e_t-d_t} \right]
\]

where \( CR_t \) is the \( t \)-year relative survival estimate, and for \( i = 1, \ldots, t \),
\( q_i \) is the probability of dying in year \( i \) after diagnosis,
\( e_i \) is the effective number of patients at risk in year \( i \) after diagnosis, and
\( d_i \) is the number of deaths in year \( i \) after diagnosis.

**Incidence and mortality rates:** The standard errors of age-adjusted incidence and mortality rates are often not specified. However, the reader can approximate the SE of a particular incidence or mortality rate by the SE of a crude incidence or mortality rate (Keyfitz, 1966), that is, the SE can be approximated by the rate divided by the square root of the number of cancer cases (or the number of deaths).

Appendix tables provide numbers of cancer diagnoses within SEER areas and numbers of deaths in the entire US, respectively, by race and sex for the most recent 5-year period. These can be used to obtain approximations of the standard errors for associated age-adjusted rates for the same time period using the above formula. To approximate the standard error of a rate for a single year, use the formula but replace the number of cancer cases or deaths with the number of cancer cases or deaths divided by 5.

**DEFINITIONS**

Several technical terms are used in presenting the data in this report. Their definitions are presented here to clarify them for the reader.

**Incidence rate:** The cancer incidence rate is the number of new cancers of a specific site/type occurring in a specified population during a year, usually expressed as the number of cancers
Appendix 1403

per 100,000 persons at risk. That is,

\[ \text{Incidence rate} = \left( \frac{\text{New cancers}}{\text{Population}} \right) \times 100,000. \]

The numerator of the incidence rate is the number of new cancers; the denominator of the incidence rate is the size of the population. The number of new cancers may include multiple primary cancers occurring in one patient. The primary site reported is the site of origin and not the metastatic site. In general, the incidence rate would not include recurrences. The population used depends on the rate to be calculated. For cancer sites that occur in only one sex, the sex-specific population (e.g., females for cervical cancer) is used.

The incidence rate can be computed for a given type of cancer or for all cancers combined. Except for 5-year age-specific rates, all incidence rates in this report are age-adjusted (see below) to the 2000 US standard population (or, where appropriate, to the world standard million population). (In some previous editions of the CSR, the 1970 US standard million population was used; therefore, incidence rates in this edition cannot be compared to rates published in those editions.) Incidence rates are for invasive cancer only, unless otherwise specified. (Exceptions are the incidence rate for cancer of the urinary bladder (where both in situ and invasive cancers are counted) and breast cancer in situ, which is shown separately.)

Death rate: The cancer death (or mortality) rate is the number of deaths with cancer given as the underlying cause of death occurring in a specified population during a year, usually expressed as the number of deaths due to cancer per 100,000 persons. That is,

\[ \text{Death Rate} = \left( \frac{\text{Cancer Deaths}}{\text{Population}} \right) \times 100,000. \]

The numerator of the death rate is the number of deaths; the denominator of the death rate is the size of the population. As with the incidence rate, the population used depends on the rate to be calculated. The death rate can be computed for a given cancer site or for all cancers combined. Except for 5-year age-specific rates, all death rates in this report are age-adjusted (see below) to the 2000 US standard population (or, where appropriate, to the world standard million population). (In some previous editions of the CSR, the 1970 US standard million population was used; therefore, death rates in this edition cannot be compared to rates published in those editions.)

Age distribution: A table showing a partition of the entire lifespan into disjoint age intervals, along with the proportion of the population in each interval.

Median age: The age at which half of a population is younger and half is older.

Standard population: A standard population for a geographic area, such as the US or the world, is a table giving the proportions of the population falling into the age groups 0, 1-4, 5-9, ..., 80-84, and 85+. A standard million population for a geographic area is a table giving the number of persons in each age group 0, 1-4, ..., 85+ out of a theoretical cohort of 1,000,000 persons that is distributed by age in the same proportions as the standard population. Table A-7 shows the US 2000 standard population and the world standard million population. (Some
World Health Organization mortality publications use a different world standard million population.)

**Age-adjusted rate:** An age-adjusted incidence or mortality rate is a weighted average of the age-specific incidence or mortality rates, where the weights are the counts of persons in the corresponding age groups of a standard population. The potential confounding effect of age is reduced when comparing age-adjusted rates based on the same standard population. For this report, the 2000 US standard population (or, where appropriate, the world standard million population) is used in computing age-adjusted rates, unless otherwise noted.

**Percent change:** The percent change (PC) in a statistic over a given time interval is

\[ \text{Percent change} = \frac{\text{Final value} - \text{Initial value}}{\text{Initial value}} \times 100. \]

A positive PC corresponds to an increasing trend, a negative PC to a decreasing trend.

**Annual percent change:** The annual percent change (APC) is calculated by first fitting a regression line to the natural logarithms of the rates (r) using calendar year (x) as a regressor variable. In this report the method of weighted least squares is used to calculate the regression equation. If \( \ln(r) = mx + b \) is the resulting regression equation (with slope \( m \)), then

\[ \text{APC} = 100 \times (e^m - 1). \]

A positive APC corresponds to an increasing trend, a negative APC to a decreasing trend.

Because the methods used in their calculation are mathematically different, *the signs of the PC and the APC for a given statistic and time interval may differ*, as occurs in a few of the tables presented. That is, one of these statistics may show an increasing trend, the other a decreasing trend.

Testing the hypothesis that the actual mean annual percent change is 0 is equivalent to testing the hypothesis that the theoretical slope estimated by the slope \( m \) of the line representing the equation \( \ln(r) = mx + b \) is 0. The latter hypothesis is tested using the \( t \) distribution of \( m / SE_m \) with \( n - 2 \) degrees of freedom. The standard error of \( m \), called \( SE_m \), is obtained from the fit of the regression (Kleinbaum et al., 1988). (This calculation assumes that the rates increased or decreased at a constant rate over the entire calendar year interval; the validity of this assumption was not assessed.) In those few instances where at least one of the rates was 0, the linear regression was not calculated.

**Average Annual Percent Change:** The average annual percent change (AAPC) is a summary measure of a trend over a pre-specified fixed interval based on an underlying joinpoint model. It allows us to use a single number to describe the average trend over a period of multiple years. It can be estimated even if the joinpoint model indicates that there were changes in trends during those years, since it is estimated as a weighted average of the joinpoint APCs, with the weights equal to the lengths of each subinterval over the pre-specified fixed interval.

**Life table:** A table for a given population listing, for each sex and each age from 0 to 120, how many members die at that age and how many survive one more year.
**Observed survival:** The observed survival estimate represents the proportion of cancer patients surviving for a specified time interval after diagnosis. Note that some of those not surviving died of the given cancer and some died of other causes.

**Relative survival:** The relative survival estimate is calculated using a procedure (Ederer et al., 1961; Ederer and Heise, 1959) whereby the observed survival estimate is adjusted for expected mortality. The relative survival estimate approximates the likelihood that a patient will not die from causes associated specifically with the given cancer before some specified time after diagnosis. It is always larger than the observed survival estimate for the same group of patients.

**Standard error:** The standard error of a rate is a measure of the sampling variability of the rate.

**Person-years of life lost:** The person-years of life lost (PYLL) is calculated as follows: For each individual who dies of the cancer of interest, the number of years of expected additional life for an average person of that age, race, and sex is obtained from life tables for the US population (available from the NCHS). The PYLL in the general population associated with a particular cancer for a given year is simply the sum of this expectation over all those individuals who died of that cancer in that year.

**Average years of life lost:** The average years of life lost (AYLL) associated with a particular cancer for a given year is the PYLL associated with that cancer in the general population divided by the number of deaths from that cancer in the general population in that year.

**Prevalence:** Prevalence is defined as the number or percent of people alive on a certain date in a population who previously had a diagnosis of the disease. It includes new (incident) and pre-existing cases and is a function of past incidence, past survival, and the size and age structure of the population. **Limited-duration prevalence** represents the proportion of people alive on a certain day who had a diagnosis of the disease within the past $x$ years (e.g. $x = 5, 10, \text{ or } 20$ years). **Complete prevalence** is an estimate of the number of persons (or the proportion of the population) alive on a specified date who had been diagnosed with the given disease, no matter how long ago that diagnosis was. For more details on cancer prevalence definitions and methods, refer to [http://surveillance.cancer.gov/prevalence/](http://surveillance.cancer.gov/prevalence/).

**Stage of disease at diagnosis:** Extent-of-disease information determines stage of disease at diagnosis. The **SEER summary stage** presented has four levels. An invasive neoplasm confined entirely to the organ of origin is said to be **localized**. A neoplasm that has extended beyond the limits of the organ of origin, either directly into surrounding organs or tissues or into regional lymph nodes, is said to be **regional**. A neoplasm that has spread to parts of the body remote from the primary tumor, either by direct extension or by discontinuous metastasis, is said to be **distant**. When information is not sufficient to assign a stage, a neoplasm is said to be **unstaged**. In situ tumors (except those of the cervix uteri) are also collected by SEER but generally are not published in this series. For some cancers and diagnosis years, the extent of
disease information can also be converted to Stages 0-IV as defined by the American Joint Committee on Cancer (Greene et al, 2002; Edge et al., 2010).

SOFTWARE USED TO GENERATE THE SEER CANCER STATISTICS REVIEW

The SEER Cancer Statistics Review includes statistics generated by a variety of statistical software including:

- **SEER*Stat**, statistical software for the analysis of SEER and other cancer databases, was used to generate incidence, mortality, prevalence, and survival statistics presented in the CSR.
- Analysis generated by the **Joinpoint Regression Program** are presented to better describe trends that are not constant over time.
- The **DevCan** system generated the probability of developing cancer from twelve SEER areas and the probability of dying from cancer from the total United States.
- The **ComPrev** software was used to calculate complete prevalence estimates.

Additional statistics can be obtained via SEER’s **Cancer Query Systems**. These data retrieval applications provide access to pre-calculated cancer statistics stored in online databases.
REFERENCES


Ederer F, Heise H. Instructions to IBM 650 Programmers in Processing Survival Computations, Technical, End Results Evaluation Section, National Cancer Institute, 1959.


Howlader N, Ries LAG, Stinchcomb DG, Edwards BK. The impact of underreported Veterans


## Table 1.1
Estimated New Cancer Cases and Deaths for 2014
All Races, By Sex

<table>
<thead>
<tr>
<th>Primary Site</th>
<th>Estimated New Cases</th>
<th>Estimated Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All Sites</strong></td>
<td>1,665,540</td>
<td>855,220</td>
</tr>
<tr>
<td><strong>Males</strong></td>
<td>840,720</td>
<td>305,010</td>
</tr>
<tr>
<td><strong>Females</strong></td>
<td>824,820</td>
<td>550,210</td>
</tr>
<tr>
<td><strong>Tongue</strong></td>
<td>42,440</td>
<td>13,590</td>
</tr>
<tr>
<td><strong>Rack and Pharynx</strong></td>
<td>63,980</td>
<td>11,920</td>
</tr>
<tr>
<td><strong>Pharynx</strong></td>
<td>82,480</td>
<td>14,410</td>
</tr>
<tr>
<td><strong>Other Oral Cavity</strong></td>
<td>63,980</td>
<td>2,520</td>
</tr>
<tr>
<td><strong>Digestive System</strong></td>
<td>126,730</td>
<td>289,610</td>
</tr>
<tr>
<td><strong>Esophagus</strong></td>
<td>14,660</td>
<td>18,170</td>
</tr>
<tr>
<td><strong>Stomach</strong></td>
<td>8,490</td>
<td>22,220</td>
</tr>
<tr>
<td><strong>Small Intestine</strong></td>
<td>4,280</td>
<td>9,160</td>
</tr>
<tr>
<td>*<em>Colon</em></td>
<td>64,120</td>
<td>96,830</td>
</tr>
<tr>
<td><strong>Rectum</strong></td>
<td>16,620</td>
<td>40,000</td>
</tr>
<tr>
<td><strong>Anus, Anal Canal, and Anorectum</strong></td>
<td>4,550</td>
<td>7,210</td>
</tr>
<tr>
<td><strong>Liver and Intrahepatic</strong></td>
<td>4,960</td>
<td>10,650</td>
</tr>
<tr>
<td><strong>Biliary</strong></td>
<td>5,690</td>
<td>16,240</td>
</tr>
<tr>
<td><strong>Pancreas</strong></td>
<td>2,280</td>
<td>46,420</td>
</tr>
<tr>
<td><strong>Respiratory System</strong></td>
<td>112,550</td>
<td>242,550</td>
</tr>
<tr>
<td><strong>Larynx</strong></td>
<td>2,630</td>
<td>12,630</td>
</tr>
<tr>
<td><strong>Lung and Bronchus</strong></td>
<td>108,210</td>
<td>224,210</td>
</tr>
<tr>
<td><strong>Other Respiratory</strong></td>
<td>1,710</td>
<td>5,790</td>
</tr>
<tr>
<td><strong>Bones and Joints</strong></td>
<td>1,340</td>
<td>3,020</td>
</tr>
<tr>
<td><strong>Soft Tissue</strong></td>
<td>5,470</td>
<td>12,020</td>
</tr>
<tr>
<td><strong>Skin (excl. basal &amp; squamous)</strong></td>
<td>34,590</td>
<td>81,220</td>
</tr>
<tr>
<td><strong>Melanoma of the Skin</strong></td>
<td>3,220</td>
<td>76,100</td>
</tr>
<tr>
<td><strong>Other non-epithelial skin</strong></td>
<td>2,380</td>
<td>5,120</td>
</tr>
<tr>
<td><strong>Breast</strong></td>
<td>232,670</td>
<td>235,030</td>
</tr>
<tr>
<td><strong>Genital Organs</strong></td>
<td>43,000</td>
<td>338,450</td>
</tr>
<tr>
<td><strong>Cervix (uterus)</strong></td>
<td>4,020</td>
<td>12,360</td>
</tr>
<tr>
<td><strong>Endometrium (uterus)</strong></td>
<td>8,590</td>
<td>52,630</td>
</tr>
<tr>
<td><strong>Ovary</strong></td>
<td>14,270</td>
<td>21,980</td>
</tr>
<tr>
<td><strong>Vulva</strong></td>
<td>2,370</td>
<td>4,850</td>
</tr>
<tr>
<td><strong>Vagina and other genital organs, female</strong></td>
<td>880</td>
<td>3,170</td>
</tr>
<tr>
<td><strong>Prostate</strong></td>
<td>29,480</td>
<td>233,000</td>
</tr>
<tr>
<td><strong>Testis</strong></td>
<td>380</td>
<td>8,820</td>
</tr>
<tr>
<td><strong>Penis and other genital organs, male</strong></td>
<td>120</td>
<td>1,640</td>
</tr>
<tr>
<td><strong>Urinary System</strong></td>
<td>44,190</td>
<td>141,610</td>
</tr>
<tr>
<td><strong>Urineary Bladder</strong></td>
<td>18,300</td>
<td>74,690</td>
</tr>
<tr>
<td><strong>Kidney and Renal Pelvis</strong></td>
<td>24,780</td>
<td>63,920</td>
</tr>
<tr>
<td><strong>Ureter and other urinary organs</strong></td>
<td>930</td>
<td>3,000</td>
</tr>
<tr>
<td><strong>Eye and Orbit</strong></td>
<td>310</td>
<td>2,730</td>
</tr>
<tr>
<td><strong>Brain and Other Nervous System</strong></td>
<td>8,090</td>
<td>23,380</td>
</tr>
<tr>
<td><strong>Endocrine System</strong></td>
<td>6,230</td>
<td>65,630</td>
</tr>
<tr>
<td><strong>Thyroid</strong></td>
<td>1,520</td>
<td>62,980</td>
</tr>
<tr>
<td><strong>Other Endocrine</strong></td>
<td>460</td>
<td>2,650</td>
</tr>
<tr>
<td><strong>Lymphoma</strong></td>
<td>9,030</td>
<td>79,990</td>
</tr>
<tr>
<td><strong>Hodgkin Lymphoma</strong></td>
<td>510</td>
<td>9,190</td>
</tr>
<tr>
<td><strong>Non-Hodgkin Lymphoma</strong></td>
<td>8,520</td>
<td>70,850</td>
</tr>
<tr>
<td><strong>Leukemia</strong></td>
<td>8,480</td>
<td>52,380</td>
</tr>
<tr>
<td><strong>Lymphocytic Leukemias</strong></td>
<td>2,410</td>
<td>27,740</td>
</tr>
<tr>
<td><strong>Myeloid Leukemias</strong></td>
<td>3,170</td>
<td>11,780</td>
</tr>
<tr>
<td><strong>Other leukemia</strong></td>
<td>2,910</td>
<td>5,800</td>
</tr>
<tr>
<td><strong>All Other Sites</strong></td>
<td>24,780</td>
<td>31,430</td>
</tr>
</tbody>
</table>

*Estimated deaths for colon & rectum cancers are combined.

More deaths than cases suggests lack of specificity in recording underlying causes of death on death certificates.

Cancer Facts & Figures - 2014, American Cancer Society (ACS), Atlanta, Georgia, 2014.

*Excludes basal and squamous cell skin and in situ carcinomas except urinary bladder.

Incidence projections are based on rates from the North American Association of Central Cancer Registries (NAACCR) from 1995-2010, representing about 89% of the US population.

*Estimated deaths are based on data from US Mortality Data, 1995-2010, National Center for Health Statistics, Centers for Disease Control and Prevention.

*Estimated deaths for colon & rectum cancers are combined.

*Estimated deaths for colon & rectum cancers are combined.

*Studies in situ accounts for about 63,770 new cases annually.

*More deaths than cases suggests lack of specificity in recording underlying causes of death on death certificates.
Table 1.3

62-Year Trends in U.S. Cancer Death Rates\(^a\)

All Races, Males and Females

All Primary Cancer Sites Combined

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Ages 0-4</td>
<td>11.1</td>
<td>4.4</td>
<td>2.1</td>
<td>-3.2*</td>
<td>-2.6*</td>
<td>-81.1</td>
</tr>
<tr>
<td>Ages 5-14</td>
<td>6.7</td>
<td>4.1</td>
<td>2.1</td>
<td>-1.6*</td>
<td>-2.1*</td>
<td>-68.5</td>
</tr>
<tr>
<td>Ages 15-24</td>
<td>8.6</td>
<td>5.6</td>
<td>3.6</td>
<td>-1.2*</td>
<td>-1.5*</td>
<td>-57.5</td>
</tr>
<tr>
<td>Ages 25-34</td>
<td>20.4</td>
<td>13.3</td>
<td>8.5</td>
<td>-1.4*</td>
<td>-1.6*</td>
<td>-58.3</td>
</tr>
<tr>
<td>Ages 35-44</td>
<td>63.6</td>
<td>48.9</td>
<td>28.6</td>
<td>-0.8*</td>
<td>-1.8*</td>
<td>-55.1</td>
</tr>
<tr>
<td>Ages 45-54</td>
<td>174.2</td>
<td>172.9</td>
<td>106.6</td>
<td>0.1*</td>
<td>-1.7*</td>
<td>-38.8</td>
</tr>
<tr>
<td>Ages 55-64</td>
<td>391.3</td>
<td>430.7</td>
<td>292.7</td>
<td>0.4*</td>
<td>-1.5*</td>
<td>-25.2</td>
</tr>
<tr>
<td>Ages 65-74</td>
<td>710.0</td>
<td>823.9</td>
<td>660.0</td>
<td>0.5*</td>
<td>-0.8*</td>
<td>-7.0</td>
</tr>
<tr>
<td>Ages 75-84</td>
<td>1,167.2</td>
<td>1,229.5</td>
<td>1,167.2</td>
<td>0.2*</td>
<td>-0.2*</td>
<td>0.0</td>
</tr>
<tr>
<td>Ages 85+</td>
<td>1,450.7</td>
<td>1,580.4</td>
<td>1,682.7</td>
<td>0.3*</td>
<td>0.2*</td>
<td>16.0</td>
</tr>
<tr>
<td>All Ages</td>
<td>195.4</td>
<td>206.4</td>
<td>168.7</td>
<td>0.2*</td>
<td>-0.8*</td>
<td>-13.7</td>
</tr>
</tbody>
</table>

Lung and Bronchus Cancer\(^b\)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Ages 0-4</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Ages 5-14</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Ages 15-24</td>
<td>0.2</td>
<td>0.1</td>
<td>0.1</td>
<td>-2.8*</td>
<td>-0.1</td>
<td>-55.3</td>
</tr>
<tr>
<td>Ages 25-34</td>
<td>0.8</td>
<td>0.6</td>
<td>0.3</td>
<td>-0.5</td>
<td>-2.4*</td>
<td>-62.8</td>
</tr>
<tr>
<td>Ages 35-44</td>
<td>4.6</td>
<td>9.5</td>
<td>3.1</td>
<td>2.5*</td>
<td>-2.8*</td>
<td>-33.2</td>
</tr>
<tr>
<td>Ages 45-54</td>
<td>20.2</td>
<td>52.5</td>
<td>24.9</td>
<td>3.2*</td>
<td>-2.7*</td>
<td>23.1</td>
</tr>
<tr>
<td>Ages 55-64</td>
<td>48.9</td>
<td>138.8</td>
<td>82.6</td>
<td>3.3*</td>
<td>-2.0*</td>
<td>69.0</td>
</tr>
<tr>
<td>Ages 65-74</td>
<td>59.4</td>
<td>238.1</td>
<td>218.8</td>
<td>4.1*</td>
<td>-0.4*</td>
<td>268.3</td>
</tr>
<tr>
<td>Ages 75-84</td>
<td>55.4</td>
<td>242.9</td>
<td>345.0</td>
<td>4.9*</td>
<td>1.0*</td>
<td>522.9</td>
</tr>
<tr>
<td>Ages 85+</td>
<td>42.3</td>
<td>178.9</td>
<td>325.5</td>
<td>5.1*</td>
<td>1.9*</td>
<td>669.6</td>
</tr>
<tr>
<td>All Ages</td>
<td>14.9</td>
<td>50.2</td>
<td>46.1</td>
<td>3.8*</td>
<td>-0.4*</td>
<td>208.4</td>
</tr>
</tbody>
</table>

Source: US Mortality Files, National Center for Health Statistics, Centers for Disease Control and Prevention.

\(^a\) Rates are per 100,000 and age-adjusted to the 2000 US Std Population (18 age groups - Census P25-1130).

\(^b\) Due to coding changes throughout the years, Lung and Bronchus includes trachea and pleura.

* The APC is significantly different from zero (p<.05).

- Statistic not shown. Rate based on less than 16 cases for the time interval.
- Trend based on less than 10 cases for at least one year within the time interval.
### Table 1.4

Summary of Changes in Cancer Mortality, 1950-2011 and 5-Year Relative Survival (Percent), 1950-2010  
Males and Females, By Primary Cancer Site

<table>
<thead>
<tr>
<th>Primary Site</th>
<th>U.S. Mortality Percent Change 1950-2011*</th>
<th>Whitest APC</th>
<th>1950-2014 5-Year Relative Survival (Percent)b</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral cavity and pharynx</td>
<td>-51.9</td>
<td>-1.3*</td>
<td>46</td>
</tr>
<tr>
<td>Esophagus</td>
<td>28.3</td>
<td>0.8*</td>
<td>4</td>
</tr>
<tr>
<td>Stomach</td>
<td>-88.1</td>
<td>-3.4*</td>
<td>12</td>
</tr>
<tr>
<td>Colon and rectum</td>
<td>-55.3</td>
<td>-1.3*</td>
<td>37</td>
</tr>
<tr>
<td>Colon</td>
<td>-48.6</td>
<td>-1.0*</td>
<td>41</td>
</tr>
<tr>
<td>Rectum</td>
<td>-70.3</td>
<td>-2.3*</td>
<td>40</td>
</tr>
<tr>
<td>Liver and intrahepatic bile duct</td>
<td>53.0</td>
<td>0.8*</td>
<td>1</td>
</tr>
<tr>
<td>Pancreas</td>
<td>26.1</td>
<td>0.1*</td>
<td>1</td>
</tr>
<tr>
<td>Larynx</td>
<td>-39.2</td>
<td>-0.7*</td>
<td>52</td>
</tr>
<tr>
<td>Lung and bronchus</td>
<td>207.5</td>
<td>1.4*</td>
<td>6</td>
</tr>
<tr>
<td>Males</td>
<td>131.9</td>
<td>0.7*</td>
<td>5</td>
</tr>
<tr>
<td>Females</td>
<td>543.9</td>
<td>2.9*</td>
<td>9</td>
</tr>
<tr>
<td>Melanoma of the skin</td>
<td>173.7</td>
<td>1.3*</td>
<td>49</td>
</tr>
<tr>
<td>Breast (females)</td>
<td>-35.8</td>
<td>-0.6*</td>
<td>60</td>
</tr>
<tr>
<td>Cervix uteri</td>
<td>-81.9</td>
<td>-3.2*</td>
<td>59</td>
</tr>
<tr>
<td>Corpus and uterus, NOS</td>
<td>-66.2</td>
<td>-1.6*</td>
<td>72</td>
</tr>
<tr>
<td>Ovary</td>
<td>-12.1</td>
<td>-0.3*</td>
<td>30</td>
</tr>
<tr>
<td>Prostate</td>
<td>-33.9</td>
<td>-0.4*</td>
<td>43</td>
</tr>
<tr>
<td>Testis</td>
<td>-70.5</td>
<td>-2.8*</td>
<td>57</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>-28.7</td>
<td>-0.7*</td>
<td>53</td>
</tr>
<tr>
<td>Kidney and renal pelvis</td>
<td>33.7</td>
<td>0.5*</td>
<td>34</td>
</tr>
<tr>
<td>Brain and nervous system</td>
<td>50.5</td>
<td>0.5*</td>
<td>21</td>
</tr>
<tr>
<td>Thyroid</td>
<td>-40.4</td>
<td>-1.0*</td>
<td>80</td>
</tr>
<tr>
<td>Hodgkin lymphoma</td>
<td>-80.9</td>
<td>-3.3*</td>
<td>30</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>82.6</td>
<td>0.9*</td>
<td>33</td>
</tr>
<tr>
<td>Myeloma</td>
<td>217.3</td>
<td>1.2*</td>
<td>6</td>
</tr>
<tr>
<td>Leukemia</td>
<td>-0.8</td>
<td>-0.3*</td>
<td>10</td>
</tr>
<tr>
<td>Childhood (Ages 0-14)</td>
<td>-74.3</td>
<td>-2.7*</td>
<td>20</td>
</tr>
<tr>
<td>All Sites</td>
<td>-14.1</td>
<td>-0.1*</td>
<td>35</td>
</tr>
</tbody>
</table>

The APC is the Annual Percent Change over the time interval.  
Rates used in the calculation of the APC are age-adjusted to the 2000 U.S. standard population (18 age groups - Census P25-1130).  
Due to coding changes throughout the years: Colon excludes other digestive tract; Rectum includes anal canal; Liver & intrahepatic bile duct includes gallbladder & biliary tract, NOS; Lung & bronchus includes trachea & pleura; Ovary includes fallopian tube; Urinary bladder includes other urinary organs; Kidney & Renal pelvis includes ureter; NHL and myeloma each include a small number of leukemias; NHL includes a small number of ill-defined sites.

Survival estimates for 1950-54 are from NCI Survival Report 5 with the exception of All Sites, Oral cavity & pharynx, Colon & rectum, Non-Hodgkin lymphoma and Childhood cancers which come from historical Connecticut data.

Survival estimates for 2004-2010 are from the SEER 9 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, and Atlanta).

Rates are based on follow-up of patients into 2011.

* The APC is significantly different from zero (p<.05).
### Table 1.5

Age-Adjusted SEER Incidence and U.S. Death Rates and 5-Year Relative Survival (Percent) By Primary Cancer Site, Sex and Time Period

<table>
<thead>
<tr>
<th>Site</th>
<th>Incidencea</th>
<th>US Mortalityb</th>
<th>Survivalc (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Males</td>
<td>Females</td>
</tr>
<tr>
<td>All Sites</td>
<td>460.4</td>
<td>529.4</td>
<td>411.3</td>
</tr>
<tr>
<td>Oral Cavity &amp; Pharynx:</td>
<td>11.0</td>
<td>16.5</td>
<td>6.2</td>
</tr>
<tr>
<td>Lip</td>
<td>0.7</td>
<td>1.1</td>
<td>0.3</td>
</tr>
<tr>
<td>Tongue</td>
<td>3.2</td>
<td>4.8</td>
<td>1.8</td>
</tr>
<tr>
<td>Salivary gland</td>
<td>1.3</td>
<td>1.7</td>
<td>1.0</td>
</tr>
<tr>
<td>Floor of mouth</td>
<td>0.6</td>
<td>0.8</td>
<td>0.3</td>
</tr>
<tr>
<td>Gum &amp; other oral cavity</td>
<td>1.5</td>
<td>1.8</td>
<td>1.3</td>
</tr>
<tr>
<td>Nasopharynx</td>
<td>0.7</td>
<td>1.0</td>
<td>0.4</td>
</tr>
<tr>
<td>Tongue</td>
<td>1.8</td>
<td>3.1</td>
<td>0.6</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>0.4</td>
<td>0.7</td>
<td>0.2</td>
</tr>
<tr>
<td>Hypopharynx</td>
<td>0.6</td>
<td>1.1</td>
<td>0.2</td>
</tr>
<tr>
<td>Other oral cavity &amp; pharynx</td>
<td>0.2</td>
<td>0.3</td>
<td>0.1</td>
</tr>
<tr>
<td>Digestive System:</td>
<td>84.3</td>
<td>103.2</td>
<td>68.9</td>
</tr>
<tr>
<td>Esophagus</td>
<td>4.4</td>
<td>7.7</td>
<td>1.8</td>
</tr>
<tr>
<td>Stomach</td>
<td>7.5</td>
<td>10.3</td>
<td>5.3</td>
</tr>
<tr>
<td>Small intestine</td>
<td>2.1</td>
<td>2.5</td>
<td>1.8</td>
</tr>
<tr>
<td>Colon &amp; Rectum:</td>
<td>43.7</td>
<td>50.6</td>
<td>38.2</td>
</tr>
<tr>
<td>Colon</td>
<td>31.1</td>
<td>34.8</td>
<td>28.2</td>
</tr>
<tr>
<td>Rectum</td>
<td>12.6</td>
<td>15.7</td>
<td>10.0</td>
</tr>
<tr>
<td>Anus, anal canal &amp; anorectum</td>
<td>1.8</td>
<td>1.5</td>
<td>2.0</td>
</tr>
<tr>
<td>Liver &amp; intrahepatic bile duct</td>
<td>7.9</td>
<td>12.4</td>
<td>4.1</td>
</tr>
<tr>
<td>Gallbladder</td>
<td>1.2</td>
<td>0.8</td>
<td>1.4</td>
</tr>
<tr>
<td>Other biliary</td>
<td>1.9</td>
<td>2.3</td>
<td>1.5</td>
</tr>
<tr>
<td>Pancreas</td>
<td>12.3</td>
<td>14.0</td>
<td>10.9</td>
</tr>
<tr>
<td>Retropertitoneum</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
</tr>
<tr>
<td>Peritoneum, omentum &amp; mesentery</td>
<td>0.6</td>
<td>0.1</td>
<td>1.1</td>
</tr>
<tr>
<td>Other digestive system</td>
<td>0.6</td>
<td>0.7</td>
<td>0.5</td>
</tr>
<tr>
<td>Respiratory System:</td>
<td>64.3</td>
<td>79.3</td>
<td>53.0</td>
</tr>
<tr>
<td>Nose, nasal cavity &amp; middle ear</td>
<td>0.7</td>
<td>0.9</td>
<td>0.5</td>
</tr>
<tr>
<td>Larynx</td>
<td>3.3</td>
<td>5.9</td>
<td>1.2</td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
<td>60.1</td>
<td>72.2</td>
<td>51.1</td>
</tr>
<tr>
<td>Pleura</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Trachea &amp; other respiratory organs</td>
<td>0.2</td>
<td>0.3</td>
<td>0.1</td>
</tr>
<tr>
<td>Bones &amp; joints</td>
<td>0.9</td>
<td>1.1</td>
<td>0.8</td>
</tr>
<tr>
<td>Soft tissue (including heart)</td>
<td>3.3</td>
<td>4.0</td>
<td>2.8</td>
</tr>
<tr>
<td>Skin (excl. basal &amp; squamous)</td>
<td>23.3</td>
<td>30.5</td>
<td>18.1</td>
</tr>
<tr>
<td>Melanoma of the skin</td>
<td>21.3</td>
<td>27.7</td>
<td>16.7</td>
</tr>
<tr>
<td>Other non-epithelial skin</td>
<td>2.0</td>
<td>2.8</td>
<td>1.4</td>
</tr>
<tr>
<td>Breast</td>
<td>67.1</td>
<td>1.2</td>
<td>124.6</td>
</tr>
<tr>
<td>Breast (in situ)</td>
<td>16.8</td>
<td>0.2</td>
<td>31.7</td>
</tr>
</tbody>
</table>

Note: Incidence and death rates are per 100,000 and are age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1130).

a SEER 18 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, Alaska Native Registry, Rural Georgia, California excluding SF/SJM/LA, Kentucky, Louisiana, New Jersey and Georgia excluding ATL/RG).

b US Mortality Files, National Center for Health Statistics, Centers for Disease Control and Prevention.

c SEER 18 areas. Based on follow-up of patients into 2011.

d Mesotheliomas of the Pleura are included in the separate group Mesothelioma for incidence but are included in the Pleura grouping for mortality.

- Statistic could not be calculated due to less than 16 cases in the time interval.
### Table 15 - continued

Age-Adjusted SEER Incidence and U.S. Death Rates and 5-Year Relative Survival (Percent) By Primary Cancer Site, Sex and Time Period

#### All Races

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total Males Females</td>
<td>Total Males Females</td>
<td>Total Males Females</td>
</tr>
<tr>
<td><strong>Female Genital System:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cervix uteri</td>
<td>26.1 - 48.8</td>
<td>8.6 - 15.5</td>
<td>68.4 - 68.4</td>
</tr>
<tr>
<td>Corpus uteri</td>
<td>12.8 - 23.9</td>
<td>1.1 - 2.2</td>
<td>82.8 - 82.8</td>
</tr>
<tr>
<td>Uterus, NOS</td>
<td>0.4 - 0.7</td>
<td>1.4 - 2.4</td>
<td>26.4 - 26.4</td>
</tr>
<tr>
<td>Ovary</td>
<td>6.6 - 12.3</td>
<td>4.4 - 7.9</td>
<td>44.6 - 44.6</td>
</tr>
<tr>
<td>Vagina</td>
<td>0.4 - 0.7</td>
<td>0.1 - 0.2</td>
<td>51.8 - 51.8</td>
</tr>
<tr>
<td>Vulva</td>
<td>1.3 - 2.4</td>
<td>0.3 - 0.5</td>
<td>70.5 - 70.5</td>
</tr>
<tr>
<td>Other female genital system</td>
<td>0.5 - 1.0</td>
<td>0.1 - 0.2</td>
<td>59.1 - 59.1</td>
</tr>
<tr>
<td><strong>Male Genital System:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prostate</td>
<td>70.3 154.5</td>
<td>9.0 22.8</td>
<td>98.6 98.6</td>
</tr>
<tr>
<td>Testis</td>
<td>67.0 147.8</td>
<td>8.8 22.3</td>
<td>98.9 98.9</td>
</tr>
<tr>
<td>Penis</td>
<td>2.8 5.6</td>
<td>0.1 0.2</td>
<td>95.3 95.3</td>
</tr>
<tr>
<td>Other male genital system</td>
<td>0.4 0.9</td>
<td>0.1 0.2</td>
<td>67.9 67.9</td>
</tr>
<tr>
<td><strong>Urinary System:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>36.9 58.8 20.1</td>
<td>8.6 13.8 4.9</td>
<td>74.7 75.9 72.2</td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>20.5 36.2 8.8</td>
<td>4.4 7.7 2.2</td>
<td>77.4 78.9 72.7</td>
</tr>
<tr>
<td>Ureter</td>
<td>0.6 0.8 0.4</td>
<td>0.1 0.1 0.1</td>
<td>47.6 47.6 47.9</td>
</tr>
<tr>
<td>Other urinary system</td>
<td>0.3 0.5 0.2</td>
<td>0.1 0.2 0.1</td>
<td>50.7 54.6 44.8</td>
</tr>
<tr>
<td><strong>Eye &amp; Orbit:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brain &amp; Nervous System:*</td>
<td>6.4 7.6 5.4</td>
<td>4.3 5.2 3.5</td>
<td>33.4 35.2 34.5</td>
</tr>
<tr>
<td>Brain</td>
<td>6.0 7.3 5.0</td>
<td>- -</td>
<td>29.3 29.8 30.9</td>
</tr>
<tr>
<td>Cranial nerves &amp; other nervous system</td>
<td>0.4 0.4 0.4</td>
<td>- -</td>
<td>77.2 75.6 78.7</td>
</tr>
<tr>
<td><strong>Endocrine System:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thyroid</td>
<td>13.6 7.3 19.8</td>
<td>0.8 0.8 0.8</td>
<td>95.8 91.4 97.2</td>
</tr>
<tr>
<td>Other endocrine &amp; thymus</td>
<td>12.9 6.4 19.1</td>
<td>0.5 0.5 0.5</td>
<td>97.8 95.6 98.5</td>
</tr>
<tr>
<td><strong>Lymphoma:</strong></td>
<td>22.4 27.0 18.8</td>
<td>6.7 8.5 5.3</td>
<td>71.6 70.4 73.0</td>
</tr>
<tr>
<td>Hodgkin lymphoma</td>
<td>2.7 3.1 2.4</td>
<td>0.4 0.5 0.3</td>
<td>85.3 84.4 86.4</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>19.7 23.9 16.3</td>
<td>6.3 8.1 5.0</td>
<td>69.3 68.0 70.9</td>
</tr>
<tr>
<td><strong>Myeloma:</strong></td>
<td>6.1 7.7 4.9</td>
<td>3.4 4.3 2.7</td>
<td>44.9 46.0 43.5</td>
</tr>
<tr>
<td><strong>Leukemia:</strong></td>
<td>13.0 16.7 10.2</td>
<td>7.0 9.4 5.3</td>
<td>57.2 58.0 56.2</td>
</tr>
<tr>
<td>Lymphocytic:</td>
<td>6.5 8.6 4.9</td>
<td>2.0 2.8 1.4</td>
<td>76.4 76.5 76.1</td>
</tr>
<tr>
<td>Acute lymphocytic</td>
<td>1.7 1.9 1.5</td>
<td>0.5 0.5 0.4</td>
<td>66.7 67.1 66.1</td>
</tr>
<tr>
<td>Chronic lymphocytic</td>
<td>1.1 1.4 0.9</td>
<td>1.4 2.0 0.9</td>
<td>80.2 79.5 81.1</td>
</tr>
<tr>
<td>Other lymphocytic</td>
<td>1.3 0.6 0.2</td>
<td>0.1 0.2 0.1</td>
<td>81.1 85.4 69.1</td>
</tr>
<tr>
<td>Myeloid &amp; Monocytic:</td>
<td>5.9 7.3 4.8</td>
<td>3.4 4.5 2.6</td>
<td>36.3 36.0 36.7</td>
</tr>
<tr>
<td>Acute myeloid</td>
<td>3.3 4.6 3.2</td>
<td>2.8 3.7 2.2</td>
<td>24.9 23.9 26.1</td>
</tr>
<tr>
<td>Chronic myeloid</td>
<td>1.2 1.7 1.2</td>
<td>0.3 0.4 0.2</td>
<td>62.0 61.2 63.0</td>
</tr>
<tr>
<td>Acute non lymphocytic</td>
<td>0.3 0.3 0.2</td>
<td>0.0 0.0 0.0</td>
<td>22.5 21.5 23.6</td>
</tr>
<tr>
<td>Other myeloid &amp; monocytic</td>
<td>0.2 0.2 0.1</td>
<td>0.2 0.3 0.1</td>
<td>33.4 32.7 34.2</td>
</tr>
<tr>
<td>Other leukemia:</td>
<td>0.6 0.8 0.5</td>
<td>1.7 2.2 1.3</td>
<td>30.8 30.9 30.5</td>
</tr>
<tr>
<td>Acute leukemia</td>
<td>0.2 0.3 0.2</td>
<td>0.6 0.8 0.5</td>
<td>18.4 18.7 18.1</td>
</tr>
<tr>
<td>Aleukemic, subleukemic &amp; NOS</td>
<td>0.4 0.5 0.3</td>
<td>1.0 1.4 0.8</td>
<td>39.0 40.0 38.0</td>
</tr>
<tr>
<td>Kaposi Sarcoma:</td>
<td>0.5 1.0 0.1</td>
<td>- -</td>
<td>72.1 71.5 76.5</td>
</tr>
<tr>
<td>Mesothelioma:</td>
<td>1.0 1.9 0.4</td>
<td>- -</td>
<td>8.3 6.6 13.5</td>
</tr>
<tr>
<td>Ill-defined &amp; unspecified</td>
<td>8.9 10.3 7.8</td>
<td>12.9 16.3 10.3</td>
<td>17.2 21.3 13.2</td>
</tr>
</tbody>
</table>

Note: Incidence and death rates are per 100,000 and are age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1130).

a SEER 18 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, Alaska Native Registry, Rural Georgia, California excluding SF/SJM/LA, Kentucky, Louisiana, New Jersey and Georgia excluding ATL/REG).

b US Mortality Files, National Center for Health Statistics, Centers for Disease Control and Prevention.

c SEER 18 areas. Based on follow-up of patients into 2011.

d Ovary excludes borderline cases or histologies 8442, 8451, 8462, 8472, and 8473.

e Due to coding changes, Brain & Nervous System mortality are no longer shown separately.

f Rate not shown for mortality. Category did not exist in mortality coding until 1999.

SEER Cancer Statistics Review 1975-2011

National Cancer Institute
### Table 1.6
Age-Adjusted SEER Incidence and U.S. Death Rates and 5-Year Relative Survival (Percent) By Primary Cancer Site, Sex and Time Period

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Males</td>
<td>Females</td>
</tr>
<tr>
<td><strong>All Sites</strong></td>
<td>468.9</td>
<td>532.1</td>
<td>424.4</td>
</tr>
<tr>
<td><strong>Oral Cavity &amp; Pharynx</strong></td>
<td>11.4</td>
<td>17.0</td>
<td>6.4</td>
</tr>
<tr>
<td>Lip</td>
<td>0.8</td>
<td>1.3</td>
<td>0.4</td>
</tr>
<tr>
<td>Tongue</td>
<td>3.5</td>
<td>5.2</td>
<td>1.9</td>
</tr>
<tr>
<td>Salivary gland</td>
<td>1.3</td>
<td>1.8</td>
<td>1.0</td>
</tr>
<tr>
<td>Floor of mouth</td>
<td>0.6</td>
<td>0.9</td>
<td>0.4</td>
</tr>
<tr>
<td>Gum &amp; other oral cavity</td>
<td>1.5</td>
<td>1.8</td>
<td>1.3</td>
</tr>
<tr>
<td>Nasopharynx</td>
<td>0.4</td>
<td>0.6</td>
<td>0.3</td>
</tr>
<tr>
<td>Tonsil</td>
<td>2.0</td>
<td>3.4</td>
<td>0.7</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>0.4</td>
<td>0.6</td>
<td>0.2</td>
</tr>
<tr>
<td>Hypopharynx</td>
<td>0.6</td>
<td>1.1</td>
<td>0.3</td>
</tr>
<tr>
<td>Other oral cavity &amp; pharynx</td>
<td>0.2</td>
<td>0.4</td>
<td>0.1</td>
</tr>
<tr>
<td><strong>Digestive System</strong></td>
<td>81.7</td>
<td>99.9</td>
<td>66.6</td>
</tr>
<tr>
<td>Esophagus</td>
<td>4.6</td>
<td>8.0</td>
<td>1.7</td>
</tr>
<tr>
<td>Stomach</td>
<td>6.5</td>
<td>9.2</td>
<td>4.5</td>
</tr>
<tr>
<td>Small intestine</td>
<td>2.1</td>
<td>2.5</td>
<td>1.8</td>
</tr>
<tr>
<td>Colon &amp; Rectum</td>
<td>42.9</td>
<td>49.6</td>
<td>37.3</td>
</tr>
<tr>
<td>Colon</td>
<td>30.6</td>
<td>34.3</td>
<td>27.5</td>
</tr>
<tr>
<td>Rectum</td>
<td>12.3</td>
<td>15.4</td>
<td>9.7</td>
</tr>
<tr>
<td>Anus, anal canal &amp; anorectum</td>
<td>1.9</td>
<td>1.5</td>
<td>2.2</td>
</tr>
<tr>
<td><strong>Respiratory System</strong></td>
<td>66.0</td>
<td>79.6</td>
<td>55.7</td>
</tr>
<tr>
<td>Nose, nasal cavity &amp; middle ear</td>
<td>0.7</td>
<td>0.9</td>
<td>0.5</td>
</tr>
<tr>
<td>Larynx</td>
<td>3.4</td>
<td>5.9</td>
<td>1.3</td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
<td>61.7</td>
<td>72.4</td>
<td>53.8</td>
</tr>
<tr>
<td>Pleura</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td><strong>Other digestive system</strong></td>
<td>0.5</td>
<td>0.6</td>
<td>0.5</td>
</tr>
<tr>
<td><strong>Bones &amp; joints</strong></td>
<td>1.0</td>
<td>1.2</td>
<td>0.8</td>
</tr>
<tr>
<td><strong>Skin (excl. basal &amp; squamous)</strong></td>
<td>27.2</td>
<td>35.3</td>
<td>21.4</td>
</tr>
<tr>
<td>Melanoma of the skin</td>
<td>25.2</td>
<td>32.3</td>
<td>20.0</td>
</tr>
<tr>
<td>Other non-epithelial skin</td>
<td>2.1</td>
<td>2.9</td>
<td>1.4</td>
</tr>
<tr>
<td><strong>Breast</strong></td>
<td>68.3</td>
<td>1.2</td>
<td>128.0</td>
</tr>
<tr>
<td><strong>Breast (in situ)</strong></td>
<td>16.8</td>
<td>0.1</td>
<td>32.1</td>
</tr>
</tbody>
</table>

**Note:** Incidence and death rates are per 100,000 and are age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1130).

- **SEER 18 areas** (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, Alaska Native Registry, Rural Georgia, California excluding SF/SJM/LA, Kentucky, Louisiana, New Jersey and Georgia excluding ATL/UG).
- **US Mortality Files,** National Center for Health Statistics, Centers for Disease Control and Prevention.
- SEER 18 areas. Based on follow-up of patients into 2011.
- Mesotheliomas of the Pleura are included in the separate group Mesothelioma for incidence but are included in the Pleura grouping for mortality.
- Statistic could not be calculated due to less than 16 cases in the time interval.
### Incidence & Mortality Rates and 5-Year Relative Survival (Percent)

#### By Primary Cancer Site, Sex, and Time Period

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Males</td>
<td>Females</td>
</tr>
<tr>
<td>Female Genital System:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cervix uteri</td>
<td>26.7</td>
<td>50.5</td>
<td>8.4</td>
</tr>
<tr>
<td>Corpus uteri</td>
<td>13.1</td>
<td>24.8</td>
<td>1.0</td>
</tr>
<tr>
<td>Uterus, NOS</td>
<td>0.3</td>
<td>0.6</td>
<td>1.2</td>
</tr>
<tr>
<td>Ovary(^d)</td>
<td>6.9</td>
<td>13.0</td>
<td>4.5</td>
</tr>
<tr>
<td>Vagina</td>
<td>0.4</td>
<td>0.7</td>
<td>0.1</td>
</tr>
<tr>
<td>Vulva</td>
<td>1.4</td>
<td>2.6</td>
<td>0.3</td>
</tr>
<tr>
<td>Other female genital system</td>
<td>0.5</td>
<td>1.0</td>
<td>0.1</td>
</tr>
<tr>
<td>Male Genital System:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prostate</td>
<td>68.1</td>
<td>147.7</td>
<td>8.4</td>
</tr>
<tr>
<td>Testis</td>
<td>64.2</td>
<td>139.9</td>
<td>8.1</td>
</tr>
<tr>
<td>Penis</td>
<td>3.4</td>
<td>6.6</td>
<td>0.1</td>
</tr>
<tr>
<td>Other male genital system</td>
<td>0.4</td>
<td>0.9</td>
<td>0.1</td>
</tr>
<tr>
<td>Urinary System:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>39.2</td>
<td>62.5</td>
<td>21.0</td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>22.4</td>
<td>39.4</td>
<td>9.5</td>
</tr>
<tr>
<td>Ureter</td>
<td>0.6</td>
<td>0.9</td>
<td>0.4</td>
</tr>
<tr>
<td>Other urinary system</td>
<td>0.3</td>
<td>0.5</td>
<td>0.2</td>
</tr>
<tr>
<td>Eye &amp; Orbit</td>
<td>0.9</td>
<td>1.1</td>
<td>0.8</td>
</tr>
<tr>
<td>Brain &amp; Nervous System:*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brain</td>
<td>7.1</td>
<td>8.4</td>
<td>6.0</td>
</tr>
<tr>
<td>Cranial nerves &amp; other nervous system</td>
<td>6.7</td>
<td>8.0</td>
<td>5.5</td>
</tr>
<tr>
<td>Endocrine System:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thyroid</td>
<td>14.4</td>
<td>7.7</td>
<td>21.1</td>
</tr>
<tr>
<td>Other endocrine &amp; thymus</td>
<td>13.7</td>
<td>6.9</td>
<td>20.4</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>23.6</td>
<td>28.2</td>
<td>19.8</td>
</tr>
<tr>
<td>Hodgkin lymphoma</td>
<td>2.9</td>
<td>3.3</td>
<td>2.6</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>20.6</td>
<td>24.9</td>
<td>17.2</td>
</tr>
<tr>
<td>Myeloma</td>
<td>5.6</td>
<td>7.2</td>
<td>4.3</td>
</tr>
<tr>
<td>Leukemia</td>
<td>13.7</td>
<td>17.5</td>
<td>10.7</td>
</tr>
<tr>
<td>Lymphocytic:</td>
<td>7.0</td>
<td>9.2</td>
<td>5.3</td>
</tr>
<tr>
<td>Acute lymphocytic</td>
<td>1.5</td>
<td>2.1</td>
<td>1.7</td>
</tr>
<tr>
<td>Chronic lymphocytic</td>
<td>4.7</td>
<td>6.4</td>
<td>3.4</td>
</tr>
<tr>
<td>Other lymphocytic</td>
<td>0.4</td>
<td>0.7</td>
<td>0.2</td>
</tr>
<tr>
<td>Myeloid &amp; Monocytic:</td>
<td>6.1</td>
<td>7.6</td>
<td>4.9</td>
</tr>
<tr>
<td>Acute myeloid</td>
<td>3.9</td>
<td>4.8</td>
<td>3.3</td>
</tr>
<tr>
<td>Chronic myeloid</td>
<td>1.7</td>
<td>2.2</td>
<td>1.2</td>
</tr>
<tr>
<td>Other myeloid &amp; monocytic</td>
<td>0.3</td>
<td>0.4</td>
<td>0.2</td>
</tr>
<tr>
<td>Other leukemia:</td>
<td>0.4</td>
<td>0.5</td>
<td>0.3</td>
</tr>
<tr>
<td>Kaposi Sarcoma(^f)</td>
<td>0.5</td>
<td>0.9</td>
<td>0.1</td>
</tr>
<tr>
<td>Mesothelioma(^f)</td>
<td>1.1</td>
<td>2.1</td>
<td>0.5</td>
</tr>
<tr>
<td>Ill-defined &amp; unspecified</td>
<td>9.0</td>
<td>10.5</td>
<td>7.9</td>
</tr>
</tbody>
</table>

**Note:** Incidence and death rates are per 100,000 and are age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1130).

\(^a\) SEER 18 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, Alaska Native Registry, Rural Georgia, California excluding SF/BMN/LA, Kentucky, Louisiana, New Jersey and Georgia excluding ATL/RO).

\(^b\) US Mortality Files, National Center for Health Statistics, Centers for Disease Control and Prevention.

\(^c\) SEER 18 areas. Based on follow-up of patients into 2011.

\(^d\) Ovary excludes borderline cases or histologies 8442, 8451, 8462, 8472, and 8473.

\(^e\) Due to coding changes, Brain & Nervous System mortality are no longer shown separately.

\(^f\) Rate not shown for mortality. Category did not exist in mortality coding until 1999.

Statistic could not be calculated due to less than 16 cases in the time interval.
<table>
<thead>
<tr>
<th>Site</th>
<th>Total Males</th>
<th>Females</th>
<th>Total U.S. Mortality</th>
<th>Survival (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Cavity &amp; Pharynx:</td>
<td>480.8</td>
<td>600.9</td>
<td>206.4</td>
<td>269.3</td>
</tr>
<tr>
<td>Oral cavity &amp; pharynx:</td>
<td>9.4</td>
<td>10.1</td>
<td>5.3</td>
<td>6.1</td>
</tr>
<tr>
<td>Lip</td>
<td>0.1</td>
<td>0.1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Tongue</td>
<td>2.2</td>
<td>3.6</td>
<td>1.1</td>
<td>0.9</td>
</tr>
<tr>
<td>Salivary gland</td>
<td>1.0</td>
<td>1.1</td>
<td>0.2</td>
<td>0.3</td>
</tr>
<tr>
<td>Gum &amp; other oral cavity</td>
<td>1.4</td>
<td>1.7</td>
<td>1.2</td>
<td>0.9</td>
</tr>
<tr>
<td>Nasopharynx</td>
<td>0.7</td>
<td>1.1</td>
<td>0.3</td>
<td>0.4</td>
</tr>
<tr>
<td>Tonsil</td>
<td>1.6</td>
<td>2.9</td>
<td>0.6</td>
<td>0.5</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>0.6</td>
<td>1.1</td>
<td>0.3</td>
<td>0.6</td>
</tr>
<tr>
<td>Hypopharynx</td>
<td>1.0</td>
<td>1.9</td>
<td>0.3</td>
<td>0.3</td>
</tr>
<tr>
<td>Other oral cavity &amp; pharynx</td>
<td>0.3</td>
<td>0.4</td>
<td>0.2</td>
<td>0.3</td>
</tr>
<tr>
<td>Digestive System:</td>
<td>1418.7</td>
<td>1561.8</td>
<td>1294.8</td>
<td>869.4</td>
</tr>
<tr>
<td>Esophagus</td>
<td>4.9</td>
<td>7.9</td>
<td>2.6</td>
<td>4.2</td>
</tr>
<tr>
<td>Stomach</td>
<td>11.2</td>
<td>15.3</td>
<td>8.5</td>
<td>6.5</td>
</tr>
<tr>
<td>Small intestine</td>
<td>3.5</td>
<td>4.2</td>
<td>3.0</td>
<td>0.6</td>
</tr>
<tr>
<td>Colon &amp; Rectum</td>
<td>53.6</td>
<td>62.3</td>
<td>47.5</td>
<td>21.1</td>
</tr>
<tr>
<td>Colon</td>
<td>40.1</td>
<td>45.4</td>
<td>36.4</td>
<td>-</td>
</tr>
<tr>
<td>Rectum</td>
<td>13.5</td>
<td>16.9</td>
<td>11.1</td>
<td>-</td>
</tr>
<tr>
<td>Anal, anorectum &amp; anorectum</td>
<td>1.8</td>
<td>2.0</td>
<td>1.6</td>
<td>0.2</td>
</tr>
<tr>
<td>Liver, intrahepatic bile duct</td>
<td>9.4</td>
<td>15.6</td>
<td>4.6</td>
<td>7.6</td>
</tr>
<tr>
<td>Gallbladder</td>
<td>1.5</td>
<td>1.2</td>
<td>1.8</td>
<td>0.9</td>
</tr>
<tr>
<td>Pancreas</td>
<td>15.6</td>
<td>17.2</td>
<td>14.2</td>
<td>13.6</td>
</tr>
<tr>
<td>Retroperitoneum</td>
<td>0.4</td>
<td>0.3</td>
<td>0.4</td>
<td>0.0</td>
</tr>
<tr>
<td>Mesentery</td>
<td>0.4</td>
<td>0.1</td>
<td>0.5</td>
<td>0.2</td>
</tr>
<tr>
<td>Respiratory System:</td>
<td>276.6</td>
<td>340.6</td>
<td>213.2</td>
<td>147.3</td>
</tr>
<tr>
<td>Nose, nasal cavity &amp; middle ear</td>
<td>0.6</td>
<td>0.9</td>
<td>0.4</td>
<td>0.2</td>
</tr>
<tr>
<td>Larynx</td>
<td>4.8</td>
<td>9.0</td>
<td>1.7</td>
<td>1.9</td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
<td>68.0</td>
<td>93.0</td>
<td>51.2</td>
<td>52.0</td>
</tr>
<tr>
<td>Peritoneum, omentum &amp; mesentery</td>
<td>0.2</td>
<td>0.3</td>
<td>0.1</td>
<td>0.1</td>
</tr>
<tr>
<td>Bones &amp; joints</td>
<td>0.8</td>
<td>0.9</td>
<td>0.7</td>
<td>0.4</td>
</tr>
<tr>
<td>Soft tissue (including heart)</td>
<td>3.3</td>
<td>3.4</td>
<td>3.2</td>
<td>1.4</td>
</tr>
<tr>
<td>Skin (excl. basal &amp; squamous):</td>
<td>2.1</td>
<td>2.2</td>
<td>2.0</td>
<td>0.9</td>
</tr>
<tr>
<td>Melanoma of the skin</td>
<td>1.1</td>
<td>1.1</td>
<td>1.0</td>
<td>0.9</td>
</tr>
<tr>
<td>Other non-epithelial skin</td>
<td>1.1</td>
<td>2.2</td>
<td>1.1</td>
<td>0.9</td>
</tr>
<tr>
<td>Breast</td>
<td>70.0</td>
<td>122.8</td>
<td>18.0</td>
<td>30.6</td>
</tr>
<tr>
<td>Breast (in situ)</td>
<td>16.8</td>
<td>29.9</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Note: Incidence and death rates are per 100,000 and are age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1130).

a SEER 18 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, Alaska Native Registry, Rural Georgia, California excluding SF/SM/LA, Kentucky, Louisiana, New Jersey and Georgia excluding ATL/RG).
b US Mortality Files, National Center for Health Statistics, Centers for Disease Control and Prevention.
c SEER 18 areas. Based on follow-up of patients into 2011.
d Mesotheliomas of the Pleura are included in the separate group Mesothelioma for incidence but are included in the Pleura grouping for mortality.
- Statistic could not be calculated due to less than 16 cases in the time interval.
Table 1.7 - continued
Age-Adjusted SEER Incidence and U.S. Death Rates and 5-Year Relative Survival (Percent)
By Primary Cancer Site, Sex and Time Period

<table>
<thead>
<tr>
<th>Site</th>
<th>Incidencea US Mortalityb Survivalc (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female Genital System:</td>
<td></td>
</tr>
<tr>
<td>Cervix uteri</td>
<td>26.0 - 45.9 11.3 - 19.1 55.0 - 55.0</td>
</tr>
<tr>
<td>Corpus uteri</td>
<td>5.2 - 9.4 2.3 - 4.1 58.8 - 58.8</td>
</tr>
<tr>
<td>Uterus, NOS</td>
<td>12.5 - 21.9 1.8 - 3.0 63.5 - 63.5</td>
</tr>
<tr>
<td>Ovaryd</td>
<td>0.8 - 1.3 2.7 - 4.5 22.1 - 22.1</td>
</tr>
<tr>
<td>Vagina</td>
<td>5.6 - 9.8 3.9 - 6.6 35.3 - 35.3</td>
</tr>
<tr>
<td>Vulva</td>
<td>0.5 - 0.9 0.2 - 0.3 45.8 - 45.8</td>
</tr>
<tr>
<td>Other female genital system</td>
<td>1.0 - 1.7 0.2 - 0.3 70.9 - 70.9</td>
</tr>
<tr>
<td>Male Genital System:</td>
<td></td>
</tr>
<tr>
<td>Prostate</td>
<td>95.9 226.4 - 17.5 49.4 - 96.6 - 96.6</td>
</tr>
<tr>
<td>Testis</td>
<td>94.8 223.9 - 17.4 48.9 - 96.7 - 96.7</td>
</tr>
<tr>
<td>Penis</td>
<td>0.7 1.4 - 0.1 - 0.1 - 90.9 - 90.9</td>
</tr>
<tr>
<td>Other male genital system</td>
<td>0.4 0.9 - 0.1 - 0.1 61.1 - 61.1</td>
</tr>
<tr>
<td>Urinary System:</td>
<td></td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>31.1 47.0 20.2 7.7 11.2 5.4 67.5 69.3 64.5</td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>12.6 21.3 6.9 3.6 5.4 2.6 63.8 68.6 54.7</td>
</tr>
<tr>
<td>Ureter</td>
<td>0.3 0.4 - 0.1 0.1 - 0.1 41.0 34.8 45.2</td>
</tr>
<tr>
<td>Other urinary system</td>
<td>0.4 0.6 - 0.3 0.1 - 0.1 37.6 48.5 29.2</td>
</tr>
<tr>
<td>Eye &amp; Orbit</td>
<td>0.2 0.3 - 0.2 0.0 - 0.0 81.9 79.8 84.8</td>
</tr>
<tr>
<td>Brain &amp; Nervous System:e</td>
<td></td>
</tr>
<tr>
<td>Brain</td>
<td>4.1 4.7 3.6 2.5 3.0 2.1 40.4 37.8 43.0</td>
</tr>
<tr>
<td>Cranial nerves &amp; other nervous system</td>
<td>3.7 4.4 3.3 - - - 36.8 34.9 38.7</td>
</tr>
<tr>
<td>Endocrine System:</td>
<td></td>
</tr>
<tr>
<td>Thyroid</td>
<td>8.5 4.3 12.1 0.9 0.8 0.9 92.8 83.1 95.4</td>
</tr>
<tr>
<td>Other endocrine &amp; thymus</td>
<td>7.6 3.3 11.3 0.5 0.4 0.6 96.7 91.4 97.6</td>
</tr>
<tr>
<td>Lymphoma:</td>
<td>1.7 20.5 14.2 4.8 6.2 3.8 66.0 62.5 70.1</td>
</tr>
<tr>
<td>Hodgkin lymphoma</td>
<td>2.7 3.1 2.3 0.3 0.4 0.3 81.6 79.2 84.4</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>14.3 17.4 11.9 4.5 5.8 3.5 62.2 58.4 66.6</td>
</tr>
<tr>
<td>Myeloma</td>
<td>12.2 14.8 10.5 6.3 7.7 5.3 44.9 44.1 45.8</td>
</tr>
<tr>
<td>Leukemia:</td>
<td></td>
</tr>
<tr>
<td>Lymphocytic:</td>
<td>10.0 12.9 8.0 6.0 8.0 4.8 50.7 51.8 49.3</td>
</tr>
<tr>
<td>Acute lymphocytic</td>
<td>4.2 5.8 3.0 1.7 2.4 1.2 66.1 65.8 66.3</td>
</tr>
<tr>
<td>Chronic lymphocytic</td>
<td>1.0 1.2 0.8 0.3 0.4 0.2 64.1 66.1 61.0</td>
</tr>
<tr>
<td>Other lymphocytic</td>
<td>3.0 4.2 2.1 1.3 1.9 0.9 68.2 66.3 70.7</td>
</tr>
<tr>
<td>Myeloid &amp; Monocytic</td>
<td>0.2 0.4 0.1 0.1 0.1 - 0.1 51.4 57.7 32.8</td>
</tr>
<tr>
<td>Acute myeloid</td>
<td>5.1 6.3 4.5 2.7 3.4 2.2 39.8 39.7 39.8</td>
</tr>
<tr>
<td>Chronic myeloid</td>
<td>3.3 3.8 2.9 2.2 2.7 1.8 26.3 25.9 26.4</td>
</tr>
<tr>
<td>Acute leukemia</td>
<td>1.6 1.9 1.3 0.3 0.5 0.3 64.6 62.8 68.6</td>
</tr>
<tr>
<td>Other leukemia</td>
<td>0.1 0.2 0.1 0.0 - - 24.1 13.6 34.7</td>
</tr>
<tr>
<td>Other myeloid &amp; monocytic</td>
<td>0.1 0.2 0.1 0.2 0.2 0.1 38.3 38.1 39.0</td>
</tr>
<tr>
<td>Other leukaemia</td>
<td>0.7 1.0 0.6 1.7 2.2 1.4 29.6 32.1 26.4</td>
</tr>
<tr>
<td>Acute aleukemic leukemia</td>
<td>0.2 0.3 0.2 0.5 0.7 0.4 26.8 28.1 24.2</td>
</tr>
<tr>
<td>Malignant histiocytosis</td>
<td>0.5 0.6 0.4 1.2 1.5 1.0 30.8 35.0 26.8</td>
</tr>
<tr>
<td>Kaposi Sarcoma f</td>
<td>1.1 2.1 0.2 - - - 53.8 53.4 56.5</td>
</tr>
<tr>
<td>Mesothelioma f</td>
<td>0.5 1.0 0.2 - - - 10.2 8.2 15.0</td>
</tr>
<tr>
<td>Ill-defined &amp; unspecified</td>
<td>10.1 11.4 9.1 14.7 19.2 11.7 12.7 12.9 12.5</td>
</tr>
</tbody>
</table>

Note: Incidence and death rates are per 100,000 and are age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1130).

SEER 18 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, Alaska Native Registry, Rural Georgia, California excluding SF/Bay/LA, Kentucky, Louisiana, New Jersey and Georgia excluding ATL/UGA).

US Mortality Files, National Center for Health Statistics, Centers for Disease Control and Prevention.

SEER 18 areas. Based on follow-up of patients into 2011.

Du to coding changes, Brain & Nervous System mortality are no longer shown separately.

Rate not shown for mortality. Category did not exist in mortality coding until 1999.

Statistic could not be calculated due to less than 16 cases in the time interval.
**Table 1.8**  
SEER Incidence and U.S. Mortality Trends by Primary Cancer Site and Sex  
All Races, 2002-2011

<table>
<thead>
<tr>
<th>Site</th>
<th>Incidencea</th>
<th>US Mortalityb</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total   APC</td>
<td>Male APC</td>
</tr>
<tr>
<td>All Sites</td>
<td>-0.6*</td>
<td>-1.2*</td>
</tr>
<tr>
<td>Oral Cavity &amp; Pharynx:</td>
<td>0.4*</td>
<td>0.4*</td>
</tr>
<tr>
<td>Lip</td>
<td>-3.5*</td>
<td>-4.1*</td>
</tr>
<tr>
<td>Tongue</td>
<td>1.8*</td>
<td>2.2*</td>
</tr>
<tr>
<td>Salivary gland</td>
<td>0.5</td>
<td>0.4</td>
</tr>
<tr>
<td>Floor of mouth</td>
<td>-3.2*</td>
<td>-3.5*</td>
</tr>
<tr>
<td>Gum &amp; other oral cavity</td>
<td>-0.5</td>
<td>-0.8</td>
</tr>
<tr>
<td>Nasopharynx</td>
<td>-0.9</td>
<td>-0.8</td>
</tr>
<tr>
<td>Tonsil</td>
<td>2.9*</td>
<td>3.1*</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>2.6*</td>
<td>3.0*</td>
</tr>
<tr>
<td>Hypopharynx</td>
<td>-2.5*</td>
<td>-2.7*</td>
</tr>
<tr>
<td>Other oral cavity &amp; pharynx</td>
<td>-0.8</td>
<td>-0.5</td>
</tr>
<tr>
<td>Digestive System:</td>
<td>-1.2*</td>
<td>-1.2*</td>
</tr>
<tr>
<td>Esophagus</td>
<td>-0.9*</td>
<td>-0.7</td>
</tr>
<tr>
<td>Stomach</td>
<td>-1.3*</td>
<td>-1.6*</td>
</tr>
<tr>
<td>Small intestine</td>
<td>1.8*</td>
<td>1.4*</td>
</tr>
<tr>
<td>Colon &amp; Rectum:</td>
<td>-2.8*</td>
<td>-3.0*</td>
</tr>
<tr>
<td>Colon</td>
<td>-3.1*</td>
<td>-3.4*</td>
</tr>
<tr>
<td>Rectum</td>
<td>-2.9*</td>
<td>-2.2*</td>
</tr>
<tr>
<td>Anus, anal canal &amp; anorectum</td>
<td>1.9*</td>
<td>1.3</td>
</tr>
<tr>
<td>Liver &amp; intrahepatic bile duct</td>
<td>3.4*</td>
<td>3.7*</td>
</tr>
<tr>
<td>Gallbladder</td>
<td>-0.2</td>
<td>-0.4</td>
</tr>
<tr>
<td>Other biliary</td>
<td>1.0*</td>
<td>1.5*</td>
</tr>
<tr>
<td>Pancreas</td>
<td>0.7*</td>
<td>0.9*</td>
</tr>
<tr>
<td>Retroperitoneum</td>
<td>-1.0</td>
<td>-0.6</td>
</tr>
<tr>
<td>Peritoneum, omentum &amp; mesentery</td>
<td>-1.2</td>
<td>0.1</td>
</tr>
<tr>
<td>Other digestive system</td>
<td>1.8*</td>
<td>2.5*</td>
</tr>
<tr>
<td>Respiratory System:</td>
<td>-1.7*</td>
<td>-2.3*</td>
</tr>
<tr>
<td>Nose, nasal cavity &amp; middle ear</td>
<td>-0.4</td>
<td>-0.4</td>
</tr>
<tr>
<td>Larynx</td>
<td>-1.9*</td>
<td>-2.1*</td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
<td>-1.7*</td>
<td>-2.4*</td>
</tr>
<tr>
<td>Pleura</td>
<td>-3.1</td>
<td>-2.1</td>
</tr>
<tr>
<td>Trachea &amp; other respiratory organs</td>
<td>-1.1</td>
<td>-0.6</td>
</tr>
<tr>
<td>Bones &amp; joints</td>
<td>-0.1</td>
<td>-0.1</td>
</tr>
<tr>
<td>Soft tissue (including heart)</td>
<td>0.8*</td>
<td>0.8*</td>
</tr>
<tr>
<td>Skin (excl. basal &amp; squamous):</td>
<td>1.3*</td>
<td>1.7*</td>
</tr>
<tr>
<td>Melanoma of the skin</td>
<td>1.4*</td>
<td>1.6*</td>
</tr>
<tr>
<td>Other non-epithelial skin</td>
<td>1.2</td>
<td>1.9*</td>
</tr>
<tr>
<td>Breast</td>
<td>-0.3</td>
<td>1.8*</td>
</tr>
<tr>
<td>Breast (in situ)</td>
<td>0.9*</td>
<td>2.6</td>
</tr>
</tbody>
</table>

The APC is the Annual Percent Change over the time interval.  
Trends are based on rates age-adjusted to the 2000 US Std Population  
(19 age groups - Census P25-130).  
SEER 18 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, Alaska Native Registry, Rural Georgia, California excluding SF/SJM/LA, Kentucky, Louisiana, New Jersey and Georgia excluding ATL/RG).  
US Mortality Files, National Center for Health Statistics, Centers for Disease Control and Prevention.  
* The APC is significantly different from zero (p<.05).  
- Statistic could not be calculated. Trend based on less than 10 cases for at least one year within the time interval.
**Table 1.8 - continued**
SEER Incidence and U.S. Mortality Trends by Primary Cancer Site and Sex
All Races, 2002-2011

<table>
<thead>
<tr>
<th>Site</th>
<th>Incidence</th>
<th>Total</th>
<th>Males</th>
<th>Females</th>
<th>US Mortality</th>
<th>Total</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female Genital System:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cervix uteri</td>
<td>-1.7*</td>
<td>-1.6*</td>
<td>-1.3*</td>
<td>-1.1*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corpus uteri</td>
<td>1.0*</td>
<td>1.2*</td>
<td>0.7*</td>
<td>-0.4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uterus, NOS</td>
<td>2.8*</td>
<td>3.3*</td>
<td>1.4*</td>
<td>1.8*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ovary</td>
<td>-1.9*</td>
<td>-1.7*</td>
<td>-2.2*</td>
<td>-2.0*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vagina</td>
<td>0.2</td>
<td>0.5</td>
<td>-1.0*</td>
<td>-0.7</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vulva</td>
<td>0.8*</td>
<td>1.1*</td>
<td>0.8*</td>
<td>1.4*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other female genital system</td>
<td>5.6*</td>
<td>5.6*</td>
<td>1.7</td>
<td>1.9</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male Genital System:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prostate</td>
<td>-1.9*</td>
<td>-2.2*</td>
<td>-2.6*</td>
<td>-3.3*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Testis</td>
<td>0.6*</td>
<td>0.6*</td>
<td>-0.5</td>
<td>-0.6</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Penis</td>
<td>0.8</td>
<td>0.4</td>
<td>-0.9</td>
<td>-1.1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other male genital system</td>
<td>0.7</td>
<td>0.6</td>
<td>3.2</td>
<td>2.7</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary System:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>-0.8*</td>
<td>-0.8*</td>
<td>-1.2*</td>
<td>0.1</td>
<td>0.1</td>
<td>0.6*</td>
<td>0.6*</td>
<td>0.6*</td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>1.9*</td>
<td>1.8*</td>
<td>1.8*</td>
<td>-0.9*</td>
<td>-0.8*</td>
<td>1.2*</td>
<td>1.2*</td>
<td>1.2*</td>
</tr>
<tr>
<td>Ureter</td>
<td>0.2</td>
<td>0.3</td>
<td>0.5</td>
<td>0.4</td>
<td>0.4</td>
<td>0.9*</td>
<td>0.9*</td>
<td>0.9*</td>
</tr>
<tr>
<td>Other urinary system</td>
<td>2.2*</td>
<td>2.0</td>
<td>1.5</td>
<td>2.6</td>
<td>0.4</td>
<td>0.4*</td>
<td>0.4*</td>
<td>0.4*</td>
</tr>
<tr>
<td>Eye &amp; Orbit</td>
<td>-0.9*</td>
<td>-1.3*</td>
<td>-0.5</td>
<td>0.8</td>
<td>0.1</td>
<td>1.2*</td>
<td>1.2*</td>
<td>1.2*</td>
</tr>
<tr>
<td><strong>Brain &amp; Nervous System:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brain</td>
<td>-0.6*</td>
<td>-0.5*</td>
<td>0.7*</td>
<td>-0.4</td>
<td>-0.4</td>
<td>-0.5*</td>
<td>-0.5*</td>
<td>-0.5*</td>
</tr>
<tr>
<td>Cranial nerves &amp; other nervous system</td>
<td>-0.5</td>
<td>0.5</td>
<td>0.4</td>
<td>0.6</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Endocrine System:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thyroid</td>
<td>5.8*</td>
<td>5.3*</td>
<td>6.0*</td>
<td>1.3*</td>
<td>1.8*</td>
<td>0.9*</td>
<td>0.9*</td>
<td>0.9*</td>
</tr>
<tr>
<td>Other endocrine &amp; thymus</td>
<td>0.9</td>
<td>0.2</td>
<td>0.9</td>
<td>0.2</td>
<td>0.9</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td><strong>Lymphoma:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hodgkin lymphoma</td>
<td>-0.4</td>
<td>-0.3</td>
<td>-0.9</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5*</td>
<td>1.5*</td>
<td>1.5*</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>-0.1</td>
<td>0.0</td>
<td>0.3</td>
<td>-2.6*</td>
<td>-2.3*</td>
<td>-3.0*</td>
<td>-3.0*</td>
<td>-3.0*</td>
</tr>
<tr>
<td><strong>Myeloma:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leukemia:</td>
<td>0.7*</td>
<td>0.7*</td>
<td>0.6</td>
<td>1.5*</td>
<td>-1.3*</td>
<td>1.9*</td>
<td>1.9*</td>
<td>1.9*</td>
</tr>
<tr>
<td>Acute lymphocytic</td>
<td>-0.4</td>
<td>0.7*</td>
<td>-0.1</td>
<td>-0.9</td>
<td>-1.0*</td>
<td>-1.0*</td>
<td>-1.0*</td>
<td>-1.0*</td>
</tr>
<tr>
<td>Chronic lymphocytic</td>
<td>1.1*</td>
<td>0.6</td>
<td>1.8*</td>
<td>-1.2*</td>
<td>-1.7*</td>
<td>-0.5</td>
<td>-0.5</td>
<td>-0.5</td>
</tr>
<tr>
<td><strong>Myeloid &amp; Monocytic:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute myeloid</td>
<td>-0.3*</td>
<td>-1.1*</td>
<td>0.8*</td>
<td>-0.8</td>
<td>-1.6*</td>
<td>-1.6*</td>
<td>-1.6*</td>
<td>-1.6*</td>
</tr>
<tr>
<td>Chronic myeloid</td>
<td>1.2*</td>
<td>1.2*</td>
<td>3.1</td>
<td>-1.0</td>
<td>1.5*</td>
<td>-1.1</td>
<td>-1.1</td>
<td>-1.1</td>
</tr>
<tr>
<td>Acute monocytic</td>
<td>0.9*</td>
<td>0.8*</td>
<td>0.9*</td>
<td>-0.2</td>
<td>-0.3</td>
<td>-0.4</td>
<td>-0.4</td>
<td>-0.4</td>
</tr>
<tr>
<td>Other myeloid</td>
<td>1.3*</td>
<td>0.9</td>
<td>1.7*</td>
<td>0.3</td>
<td>0.3</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
</tr>
<tr>
<td><strong>Other leukemia:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other acute leukemia</td>
<td>-3.1*</td>
<td>-4.1*</td>
<td>-4.1*</td>
<td>-3.8*</td>
<td>-4.9*</td>
<td>-3.2</td>
<td>-3.2</td>
<td>-3.2</td>
</tr>
<tr>
<td>Myelodemic, subleukemic &amp; NOS</td>
<td>-3.7*</td>
<td>-4.1*</td>
<td>-3.3</td>
<td>0.1</td>
<td>0.3</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
</tr>
<tr>
<td>Kaposi Sarcoma</td>
<td>-3.1*</td>
<td>-3.3*</td>
<td>-1.7</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Mesothelioma</td>
<td>-1.0</td>
<td>-1.3</td>
<td>-0.4</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Ill-defined &amp; unspecified</td>
<td>-2.8*</td>
<td>-2.5*</td>
<td>-3.1*</td>
<td>-2.2*</td>
<td>-2.1*</td>
<td>-2.4*</td>
<td>-2.4*</td>
<td>-2.4*</td>
</tr>
</tbody>
</table>

The APC is the Annual Percent Change over the time interval. Trends are based on rates age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1130).

a  SEER 18 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, Alaska Native Registry, Rural Georgia, California excluding SP/BJM/EA, Kentucky, Louisiana, New Jersey and Georgia excluding ATL/MS).

b  US Mortality Files, National Center for Health Statistics, Centers for Disease Control and Prevention.

c  Ovary excludes borderline cases or histologies 8442, 8451, 8462, 8472, and 8473.

d  Due to coding changes, Brain & Nervous System mortality are no longer shown separately.

*  Trend not shown for mortality. Category did not exist in mortality coding until 1999.

*  The APC is significantly different from zero (p<.05).

-  Statistic could not be calculated. Trend based on less than 10 cases for at least one year within the time interval.
### Table 1.9

SEER Incidence and U.S. Mortality Trends by Primary Cancer Site and Sex (Whites, 2002-2011)

<table>
<thead>
<tr>
<th>Site</th>
<th>Incidence(^a)</th>
<th>US Mortality(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total APC</td>
<td>Males APC</td>
</tr>
<tr>
<td>All Sites</td>
<td>-0.6*</td>
<td>-1.2*</td>
</tr>
<tr>
<td>Oral Cavity &amp; Pharynx</td>
<td>0.8*</td>
<td>0.8*</td>
</tr>
<tr>
<td>Lip</td>
<td>-3.7*</td>
<td>-4.3*</td>
</tr>
<tr>
<td>Tongue</td>
<td>2.1*</td>
<td>2.4*</td>
</tr>
<tr>
<td>Salivary gland</td>
<td>0.9</td>
<td>0.7</td>
</tr>
<tr>
<td>Floor of mouth</td>
<td>-2.5*</td>
<td>-3.0*</td>
</tr>
<tr>
<td>Gum &amp; other oral cavity</td>
<td>-0.4</td>
<td>-0.7</td>
</tr>
<tr>
<td>Nasopharynx</td>
<td>-0.5</td>
<td>-0.8</td>
</tr>
<tr>
<td>Tonsil</td>
<td>3.8*</td>
<td>4.0*</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>3.1*</td>
<td>3.4*</td>
</tr>
<tr>
<td>Hypopharynx</td>
<td>-2.1*</td>
<td>-2.4*</td>
</tr>
<tr>
<td>Other oral cavity &amp; pharynx</td>
<td>-0.5</td>
<td>0.3</td>
</tr>
<tr>
<td>Digestive System:</td>
<td>-1.2*</td>
<td>-1.2*</td>
</tr>
<tr>
<td>Esophagus</td>
<td>-0.3</td>
<td>-0.1</td>
</tr>
<tr>
<td>Stomach</td>
<td>-1.0*</td>
<td>-1.2*</td>
</tr>
<tr>
<td>Small intestine</td>
<td>1.5*</td>
<td>1.6*</td>
</tr>
<tr>
<td>Colon &amp; Rectum:</td>
<td>-2.9*</td>
<td>-3.2*</td>
</tr>
<tr>
<td>Colon</td>
<td>-3.2*</td>
<td>-3.5*</td>
</tr>
<tr>
<td>Rectum</td>
<td>-2.8*</td>
<td>-2.6*</td>
</tr>
<tr>
<td>Anus, anal canal &amp; anorectum</td>
<td>2.0*</td>
<td>1.0</td>
</tr>
<tr>
<td>Liver &amp; intrahepatic bile duct</td>
<td>4.1*</td>
<td>4.3*</td>
</tr>
<tr>
<td>Gallbladder</td>
<td>-0.1</td>
<td>-0.3</td>
</tr>
<tr>
<td>Other biliary</td>
<td>0.9*</td>
<td>1.4*</td>
</tr>
<tr>
<td>Pancreas</td>
<td>0.9*</td>
<td>1.0*</td>
</tr>
<tr>
<td>Retropertitoneum</td>
<td>-1.4</td>
<td>-1.6</td>
</tr>
<tr>
<td>Peritoneum, omentum &amp; mesentery</td>
<td>-1.1</td>
<td>0.7</td>
</tr>
<tr>
<td>Other digestive system</td>
<td>1.4*</td>
<td>1.7*</td>
</tr>
<tr>
<td>Respiratory System:</td>
<td>-1.6*</td>
<td>-2.2*</td>
</tr>
<tr>
<td>Nose, nasal cavity &amp; middle ear</td>
<td>-0.1</td>
<td>0.0</td>
</tr>
<tr>
<td>Larynx</td>
<td>-1.6*</td>
<td>-1.8*</td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
<td>-1.6*</td>
<td>-2.3*</td>
</tr>
<tr>
<td>Pleura</td>
<td>-3.4*</td>
<td>-1.8</td>
</tr>
<tr>
<td>Trachea &amp; other respiratory organs</td>
<td>-1.2</td>
<td>-1.3</td>
</tr>
<tr>
<td>Bones &amp; joints</td>
<td>0.3</td>
<td>0.4</td>
</tr>
<tr>
<td>Soft tissue (including heart)</td>
<td>0.9*</td>
<td>1.0*</td>
</tr>
<tr>
<td>Skin (excl. basal &amp; squamous):</td>
<td>1.3*</td>
<td>1.6*</td>
</tr>
<tr>
<td>Melanoma of the skin</td>
<td>1.3*</td>
<td>1.6*</td>
</tr>
<tr>
<td>Other non-epithelial skin</td>
<td>1.3*</td>
<td>1.9*</td>
</tr>
<tr>
<td>Breast</td>
<td>-0.5</td>
<td>1.8*</td>
</tr>
<tr>
<td>Breast (in situ)</td>
<td>0.6</td>
<td>2.3</td>
</tr>
</tbody>
</table>

The APC is the Annual Percent Change over the time interval. Trends are based on rates age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1130).

\(^a\) SEER 18 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, Alaska Native Registry, Rural Georgia, California excluding SF/SJ/LA, Kentucky, Louisiana, New Jersey and Georgia excluding ATL/RG).

\(^b\) US Mortality Files, National Center for Health Statistics, Centers for Disease Control and Prevention.

* The APC is significantly different from zero (p<.05).
- Statistic could not be calculated. Trend based on less than 10 cases for at least one year within the time interval.
The APC is the Annual Percent Change over the time interval. Trends are based on rates age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1130).

<table>
<thead>
<tr>
<th>Site</th>
<th>Incidencea US Mortalityb</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>APC</td>
</tr>
<tr>
<td>Female Genital System:</td>
<td></td>
</tr>
<tr>
<td>Female Genital System:</td>
<td></td>
</tr>
<tr>
<td>Cervix uteri</td>
<td>-1.3*</td>
</tr>
<tr>
<td>Corpus uteri</td>
<td>0.8*</td>
</tr>
<tr>
<td>Uterus, NOS</td>
<td>1.9*</td>
</tr>
<tr>
<td>Ovary</td>
<td>-1.8*</td>
</tr>
<tr>
<td>Vagina</td>
<td>0.7*</td>
</tr>
<tr>
<td>Vulva</td>
<td>1.2*</td>
</tr>
<tr>
<td>Other female genital system</td>
<td>6.3*</td>
</tr>
<tr>
<td>Male Genital System:</td>
<td></td>
</tr>
<tr>
<td>Male Genital System:</td>
<td></td>
</tr>
<tr>
<td>Prostate</td>
<td>-2.2*</td>
</tr>
<tr>
<td>Testis</td>
<td>0.6*</td>
</tr>
<tr>
<td>Penis</td>
<td>0.9*</td>
</tr>
<tr>
<td>Other male genital system</td>
<td>0.6</td>
</tr>
<tr>
<td>Urinary System:</td>
<td></td>
</tr>
<tr>
<td>Urinary System:</td>
<td></td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>-0.7*</td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>1.9*</td>
</tr>
<tr>
<td>Ureter</td>
<td>0.5*</td>
</tr>
<tr>
<td>Other urinary system</td>
<td>2.4*</td>
</tr>
<tr>
<td>Eye &amp; Orbit</td>
<td>-0.9*</td>
</tr>
<tr>
<td>Brain &amp; Nervous System:d</td>
<td></td>
</tr>
<tr>
<td>Brain &amp; Nervous System:d</td>
<td></td>
</tr>
<tr>
<td>Brain</td>
<td>-0.5</td>
</tr>
<tr>
<td>Cranial nerves &amp; other nervous system</td>
<td>-1.3</td>
</tr>
<tr>
<td>Endocrine System:</td>
<td></td>
</tr>
<tr>
<td>Endocrine System:</td>
<td></td>
</tr>
<tr>
<td>Thyroid</td>
<td>5.6*</td>
</tr>
<tr>
<td>Other endocrine &amp; thymus</td>
<td>5.6*</td>
</tr>
<tr>
<td>Lymphoma:</td>
<td></td>
</tr>
<tr>
<td>Lymphoma:</td>
<td></td>
</tr>
<tr>
<td>Hodgkin lymphoma</td>
<td>-0.2</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>-0.2</td>
</tr>
<tr>
<td>Myeloma</td>
<td>0.6*</td>
</tr>
<tr>
<td>Leukemia:</td>
<td></td>
</tr>
<tr>
<td>Leukemia:</td>
<td></td>
</tr>
<tr>
<td>Lymphocytic:</td>
<td></td>
</tr>
<tr>
<td>Acute lymphocytic:</td>
<td>-0.5</td>
</tr>
<tr>
<td>Chronic lymphocytic:</td>
<td>-1.1*</td>
</tr>
<tr>
<td>Myeloid &amp; Monocytic:</td>
<td>1.7*</td>
</tr>
<tr>
<td>Acute myeloid</td>
<td>1.9*</td>
</tr>
<tr>
<td>Chronic myeloid</td>
<td>1.9*</td>
</tr>
<tr>
<td>Acute monocytic</td>
<td>-2.6</td>
</tr>
<tr>
<td>Other myeloid &amp; monocytic</td>
<td>1.3</td>
</tr>
<tr>
<td>Other acute leukemia</td>
<td>-4.3</td>
</tr>
<tr>
<td>Aleukemic, subleukemic &amp; NOS</td>
<td>-3.5</td>
</tr>
<tr>
<td>Kaposi Sarcoma</td>
<td>-3.7</td>
</tr>
<tr>
<td>Mesothelioma</td>
<td>-0.9</td>
</tr>
<tr>
<td>Ill-defined &amp; unspecified</td>
<td>-2.7</td>
</tr>
</tbody>
</table>

Table 1.9 - continued
SEER Incidence and U.S. Mortality Trends by Primary Cancer Site and Sex Whites, 2002-2011

a SEER 18 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, Alaska Native Registry, Rural Georgia, California excluding SP/SJM/IA, Kentucky, Louisiana, New Jersey and Georgia excluding ATL/KG).

b US Mortality Files, National Center for Health Statistics, Centers for Disease Control and Prevention.

c Ovary excludes borderline cases or histologies 8442, 8451, 8462, 8472, and 8473.

d Due to coding changes, Brain & Nervous System mortality are no longer shown separately.

e Trend not shown for mortality. Category did not exist in mortality coding until 1999.

* The APC is significantly different from zero (p<.05).

- Statistic could not be calculated. Trend based on less than 10 cases for at least one year within the time interval.
## Table 1.10
SEER Incidence and U.S. Mortality Trends by Primary Cancer Site and Sex
Blacks, 2002-2011

<table>
<thead>
<tr>
<th>Site</th>
<th>Incidence</th>
<th>US Mortality</th>
<th>Site</th>
<th>Incidence</th>
<th>US Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Males</td>
<td>Females</td>
<td>Total</td>
<td>Males</td>
</tr>
<tr>
<td>All Sites</td>
<td>-1.0*</td>
<td>-1.9*</td>
<td>-0.2</td>
<td>-2.1*</td>
<td>-2.6*</td>
</tr>
<tr>
<td>Oral Cavity &amp; Pharynx:</td>
<td>-2.5*</td>
<td>-2.9*</td>
<td>-1.7</td>
<td>-3.4*</td>
<td>-3.7*</td>
</tr>
<tr>
<td>Lip</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Tongue</td>
<td>-1.2</td>
<td>-1.2</td>
<td>-1.2</td>
<td>-3.7*</td>
<td>-4.4*</td>
</tr>
<tr>
<td>Salivary gland</td>
<td>-0.9</td>
<td>-0.8</td>
<td>-1.1</td>
<td>1.2</td>
<td>2.3</td>
</tr>
<tr>
<td>Floor of mouth</td>
<td>-6.5*</td>
<td>-6.7*</td>
<td>-5.4*</td>
<td>-11.6*</td>
<td>-</td>
</tr>
<tr>
<td>Gum &amp; other oral cavity</td>
<td>-3.7*</td>
<td>-5.5*</td>
<td>-1.5</td>
<td>-5.4*</td>
<td>-5.8*</td>
</tr>
<tr>
<td>Nasopharynx</td>
<td>-3.1*</td>
<td>-2.9</td>
<td>-3.3</td>
<td>-3.4*</td>
<td>2.8</td>
</tr>
<tr>
<td>Tonsil</td>
<td>-1.1</td>
<td>-1.3</td>
<td>-0.3</td>
<td>1.5</td>
<td>-1.7*</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>0.2</td>
<td>-0.1</td>
<td>-</td>
<td>0.5</td>
<td>1.2</td>
</tr>
<tr>
<td>Hypopharynx</td>
<td>-5.0*</td>
<td>-5.2*</td>
<td>-4.4</td>
<td>-2.5</td>
<td>4.6</td>
</tr>
<tr>
<td>Other oral cavity &amp; pharynx</td>
<td>-3.9</td>
<td>-6.8*</td>
<td>-</td>
<td>4.8*</td>
<td>-4.5*</td>
</tr>
<tr>
<td>Digestive System:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Esophagus</td>
<td>-1.3*</td>
<td>-1.5*</td>
<td>-1.8*</td>
<td>-1.6*</td>
<td>-1.5*</td>
</tr>
<tr>
<td>Stomach</td>
<td>-2.1*</td>
<td>-3.1*</td>
<td>-1.1</td>
<td>-3.3*</td>
<td>-3.3*</td>
</tr>
<tr>
<td>Small intestine</td>
<td>2.1*</td>
<td>1.9</td>
<td>2.4</td>
<td>1.0</td>
<td>1.3</td>
</tr>
<tr>
<td>Colon &amp; Rectum:</td>
<td>-2.7*</td>
<td>-2.8*</td>
<td>-2.7*</td>
<td>-2.8*</td>
<td>-2.6*</td>
</tr>
<tr>
<td>Colon</td>
<td>-3.1*</td>
<td>-3.3*</td>
<td>-3.0*</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Rectum</td>
<td>-1.5*</td>
<td>-1.0</td>
<td>-1.8*</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Anus, anal canal &amp; anorectum</td>
<td>2.3*</td>
<td>3.3*</td>
<td>1.2</td>
<td>4.4*</td>
<td>7.0*</td>
</tr>
<tr>
<td>Liver &amp; intrahepatic bile duct</td>
<td>3.4*</td>
<td>3.6*</td>
<td>2.5</td>
<td>2.5*</td>
<td>2.7*</td>
</tr>
<tr>
<td>Other digestive system</td>
<td>2.6</td>
<td>6.0</td>
<td>0.2</td>
<td>0.8</td>
<td>0.6</td>
</tr>
<tr>
<td>Respiratory System:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nose, nasal cavity &amp; middle ear</td>
<td>-2.0*</td>
<td>-2.8*</td>
<td>-0.8</td>
<td>-2.6*</td>
<td>-3.4*</td>
</tr>
<tr>
<td>Larynx</td>
<td>-3.5*</td>
<td>-3.5*</td>
<td>-3.5</td>
<td>-3.8*</td>
<td>-3.9*</td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
<td>-1.9*</td>
<td>-2.8*</td>
<td>-0.7</td>
<td>-2.6*</td>
<td>-3.4*</td>
</tr>
<tr>
<td>Pleura</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Trachea &amp; other respiratory organs</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Bones &amp; joints</td>
<td>-1.5</td>
<td>-1.4</td>
<td>-1.0</td>
<td>-0.2</td>
<td>0.1</td>
</tr>
<tr>
<td>Soft tissue (including heart)</td>
<td>-0.4</td>
<td>-1.5</td>
<td>0.6</td>
<td>0.4</td>
<td>0.2</td>
</tr>
<tr>
<td>Skin (excl. basal &amp; squamous):</td>
<td>-1.1</td>
<td>-1.2</td>
<td>-1.0</td>
<td>-1.5*</td>
<td>-2.2</td>
</tr>
<tr>
<td>Melanoma of the skin</td>
<td>-0.9</td>
<td>-2.4</td>
<td>-0.1</td>
<td>-0.3</td>
<td>-0.9</td>
</tr>
<tr>
<td>Other non-epithelial skin</td>
<td>-1.1</td>
<td>-0.2</td>
<td>-1.8</td>
<td>-2.6*</td>
<td>-3.0*</td>
</tr>
<tr>
<td>Breast (in situ)</td>
<td>0.3</td>
<td>1.5</td>
<td>0.5</td>
<td>-1.6*</td>
<td>-0.4</td>
</tr>
<tr>
<td>Breast</td>
<td>2.2*</td>
<td>-</td>
<td>2.3*</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

The APC is the Annual Percent Change over the time interval. 
Trends are based on rates age-adjusted to the 2000 US Std Population (19 age groups - Census P25-130) 
\(a\) SEER 18 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, Alaska Native Registry, Rural Georgia, California excluding SP/SJ/LA, Kentucky, Louisiana, New Jersey and Georgia excluding ATL/RG). 
\(b\) US Mortality Files, National Center for Health Statistics, Centers for Disease Control and Prevention. 
* The APC is significantly different from zero (p<.05). 
- Statistic could not be calculated. Trend based on less than 10 cases for at least one year within the time interval.
### Table 1.10 - continued

<table>
<thead>
<tr>
<th>Site</th>
<th>Incidence</th>
<th>US Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total APC</td>
<td>Males APC</td>
</tr>
<tr>
<td>Female Genital System:</td>
<td>-0.1</td>
<td>-0.1</td>
</tr>
<tr>
<td>Cervix uteri</td>
<td>-3.4</td>
<td>-3.3</td>
</tr>
<tr>
<td>Corpus uteri</td>
<td>2.2</td>
<td>2.4</td>
</tr>
<tr>
<td>Uterus, NOS</td>
<td>3.8</td>
<td>4.1</td>
</tr>
<tr>
<td>Ovary</td>
<td>-1.6</td>
<td>-1.4</td>
</tr>
<tr>
<td>Vagina</td>
<td>-2.0</td>
<td>-1.9</td>
</tr>
<tr>
<td>Vulva</td>
<td>-0.8</td>
<td>-0.7</td>
</tr>
<tr>
<td>Other female genital system</td>
<td>1.5</td>
<td>1.2</td>
</tr>
<tr>
<td>Male Genital System:</td>
<td>-2.0</td>
<td>-2.5</td>
</tr>
<tr>
<td>Prostate</td>
<td>-2.0</td>
<td>-2.5</td>
</tr>
<tr>
<td>Testis</td>
<td>0.7</td>
<td>0.6</td>
</tr>
<tr>
<td>Penis</td>
<td>-1.1</td>
<td>-1.2</td>
</tr>
<tr>
<td>Other male genital system</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary System:</td>
<td>1.3</td>
<td>1.2</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>-0.5</td>
<td>0.1</td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>2.7</td>
<td>2.1</td>
</tr>
<tr>
<td>Ureter</td>
<td>-2.3</td>
<td></td>
</tr>
<tr>
<td>Other urinary system</td>
<td>2.1</td>
<td></td>
</tr>
<tr>
<td>Eye &amp; Orbit</td>
<td>-1.2</td>
<td></td>
</tr>
<tr>
<td>Brain &amp; Nervous System:d</td>
<td>-0.3</td>
<td>-0.5</td>
</tr>
<tr>
<td>Brain</td>
<td>0.2</td>
<td>-0.3</td>
</tr>
<tr>
<td>Cranial nerves &amp; other nervous system</td>
<td>-4.6</td>
<td>-3.8</td>
</tr>
<tr>
<td>Endocrine System:</td>
<td>5.5</td>
<td>3.8</td>
</tr>
<tr>
<td>Thyroid</td>
<td>5.9</td>
<td>4.2</td>
</tr>
<tr>
<td>Other endocrine &amp; thymus</td>
<td>2.9</td>
<td>2.4</td>
</tr>
<tr>
<td>Lymphoma:</td>
<td>-0.2</td>
<td>-0.3</td>
</tr>
<tr>
<td>Hodgkin lymphoma</td>
<td>0.8</td>
<td>1.3</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>-0.3</td>
<td>-0.5</td>
</tr>
<tr>
<td>Myeloma</td>
<td>0.4</td>
<td>0.3</td>
</tr>
<tr>
<td>Leukemia:</td>
<td>-1.0</td>
<td>-1.3</td>
</tr>
<tr>
<td>Lymphocytic:</td>
<td>-1.8</td>
<td>-2.2</td>
</tr>
<tr>
<td>Acute lymphocytic</td>
<td>1.2</td>
<td>1.0</td>
</tr>
<tr>
<td>Chronic lymphocytic</td>
<td>-2.7</td>
<td>-3.2</td>
</tr>
<tr>
<td>Other lymphocytic</td>
<td>-2.9</td>
<td></td>
</tr>
<tr>
<td>Myeloid &amp; Monocytic</td>
<td>0.4</td>
<td>0.1</td>
</tr>
<tr>
<td>Acute myeloid</td>
<td>1.0</td>
<td>0.8</td>
</tr>
<tr>
<td>Chronic myeloid</td>
<td>0.3</td>
<td>0.7</td>
</tr>
<tr>
<td>Acute monocytic</td>
<td>-5.0</td>
<td></td>
</tr>
<tr>
<td>Other myeloid &amp; monocytic</td>
<td>-5.2</td>
<td>-4.1</td>
</tr>
<tr>
<td>Other leukemia:</td>
<td>7.3</td>
<td></td>
</tr>
<tr>
<td>Aleukemic, subleukemic &amp; NOS</td>
<td>-4.0</td>
<td>-3.3</td>
</tr>
<tr>
<td>Kaposi Sarcoma</td>
<td>-1.3</td>
<td>-1.4</td>
</tr>
<tr>
<td>Mesothelioma</td>
<td>0.5</td>
<td>-0.2</td>
</tr>
<tr>
<td>Ill-defined &amp; unspecified</td>
<td>-3.3</td>
<td>-3.7</td>
</tr>
</tbody>
</table>

The APC is the Annual Percent Change over the time interval. Trends are based on rates age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1130).

a SEER 18 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, Alaska Native Registry, Rural Georgia, California excluding SF/SJM/LA, Kentucky, Louisiana, New Jersey and Georgia excluding ATL/RO).

b US Mortality Files, National Center for Health Statistics, Centers for Disease Control and Prevention.

c Ovary excludes borderline cases or histologies 8442, 8451, 8462, 8472, and 8473.

d Due to coding changes, Brain & Nervous System mortality are no longer shown separately.

* Trend not shown for mortality. Category did not exist in mortality coding until 1999.

* The APC is significantly different from zero (p<.05).

- Statistic could not be calculated. Trend based on less than 10 cases for at least one year within the time interval.
1426

Appendix

Table 1.11
Age Distribution (%) of Incidence Cases by Site, 2007-2011
All Races, Both Sexes

Age at Diagnosis
All
Ages

Site

<20

20-34

35-44

45-54

55-64

65-74

75-84

85+

All Sites

1.0

2.7

5.2

14.1

24.1

25.4

19.6

7.8

Oral Cavity & Pharynx:
Lip
Tongue
Salivary gland
Floor of mouth
Gum & other oral cavity
Nasopharynx
Tonsil
Oropharynx
Hypopharynx
Other oral cavity & pharynx

0.6
0.2
0.1
2.1
0.0
0.7
3.5
0.0
0.1
0.0
0.2

2.1
1.1
1.9
6.4
0.3
2.1
5.9
0.5
0.2
0.2
0.8

5.6
5.4
5.1
7.7
3.1
4.6
13.3
6.1
3.9
1.4
3.1

19.8
15.0
19.7
14.2
20.0
12.8
24.5
30.6
20.1
16.7
16.8

29.5
18.9
32.7
19.8
32.7
22.9
25.5
38.0
34.0
31.8
27.8

21.9
23.9
23.0
19.7
25.2
23.7
15.6
17.0
24.7
28.1
27.7

14.4
22.6
12.9
19.7
14.1
21.6
9.4
6.3
12.7
17.2
15.4

6.1
12.8
4.7
10.5
4.6
11.6
2.3
1.5
4.2
4.5
8.1

100.0%
100.0%
100.0%
100.0%
100.0%
100.0%
100.0%
100.0%
100.0%
100.0%
100.0%

48,868
2,908
14,368
5,494
2,569
6,582
2,866
8,475
1,797
2,835
974

Digestive System:
Esophagus
Stomach
Small intestine
Colon & Rectum:
Colon
Rectum
Colon & Rectum (Male)
Colon & Rectum (Female)
Anus, anal canal & anorectum
Liver & intrahepatic
bile duct
Gallbladder
Other biliary
Pancreas
Retroperitoneum
Peritoneum, omentum &
mesentery
Other digestive system

0.2
0.0
0.1
0.1
0.1
0.1
0.1
0.1
0.1
0.0
0.9

1.0
0.3
1.7
1.4
1.2
1.0
1.6
1.2
1.2
1.1
0.8

3.6
2.0
4.5
5.1
4.1
3.5
5.6
4.1
4.1
7.3
2.3

13.5
11.7
12.2
15.7
14.2
11.9
19.9
15.0
13.4
25.2
16.8

22.9
27.1
20.4
25.4
21.2
19.7
24.8
23.6
18.6
27.6
33.5

24.4
27.7
24.7
25.1
23.9
24.4
22.5
25.7
22.0
18.7
22.5

23.1
22.6
24.3
19.5
23.2
25.5
17.7
21.5
25.1
13.9
17.1

11.3
8.5
12.2
7.6
12.1
13.9
7.7
8.8
15.6
6.2
6.0

100.0%
100.0%
100.0%
100.0%
100.0%
100.0%
100.0%
100.0%
100.0%
100.0%
100.0%

365,536
19,290
32,063
9,263
188,874
133,670
55,204
97,463
91,411
7,834
35,695

0.0
0.1
0.1
9.0
0.4

0.3
0.5
0.4
4.8
1.0

2.6
2.4
2.1
7.3
2.7

8.6
8.4
9.4
15.3
9.7

19.4
19.8
21.5
22.5
24.4

25.7
25.4
26.3
21.4
33.1

28.5
28.5
26.8
15.2
22.9

14.8
14.8
13.4
4.5
5.9

100.0%
100.0%
100.0%
100.0%
100.0%

4,919
7,960
52,863
1,677
2,698

0.3

0.8

2.8

10.8

20.5

23.0

28.1

13.7

100.0%

2,400

Respiratory System:
Nose, nasal cavity &
middle ear
Larynx
Lung & bronchus
Lung & bronchus (Male)
Lung & bronchus (Female)
Pleura
Trachea & other
respiratory organs

0.1
1.8

0.4
4.0

1.4
7.3

9.0
14.9

21.9
23.7

31.3
21.4

27.1
17.9

8.7
8.9

100.0%
100.0%

274,682
2,995

0.0
0.0
0.0
0.0
5.6
17.7

0.4
0.3
0.2
0.3
1.6
20.0

2.6
1.3
1.2
1.4
3.2
9.1

15.4
8.6
8.4
8.9
10.5
11.3

30.8
21.4
22.5
20.2
15.3
13.0

28.7
31.7
32.2
31.0
21.8
12.8

17.2
27.9
27.5
28.3
27.4
10.9

4.9
8.9
8.1
9.9
14.5
5.2

100.0%
100.0%
100.0%
100.0%
100.0%
100.0%

14,687
256,086
135,278
120,808
124
790

26.9

15.7

9.3

12.9

12.4

10.1

9.0

3.7

100.0%

3,972

Soft tissue (including heart)

9.0

9.2

9.4

14.7

17.9

16.5

16.0

7.3

100.0%

14,395

Skin (excl. basal & squamous):
Melanoma of the skin
Other non-epithelial skin

0.6
0.5
1.3

6.2
6.2
5.4

9.2
9.4
6.7

16.7
17.3
9.7

21.4
22.0
14.8

20.1
20.2
19.4

17.6
16.8
26.2

8.1
7.4
16.5

100.0%
100.0%
100.0%

100,797
92,417
8,380

Breast (Female)

0.0

1.8

9.3

22.0

25.5

21.3

14.4

5.7

100.0%

292,397

Breast (Female -in situ )

0.0

0.7

10.4

28.5

27.1

20.3

10.8

2.2

100.0%

74,063

Bones & joints

Cases

100.0% 2,001,481

Source: SEER 18 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah,
Atlanta, San Jose-Monterey, Los Angeles, Alaska Native Registry, Rural Georgia,
California excluding SF/SJM/LA, Kentucky, Louisiana, New Jersey and Georgia excluding ATL/RG).
Percents may not sum to 100 due to rounding.

SEER Cancer Statistics Review 1975-2011

National Cancer Institute


Appendix

1427

Table 1.11 - continued
Age Distribution (%) of Incidence Cases by Site, 2007-2011
All Races, Both Sexes

Age at Diagnosis
All
Ages

Site

<20

20-34

35-44

45-54

55-64

65-74

75-84

85+

Female Genital System:
Cervix uteri
Corpus uteri
Uterus, NOS
Ovarya
Vagina
Vulva
Other female genital system

0.4
0.1
0.0
0.1
1.2
0.9
0.2
0.9

4.1
13.8
1.6
1.7
3.7
1.8
2.1
6.3

8.9
24.9
5.6
5.4
7.2
5.1
6.4
6.2

19.0
24.2
18.4
15.8
18.6
13.5
15.1
14.6

27.9
17.6
34.1
25.4
23.9
23.9
19.7
24.9

20.6
10.7
23.5
20.4
20.7
22.4
19.3
23.5

13.3
5.9
12.5
16.7
16.6
20.8
22.5
16.8

5.8
2.7
4.3
14.6
8.1
11.6
14.6
6.9

100.0%
100.0%
100.0%
100.0%
100.0%
100.0%
100.0%
100.0%

115,291
17,223
57,667
1,644
29,010
1,759
5,699
2,289

Male Genital System:
Prostate
Testis
Penis
Other male genital system

0.3
0.0
6.6
0.1
3.1

1.9
0.0
48.9
1.7
2.8

1.5
0.6
23.8
5.8
6.9

9.9
9.7
13.5
11.7
13.2

31.6
32.7
5.0
22.9
21.5

34.9
36.3
1.3
25.0
18.7

16.3
16.8
0.6
22.3
21.5

3.7
3.8
0.2
10.5
12.4

100.0%
100.0%
100.0%
100.0%
100.0%

311,294
297,322
11,801
1,663
508

Urinary System:
Urinary bladder
Kidney & renal pelvis
Ureter
Other urinary system

0.6
0.1
1.2
0.0
0.0

1.0
0.4
1.8
0.1
0.7

3.4
1.5
6.0
0.6
1.7

11.0
7.1
16.4
4.1
7.1

21.7
18.5
26.2
14.3
17.4

26.7
27.9
25.2
28.7
24.6

25.0
30.5
17.4
36.1
31.5

10.5
14.0
5.7
16.0
17.0

100.0%
100.0%
100.0%
100.0%
100.0%

158,403
86,940
67,743
2,399
1,321

Eye & Orbit

12.9

3.2

6.4

14.9

19.9

20.4

15.7

6.5

100.0%

3,454

Brain & Nervous System:
Brain
Cranial nerves & other
nervous system

13.1
12.4
23.7

8.9
8.8
10.4

8.4
8.2
11.8

14.8
14.7
15.9

19.7
20.0
16.0

17.0
17.4
10.7

13.3
13.6
8.6

4.8
5.0
2.9

100.0%
100.0%
100.0%

27,816
26,100
1,716

Endocrine System:
Thyroid
Other endocrine & thymus

2.9
1.8
21.7

14.7
15.1
7.6

19.0
19.6
8.2

23.7
24.2
14.5

19.8
19.9
19.0

12.5
12.3
16.6

5.9
5.7
9.8

1.5
1.4
2.7

100.0%
100.0%
100.0%

59,131
55,834
3,297

Lymphoma:
Hodgkin lymphoma
Non-Hodgkin lymphoma

3.0
12.8
1.6

7.1
31.0
3.8

7.2
14.5
6.2

13.1
12.7
13.2

19.5
10.9
20.7

21.4
9.1
23.1

20.2
6.6
22.1

8.5
2.3
9.3

100.0%
100.0%
100.0%

96,350
11,757
84,593

0.0

0.6

3.1

11.4

23.0

27.7

24.7

9.5

100.0%

26,346

Leukemia:
10.1
Lymphocytic:
15.2
Acute lymphocytic
58.8
Chronic lymphocytic
0.0
Other lymphocytic
0.2
Myeloid & Monocytic:
4.9
Acute myeloid
5.6
Chronic myeloid
2.7
Acute monocytic
9.6
Other myeloid & monocytic
4.0
Other leukemia:
4.5
Other acute leukemia
8.0
Aleukemic, subleukemic & NOS
2.3

4.6
2.9
10.2
0.2
2.0
6.7
6.4
7.6
5.7
5.7
3.5
4.3
3.0

5.0
3.1
5.5
1.6
10.4
7.2
6.3
9.2
8.4
6.8
4.0
3.5
4.4

10.3
9.2
7.0
9.0
19.3
12.0
11.0
14.2
12.6
10.9
7.6
7.8
7.4

17.1
17.9
7.3
21.5
23.6
16.6
16.2
17.9
17.9
11.8
12.5
10.7
13.6

20.6
21.1
5.5
27.2
18.3
20.5
21.3
18.9
17.0
22.6
16.1
14.8
16.9

21.3
20.3
4.2
26.7
17.8
22.0
23.1
19.5
19.6
22.6
26.1
24.5
27.1

11.0
10.2
1.5
13.7
8.3
10.2
10.1
10.0
9.1
15.6
25.7
26.4
25.3

100.0%
100.0%
100.0%
100.0%
100.0%
100.0%
100.0%
100.0%
100.0%
100.0%
100.0%
100.0%
100.0%

55,604
27,868
7,190
18,934
1,744
25,048
16,173
7,113
1,082
680
2,688
1,036
1,652

Kaposi Sarcoma
Mesothelioma

0.4
0.1

20.3
0.7

26.5
1.9

21.1
6.0

9.7
16.1

7.7
27.2

8.1
33.8

6.3
14.3

100.0%
100.0%

2,258
4,267

Ill-defined & unspecified

0.4

0.9

2.4

9.4

18.4

22.2

27.0

19.3

100.0%

38,242

Myeloma

Cases

Source: SEER 18 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah,
Atlanta, San Jose-Monterey, Los Angeles, Alaska Native Registry, Rural Georgia,
California excluding SF/SJM/LA, Kentucky, Louisiana, New Jersey and Georgia excluding ATL/RG).
Percents may not sum to 100 due to rounding.
a
Ovary excludes borderline cases or histologies 8442, 8451, 8462, 8472, and 8473.

SEER Cancer Statistics Review 1975-2011

National Cancer Institute


### Table 1.12
Median Age of Cancer Patients at Diagnosis, 2007-2011
By Primary Cancer Site, Race and Sex

<table>
<thead>
<tr>
<th>Site</th>
<th>All Races</th>
<th>Whites</th>
<th>Blacks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Males</td>
<td>Females</td>
</tr>
<tr>
<td>All Sites</td>
<td>66.0</td>
<td>66.0</td>
<td>65.0</td>
</tr>
<tr>
<td>Oral Cavity &amp; Pharynx:</td>
<td>62.0</td>
<td>61.0</td>
<td>65.0</td>
</tr>
<tr>
<td>Lip</td>
<td>68.0</td>
<td>67.0</td>
<td>72.0</td>
</tr>
<tr>
<td>Tongue</td>
<td>62.0</td>
<td>61.0</td>
<td>64.0</td>
</tr>
<tr>
<td>Salivary gland</td>
<td>64.0</td>
<td>67.0</td>
<td>61.0</td>
</tr>
<tr>
<td>Floor of mouth</td>
<td>63.0</td>
<td>62.0</td>
<td>66.0</td>
</tr>
<tr>
<td>Gum &amp; other oral cavity</td>
<td>67.0</td>
<td>65.0</td>
<td>71.0</td>
</tr>
<tr>
<td>Nasopharynx</td>
<td>55.0</td>
<td>55.0</td>
<td>55.0</td>
</tr>
<tr>
<td>Tonsil</td>
<td>58.0</td>
<td>57.0</td>
<td>60.0</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>62.0</td>
<td>61.0</td>
<td>64.0</td>
</tr>
<tr>
<td>Hypopharynx</td>
<td>64.0</td>
<td>64.0</td>
<td>67.0</td>
</tr>
<tr>
<td>Other oral cavity &amp; pharynx</td>
<td>65.0</td>
<td>63.0</td>
<td>70.0</td>
</tr>
<tr>
<td>Digestive System:</td>
<td>68.0</td>
<td>66.0</td>
<td>71.0</td>
</tr>
<tr>
<td>Esophagus</td>
<td>67.0</td>
<td>66.0</td>
<td>72.0</td>
</tr>
<tr>
<td>Stomach</td>
<td>69.0</td>
<td>68.0</td>
<td>71.0</td>
</tr>
<tr>
<td>Small intestine</td>
<td>65.0</td>
<td>65.0</td>
<td>66.0</td>
</tr>
<tr>
<td>Colon &amp; Rectum:</td>
<td>68.0</td>
<td>67.0</td>
<td>70.0</td>
</tr>
<tr>
<td>Colon</td>
<td>70.0</td>
<td>68.0</td>
<td>72.0</td>
</tr>
<tr>
<td>Rectum</td>
<td>64.0</td>
<td>63.0</td>
<td>65.0</td>
</tr>
<tr>
<td>Anus, anal canal &amp; anorectum</td>
<td>60.0</td>
<td>58.0</td>
<td>61.0</td>
</tr>
<tr>
<td>Liver &amp; intrahepatic bile duct</td>
<td>63.0</td>
<td>61.0</td>
<td>69.0</td>
</tr>
<tr>
<td>Gallbladder</td>
<td>72.0</td>
<td>72.0</td>
<td>72.0</td>
</tr>
<tr>
<td>Other biliary</td>
<td>72.0</td>
<td>71.0</td>
<td>74.0</td>
</tr>
<tr>
<td>Pancreas</td>
<td>71.0</td>
<td>69.0</td>
<td>73.0</td>
</tr>
<tr>
<td>Retroperitoneum</td>
<td>61.0</td>
<td>61.0</td>
<td>60.5</td>
</tr>
<tr>
<td>Peritoneum, omentum &amp; mesentery</td>
<td>68.0</td>
<td>65.0</td>
<td>68.0</td>
</tr>
<tr>
<td>Other digestive system</td>
<td>71.0</td>
<td>70.0</td>
<td>72.0</td>
</tr>
<tr>
<td>Respiratory System:</td>
<td>70.0</td>
<td>70.0</td>
<td>71.0</td>
</tr>
<tr>
<td>Nose, nasal cavity &amp; middle ear</td>
<td>64.0</td>
<td>63.0</td>
<td>66.0</td>
</tr>
<tr>
<td>Larynx</td>
<td>65.0</td>
<td>65.0</td>
<td>64.0</td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
<td>70.0</td>
<td>70.0</td>
<td>71.0</td>
</tr>
<tr>
<td>Pleura</td>
<td>69.0</td>
<td>69.0</td>
<td>68.0</td>
</tr>
<tr>
<td>Trachea &amp; other respiratory organs</td>
<td>47.0</td>
<td>42.0</td>
<td>57.0</td>
</tr>
<tr>
<td>Bones &amp; joints</td>
<td>43.0</td>
<td>40.0</td>
<td>45.0</td>
</tr>
<tr>
<td>Soft tissue (including heart)</td>
<td>59.0</td>
<td>59.0</td>
<td>58.0</td>
</tr>
<tr>
<td>Skin (excl. basal &amp; squamous):</td>
<td>63.0</td>
<td>65.0</td>
<td>58.0</td>
</tr>
<tr>
<td>Melanoma of the skin</td>
<td>62.0</td>
<td>65.0</td>
<td>58.0</td>
</tr>
<tr>
<td>Other non-epithelial skin</td>
<td>71.0</td>
<td>72.0</td>
<td>69.0</td>
</tr>
<tr>
<td>Breast (in situ)</td>
<td>61.0</td>
<td>68.0</td>
<td>61.0</td>
</tr>
<tr>
<td>Breast</td>
<td>58.0</td>
<td>63.0</td>
<td>58.0</td>
</tr>
</tbody>
</table>

*a* SEER 18 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, Alaska Native Registry, Rural Georgia, California excluding SF/SJN/LA, Kentucky, Louisiana, New Jersey and Georgia excluding ATL/RO).
- Statistic could not be calculated. Less than 16 cases were diagnosed during the time interval.
### Appendix

**SEER Cancer Statistics Review 1975-2011 National Cancer Institute**

#### Table 1.12 - continued

<table>
<thead>
<tr>
<th>Site</th>
<th>All Races</th>
<th>Whites</th>
<th>Blacks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total Males</td>
<td>Females</td>
<td>Total Males</td>
</tr>
<tr>
<td>Female Genital System:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cervix uteri</td>
<td>61.0</td>
<td>61.0</td>
<td>61.0</td>
</tr>
<tr>
<td>Corpus uteri</td>
<td>62.0</td>
<td>62.0</td>
<td>62.0</td>
</tr>
<tr>
<td>Uterus, NOS</td>
<td>65.0</td>
<td>65.0</td>
<td>65.0</td>
</tr>
<tr>
<td>Ovary</td>
<td>63.0</td>
<td>63.0</td>
<td>63.0</td>
</tr>
<tr>
<td>Vagina</td>
<td>67.0</td>
<td>67.0</td>
<td>68.0</td>
</tr>
<tr>
<td>Vulva</td>
<td>68.0</td>
<td>68.0</td>
<td>69.0</td>
</tr>
<tr>
<td>Other female genital system</td>
<td>63.0</td>
<td>63.0</td>
<td>64.0</td>
</tr>
<tr>
<td>Male Genital System:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prostate</td>
<td>66.0</td>
<td>66.0</td>
<td>66.0</td>
</tr>
<tr>
<td>Testis</td>
<td>33.0</td>
<td>33.0</td>
<td>33.0</td>
</tr>
<tr>
<td>Penis</td>
<td>68.0</td>
<td>68.0</td>
<td>68.0</td>
</tr>
<tr>
<td>Other male genital system</td>
<td>66.0</td>
<td>66.0</td>
<td>67.0</td>
</tr>
<tr>
<td>Urinary System:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>69.0</td>
<td>69.0</td>
<td>70.0</td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>73.0</td>
<td>72.0</td>
<td>74.0</td>
</tr>
<tr>
<td>Ureter</td>
<td>64.0</td>
<td>63.0</td>
<td>64.0</td>
</tr>
<tr>
<td>Other urinary system</td>
<td>75.0</td>
<td>74.0</td>
<td>76.0</td>
</tr>
<tr>
<td>Eye &amp; Orbit</td>
<td>61.0</td>
<td>61.0</td>
<td>62.0</td>
</tr>
<tr>
<td>Brain &amp; Nervous System:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brain</td>
<td>57.0</td>
<td>57.0</td>
<td>58.0</td>
</tr>
<tr>
<td>Cranial nerves &amp; other</td>
<td>47.0</td>
<td>45.0</td>
<td>48.0</td>
</tr>
<tr>
<td>Endocrine System:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thyroid</td>
<td>50.0</td>
<td>54.0</td>
<td>51.0</td>
</tr>
<tr>
<td>Other endocrine &amp; thymus</td>
<td>53.0</td>
<td>51.0</td>
<td>54.0</td>
</tr>
<tr>
<td>Hodgkin lymphoma</td>
<td>65.0</td>
<td>63.0</td>
<td>66.0</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>39.0</td>
<td>40.0</td>
<td>40.0</td>
</tr>
<tr>
<td>Myeloma</td>
<td>66.0</td>
<td>65.0</td>
<td>68.0</td>
</tr>
<tr>
<td>Leukemia:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphocytic</td>
<td>66.0</td>
<td>65.0</td>
<td>67.0</td>
</tr>
<tr>
<td>Chronic lymphocytic</td>
<td>14.0</td>
<td>14.0</td>
<td>14.0</td>
</tr>
<tr>
<td>Other lymphocytic</td>
<td>71.0</td>
<td>70.0</td>
<td>73.0</td>
</tr>
<tr>
<td>Myeloid &amp; monocytic</td>
<td>62.0</td>
<td>61.0</td>
<td>67.0</td>
</tr>
<tr>
<td>Acute myeloid</td>
<td>67.0</td>
<td>67.0</td>
<td>68.0</td>
</tr>
<tr>
<td>Chronic myeloid</td>
<td>64.0</td>
<td>63.0</td>
<td>65.0</td>
</tr>
<tr>
<td>Acute monocytic</td>
<td>62.0</td>
<td>64.0</td>
<td>60.0</td>
</tr>
<tr>
<td>Other myeloid &amp; monocytic</td>
<td>70.0</td>
<td>70.0</td>
<td>69.0</td>
</tr>
<tr>
<td>Other leukemia:</td>
<td>76.0</td>
<td>73.0</td>
<td>78.0</td>
</tr>
<tr>
<td>Aleukemic, subleukemic &amp; NOS</td>
<td>76.0</td>
<td>73.0</td>
<td>78.0</td>
</tr>
<tr>
<td>Kaposi Sarcoma</td>
<td>46.0</td>
<td>44.0</td>
<td>48.0</td>
</tr>
<tr>
<td>Mesothelioma</td>
<td>74.0</td>
<td>75.0</td>
<td>71.0</td>
</tr>
<tr>
<td>Ill-defined &amp; unspecified</td>
<td>73.0</td>
<td>70.0</td>
<td>76.0</td>
</tr>
</tbody>
</table>

* SEER 18 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, Alaska Native Registry, Rural Georgia, California excluding SF/SJM/LA, Kentucky, Louisiana, New Jersey and Georgia excluding ATL/RG).

- Ovary excludes borderline cases or histologies 8442, 8451, 8462, 8472, and 8473.

- Statistic could not be calculated. Less than 16 cases were diagnosed during the time interval.
Table 1.13
Age Distribution (%) of Deaths by Site, 2007-2011
All Races, Both Sexes

<table>
<thead>
<tr>
<th>Age at Death</th>
<th>&lt;20</th>
<th>20-34</th>
<th>35-44</th>
<th>45-54</th>
<th>55-64</th>
<th>65-74</th>
<th>75-84</th>
<th>85+</th>
<th>All Ages</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Sites</td>
<td>0.3</td>
<td>0.8</td>
<td>2.2</td>
<td>8.8</td>
<td>18.8</td>
<td>25.0</td>
<td>27.9</td>
<td>16.1</td>
<td>100.0%</td>
<td>2,847,364</td>
</tr>
<tr>
<td>Oral Cavity &amp; Pharynx:</td>
<td>0.1</td>
<td>0.8</td>
<td>2.7</td>
<td>13.7</td>
<td>25.7</td>
<td>24.0</td>
<td>20.8</td>
<td>12.3</td>
<td>100.0%</td>
<td>41,139</td>
</tr>
<tr>
<td>Lip</td>
<td>0.3</td>
<td>0.9</td>
<td>2.0</td>
<td>8.2</td>
<td>12.2</td>
<td>17.5</td>
<td>28.0</td>
<td>30.9</td>
<td>100.0%</td>
<td>343</td>
</tr>
<tr>
<td>Tongue</td>
<td>0.1</td>
<td>1.0</td>
<td>3.2</td>
<td>14.4</td>
<td>26.8</td>
<td>23.7</td>
<td>19.8</td>
<td>10.9</td>
<td>100.0%</td>
<td>10,202</td>
</tr>
<tr>
<td>Salivary gland</td>
<td>0.1</td>
<td>0.9</td>
<td>2.6</td>
<td>9.1</td>
<td>16.8</td>
<td>21.2</td>
<td>27.9</td>
<td>21.4</td>
<td>100.0%</td>
<td>3,902</td>
</tr>
<tr>
<td>Floor of mouth</td>
<td>0.0</td>
<td>0.0</td>
<td>2.7</td>
<td>11.3</td>
<td>32.2</td>
<td>28.1</td>
<td>17.9</td>
<td>7.8</td>
<td>100.0%</td>
<td>487</td>
</tr>
<tr>
<td>Gum &amp; other oral cavity</td>
<td>0.1</td>
<td>0.5</td>
<td>1.9</td>
<td>8.9</td>
<td>18.8</td>
<td>22.0</td>
<td>25.5</td>
<td>22.4</td>
<td>100.0%</td>
<td>5,817</td>
</tr>
<tr>
<td>Nasopharynx</td>
<td>0.8</td>
<td>3.3</td>
<td>6.0</td>
<td>19.2</td>
<td>26.5</td>
<td>20.3</td>
<td>16.5</td>
<td>7.5</td>
<td>100.0%</td>
<td>3,315</td>
</tr>
<tr>
<td>Tonsil</td>
<td>0.0</td>
<td>0.2</td>
<td>2.8</td>
<td>19.9</td>
<td>33.9</td>
<td>23.9</td>
<td>14.2</td>
<td>5.1</td>
<td>100.0%</td>
<td>3,785</td>
</tr>
<tr>
<td>Hypopharynx</td>
<td>0.0</td>
<td>0.3</td>
<td>1.2</td>
<td>12.9</td>
<td>28.8</td>
<td>29.4</td>
<td>21.2</td>
<td>6.4</td>
<td>100.0%</td>
<td>1,543</td>
</tr>
<tr>
<td>Digestive System:</td>
<td>0.1</td>
<td>0.5</td>
<td>2.1</td>
<td>9.6</td>
<td>20.3</td>
<td>23.9</td>
<td>26.9</td>
<td>16.7</td>
<td>100.0%</td>
<td>701,293</td>
</tr>
<tr>
<td>Esophagus</td>
<td>0.0</td>
<td>0.2</td>
<td>1.7</td>
<td>10.5</td>
<td>25.0</td>
<td>27.4</td>
<td>24.4</td>
<td>10.7</td>
<td>100.0%</td>
<td>70,150</td>
</tr>
<tr>
<td>Stomach</td>
<td>0.0</td>
<td>1.3</td>
<td>3.8</td>
<td>10.3</td>
<td>17.5</td>
<td>22.6</td>
<td>26.8</td>
<td>17.6</td>
<td>100.0%</td>
<td>56,349</td>
</tr>
<tr>
<td>Small intestine</td>
<td>0.0</td>
<td>0.8</td>
<td>2.6</td>
<td>9.5</td>
<td>20.7</td>
<td>23.3</td>
<td>27.0</td>
<td>16.1</td>
<td>100.0%</td>
<td>5,944</td>
</tr>
<tr>
<td>Colon &amp; Rectum:</td>
<td>0.0</td>
<td>0.6</td>
<td>2.5</td>
<td>9.1</td>
<td>17.6</td>
<td>21.9</td>
<td>27.3</td>
<td>20.9</td>
<td>100.0%</td>
<td>261,752</td>
</tr>
<tr>
<td>Colon &amp; Rectum (Male)</td>
<td>0.0</td>
<td>0.7</td>
<td>2.7</td>
<td>10.0</td>
<td>20.2</td>
<td>24.6</td>
<td>26.6</td>
<td>15.1</td>
<td>100.0%</td>
<td>134,620</td>
</tr>
<tr>
<td>Colon &amp; Rectum (Female)</td>
<td>0.0</td>
<td>0.6</td>
<td>2.3</td>
<td>8.2</td>
<td>14.7</td>
<td>19.1</td>
<td>28.0</td>
<td>27.1</td>
<td>100.0%</td>
<td>127,132</td>
</tr>
<tr>
<td>Other digestive system</td>
<td>0.0</td>
<td>0.6</td>
<td>2.1</td>
<td>13.1</td>
<td>27.6</td>
<td>23.0</td>
<td>23.3</td>
<td>10.4</td>
<td>100.0%</td>
<td>96,623</td>
</tr>
<tr>
<td>Respiratory System:</td>
<td>0.0</td>
<td>0.1</td>
<td>1.0</td>
<td>7.8</td>
<td>19.8</td>
<td>30.5</td>
<td>29.6</td>
<td>11.1</td>
<td>100.0%</td>
<td>813,550</td>
</tr>
<tr>
<td>Nose, nasal cavity &amp; middle ear</td>
<td>0.2</td>
<td>1.8</td>
<td>5.7</td>
<td>12.9</td>
<td>19.4</td>
<td>21.1</td>
<td>23.4</td>
<td>15.4</td>
<td>100.0%</td>
<td>2,432</td>
</tr>
<tr>
<td>Larynx</td>
<td>0.0</td>
<td>0.1</td>
<td>1.3</td>
<td>11.4</td>
<td>26.2</td>
<td>28.6</td>
<td>23.2</td>
<td>9.3</td>
<td>100.0%</td>
<td>18,447</td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
<td>0.0</td>
<td>0.1</td>
<td>1.0</td>
<td>7.7</td>
<td>19.7</td>
<td>30.6</td>
<td>29.8</td>
<td>11.2</td>
<td>100.0%</td>
<td>790,557</td>
</tr>
<tr>
<td>Lung &amp; bronchus (Male)</td>
<td>0.0</td>
<td>0.1</td>
<td>0.9</td>
<td>7.7</td>
<td>21.0</td>
<td>31.4</td>
<td>29.2</td>
<td>9.7</td>
<td>100.0%</td>
<td>438,998</td>
</tr>
<tr>
<td>Pleura</td>
<td>0.3</td>
<td>0.5</td>
<td>1.2</td>
<td>2.9</td>
<td>14.4</td>
<td>26.4</td>
<td>38.5</td>
<td>15.7</td>
<td>100.0%</td>
<td>1,018</td>
</tr>
<tr>
<td>Trachea &amp; other respiratory organs</td>
<td>0.9</td>
<td>4.9</td>
<td>4.0</td>
<td>12.7</td>
<td>17.4</td>
<td>21.2</td>
<td>24.3</td>
<td>14.6</td>
<td>100.0%</td>
<td>1,096</td>
</tr>
<tr>
<td>Bones &amp; joints</td>
<td>12.6</td>
<td>15.1</td>
<td>6.1</td>
<td>10.6</td>
<td>12.5</td>
<td>14.2</td>
<td>16.7</td>
<td>12.2</td>
<td>100.0%</td>
<td>6,904</td>
</tr>
<tr>
<td>Soft tissue (including heart)</td>
<td>3.6</td>
<td>6.2</td>
<td>6.5</td>
<td>13.2</td>
<td>19.4</td>
<td>19.3</td>
<td>20.3</td>
<td>11.5</td>
<td>100.0%</td>
<td>21,139</td>
</tr>
<tr>
<td>Skin (excl. basal &amp; squamous):</td>
<td>0.1</td>
<td>1.8</td>
<td>4.2</td>
<td>11.4</td>
<td>19.4</td>
<td>21.2</td>
<td>24.9</td>
<td>17.2</td>
<td>100.0%</td>
<td>59,224</td>
</tr>
<tr>
<td>Melanoma of the skin</td>
<td>0.1</td>
<td>2.3</td>
<td>5.1</td>
<td>12.7</td>
<td>20.5</td>
<td>21.7</td>
<td>24.0</td>
<td>13.6</td>
<td>100.0%</td>
<td>44,565</td>
</tr>
<tr>
<td>Other non-epithelial skin</td>
<td>0.0</td>
<td>0.3</td>
<td>1.4</td>
<td>7.4</td>
<td>16.0</td>
<td>19.5</td>
<td>27.4</td>
<td>28.0</td>
<td>100.0%</td>
<td>14,659</td>
</tr>
<tr>
<td>Breast (Female)</td>
<td>0.0</td>
<td>0.9</td>
<td>5.2</td>
<td>14.5</td>
<td>21.7</td>
<td>20.6</td>
<td>21.0</td>
<td>16.2</td>
<td>100.0%</td>
<td>203,790</td>
</tr>
</tbody>
</table>

Source: US Mortality Files, National Center for Health Statistics, Centers for Disease Control and Prevention.
Percentages may not sum to 100 due to rounding.
Table 1.13 - continued
Age Distribution (%) of Deaths by Site, 2007-2011
All Races, Both Sexes

<table>
<thead>
<tr>
<th>Site</th>
<th>&lt;20</th>
<th>20-34</th>
<th>35-44</th>
<th>45-54</th>
<th>55-64</th>
<th>65-74</th>
<th>75-84</th>
<th>85+</th>
<th>All Ages</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female Genital System:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cervix uteri</td>
<td>0.0</td>
<td>4.8</td>
<td>14.5</td>
<td>24.0</td>
<td>22.6</td>
<td>15.8</td>
<td>11.8</td>
<td>6.4</td>
<td>100.0%</td>
<td>19,969</td>
</tr>
<tr>
<td>Corpus uteri</td>
<td>0.0</td>
<td>0.3</td>
<td>1.8</td>
<td>7.5</td>
<td>23.2</td>
<td>28.4</td>
<td>24.6</td>
<td>14.1</td>
<td>100.0%</td>
<td>17,504</td>
</tr>
<tr>
<td>Uterus, NOS</td>
<td>0.0</td>
<td>0.4</td>
<td>2.2</td>
<td>8.7</td>
<td>21.8</td>
<td>26.4</td>
<td>24.4</td>
<td>16.2</td>
<td>100.0%</td>
<td>22,383</td>
</tr>
<tr>
<td>Ovary</td>
<td>0.1</td>
<td>0.7</td>
<td>2.5</td>
<td>10.5</td>
<td>21.1</td>
<td>25.2</td>
<td>25.8</td>
<td>14.2</td>
<td>100.0%</td>
<td>72,337</td>
</tr>
<tr>
<td>Vagina</td>
<td>0.0</td>
<td>0.8</td>
<td>2.7</td>
<td>6.6</td>
<td>16.0</td>
<td>19.7</td>
<td>28.2</td>
<td>26.0</td>
<td>100.0%</td>
<td>2,042</td>
</tr>
<tr>
<td>Vulva</td>
<td>0.0</td>
<td>0.5</td>
<td>2.3</td>
<td>7.5</td>
<td>13.1</td>
<td>16.7</td>
<td>29.7</td>
<td>30.1</td>
<td>100.0%</td>
<td>4,696</td>
</tr>
<tr>
<td>Other female genital system</td>
<td>0.1</td>
<td>1.3</td>
<td>2.9</td>
<td>9.9</td>
<td>21.5</td>
<td>25.9</td>
<td>24.2</td>
<td>14.3</td>
<td>100.0%</td>
<td>2,235</td>
</tr>
<tr>
<td>Male Genital System:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Testis</td>
<td>1.8</td>
<td>34.8</td>
<td>20.4</td>
<td>18.4</td>
<td>11.2</td>
<td>5.0</td>
<td>5.1</td>
<td>3.3</td>
<td>100.0%</td>
<td>1,839</td>
</tr>
<tr>
<td>Penis</td>
<td>0.1</td>
<td>0.8</td>
<td>4.7</td>
<td>10.6</td>
<td>20.6</td>
<td>23.7</td>
<td>22.6</td>
<td>16.8</td>
<td>100.0%</td>
<td>1,223</td>
</tr>
<tr>
<td>Other male genital system</td>
<td>0.4</td>
<td>0.9</td>
<td>3.5</td>
<td>9.6</td>
<td>14.0</td>
<td>22.3</td>
<td>26.6</td>
<td>22.7</td>
<td>100.0%</td>
<td>229</td>
</tr>
<tr>
<td>Urinary System:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>0.2</td>
<td>0.3</td>
<td>1.2</td>
<td>6.6</td>
<td>15.9</td>
<td>23.0</td>
<td>30.7</td>
<td>22.1</td>
<td>100.0%</td>
<td>140,985</td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>0.4</td>
<td>0.6</td>
<td>1.8</td>
<td>9.6</td>
<td>21.1</td>
<td>25.3</td>
<td>26.2</td>
<td>15.0</td>
<td>100.0%</td>
<td>65,371</td>
</tr>
<tr>
<td>Ureter</td>
<td>0.1</td>
<td>0.4</td>
<td>0.9</td>
<td>3.2</td>
<td>9.2</td>
<td>24.1</td>
<td>37.5</td>
<td>25.3</td>
<td>100.0%</td>
<td>1,753</td>
</tr>
<tr>
<td>Other urinary system</td>
<td>0.0</td>
<td>0.2</td>
<td>1.3</td>
<td>5.9</td>
<td>12.0</td>
<td>21.6</td>
<td>35.5</td>
<td>23.4</td>
<td>100.0%</td>
<td>2,037</td>
</tr>
<tr>
<td>Eye &amp; Orbit</td>
<td>2.0</td>
<td>1.8</td>
<td>4.7</td>
<td>11.2</td>
<td>19.8</td>
<td>21.4</td>
<td>23.6</td>
<td>15.5</td>
<td>100.0%</td>
<td>1,352</td>
</tr>
<tr>
<td>Brain &amp; Nervous System:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endocrine System:</td>
<td>3.8</td>
<td>3.5</td>
<td>5.9</td>
<td>14.2</td>
<td>23.4</td>
<td>23.1</td>
<td>18.9</td>
<td>7.2</td>
<td>100.0%</td>
<td>69,789</td>
</tr>
<tr>
<td>Thyroid</td>
<td>6.3</td>
<td>2.5</td>
<td>3.9</td>
<td>9.6</td>
<td>18.0</td>
<td>22.1</td>
<td>23.8</td>
<td>13.8</td>
<td>100.0%</td>
<td>13,007</td>
</tr>
<tr>
<td>Other endocrine &amp; thymus</td>
<td>17.4</td>
<td>5.6</td>
<td>7.1</td>
<td>12.8</td>
<td>18.7</td>
<td>18.7</td>
<td>14.5</td>
<td>6.0</td>
<td>100.0%</td>
<td>4,656</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>0.4</td>
<td>2.0</td>
<td>2.7</td>
<td>6.7</td>
<td>14.4</td>
<td>21.9</td>
<td>31.7</td>
<td>20.2</td>
<td>100.0%</td>
<td>107,987</td>
</tr>
<tr>
<td>Hodgkin lymphoma</td>
<td>1.4</td>
<td>12.3</td>
<td>10.2</td>
<td>11.1</td>
<td>14.9</td>
<td>17.8</td>
<td>23.5</td>
<td>10.8</td>
<td>100.0%</td>
<td>6,091</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>0.4</td>
<td>1.4</td>
<td>2.3</td>
<td>6.4</td>
<td>14.4</td>
<td>22.1</td>
<td>32.3</td>
<td>20.7</td>
<td>100.0%</td>
<td>101,896</td>
</tr>
<tr>
<td>Myeloma</td>
<td>0.0</td>
<td>0.1</td>
<td>1.0</td>
<td>5.8</td>
<td>16.4</td>
<td>26.3</td>
<td>33.1</td>
<td>17.3</td>
<td>100.0%</td>
<td>54,601</td>
</tr>
<tr>
<td>Leukemia:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute lymphocytic:</td>
<td>2.5</td>
<td>3.0</td>
<td>2.8</td>
<td>6.3</td>
<td>13.1</td>
<td>21.7</td>
<td>30.5</td>
<td>20.1</td>
<td>100.0%</td>
<td>112,914</td>
</tr>
<tr>
<td>Acute myeloid</td>
<td>17.4</td>
<td>15.4</td>
<td>8.3</td>
<td>11.1</td>
<td>14.0</td>
<td>14.2</td>
<td>13.0</td>
<td>6.6</td>
<td>100.0%</td>
<td>31,589</td>
</tr>
<tr>
<td>Chronic lymphocytic</td>
<td>0.0</td>
<td>0.1</td>
<td>0.4</td>
<td>2.8</td>
<td>10.7</td>
<td>20.7</td>
<td>34.2</td>
<td>31.2</td>
<td>100.0%</td>
<td>22,517</td>
</tr>
<tr>
<td>Acute myeloid</td>
<td>1.6</td>
<td>1.6</td>
<td>1.4</td>
<td>5.5</td>
<td>11.1</td>
<td>20.0</td>
<td>31.1</td>
<td>27.7</td>
<td>100.0%</td>
<td>1,939</td>
</tr>
<tr>
<td>Acute monocytic</td>
<td>1.9</td>
<td>2.9</td>
<td>3.4</td>
<td>7.8</td>
<td>15.2</td>
<td>24.1</td>
<td>31.0</td>
<td>14.7</td>
<td>100.0%</td>
<td>54,525</td>
</tr>
<tr>
<td>Acute monocytic</td>
<td>2.1</td>
<td>3.0</td>
<td>3.4</td>
<td>7.9</td>
<td>15.8</td>
<td>24.9</td>
<td>29.8</td>
<td>13.2</td>
<td>100.0%</td>
<td>45,394</td>
</tr>
<tr>
<td>Chronic myeloid</td>
<td>0.5</td>
<td>3.5</td>
<td>4.8</td>
<td>8.7</td>
<td>12.2</td>
<td>17.6</td>
<td>28.7</td>
<td>24.1</td>
<td>100.0%</td>
<td>5,097</td>
</tr>
<tr>
<td>Acute myeloid</td>
<td>1.2</td>
<td>1.6</td>
<td>1.8</td>
<td>5.7</td>
<td>10.9</td>
<td>24.8</td>
<td>32.4</td>
<td>21.4</td>
<td>100.0%</td>
<td>487</td>
</tr>
<tr>
<td>Other leukemia</td>
<td>1.5</td>
<td>1.2</td>
<td>1.8</td>
<td>4.9</td>
<td>12.3</td>
<td>23.1</td>
<td>34.7</td>
<td>20.4</td>
<td>100.0%</td>
<td>3,547</td>
</tr>
<tr>
<td>ALeukemic, subleukemic &amp; NOS</td>
<td>2.7</td>
<td>2.1</td>
<td>2.2</td>
<td>5.0</td>
<td>11.1</td>
<td>20.9</td>
<td>33.5</td>
<td>23.5</td>
<td>100.0%</td>
<td>10,055</td>
</tr>
<tr>
<td>Ill-defined &amp; unspecified</td>
<td>0.2</td>
<td>0.7</td>
<td>1.9</td>
<td>8.0</td>
<td>17.7</td>
<td>23.3</td>
<td>28.8</td>
<td>19.4</td>
<td>100.0%</td>
<td>210,961</td>
</tr>
</tbody>
</table>

Source: US Mortality Files, National Center for Health Statistics, Centers for Disease Control and Prevention.
Percent may not sum to 100 due to rounding.
Table 1.14
Median Age of Cancer Patients at Deatha, 2007-2011
By Primary Cancer Site, Race and Sex

<table>
<thead>
<tr>
<th>Site</th>
<th>All Races</th>
<th></th>
<th></th>
<th></th>
<th>Whites</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th>Blacks</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total Males</td>
<td>Females</td>
<td>Total Males</td>
<td>Females</td>
<td>Total Males</td>
<td>Females</td>
<td>Total Males</td>
<td>Females</td>
<td>Total Males</td>
<td>Females</td>
<td>Total Males</td>
<td>Females</td>
<td>Total Males</td>
</tr>
<tr>
<td>All Sites</td>
<td>72.0</td>
<td>72.0</td>
<td>73.0</td>
<td>73.0</td>
<td>72.0</td>
<td>74.0</td>
<td>67.0</td>
<td>67.0</td>
<td>68.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral Cavity &amp; Pharynx:</td>
<td>67.0</td>
<td>65.0</td>
<td>73.0</td>
<td>68.0</td>
<td>66.0</td>
<td>74.0</td>
<td>62.0</td>
<td>61.0</td>
<td>63.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lip</td>
<td>78.0</td>
<td>76.0</td>
<td>85.0</td>
<td>78.0</td>
<td>76.0</td>
<td>85.0</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tongue</td>
<td>66.0</td>
<td>64.0</td>
<td>72.0</td>
<td>67.0</td>
<td>65.0</td>
<td>72.0</td>
<td>61.0</td>
<td>61.0</td>
<td>60.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salivary gland</td>
<td>74.0</td>
<td>73.0</td>
<td>76.0</td>
<td>75.0</td>
<td>74.0</td>
<td>78.0</td>
<td>62.0</td>
<td>61.5</td>
<td>65.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Floor of mouth</td>
<td>66.0</td>
<td>64.0</td>
<td>71.0</td>
<td>67.0</td>
<td>64.0</td>
<td>72.0</td>
<td>61.0</td>
<td>61.0</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gum &amp; other oral cavity</td>
<td>74.0</td>
<td>68.0</td>
<td>80.0</td>
<td>75.0</td>
<td>69.0</td>
<td>81.0</td>
<td>64.0</td>
<td>62.0</td>
<td>68.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nasopharynx</td>
<td>62.0</td>
<td>61.0</td>
<td>66.0</td>
<td>65.0</td>
<td>63.0</td>
<td>71.0</td>
<td>59.0</td>
<td>58.0</td>
<td>59.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tonsil</td>
<td>62.0</td>
<td>61.0</td>
<td>67.0</td>
<td>63.0</td>
<td>61.0</td>
<td>68.0</td>
<td>61.0</td>
<td>61.0</td>
<td>61.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oropharynx</td>
<td>65.0</td>
<td>64.0</td>
<td>72.0</td>
<td>67.0</td>
<td>65.0</td>
<td>73.0</td>
<td>61.0</td>
<td>61.0</td>
<td>61.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypopharynx</td>
<td>67.0</td>
<td>66.0</td>
<td>69.5</td>
<td>67.0</td>
<td>67.0</td>
<td>70.0</td>
<td>62.0</td>
<td>61.0</td>
<td>63.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other oral cavity &amp; pharynx</td>
<td>67.0</td>
<td>66.0</td>
<td>71.0</td>
<td>68.0</td>
<td>67.0</td>
<td>72.0</td>
<td>63.0</td>
<td>63.0</td>
<td>66.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Digestive System:</td>
<td>72.0</td>
<td>69.0</td>
<td>75.0</td>
<td>73.0</td>
<td>70.0</td>
<td>76.0</td>
<td>67.0</td>
<td>65.0</td>
<td>70.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Esophagus</td>
<td>69.0</td>
<td>68.0</td>
<td>74.0</td>
<td>70.0</td>
<td>68.0</td>
<td>75.0</td>
<td>64.0</td>
<td>64.0</td>
<td>66.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stomach</td>
<td>72.0</td>
<td>71.0</td>
<td>75.0</td>
<td>73.0</td>
<td>71.0</td>
<td>76.0</td>
<td>70.0</td>
<td>68.0</td>
<td>73.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Small intestine</td>
<td>72.0</td>
<td>70.0</td>
<td>74.0</td>
<td>73.0</td>
<td>71.0</td>
<td>75.0</td>
<td>65.0</td>
<td>63.0</td>
<td>67.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colon &amp; Rectum</td>
<td>74.0</td>
<td>71.0</td>
<td>77.0</td>
<td>75.0</td>
<td>72.0</td>
<td>78.0</td>
<td>68.0</td>
<td>66.0</td>
<td>71.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anus, anal canal &amp; anorectum</td>
<td>64.0</td>
<td>62.0</td>
<td>66.0</td>
<td>65.0</td>
<td>63.0</td>
<td>66.0</td>
<td>57.0</td>
<td>54.0</td>
<td>61.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver &amp; intrahepatic bile duct</td>
<td>67.0</td>
<td>64.0</td>
<td>74.0</td>
<td>69.0</td>
<td>66.0</td>
<td>74.0</td>
<td>61.0</td>
<td>60.0</td>
<td>67.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gallbladder</td>
<td>74.0</td>
<td>73.0</td>
<td>74.0</td>
<td>74.0</td>
<td>73.0</td>
<td>75.0</td>
<td>69.0</td>
<td>70.0</td>
<td>68.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other biliary</td>
<td>76.0</td>
<td>74.0</td>
<td>78.0</td>
<td>77.0</td>
<td>75.0</td>
<td>78.0</td>
<td>71.0</td>
<td>70.0</td>
<td>73.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pancreas</td>
<td>73.0</td>
<td>70.0</td>
<td>75.0</td>
<td>73.0</td>
<td>71.0</td>
<td>76.0</td>
<td>69.0</td>
<td>66.0</td>
<td>72.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retroperitoneum</td>
<td>71.0</td>
<td>70.0</td>
<td>71.0</td>
<td>72.0</td>
<td>71.0</td>
<td>73.0</td>
<td>64.0</td>
<td>64.0</td>
<td>65.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peritoneum, omentum &amp; mesentery</td>
<td>72.0</td>
<td>68.0</td>
<td>72.0</td>
<td>72.0</td>
<td>68.5</td>
<td>73.0</td>
<td>68.0</td>
<td>64.0</td>
<td>69.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other digestive system</td>
<td>75.0</td>
<td>73.0</td>
<td>78.0</td>
<td>76.0</td>
<td>74.0</td>
<td>79.0</td>
<td>69.0</td>
<td>65.0</td>
<td>74.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory System:</td>
<td>72.0</td>
<td>71.0</td>
<td>72.0</td>
<td>72.0</td>
<td>71.0</td>
<td>73.0</td>
<td>67.0</td>
<td>67.0</td>
<td>69.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nose, nasal cavity &amp; middle ear</td>
<td>69.0</td>
<td>66.0</td>
<td>74.0</td>
<td>71.0</td>
<td>67.0</td>
<td>76.0</td>
<td>63.0</td>
<td>62.0</td>
<td>66.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Larynx</td>
<td>68.0</td>
<td>68.0</td>
<td>70.0</td>
<td>69.0</td>
<td>68.0</td>
<td>71.0</td>
<td>65.0</td>
<td>65.0</td>
<td>65.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
<td>72.0</td>
<td>71.0</td>
<td>72.0</td>
<td>72.0</td>
<td>72.0</td>
<td>73.0</td>
<td>68.0</td>
<td>67.0</td>
<td>69.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pleura</td>
<td>75.5</td>
<td>76.0</td>
<td>75.0</td>
<td>76.0</td>
<td>76.0</td>
<td>75.0</td>
<td>70.0</td>
<td>68.0</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trachea &amp; other respiratory organs</td>
<td>69.0</td>
<td>66.0</td>
<td>74.0</td>
<td>70.0</td>
<td>66.0</td>
<td>74.0</td>
<td>60.0</td>
<td>61.0</td>
<td>57.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bones &amp; joints</td>
<td>59.0</td>
<td>57.0</td>
<td>63.0</td>
<td>61.0</td>
<td>58.0</td>
<td>65.0</td>
<td>52.0</td>
<td>50.0</td>
<td>56.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soft tissue (including heart)</td>
<td>65.0</td>
<td>65.0</td>
<td>65.0</td>
<td>66.0</td>
<td>66.0</td>
<td>67.0</td>
<td>57.0</td>
<td>55.0</td>
<td>59.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin (excl. basal &amp; squamous):</td>
<td>71.0</td>
<td>70.0</td>
<td>72.0</td>
<td>71.0</td>
<td>71.0</td>
<td>72.0</td>
<td>63.0</td>
<td>61.0</td>
<td>69.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Melanoma of the skin</td>
<td>69.0</td>
<td>69.0</td>
<td>69.0</td>
<td>69.0</td>
<td>69.0</td>
<td>69.0</td>
<td>68.0</td>
<td>65.0</td>
<td>70.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other non-epithelial skin</td>
<td>77.0</td>
<td>75.0</td>
<td>81.0</td>
<td>78.0</td>
<td>76.0</td>
<td>82.0</td>
<td>60.0</td>
<td>59.0</td>
<td>66.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast</td>
<td>68.0</td>
<td>71.0</td>
<td>68.0</td>
<td>69.0</td>
<td>72.0</td>
<td>69.0</td>
<td>62.0</td>
<td>65.0</td>
<td>61.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*a US Mortality Files, National Center for Health Statistics, Centers for Disease Control and Prevention.
- Statistic could not be calculated. Less than 16 deaths occurred during the time interval.
<table>
<thead>
<tr>
<th>Site</th>
<th>All Races</th>
<th>Whites</th>
<th>Blacks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Males</td>
<td>Females</td>
</tr>
<tr>
<td>Female Genital System:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cervix uteri</td>
<td>69.0</td>
<td>-</td>
<td>69.0</td>
</tr>
<tr>
<td>Corpus uteri</td>
<td>70.0</td>
<td>-</td>
<td>70.0</td>
</tr>
<tr>
<td>Uterus, NOS</td>
<td>71.0</td>
<td>- 71.0</td>
<td>72.0</td>
</tr>
<tr>
<td>Ovary</td>
<td>71.0</td>
<td>- 71.0</td>
<td>71.0</td>
</tr>
<tr>
<td>Vagina</td>
<td>76.0</td>
<td>- 76.0</td>
<td>78.0</td>
</tr>
<tr>
<td>Vagina</td>
<td>78.0</td>
<td>- 78.0</td>
<td>79.0</td>
</tr>
<tr>
<td>Other female genital system</td>
<td>70.0</td>
<td>- 70.0</td>
<td>71.0</td>
</tr>
<tr>
<td>Male Genital System:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prostate</td>
<td>80.0</td>
<td>80.0</td>
<td>- 81.0</td>
</tr>
<tr>
<td>Testis</td>
<td>41.0</td>
<td>41.0</td>
<td>41.0</td>
</tr>
<tr>
<td>Penis</td>
<td>70.0</td>
<td>70.0</td>
<td>70.0</td>
</tr>
<tr>
<td>Other male genital system</td>
<td>74.0</td>
<td>74.0</td>
<td>75.0</td>
</tr>
<tr>
<td>Urinary System:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>76.0</td>
<td>74.0</td>
<td>78.0</td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>79.0</td>
<td>78.0</td>
<td>80.0</td>
</tr>
<tr>
<td>Ureter</td>
<td>78.0</td>
<td>77.0</td>
<td>79.0</td>
</tr>
<tr>
<td>Other urinary system</td>
<td>77.0</td>
<td>77.0</td>
<td>78.0</td>
</tr>
<tr>
<td>Eye &amp; Orbit</td>
<td>69.0</td>
<td>67.0</td>
<td>72.0</td>
</tr>
<tr>
<td>Brain &amp; Nervous System</td>
<td>64.0</td>
<td>63.0</td>
<td>66.0</td>
</tr>
<tr>
<td>Endocrine System:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thyroid</td>
<td>73.0</td>
<td>71.0</td>
<td>76.0</td>
</tr>
<tr>
<td>Other endocrine &amp; thymus</td>
<td>58.0</td>
<td>57.0</td>
<td>59.0</td>
</tr>
<tr>
<td>Lymphoma:</td>
<td>75.0</td>
<td>73.0</td>
<td>78.0</td>
</tr>
<tr>
<td>Hodgkin lymphoma</td>
<td>65.0</td>
<td>62.0</td>
<td>68.0</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>76.0</td>
<td>73.0</td>
<td>78.0</td>
</tr>
<tr>
<td>Myeloma</td>
<td>75.0</td>
<td>74.0</td>
<td>76.0</td>
</tr>
<tr>
<td>Leukemia:</td>
<td>75.0</td>
<td>74.0</td>
<td>76.0</td>
</tr>
<tr>
<td>Acute lymphocytic</td>
<td>53.0</td>
<td>50.0</td>
<td>56.0</td>
</tr>
<tr>
<td>Chronic lymphocytic</td>
<td>80.0</td>
<td>78.0</td>
<td>83.0</td>
</tr>
<tr>
<td>Other lymphocytic</td>
<td>78.0</td>
<td>76.0</td>
<td>81.0</td>
</tr>
<tr>
<td>Acute myeloid</td>
<td>73.0</td>
<td>72.0</td>
<td>73.0</td>
</tr>
<tr>
<td>Chronic myeloid</td>
<td>76.0</td>
<td>73.0</td>
<td>79.0</td>
</tr>
<tr>
<td>Other myeloid &amp; monocytic</td>
<td>76.0</td>
<td>76.0</td>
<td>76.0</td>
</tr>
<tr>
<td>Other leukemia</td>
<td>77.0</td>
<td>76.0</td>
<td>79.0</td>
</tr>
<tr>
<td>Ill-defined &amp; unspecified</td>
<td>74.0</td>
<td>72.0</td>
<td>76.0</td>
</tr>
</tbody>
</table>

*US Mortality Files, National Center for Health Statistics, Centers for Disease Control and Prevention.
- Statistic could not be calculated. Less than 16 deaths occurred during the time interval.*
### Table 1.15

<table>
<thead>
<tr>
<th>Site</th>
<th>All Races</th>
<th>Whites</th>
<th>Blacks</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Percent ( 95% C.I. )</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All Sites</td>
<td>40.37 (40.28, 40.46)</td>
<td>40.55 (40.46, 40.65)</td>
<td>37.63 (37.37, 37.89)</td>
</tr>
<tr>
<td><strong>Percent Invasive and In Situ</strong></td>
<td>42.73 (42.64, 42.82)</td>
<td>42.91 (42.81, 43.01)</td>
<td>38.95 (38.69, 39.22)</td>
</tr>
<tr>
<td>Oral Cavity and Pharynx</td>
<td>1.10 (1.09, 1.11)</td>
<td>1.15 (1.13, 1.16)</td>
<td>0.80 (0.76, 0.83)</td>
</tr>
<tr>
<td>Esophagus</td>
<td>0.50 (0.50, 0.51)</td>
<td>0.53 (0.52, 0.54)</td>
<td>0.46 (0.42, 0.48)</td>
</tr>
<tr>
<td>Stomach</td>
<td>0.87 (0.85, 0.88)</td>
<td>0.76 (0.75, 0.78)</td>
<td>1.10 (1.06, 1.15)</td>
</tr>
<tr>
<td>Colon and Rectum</td>
<td>4.66 (4.63, 4.69)</td>
<td>4.56 (4.53, 4.59)</td>
<td>4.85 (4.75, 4.94)</td>
</tr>
<tr>
<td><strong>Percent Invasive and In Situ</strong></td>
<td>4.83 (4.80, 4.86)</td>
<td>4.72 (4.68, 4.75)</td>
<td>5.07 (4.97, 5.17)</td>
</tr>
<tr>
<td>Liver and Intrahepatic Bile Duct</td>
<td>0.89 (0.88, 0.90)</td>
<td>0.79 (0.77, 0.80)</td>
<td>0.91 (0.88, 0.95)</td>
</tr>
<tr>
<td>Pancreas</td>
<td>1.50 (1.49, 1.52)</td>
<td>1.49 (1.47, 1.51)</td>
<td>1.59 (1.54, 1.65)</td>
</tr>
<tr>
<td>Larynx</td>
<td>0.35 (0.35, 0.36)</td>
<td>0.36 (0.35, 0.37)</td>
<td>0.44 (0.41, 0.47)</td>
</tr>
<tr>
<td><strong>Percent Invasive and In Situ</strong></td>
<td>0.38 (0.37, 0.39)</td>
<td>0.38 (0.38, 0.39)</td>
<td>0.47 (0.44, 0.50)</td>
</tr>
<tr>
<td>Lung and Bronchus</td>
<td>6.75 (6.71, 6.79)</td>
<td>6.92 (6.88, 6.96)</td>
<td>6.47 (6.36, 6.58)</td>
</tr>
<tr>
<td>Melanoma of the Skin</td>
<td>2.05 (2.03, 2.07)</td>
<td>2.39 (2.36, 2.41)</td>
<td>0.09 (0.08, 0.11)</td>
</tr>
<tr>
<td>Invasive and In Situ</td>
<td>3.44 (3.42, 3.47)</td>
<td>3.80 (3.87, 3.93)</td>
<td>0.12 (0.11, 0.14)</td>
</tr>
<tr>
<td><strong>Percent Invasive and In Situ</strong></td>
<td>6.38 (6.35, 6.42)</td>
<td>6.50 (6.47, 6.54)</td>
<td>5.88 (5.79, 5.98)</td>
</tr>
<tr>
<td>Urinary Bladder (Invasive and In Situ)</td>
<td>7.62 (7.58, 7.65)</td>
<td>7.73 (7.69, 7.77)</td>
<td>7.05 (6.94, 7.15)</td>
</tr>
<tr>
<td>Kidney and Renal Pelvis</td>
<td>1.60 (1.59, 1.62)</td>
<td>1.65 (1.63, 1.67)</td>
<td>1.60 (1.55, 1.65)</td>
</tr>
<tr>
<td><strong>Brain and Other Nervous System</strong></td>
<td>0.62 (0.61, 0.63)</td>
<td>0.68 (0.67, 0.69)</td>
<td>0.35 (0.32, 0.37)</td>
</tr>
<tr>
<td>Thyroid</td>
<td>1.13 (1.11, 1.14)</td>
<td>1.18 (1.17, 1.20)</td>
<td>0.64 (0.62, 0.67)</td>
</tr>
<tr>
<td>Hodgkin Lymphoma</td>
<td>0.22 (0.22, 0.23)</td>
<td>0.24 (0.23, 0.24)</td>
<td>0.19 (0.18, 0.21)</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>2.12 (2.11, 2.14)</td>
<td>2.22 (2.20, 2.25)</td>
<td>1.28 (1.24, 1.33)</td>
</tr>
<tr>
<td>Myeloma</td>
<td>0.72 (0.71, 0.73)</td>
<td>0.66 (0.65, 0.67)</td>
<td>1.21 (1.17, 1.26)</td>
</tr>
<tr>
<td>Leukemia</td>
<td>1.43 (1.42, 1.45)</td>
<td>1.50 (1.48, 1.51)</td>
<td>0.96 (0.92, 1.01)</td>
</tr>
<tr>
<td><strong>Acute Lymphocytic Leukemia</strong></td>
<td>0.13 (0.13, 0.14)</td>
<td>0.14 (0.14, 0.15)</td>
<td>0.07 (0.07, 0.08)</td>
</tr>
<tr>
<td>Chronic Lymphocytic Leukemia</td>
<td>0.54 (0.53, 0.55)</td>
<td>0.57 (0.56, 0.58)</td>
<td>0.32 (0.29, 0.35)</td>
</tr>
<tr>
<td><strong>Acute Myeloid Leukemia</strong></td>
<td>0.43 (0.42, 0.44)</td>
<td>0.45 (0.44, 0.46)</td>
<td>0.31 (0.29, 0.34)</td>
</tr>
<tr>
<td>Chronic Myeloid Leukemia</td>
<td>0.18 (0.18, 0.19)</td>
<td>0.18 (0.18, 0.19)</td>
<td>0.14 (0.13, 0.16)</td>
</tr>
<tr>
<td>Kaposi Sarcoma</td>
<td>0.05 (0.04, 0.05)</td>
<td>0.04 (0.04, 0.04)</td>
<td>0.08 (0.07, 0.09)</td>
</tr>
<tr>
<td>Mesothehlioma</td>
<td>0.12 (0.12, 0.13)</td>
<td>0.14 (0.13, 0.15)</td>
<td>0.06 (0.05, 0.07)</td>
</tr>
</tbody>
</table>
Table 1.15 - continued

<table>
<thead>
<tr>
<th>Site</th>
<th>Asian/Pacific Islanders</th>
<th>American Indian/Alaska Natives</th>
<th>Hispanic*</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Sites</td>
<td>34.75 (34.40, 35.11)</td>
<td>29.15 (27.99, 30.41)</td>
<td>37.15 (36.83, 37.47)</td>
</tr>
<tr>
<td>Invasive and In Situ</td>
<td>36.13 (35.77, 36.48)</td>
<td>29.95 (28.77, 31.21)</td>
<td>38.36 (38.04, 38.69)</td>
</tr>
<tr>
<td>Oral Cavity and Pharynx</td>
<td>0.88 (0.83, 0.93)</td>
<td>0.80 (0.75, 0.85)</td>
<td>0.81 (0.76, 0.86)</td>
</tr>
<tr>
<td>Esophagus</td>
<td>0.34 (0.30, 0.39)</td>
<td>0.32 (0.21, 0.56)</td>
<td>0.38 (0.34, 0.42)</td>
</tr>
<tr>
<td>Stomach</td>
<td>1.78 (1.69, 1.87)</td>
<td>1.07 (0.86, 1.40)</td>
<td>1.49 (1.43, 1.57)</td>
</tr>
<tr>
<td>Colon and Rectum</td>
<td>4.99 (4.85, 5.14)</td>
<td>4.23 (3.79, 4.77)</td>
<td>4.56 (4.44, 4.68)</td>
</tr>
<tr>
<td>Invasive and In Situ</td>
<td>5.17 (5.03, 5.31)</td>
<td>4.33 (3.89, 4.88)</td>
<td>4.70 (4.58, 4.82)</td>
</tr>
<tr>
<td>Liver and Intrahepatic Bile Duct</td>
<td>1.92 (1.84, 2.01)</td>
<td>1.47 (1.24, 1.81)</td>
<td>1.59 (1.53, 1.66)</td>
</tr>
<tr>
<td>Pancreas</td>
<td>1.58 (1.50, 1.67)</td>
<td>1.23 (0.99, 1.58)</td>
<td>1.64 (1.57, 1.72)</td>
</tr>
<tr>
<td>Larynx</td>
<td>0.18 (0.16, 0.21)</td>
<td>0.25 (0.16, 0.48)</td>
<td>0.30 (0.27, 0.33)</td>
</tr>
<tr>
<td>Invasive and In Situ</td>
<td>0.19 (0.17, 0.22)</td>
<td>0.26 (0.17, 0.49)</td>
<td>0.31 (0.29, 0.35)</td>
</tr>
<tr>
<td>Lung and Bronchue</td>
<td>5.55 (5.41, 5.70)</td>
<td>4.46 (4.00, 5.01)</td>
<td>4.28 (4.17, 4.40)</td>
</tr>
<tr>
<td>Melanoma of the Skin</td>
<td>0.18 (0.15, 0.22)</td>
<td>0.38 (0.28, 0.61)</td>
<td>0.49 (0.46, 0.54)</td>
</tr>
<tr>
<td>Invasive and In Situ</td>
<td>0.24 (0.21, 0.28)</td>
<td>0.59 (0.45, 0.85)</td>
<td>0.78 (0.73, 0.83)</td>
</tr>
<tr>
<td>Breast</td>
<td>5.38 (5.27, 5.50)</td>
<td>4.06 (3.68, 4.54)</td>
<td>5.12 (5.01, 5.23)</td>
</tr>
<tr>
<td>Invasive and In Situ</td>
<td>6.67 (6.55, 6.80)</td>
<td>4.60 (4.20, 5.09)</td>
<td>5.99 (5.88, 6.10)</td>
</tr>
<tr>
<td>Urinary Bladder (Invasive and In Situ)</td>
<td>1.40 (1.33, 1.49)</td>
<td>0.93 (0.71, 1.28)</td>
<td>1.64 (1.56, 1.72)</td>
</tr>
<tr>
<td>Kidney and Renal Pelvis</td>
<td>1.03 (0.97, 1.09)</td>
<td>1.16 (1.13, 1.22)</td>
<td>1.75 (1.69, 1.82)</td>
</tr>
<tr>
<td>Brain and Other Nervous System</td>
<td>0.39 (0.36, 0.43)</td>
<td>0.30 (0.18, 0.57)</td>
<td>0.54 (0.51, 0.58)</td>
</tr>
<tr>
<td>Thyroid</td>
<td>1.21 (1.16, 1.27)</td>
<td>0.75 (0.59, 1.04)</td>
<td>1.04 (1.01, 1.09)</td>
</tr>
<tr>
<td>Hodgkin Lymphoma</td>
<td>0.12 (0.10, 0.14)</td>
<td>0.09 (0.05, 0.20)</td>
<td>0.21 (0.20, 0.24)</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>1.83 (1.75, 1.92)</td>
<td>1.33 (1.10, 1.68)</td>
<td>2.23 (2.16, 2.31)</td>
</tr>
<tr>
<td>Myeloma</td>
<td>0.54 (0.50, 0.59)</td>
<td>0.44 (0.31, 0.71)</td>
<td>0.76 (0.72, 0.81)</td>
</tr>
<tr>
<td>Leukemia</td>
<td>0.96 (0.90, 1.02)</td>
<td>0.78 (0.60, 1.07)</td>
<td>1.21 (1.15, 1.27)</td>
</tr>
<tr>
<td>Acute Lymphocytic Leukemia</td>
<td>0.10 (0.09, 0.12)</td>
<td>0.09 (0.06, 0.20)</td>
<td>0.19 (0.18, 0.21)</td>
</tr>
<tr>
<td>Chronic Lymphocytic Leukemia</td>
<td>0.17 (0.14, 0.20)</td>
<td>0.18 (0.10, 0.33)</td>
<td>0.30 (0.27, 0.33)</td>
</tr>
<tr>
<td>Acute Myeloid Leukemia</td>
<td>0.43 (0.39, 0.47)</td>
<td>0.26 (0.14, 0.51)</td>
<td>0.41 (0.38, 0.45)</td>
</tr>
<tr>
<td>Chronic Myeloid Leukemia</td>
<td>0.15 (0.13, 0.18)</td>
<td>0.10 (0.06, 0.31)</td>
<td>0.18 (0.15, 0.21)</td>
</tr>
<tr>
<td>Kaposi Sarcoma</td>
<td>0.02 (0.01, 0.03)</td>
<td>0.02 (0.00, 0.04)</td>
<td>0.09 (0.07, 0.11)</td>
</tr>
<tr>
<td>Mesothelioma</td>
<td>0.06 (0.04, 0.08)</td>
<td>0.06 (0.01, 0.29)</td>
<td>0.11 (0.10, 0.14)</td>
</tr>
</tbody>
</table>
### Table 1.16

**Lifetime Risk (Percent) of Being Diagnosed with Cancer by Site and Race/Ethnicity**

**Males, 18 SEER Areas, 2009-2011**

<table>
<thead>
<tr>
<th>Site</th>
<th>All Races</th>
<th>Whites</th>
<th>Blacks</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Sites</td>
<td>43.31 (43.17, 43.44)</td>
<td>42.90 (42.75, 43.04)</td>
<td>41.63 (41.22, 42.04)</td>
</tr>
<tr>
<td>Invasive and In Situ</td>
<td>44.76 (44.63, 44.90)</td>
<td>44.34 (44.19, 44.49)</td>
<td>41.96 (41.55, 42.37)</td>
</tr>
<tr>
<td>Oral Cavity and Pharynx</td>
<td>1.55 (1.52, 1.57)</td>
<td>1.61 (1.58, 1.63)</td>
<td>1.15 (1.09, 1.22)</td>
</tr>
<tr>
<td>Esophagus</td>
<td>0.80 (0.78, 0.82)</td>
<td>0.85 (0.83, 0.87)</td>
<td>0.63 (0.59, 0.69)</td>
</tr>
<tr>
<td>Stomach</td>
<td>1.08 (1.06, 1.11)</td>
<td>0.98 (0.96, 1.01)</td>
<td>1.23 (1.16, 1.31)</td>
</tr>
<tr>
<td>Colon and Rectum</td>
<td>4.84 (4.80, 4.89)</td>
<td>4.73 (4.69, 4.78)</td>
<td>4.93 (4.79, 5.07)</td>
</tr>
<tr>
<td>Invasive and In Situ</td>
<td>5.03 (4.99, 5.08)</td>
<td>4.91 (4.86, 4.96)</td>
<td>5.17 (5.03, 5.32)</td>
</tr>
<tr>
<td>Liver and Intrahepatic Bile Duct</td>
<td>1.27 (1.25, 1.29)</td>
<td>1.13 (1.10, 1.15)</td>
<td>1.36 (1.30, 1.43)</td>
</tr>
<tr>
<td>Pancreas</td>
<td>1.52 (1.50, 1.55)</td>
<td>1.52 (1.49, 1.55)</td>
<td>1.51 (1.43, 1.59)</td>
</tr>
<tr>
<td>Larynx</td>
<td>0.59 (0.58, 0.61)</td>
<td>0.59 (0.58, 0.61)</td>
<td>0.75 (0.70, 0.81)</td>
</tr>
<tr>
<td>Invasive and In Situ</td>
<td>0.64 (0.62, 0.65)</td>
<td>0.64 (0.62, 0.65)</td>
<td>0.80 (0.75, 0.86)</td>
</tr>
<tr>
<td>Lung and Bronchus</td>
<td>7.43 (7.38, 7.49)</td>
<td>7.46 (7.40, 7.52)</td>
<td>7.78 (7.60, 7.96)</td>
</tr>
<tr>
<td>Melanoma of the Skin</td>
<td>2.56 (2.53, 2.59)</td>
<td>2.95 (2.91, 2.99)</td>
<td>0.08 (0.06, 0.11)</td>
</tr>
<tr>
<td>Invasive and In Situ</td>
<td>4.26 (4.22, 4.30)</td>
<td>4.77 (4.72, 4.82)</td>
<td>0.11 (0.09, 0.14)</td>
</tr>
<tr>
<td>Breast</td>
<td>0.13 (0.12, 0.14)</td>
<td>0.13 (0.12, 0.14)</td>
<td>0.15 (0.12, 0.18)</td>
</tr>
<tr>
<td>Invasive and In Situ</td>
<td>0.14 (0.14, 0.15)</td>
<td>0.14 (0.13, 0.15)</td>
<td>0.17 (0.14, 0.20)</td>
</tr>
<tr>
<td>Prostate</td>
<td>18.02 (14.95, 15.10)</td>
<td>14.16 (14.08, 14.24)</td>
<td>19.08 (18.82, 19.35)</td>
</tr>
<tr>
<td>Testis</td>
<td>0.38 (0.37, 0.39)</td>
<td>0.46 (0.45, 0.47)</td>
<td>0.09 (0.08, 0.11)</td>
</tr>
<tr>
<td>Urinary Bladder (Invasive and In Situ)</td>
<td>3.85 (3.79, 3.87)</td>
<td>4.15 (4.10, 4.19)</td>
<td>1.79 (1.70, 1.89)</td>
</tr>
<tr>
<td>Kidney and Renal Pelvis</td>
<td>2.04 (2.02, 2.07)</td>
<td>2.10 (2.07, 2.13)</td>
<td>1.94 (1.86, 2.03)</td>
</tr>
<tr>
<td>Brain and Other Nervous System</td>
<td>0.69 (0.67, 0.71)</td>
<td>0.76 (0.74, 0.78)</td>
<td>0.36 (0.33, 0.40)</td>
</tr>
<tr>
<td>Thyroid</td>
<td>0.57 (0.56, 0.59)</td>
<td>0.61 (0.60, 0.63)</td>
<td>0.26 (0.23, 0.29)</td>
</tr>
<tr>
<td>Hodgkin Lymphoma</td>
<td>0.24 (0.23, 0.25)</td>
<td>0.26 (0.25, 0.27)</td>
<td>0.21 (0.19, 0.24)</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>2.36 (2.33, 2.39)</td>
<td>2.46 (2.43, 2.50)</td>
<td>1.41 (1.34, 1.49)</td>
</tr>
<tr>
<td>Myeloma</td>
<td>0.83 (0.81, 0.85)</td>
<td>0.78 (0.76, 0.80)</td>
<td>1.25 (1.18, 1.33)</td>
</tr>
<tr>
<td>Leukemia</td>
<td>1.70 (1.67, 1.72)</td>
<td>1.77 (1.74, 1.80)</td>
<td>1.07 (1.00, 1.14)</td>
</tr>
<tr>
<td>Acute Lymphocytic Leukemia</td>
<td>0.14 (0.14, 0.15)</td>
<td>0.16 (0.15, 0.17)</td>
<td>0.08 (0.07, 0.10)</td>
</tr>
<tr>
<td>Chronic Lymphocytic Leukemia</td>
<td>0.66 (0.65, 0.68)</td>
<td>0.70 (0.68, 0.71)</td>
<td>0.37 (0.33, 0.42)</td>
</tr>
<tr>
<td>Acute Myeloid Leukemia</td>
<td>0.49 (0.48, 0.51)</td>
<td>0.51 (0.50, 0.53)</td>
<td>0.34 (0.30, 0.38)</td>
</tr>
<tr>
<td>Chronic Myeloid Leukemia</td>
<td>0.22 (0.21, 0.23)</td>
<td>0.22 (0.21, 0.23)</td>
<td>0.15 (0.13, 0.18)</td>
</tr>
<tr>
<td>Kaposi Sarcoma</td>
<td>0.08 (0.07, 0.08)</td>
<td>0.07 (0.06, 0.07)</td>
<td>0.14 (0.12, 0.16)</td>
</tr>
<tr>
<td>Mesothelioma</td>
<td>0.21 (0.20, 0.22)</td>
<td>0.23 (0.22, 0.24)</td>
<td>0.10 (0.08, 0.13)</td>
</tr>
</tbody>
</table>

**Note:** Invasive cancer only unless specified otherwise.

A percent or confidence interval value of 0.00 represents a value that is below 0.005.

Source: SEER 18 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, Alaska Native Registry, Rural Georgia, California excluding SF/SJM/LA, Kentucky, Louisiana, New Jersey, and Georgia excluding ATL/RG).

Note: Invasive cancer only unless specified otherwise.
Table 1.16 - continued

Lifetime Risk (Percent) of Being Diagnosed with Cancer by Site and Race/Ethnicity

Males, 18 SEER Areas, 2009-2011

<table>
<thead>
<tr>
<th>Site</th>
<th>Asian/Pacific Islanders</th>
<th>American Indian/Alaska Natives</th>
<th>Hispanics b</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Percent (95% C.I.)</td>
<td>Percent (95% C.I.)</td>
<td>Percent (95% C.I.)</td>
</tr>
<tr>
<td>All Sites</td>
<td>36.92 (36.39, 37.47)</td>
<td>29.98 (28.29, 31.89)</td>
<td>40.34 (39.85, 40.85)</td>
</tr>
<tr>
<td>Invasive and In Situ</td>
<td>37.26 (36.72, 37.81)</td>
<td>30.25 (28.55, 32.16)</td>
<td>40.78 (40.28, 41.29)</td>
</tr>
<tr>
<td>Oral Cavity and Pharynx</td>
<td>1.25 (1.16, 1.36)</td>
<td>1.24 (1.04, 1.44)</td>
<td>1.12 (1.04, 1.21)</td>
</tr>
<tr>
<td>Esophagus</td>
<td>0.53 (0.47, 0.62)</td>
<td>0.49 (0.30, 1.03)</td>
<td>0.61 (0.56, 0.68)</td>
</tr>
<tr>
<td>Stomach</td>
<td>2.11 (1.97, 2.26)</td>
<td>1.36 (1.09, 2.01)</td>
<td>1.80 (1.70, 1.93)</td>
</tr>
<tr>
<td>Colon and Rectum</td>
<td>5.33 (5.13, 5.54)</td>
<td>4.62 (3.96, 5.52)</td>
<td>4.92 (4.75, 5.11)</td>
</tr>
<tr>
<td>Invasive and In Situ</td>
<td>5.53 (5.32, 5.74)</td>
<td>4.73 (4.07, 5.64)</td>
<td>5.08 (4.90, 5.26)</td>
</tr>
<tr>
<td>Liver and Intrahepatic Bile Duct</td>
<td>2.66 (2.53, 2.80)</td>
<td>2.09 (1.69, 2.76)</td>
<td>2.21 (2.11, 2.33)</td>
</tr>
<tr>
<td>Pancreas</td>
<td>1.56 (1.45, 1.69)</td>
<td>1.28 (0.98, 1.87)</td>
<td>1.55 (1.45, 1.66)</td>
</tr>
<tr>
<td>Larynx</td>
<td>0.35 (0.30, 0.41)</td>
<td>0.40 (0.25, 0.90)</td>
<td>0.56 (0.51, 0.64)</td>
</tr>
<tr>
<td>Invasive and In Situ</td>
<td>0.37 (0.32, 0.44)</td>
<td>0.41 (0.25, 0.91)</td>
<td>0.59 (0.54, 0.66)</td>
</tr>
<tr>
<td>Lung and Bronchus</td>
<td>6.83 (6.59, 7.09)</td>
<td>4.89 (4.21, 5.81)</td>
<td>4.96 (4.77, 5.17)</td>
</tr>
<tr>
<td>Melanoma of the Skin</td>
<td>0.21 (0.17, 0.28)</td>
<td>0.39 (0.24, 0.89)</td>
<td>0.49 (0.44, 0.55)</td>
</tr>
<tr>
<td>Invasive and In Situ</td>
<td>0.29 (0.24, 0.36)</td>
<td>0.57 (0.38, 1.08)</td>
<td>0.78 (0.71, 0.87)</td>
</tr>
<tr>
<td>Breast</td>
<td>0.09 (0.07, 0.14)</td>
<td>0.02 (0.00, 0.52)</td>
<td>0.07 (0.06, 0.11)</td>
</tr>
<tr>
<td>Invasive and In Situ</td>
<td>0.10 (0.07, 0.15)</td>
<td>0.03 (0.01, 0.53)</td>
<td>0.08 (0.06, 0.12)</td>
</tr>
<tr>
<td>Prostate</td>
<td>10.10 (9.84, 10.37)</td>
<td>7.01 (6.25, 8.01)</td>
<td>14.03 (13.76, 14.31)</td>
</tr>
<tr>
<td>Testis</td>
<td>0.14 (0.12, 0.18)</td>
<td>0.34 (0.25, 0.79)</td>
<td>0.35 (0.33, 0.39)</td>
</tr>
<tr>
<td>Urinary Bladder (Invasive and In Situ)</td>
<td>2.23 (2.09, 2.39)</td>
<td>1.64 (1.18, 2.38)</td>
<td>2.65 (2.50, 2.81)</td>
</tr>
<tr>
<td>Kidney and Renal Pelvis</td>
<td>1.37 (1.27, 1.47)</td>
<td>2.43 (2.03, 3.08)</td>
<td>2.19 (2.08, 2.30)</td>
</tr>
<tr>
<td>Brain and Other Nervous System</td>
<td>0.95 (0.89, 0.52)</td>
<td>0.28 (0.15, 0.75)</td>
<td>0.55 (0.51, 0.61)</td>
</tr>
<tr>
<td>Thyroid</td>
<td>0.58 (0.53, 0.65)</td>
<td>0.35 (0.23, 0.82)</td>
<td>0.46 (0.42, 0.51)</td>
</tr>
<tr>
<td>Hodgkin Lymphoma</td>
<td>0.13 (0.11, 0.17)</td>
<td>0.09 (0.04, 0.57)</td>
<td>0.24 (0.21, 0.29)</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>2.06 (1.93, 2.19)</td>
<td>1.36 (1.06, 1.94)</td>
<td>2.39 (2.28, 2.52)</td>
</tr>
<tr>
<td>Myeloma</td>
<td>0.63 (0.56, 0.71)</td>
<td>0.48 (0.28, 1.02)</td>
<td>0.88 (0.80, 0.97)</td>
</tr>
<tr>
<td>Leukemia</td>
<td>1.17 (1.08, 1.27)</td>
<td>0.84 (0.58, 1.40)</td>
<td>1.37 (1.28, 1.47)</td>
</tr>
<tr>
<td>Acute Lymphocytic Leukemia</td>
<td>0.12 (0.10, 0.16)</td>
<td>0.09 (0.04, 0.57)</td>
<td>0.19 (0.17, 0.23)</td>
</tr>
<tr>
<td>Chronic Lymphocytic Leukemia</td>
<td>0.23 (0.19, 0.29)</td>
<td>0.21 (0.08, 0.73)</td>
<td>0.35 (0.30, 0.42)</td>
</tr>
<tr>
<td>Acute Myeloid Leukemia</td>
<td>0.49 (0.44, 0.57)</td>
<td>0.22 (0.11, 0.71)</td>
<td>0.45 (0.41, 0.52)</td>
</tr>
<tr>
<td>Chronic Myeloid Leukemia</td>
<td>0.21 (0.17, 0.26)</td>
<td>0.08 (0.03, 0.57)</td>
<td>0.20 (0.17, 0.26)</td>
</tr>
<tr>
<td>Kaposi Sarcoma</td>
<td>0.04 (0.02, 0.07)</td>
<td>0.04 (0.00, 0.54)</td>
<td>0.12 (0.10, 0.16)</td>
</tr>
<tr>
<td>Mesothelioma</td>
<td>0.10 (0.07, 0.15)</td>
<td>0.08 (0.01, 0.59)</td>
<td>0.19 (0.16, 0.24)</td>
</tr>
</tbody>
</table>
Table 1.17
Lifetime Risk (Percent) of Being Diagnosed with Cancer by Site and Race/Ethnicity
Females, 18 SEER Areas, 2009-2011

<table>
<thead>
<tr>
<th>Site</th>
<th>All Races</th>
<th>Whites</th>
<th>Blacks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Percent (95% C.I.)</td>
<td>Percent (95% C.I.)</td>
<td>Percent (95% C.I.)</td>
</tr>
<tr>
<td>All Sites</td>
<td>37.81 (37.70, 37.93)</td>
<td>38.53 (38.40, 38.67)</td>
<td>34.18 (33.84, 34.53)</td>
</tr>
<tr>
<td>Invasive and In Situ</td>
<td>41.08 (40.96, 41.20)</td>
<td>41.83 (41.69, 41.97)</td>
<td>36.42 (36.08, 36.77)</td>
</tr>
<tr>
<td>Oral Cavity and Pharynx</td>
<td>0.67 (0.66, 0.69)</td>
<td>0.70 (0.68, 0.72)</td>
<td>0.48 (0.45, 0.52)</td>
</tr>
<tr>
<td>Esophagus</td>
<td>0.23 (0.22, 0.24)</td>
<td>0.23 (0.22, 0.24)</td>
<td>0.28 (0.25, 0.32)</td>
</tr>
<tr>
<td>Stomach</td>
<td>0.67 (0.65, 0.69)</td>
<td>0.56 (0.54, 0.57)</td>
<td>1.00 (0.94, 1.07)</td>
</tr>
<tr>
<td>Colon and Rectum</td>
<td>4.49 (4.45, 4.53)</td>
<td>4.40 (4.35, 4.44)</td>
<td>4.79 (4.66, 4.92)</td>
</tr>
<tr>
<td>Invasive and In Situ</td>
<td>4.64 (4.60, 4.69)</td>
<td>4.54 (4.49, 4.58)</td>
<td>4.99 (4.86, 5.12)</td>
</tr>
<tr>
<td>Liver and Intrahepatic Bile Duct</td>
<td>0.53 (0.51, 0.54)</td>
<td>0.46 (0.44, 0.47)</td>
<td>0.51 (0.47, 0.55)</td>
</tr>
<tr>
<td>Pancreas</td>
<td>1.48 (1.46, 1.51)</td>
<td>1.45 (1.43, 1.48)</td>
<td>1.66 (1.58, 1.74)</td>
</tr>
<tr>
<td>Larynx</td>
<td>0.13 (0.13, 0.14)</td>
<td>0.14 (0.13, 0.15)</td>
<td>0.17 (0.14, 0.19)</td>
</tr>
<tr>
<td>Invasive and In Situ</td>
<td>0.14 (0.13, 0.15)</td>
<td>0.15 (0.14, 0.16)</td>
<td>0.17 (0.15, 0.20)</td>
</tr>
<tr>
<td>Lung and Bronchus</td>
<td>6.17 (6.12, 6.22)</td>
<td>6.46 (6.41, 6.52)</td>
<td>5.39 (5.26, 5.53)</td>
</tr>
<tr>
<td>Melanoma of the Skin</td>
<td>1.61 (1.58, 1.63)</td>
<td>1.89 (1.86, 1.91)</td>
<td>0.10 (0.09, 0.13)</td>
</tr>
<tr>
<td>Invasive and In Situ</td>
<td>2.74 (2.71, 2.77)</td>
<td>3.13 (3.09, 3.17)</td>
<td>0.13 (0.11, 0.15)</td>
</tr>
<tr>
<td>Breast</td>
<td>12.33 (12.27, 12.40)</td>
<td>12.70 (12.63, 12.77)</td>
<td>10.99 (10.82, 11.18)</td>
</tr>
<tr>
<td>Invasive and In Situ</td>
<td>14.75 (14.68, 14.82)</td>
<td>15.13 (15.05, 15.20)</td>
<td>13.19 (13.00, 13.39)</td>
</tr>
<tr>
<td>Cervix Uteri</td>
<td>0.65 (0.63, 0.66)</td>
<td>0.64 (0.62, 0.65)</td>
<td>0.78 (0.73, 0.82)</td>
</tr>
<tr>
<td>Corpus and Uterus, NOS</td>
<td>2.73 (2.71, 2.75)</td>
<td>2.81 (2.78, 2.85)</td>
<td>2.48 (2.39, 2.57)</td>
</tr>
<tr>
<td>Invasive and In Situ</td>
<td>2.76 (2.73, 2.79)</td>
<td>2.84 (2.80, 2.87)</td>
<td>2.51 (2.42, 2.60)</td>
</tr>
<tr>
<td>Ovary</td>
<td>1.33 (1.31, 1.35)</td>
<td>1.41 (1.38, 1.43)</td>
<td>0.99 (0.93, 1.05)</td>
</tr>
<tr>
<td>Urinary Bladder (Invasive and In Situ)</td>
<td>1.14 (1.12, 1.16)</td>
<td>1.21 (1.19, 1.24)</td>
<td>0.81 (0.76, 0.87)</td>
</tr>
<tr>
<td>Kidney and Renal Pelvis</td>
<td>1.19 (1.17, 1.21)</td>
<td>1.23 (1.20, 1.25)</td>
<td>1.29 (1.23, 1.36)</td>
</tr>
<tr>
<td>Brain and Other Nervous System</td>
<td>0.55 (0.54, 0.56)</td>
<td>0.10 (0.09, 0.11)</td>
<td>0.34 (0.31, 0.37)</td>
</tr>
<tr>
<td>Thyroid</td>
<td>1.68 (1.66, 1.70)</td>
<td>1.77 (1.75, 1.80)</td>
<td>1.00 (0.95, 1.05)</td>
</tr>
<tr>
<td>Hodgkin Lymphoma</td>
<td>0.20 (0.19, 0.21)</td>
<td>0.22 (0.21, 0.23)</td>
<td>0.18 (0.16, 0.20)</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>1.91 (1.89, 1.94)</td>
<td>2.01 (1.98, 2.04)</td>
<td>1.17 (1.11, 1.23)</td>
</tr>
<tr>
<td>Myeloma</td>
<td>0.62 (0.61, 0.64)</td>
<td>0.55 (0.53, 0.57)</td>
<td>1.19 (1.12, 1.25)</td>
</tr>
<tr>
<td>Leukemia</td>
<td>1.19 (1.17, 1.22)</td>
<td>1.24 (1.22, 1.27)</td>
<td>0.87 (0.82, 0.93)</td>
</tr>
<tr>
<td>Acute Lymphocytic Leukemia</td>
<td>0.12 (0.11, 0.12)</td>
<td>0.13 (0.12, 0.14)</td>
<td>0.07 (0.06, 0.09)</td>
</tr>
<tr>
<td>Chronic Lymphocytic Leukemia</td>
<td>0.43 (0.42, 0.44)</td>
<td>0.45 (0.44, 0.47)</td>
<td>0.27 (0.24, 0.31)</td>
</tr>
<tr>
<td>Acute Myeloid Leukemia</td>
<td>0.38 (0.37, 0.39)</td>
<td>0.39 (0.38, 0.40)</td>
<td>0.29 (0.26, 0.31)</td>
</tr>
<tr>
<td>Chronic Myeloid Leukemia</td>
<td>0.15 (0.14, 0.15)</td>
<td>0.15 (0.14, 0.16)</td>
<td>0.13 (0.11, 0.16)</td>
</tr>
<tr>
<td>Kaposi Sarcoma</td>
<td>0.01 (0.01, 0.02)</td>
<td>0.01 (0.01, 0.02)</td>
<td>0.01 (0.01, 0.02)</td>
</tr>
<tr>
<td>Mesothelioma</td>
<td>0.05 (0.05, 0.06)</td>
<td>0.06 (0.05, 0.06)</td>
<td>0.03 (0.02, 0.04)</td>
</tr>
</tbody>
</table>

Note: Invasive cancer only unless specified otherwise.

* Ovary excludes borderline cases or histologies 8442, 8451, 8462, 8472, and 8473.
A percent or confidence interval value of 0.00 represents a value that is below 0.005.

Source: SEER 18 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, Alaska Native Registry, Rural Georgia, California excluding SF/SJM/LA, Kentucky, Louisiana, New Jersey, and Georgia excluding ATL/RG).

### Table 1.17 - continued

**Lifetime Risk (Percent) of Being Diagnosed with Cancer by Site and Race/Ethnicity**

**Females, 18 SEER Areas, 2009-2011**

<table>
<thead>
<tr>
<th>Site</th>
<th>Asian/Pacific Islanders</th>
<th>American Indian/Alaska Natives&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Hispanics&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Percent (95% C.I.)</td>
<td>Percent (95% C.I.)</td>
<td>Percent (95% C.I.)</td>
</tr>
<tr>
<td>All Sites</td>
<td>33.08 (32.62, 33.55)</td>
<td>28.63 (27.02, 30.41)</td>
<td>34.72 (34.30, 35.14)</td>
</tr>
<tr>
<td>Invasive and In Situ</td>
<td>35.36 (34.89, 35.84)</td>
<td>29.94 (28.32, 31.74)</td>
<td>36.68 (36.26, 37.12)</td>
</tr>
<tr>
<td>Oral Cavity and Pharynx</td>
<td>0.56 (0.50, 0.63)</td>
<td>0.40 (0.27, 0.51)</td>
<td>0.54 (0.48, 0.60)</td>
</tr>
<tr>
<td>Esophagus</td>
<td>0.18 (0.14, 0.24)</td>
<td>0.16 (0.08, 0.24)</td>
<td>0.17 (0.14, 0.21)</td>
</tr>
<tr>
<td>Stomach</td>
<td>1.50 (1.39, 1.63)</td>
<td>0.84 (0.60, 1.13)</td>
<td>1.23 (1.15, 1.33)</td>
</tr>
<tr>
<td>Colon and Rectum</td>
<td>4.86 (4.67, 5.07)</td>
<td>3.96 (3.88, 4.37)</td>
<td>4.38 (4.22, 4.55)</td>
</tr>
<tr>
<td>Liver and Intrahepatic Bile Duct</td>
<td>1.30 (1.20, 1.41)</td>
<td>0.90 (0.66, 1.19)</td>
<td>1.03 (0.96, 1.11)</td>
</tr>
<tr>
<td>Pancreas</td>
<td>1.60 (1.49, 1.72)</td>
<td>1.17 (0.83, 1.74)</td>
<td>1.71 (1.60, 1.83)</td>
</tr>
<tr>
<td>Larynx</td>
<td>0.04 (0.03, 0.07)</td>
<td>0.11 (0.04, 0.50)</td>
<td>0.07 (0.05, 0.10)</td>
</tr>
<tr>
<td>Invasive and In Situ</td>
<td>0.04 (0.03, 0.07)</td>
<td>0.12 (0.05, 0.52)</td>
<td>0.07 (0.06, 0.10)</td>
</tr>
<tr>
<td>Lung and Bronchus</td>
<td>4.50 (4.33, 4.69)</td>
<td>4.11 (3.50, 4.9)</td>
<td>3.75 (3.60, 3.90)</td>
</tr>
<tr>
<td>Melanoma of the Skin</td>
<td>0.15 (0.12, 0.20)</td>
<td>0.37 (0.24, 0.77)</td>
<td>0.50 (0.45, 0.57)</td>
</tr>
<tr>
<td>Invasive and In Situ</td>
<td>0.20 (0.17, 0.26)</td>
<td>0.61 (0.42, 1.05)</td>
<td>0.79 (0.72, 0.86)</td>
</tr>
<tr>
<td>Breast</td>
<td>9.93 (9.72, 10.15)</td>
<td>7.92 (7.18, 8.83)</td>
<td>9.76 (9.56, 9.96)</td>
</tr>
<tr>
<td>Invasive and In Situ</td>
<td>12.33 (12.11, 12.58)</td>
<td>8.97 (8.14, 9.91)</td>
<td>11.45 (11.24, 11.66)</td>
</tr>
<tr>
<td>Cervix Uteri</td>
<td>0.65 (0.59, 0.72)</td>
<td>0.60 (0.45, 1.00)</td>
<td>0.91 (0.86, 0.98)</td>
</tr>
<tr>
<td>Corpus and Uterus, NOS</td>
<td>2.16 (2.07, 2.27)</td>
<td>2.05 (1.75, 2.57)</td>
<td>2.34 (2.26, 2.44)</td>
</tr>
<tr>
<td>Invasive and In Situ</td>
<td>2.18 (2.08, 2.28)</td>
<td>2.07 (1.76, 2.59)</td>
<td>2.36 (2.27, 2.46)</td>
</tr>
<tr>
<td>Ovary&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1.03 (0.96, 1.12)</td>
<td>1.13 (0.82, 1.68)</td>
<td>1.26 (1.18, 1.34)</td>
</tr>
<tr>
<td>Urinary Bladder (Invasive and In Situ)</td>
<td>0.72 (0.64, 0.82)</td>
<td>0.32 (0.17, 0.75)</td>
<td>0.80 (0.73, 0.89)</td>
</tr>
<tr>
<td>Kidney and Renal Pelvis</td>
<td>0.74 (0.67, 0.82)</td>
<td>1.51 (1.22, 2.03)</td>
<td>1.38 (1.30, 1.46)</td>
</tr>
<tr>
<td>Brain and Other Nervous System</td>
<td>0.34 (0.30, 0.40)</td>
<td>0.31 (0.12, 0.81)</td>
<td>0.52 (0.47, 0.58)</td>
</tr>
<tr>
<td>Thymus</td>
<td>1.77 (1.69, 1.86)</td>
<td>1.15 (0.85, 1.67)</td>
<td>1.62 (1.56, 1.70)</td>
</tr>
<tr>
<td>Hodgkin Lymphoma</td>
<td>0.11 (0.09, 0.14)</td>
<td>0.10 (0.04, 0.49)</td>
<td>0.19 (0.17, 0.23)</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>1.64 (1.54, 1.75)</td>
<td>1.31 (0.97, 1.87)</td>
<td>2.10 (1.99, 2.21)</td>
</tr>
<tr>
<td>Myeloma</td>
<td>0.46 (0.41, 0.53)</td>
<td>0.41 (0.24, 0.85)</td>
<td>0.67 (0.61, 0.74)</td>
</tr>
<tr>
<td>Leukemia</td>
<td>0.78 (0.71, 0.86)</td>
<td>0.73 (0.50, 1.20)</td>
<td>1.07 (1.00, 1.15)</td>
</tr>
<tr>
<td>Acute Lymphocytic Leukemia</td>
<td>0.09 (0.07, 0.12)</td>
<td>0.10 (0.05, 0.49)</td>
<td>0.18 (0.16, 0.21)</td>
</tr>
<tr>
<td>Chronic Lymphocytic Leukemia</td>
<td>0.11 (0.09, 0.15)</td>
<td>0.16 (0.06, 0.58)</td>
<td>0.25 (0.21, 0.31)</td>
</tr>
<tr>
<td>Acute Myeloid Leukemia</td>
<td>0.37 (0.33, 0.43)</td>
<td>0.30 (0.15, 0.73)</td>
<td>0.37 (0.33, 0.43)</td>
</tr>
<tr>
<td>Chronic Myeloid Leukemia</td>
<td>0.10 (0.08, 0.14)</td>
<td>0.11 (0.06, 0.50)</td>
<td>0.15 (0.12, 0.20)</td>
</tr>
<tr>
<td>Kaposi Sarcoma</td>
<td>0.00 (0.00, 0.03)</td>
<td>0.01 (0.00, 0.42)</td>
<td>0.05 (0.03, 0.08)</td>
</tr>
<tr>
<td>Mesotheiloma</td>
<td>0.02 (0.01, 0.05)</td>
<td>0.04 (0.00, 0.45)</td>
<td>0.05 (0.04, 0.08)</td>
</tr>
</tbody>
</table>

<sup>a</sup> Underlying incidence data for American Indian/Alaska Native are based on the CHSDA (Contract Health Service Delivery Area) counties.

<sup>b</sup> Hispanic is not mutually exclusive from whites, blacks, Asian Pacific Islanders, and American Indians/Alaska Natives.

<sup>c</sup> Underlying incidence data for Hispanics are based on NHIA and exclude cases from the Alaska Native Registry.

A percent or confidence interval value of 0.00 represents a value that is below 0.005.
# Table 1.18

**Lifetime Risk (Percent) of Dying from Cancer by Site and Race/Ethnicity**

**Both Sexes, Total U.S., 2009-2011**

<table>
<thead>
<tr>
<th>Site</th>
<th>All Races</th>
<th>Whites</th>
<th>Blacks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Percent ( 95% C.I. )</td>
<td>Percent ( 95% C.I. )</td>
<td>Percent ( 95% C.I. )</td>
</tr>
<tr>
<td>All Sites</td>
<td>20.84 (20.81, 20.87)</td>
<td>20.95 (20.92, 20.98)</td>
<td>21.17 (21.08, 21.27)</td>
</tr>
<tr>
<td>Oral Cavity and Pharynx</td>
<td>0.28 (0.28, 0.29)</td>
<td>0.28 (0.28, 0.29)</td>
<td>0.28 (0.27, 0.29)</td>
</tr>
<tr>
<td>Esophagus</td>
<td>0.49 (0.48, 0.49)</td>
<td>0.51 (0.50, 0.52)</td>
<td>0.40 (0.39, 0.42)</td>
</tr>
<tr>
<td>Stomach</td>
<td>0.41 (0.40, 0.41)</td>
<td>0.36 (0.35, 0.36)</td>
<td>0.67 (0.65, 0.69)</td>
</tr>
<tr>
<td>Colon and Rectum</td>
<td>1.94 (1.93, 1.95)</td>
<td>1.90 (1.89, 1.91)</td>
<td>2.29 (2.26, 2.33)</td>
</tr>
<tr>
<td>Liver and Intrahepatic Bile Duct</td>
<td>0.68 (0.67, 0.69)</td>
<td>0.64 (0.63, 0.64)</td>
<td>0.78 (0.76, 0.80)</td>
</tr>
<tr>
<td>Pancreas</td>
<td>1.34 (1.33, 1.35)</td>
<td>1.33 (1.32, 1.34)</td>
<td>1.43 (1.40, 1.46)</td>
</tr>
<tr>
<td>Larynx</td>
<td>0.12 (0.12, 0.13)</td>
<td>0.12 (0.12, 0.12)</td>
<td>0.18 (0.17, 0.19)</td>
</tr>
<tr>
<td>Lung and Bronchus</td>
<td>5.66 (5.64, 5.68)</td>
<td>5.79 (5.77, 5.81)</td>
<td>5.21 (5.17, 5.26)</td>
</tr>
<tr>
<td>Melanoma of the Skin</td>
<td>0.32 (0.31, 0.32)</td>
<td>0.36 (0.36, 0.37)</td>
<td>0.04 (0.04, 0.05)</td>
</tr>
<tr>
<td>Breast</td>
<td>1.43 (1.42, 1.44)</td>
<td>1.41 (1.40, 1.42)</td>
<td>1.78 (1.75, 1.81)</td>
</tr>
<tr>
<td>Urinary Bladder</td>
<td>0.60 (0.60, 0.61)</td>
<td>0.63 (0.62, 0.64)</td>
<td>0.42 (0.40, 0.43)</td>
</tr>
<tr>
<td>Kidney and Renal Pelvis</td>
<td>0.47 (0.47, 0.48)</td>
<td>0.49 (0.48, 0.49)</td>
<td>0.39 (0.38, 0.41)</td>
</tr>
<tr>
<td>Brain and Other Nervous System</td>
<td>0.45 (0.45, 0.46)</td>
<td>0.49 (0.49, 0.50)</td>
<td>0.23 (0.22, 0.24)</td>
</tr>
<tr>
<td>Thyroid</td>
<td>0.06 (0.06, 0.07)</td>
<td>0.06 (0.06, 0.07)</td>
<td>0.05 (0.05, 0.06)</td>
</tr>
<tr>
<td>Hodgkin Lymphoma</td>
<td>0.04 (0.04, 0.04)</td>
<td>0.04 (0.04, 0.04)</td>
<td>0.03 (0.03, 0.03)</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>0.78 (0.77, 0.78)</td>
<td>0.82 (0.81, 0.82)</td>
<td>0.45 (0.43, 0.46)</td>
</tr>
<tr>
<td>Myeloma</td>
<td>0.42 (0.41, 0.42)</td>
<td>0.39 (0.39, 0.40)</td>
<td>0.66 (0.64, 0.68)</td>
</tr>
<tr>
<td>Leukemia</td>
<td>0.86 (0.86, 0.87)</td>
<td>0.90 (0.89, 0.91)</td>
<td>0.62 (0.60, 0.64)</td>
</tr>
<tr>
<td>Acute Lymphocytic Leukemia</td>
<td>0.04 (0.04, 0.04)</td>
<td>0.04 (0.04, 0.05)</td>
<td>0.03 (0.02, 0.03)</td>
</tr>
<tr>
<td>Chronic Lymphocytic Leukemia</td>
<td>0.19 (0.19, 0.19)</td>
<td>0.20 (0.20, 0.20)</td>
<td>0.14 (0.13, 0.15)</td>
</tr>
<tr>
<td>Acute Myeloid Leukemia</td>
<td>0.33 (0.33, 0.34)</td>
<td>0.35 (0.34, 0.35)</td>
<td>0.21 (0.20, 0.22)</td>
</tr>
<tr>
<td>Chronic Myeloid Leukemia</td>
<td>0.04 (0.04, 0.04)</td>
<td>0.04 (0.04, 0.04)</td>
<td>0.03 (0.03, 0.04)</td>
</tr>
</tbody>
</table>

Source: NCHS public use data file for the total US.

A percent or confidence interval value of 0.00 represents a value that is below 0.005.
## Table 1.18 - continued

<table>
<thead>
<tr>
<th>Site</th>
<th>Asian/Pacific Islanders Percent (95% C.I.)</th>
<th>American Indian/Alaska Natives Percent (95% C.I.)</th>
<th>Hispanics Percent (95% C.I.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Sites</td>
<td>18.69 (18.45, 18.93)</td>
<td>16.99 (16.51, 17.50)</td>
<td>17.71 (17.57, 17.86)</td>
</tr>
<tr>
<td>Oral Cavity and Pharynx</td>
<td>0.30 (0.27, 0.34)</td>
<td>0.24 (0.19, 0.33)</td>
<td>0.21 (0.19, 0.23)</td>
</tr>
<tr>
<td>Esophagus</td>
<td>0.30 (0.27, 0.34)</td>
<td>0.35 (0.28, 0.45)</td>
<td>0.35 (0.32, 0.37)</td>
</tr>
<tr>
<td>Stomach</td>
<td>1.14 (1.07, 1.21)</td>
<td>0.55 (0.46, 0.67)</td>
<td>0.79 (0.76, 0.83)</td>
</tr>
<tr>
<td>Colon and Rectum</td>
<td>2.02 (1.94, 2.12)</td>
<td>1.87 (1.70, 2.08)</td>
<td>1.89 (1.84, 1.95)</td>
</tr>
<tr>
<td>Liver and Intrahepatic Bile Duct</td>
<td>1.55 (1.48, 1.62)</td>
<td>1.00 (0.89, 1.14)</td>
<td>1.20 (1.17, 1.24)</td>
</tr>
<tr>
<td>Pancreas</td>
<td>1.40 (1.33, 1.47)</td>
<td>0.93 (0.81, 1.08)</td>
<td>1.33 (1.29, 1.37)</td>
</tr>
<tr>
<td>Larynx</td>
<td>0.07 (0.05, 0.09)</td>
<td>0.10 (0.07, 0.16)</td>
<td>0.12 (0.11, 0.14)</td>
</tr>
<tr>
<td>Lung and Bronchus</td>
<td>4.30 (4.19, 4.41)</td>
<td>4.12 (3.88, 4.38)</td>
<td>3.01 (2.95, 3.07)</td>
</tr>
<tr>
<td>Melanoma of the Skin</td>
<td>0.06 (0.04, 0.08)</td>
<td>0.12 (0.08, 0.19)</td>
<td>0.12 (0.11, 0.13)</td>
</tr>
<tr>
<td>Breast</td>
<td>0.97 (0.91, 1.03)</td>
<td>0.91 (0.79, 1.06)</td>
<td>1.11 (1.07, 1.15)</td>
</tr>
<tr>
<td>Urinary Bladder</td>
<td>0.39 (0.35, 0.44)</td>
<td>0.29 (0.21, 0.39)</td>
<td>0.43 (0.40, 0.46)</td>
</tr>
<tr>
<td>Kidney and Renal Pelvis</td>
<td>0.35 (0.31, 0.39)</td>
<td>0.74 (0.63, 0.88)</td>
<td>0.50 (0.47, 0.52)</td>
</tr>
<tr>
<td>Brain and Other Nervous System</td>
<td>0.27 (0.24, 0.30)</td>
<td>0.19 (0.16, 0.26)</td>
<td>0.33 (0.32, 0.35)</td>
</tr>
<tr>
<td>Thyroid</td>
<td>0.12 (0.10, 0.15)</td>
<td>0.05 (0.03, 0.12)</td>
<td>0.08 (0.08, 0.10)</td>
</tr>
<tr>
<td>Hodgkin Lymphoma</td>
<td>0.03 (0.02, 0.05)</td>
<td>0.02 (0.01, 0.08)</td>
<td>0.05 (0.05, 0.06)</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>0.74 (0.69, 0.80)</td>
<td>0.50 (0.41, 0.61)</td>
<td>0.77 (0.74, 0.80)</td>
</tr>
<tr>
<td>Myeloma</td>
<td>0.29 (0.27, 0.33)</td>
<td>0.31 (0.25, 0.41)</td>
<td>0.42 (0.40, 0.45)</td>
</tr>
<tr>
<td>Leukemia</td>
<td>0.66 (0.62, 0.71)</td>
<td>0.50 (0.41, 0.62)</td>
<td>0.68 (0.65, 0.71)</td>
</tr>
<tr>
<td>Acute Lymphocytic Leukemia</td>
<td>0.04 (0.03, 0.06)</td>
<td>0.02 (0.01, 0.08)</td>
<td>0.07 (0.06, 0.07)</td>
</tr>
<tr>
<td>Chronic Lymphocytic Leukemia</td>
<td>0.06 (0.04, 0.08)</td>
<td>0.10 (0.05, 0.19)</td>
<td>0.09 (0.08, 0.10)</td>
</tr>
<tr>
<td>Acute Myeloid Leukemia</td>
<td>0.32 (0.30, 0.36)</td>
<td>0.19 (0.15, 0.27)</td>
<td>0.26 (0.24, 0.28)</td>
</tr>
<tr>
<td>Chronic Myeloid Leukemia</td>
<td>0.04 (0.03, 0.06)</td>
<td>0.03 (0.01, 0.09)</td>
<td>0.04 (0.03, 0.04)</td>
</tr>
</tbody>
</table>

Source: NCIS public use data file for the total US. Underlying mortality data for American Indian/Alaska Native are based on the CHSDA (Contract Health Service Delivery Area) counties. Hispanic is not mutually exclusive from whites, blacks, Asian Pacific Islanders, and American Indians/Alaska Natives. A percent or confidence interval value of 0.00 represents a value that is below 0.005.
Table 1.19
Lifetime Risk (Percent) of Dying from Cancer by Site and Race/Ethnicity
Males, Total U.S., 2009-2011

<table>
<thead>
<tr>
<th>Site</th>
<th>All Races</th>
<th>Whites</th>
<th>Blacks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Percent (95% C.I.)</td>
<td>Percent (95% C.I.)</td>
<td>Percent (95% C.I.)</td>
</tr>
<tr>
<td>All Sites</td>
<td>22.83 (22.78, 22.87)</td>
<td>22.87 (22.82, 22.92)</td>
<td>23.66 (23.51, 23.81)</td>
</tr>
<tr>
<td>Oral Cavity and Pharynx</td>
<td>0.39 (0.38, 0.39)</td>
<td>0.38 (0.38, 0.39)</td>
<td>0.44 (0.42, 0.46)</td>
</tr>
<tr>
<td>Esophagus</td>
<td>0.79 (0.78, 0.80)</td>
<td>0.83 (0.82, 0.84)</td>
<td>0.62 (0.59, 0.64)</td>
</tr>
<tr>
<td>Stomach</td>
<td>0.49 (0.48, 0.50)</td>
<td>0.43 (0.42, 0.44)</td>
<td>0.82 (0.79, 0.85)</td>
</tr>
<tr>
<td>Colon and Rectum</td>
<td>2.04 (2.02, 2.05)</td>
<td>2.00 (1.98, 2.01)</td>
<td>2.41 (2.36, 2.46)</td>
</tr>
<tr>
<td>Liver and Intrahepatic Bile Duct</td>
<td>0.90 (0.89, 0.91)</td>
<td>0.84 (0.83, 0.85)</td>
<td>1.08 (1.05, 1.11)</td>
</tr>
<tr>
<td>Pancreas</td>
<td>1.35 (1.34, 1.37)</td>
<td>1.36 (1.35, 1.38)</td>
<td>1.35 (1.31, 1.39)</td>
</tr>
<tr>
<td>Larynx</td>
<td>0.20 (0.20, 0.21)</td>
<td>0.19 (0.19, 0.20)</td>
<td>0.32 (0.30, 0.34)</td>
</tr>
<tr>
<td>Lung and Bronchus</td>
<td>6.47 (6.45, 6.50)</td>
<td>6.53 (6.51, 6.56)</td>
<td>6.49 (6.42, 6.58)</td>
</tr>
<tr>
<td>Melanoma of the Skin</td>
<td>0.43 (0.43, 0.44)</td>
<td>0.49 (0.49, 0.50)</td>
<td>0.04 (0.04, 0.05)</td>
</tr>
<tr>
<td>Breast</td>
<td>0.03 (0.03, 0.03)</td>
<td>0.03 (0.03, 0.03)</td>
<td>0.05 (0.04, 0.05)</td>
</tr>
<tr>
<td>Prostate</td>
<td>2.66 (2.65, 2.68)</td>
<td>2.48 (2.46, 2.50)</td>
<td>4.57 (4.49, 4.66)</td>
</tr>
<tr>
<td>Testis</td>
<td>0.02 (0.02, 0.02)</td>
<td>0.02 (0.02, 0.02)</td>
<td>0.01 (0.01, 0.01)</td>
</tr>
<tr>
<td>Urinary Bladder</td>
<td>0.91 (0.90, 0.92)</td>
<td>0.97 (0.95, 0.98)</td>
<td>0.51 (0.48, 0.54)</td>
</tr>
<tr>
<td>Kidney and Renal Pelvis</td>
<td>0.61 (0.60, 0.62)</td>
<td>0.63 (0.62, 0.64)</td>
<td>0.48 (0.46, 0.51)</td>
</tr>
<tr>
<td>Brain and Other Nervous System</td>
<td>0.51 (0.50, 0.51)</td>
<td>0.55 (0.54, 0.56)</td>
<td>0.24 (0.23, 0.26)</td>
</tr>
<tr>
<td>Thyroid</td>
<td>0.05 (0.05, 0.06)</td>
<td>0.06 (0.05, 0.06)</td>
<td>0.03 (0.03, 0.04)</td>
</tr>
<tr>
<td>Hodgkin Lymphoma</td>
<td>0.05 (0.04, 0.05)</td>
<td>0.05 (0.05, 0.05)</td>
<td>0.04 (0.03, 0.04)</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>0.87 (0.86, 0.88)</td>
<td>0.92 (0.90, 0.93)</td>
<td>0.51 (0.48, 0.53)</td>
</tr>
<tr>
<td>Myeloma</td>
<td>0.47 (0.46, 0.47)</td>
<td>0.45 (0.44, 0.45)</td>
<td>0.68 (0.66, 0.71)</td>
</tr>
<tr>
<td>Leukemia</td>
<td>1.03 (1.01, 1.04)</td>
<td>1.07 (1.06, 1.08)</td>
<td>0.69 (0.66, 0.72)</td>
</tr>
<tr>
<td>Acute Lymphoblastic Leukemia</td>
<td>0.05 (0.04, 0.05)</td>
<td>0.05 (0.05, 0.05)</td>
<td>0.03 (0.02, 0.03)</td>
</tr>
<tr>
<td>Chronic Lymphoblastic Leukemia</td>
<td>0.24 (0.23, 0.24)</td>
<td>0.25 (0.24, 0.25)</td>
<td>0.17 (0.15, 0.19)</td>
</tr>
<tr>
<td>Acute Myeloid Leukemia</td>
<td>0.39 (0.39, 0.40)</td>
<td>0.41 (0.41, 0.42)</td>
<td>0.23 (0.22, 0.25)</td>
</tr>
<tr>
<td>Chronic Myeloid Leukemia</td>
<td>0.04 (0.04, 0.05)</td>
<td>0.05 (0.04, 0.05)</td>
<td>0.04 (0.03, 0.05)</td>
</tr>
</tbody>
</table>
## Table 1.19 - continued

<table>
<thead>
<tr>
<th>Site</th>
<th>Asian/Pacific Islander</th>
<th>American Indian/Alaska Native</th>
<th>Hispanic*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Site Percent (95% C.I.)</td>
<td>Percent (95% C.I.)</td>
<td>Percent (95% C.I.)</td>
<td>Percent (95% C.I.)</td>
</tr>
<tr>
<td>All Sites</td>
<td>21.04 (20.68, 21.41)</td>
<td>18.46 (17.69, 19.29)</td>
<td>20.28 (20.05, 20.52)</td>
</tr>
<tr>
<td>Oral Cavity and Pharynx</td>
<td>0.41 (0.36, 0.48)</td>
<td>0.33 (0.24, 0.54)</td>
<td>0.29 (0.27, 0.32)</td>
</tr>
<tr>
<td>Esophagus</td>
<td>0.47 (0.41, 0.54)</td>
<td>0.48 (0.37, 0.70)</td>
<td>0.58 (0.54, 0.62)</td>
</tr>
<tr>
<td>Stomach</td>
<td>1.31 (1.22, 1.42)</td>
<td>0.69 (0.55, 0.92)</td>
<td>0.94 (0.89, 1.00)</td>
</tr>
<tr>
<td>Colon and Rectum</td>
<td>2.12 (1.99, 2.25)</td>
<td>1.83 (1.57, 2.16)</td>
<td>2.13 (2.05, 2.21)</td>
</tr>
<tr>
<td>Liver and Intrahepatic Bile Duct</td>
<td>2.02 (1.92, 2.14)</td>
<td>1.30 (1.12, 1.57)</td>
<td>1.55 (1.49, 1.61)</td>
</tr>
<tr>
<td>Pancreas</td>
<td>1.33 (1.24, 1.43)</td>
<td>0.86 (0.72, 1.10)</td>
<td>1.30 (1.24, 1.36)</td>
</tr>
<tr>
<td>Larynx</td>
<td>0.13 (0.10, 0.17)</td>
<td>0.16 (0.10, 0.34)</td>
<td>0.23 (0.21, 0.26)</td>
</tr>
<tr>
<td>Lung and Bronchus</td>
<td>5.43 (5.25, 5.63)</td>
<td>4.63 (4.25, 5.09)</td>
<td>3.97 (3.87, 4.08)</td>
</tr>
<tr>
<td>Melanoma of the Skin</td>
<td>0.06 (0.04, 0.09)</td>
<td>0.19 (0.12, 0.38)</td>
<td>0.15 (0.12, 0.18)</td>
</tr>
<tr>
<td>Breast</td>
<td>0.03 (0.01, 0.07)</td>
<td>0.02 (0.00, 0.20)</td>
<td>0.03 (0.02, 0.05)</td>
</tr>
<tr>
<td>Prostate</td>
<td>2.20 (2.04, 2.37)</td>
<td>2.38 (2.02, 2.84)</td>
<td>3.08 (2.96, 3.21)</td>
</tr>
<tr>
<td>Testis</td>
<td>0.00 (0.00, 0.03)</td>
<td>0.02 (0.01, 0.20)</td>
<td>0.03 (0.02, 0.04)</td>
</tr>
<tr>
<td>Urinary Bladder</td>
<td>0.58 (0.50, 0.67)</td>
<td>0.50 (0.31, 0.78)</td>
<td>0.65 (0.59, 0.71)</td>
</tr>
<tr>
<td>Kidney and Renal Pelvis</td>
<td>0.45 (0.40, 0.52)</td>
<td>0.53 (0.37, 0.76)</td>
<td>0.64 (0.60, 0.69)</td>
</tr>
<tr>
<td>Brain and Other Nervous System</td>
<td>0.31 (0.27, 0.36)</td>
<td>0.23 (0.17, 0.41)</td>
<td>0.36 (0.34, 0.39)</td>
</tr>
<tr>
<td>Thyroid</td>
<td>0.07 (0.06, 0.11)</td>
<td>0.05 (0.02, 0.23)</td>
<td>0.06 (0.05, 0.08)</td>
</tr>
<tr>
<td>Hodgkin Lymphoma</td>
<td>0.04 (0.02, 0.07)</td>
<td>0.04 (0.01, 0.22)</td>
<td>0.06 (0.05, 0.08)</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>0.83 (0.76, 0.93)</td>
<td>0.52 (0.41, 0.73)</td>
<td>0.82 (0.77, 0.87)</td>
</tr>
<tr>
<td>Myeloma</td>
<td>0.36 (0.31, 0.42)</td>
<td>0.31 (0.21, 0.51)</td>
<td>0.48 (0.45, 0.53)</td>
</tr>
<tr>
<td>Leukemia</td>
<td>0.78 (0.71, 0.85)</td>
<td>0.68 (0.52, 0.95)</td>
<td>0.77 (0.73, 0.83)</td>
</tr>
<tr>
<td>Acute Lymphocytic Leukemia</td>
<td>0.05 (0.03, 0.08)</td>
<td>0.02 (0.01, 0.20)</td>
<td>0.07 (0.06, 0.09)</td>
</tr>
<tr>
<td>Chronic Lymphocytic Leukemia</td>
<td>0.07 (0.05, 0.11)</td>
<td>0.15 (0.07, 0.35)</td>
<td>0.10 (0.08, 0.12)</td>
</tr>
<tr>
<td>Acute Myeloid Leukemia</td>
<td>0.37 (0.33, 0.43)</td>
<td>0.23 (0.15, 0.43)</td>
<td>0.29 (0.27, 0.32)</td>
</tr>
<tr>
<td>Chronic Myeloid Leukemia</td>
<td>0.04 (0.03, 0.08)</td>
<td>0.06 (0.03, 0.24)</td>
<td>0.05 (0.04, 0.07)</td>
</tr>
</tbody>
</table>

Source: NCIS public use data file for the total US.

* Underlying mortality data for American Indian/Alaska Native are based on the CHSDA (Contract Health Service Delivery Area) counties.

** Hispanic is not mutually exclusive from whites, blacks, Asian Pacific Islanders, and American Indians/Alaska Natives. A percent or confidence interval value of 0.00 represents a value that is below 0.005.
Table 1.20
Lifetime Risk (Percent) of Dying from Cancer by Site and Race/Ethnicity
Females, Total U.S., 2009-2011

<table>
<thead>
<tr>
<th>Site</th>
<th>All Races</th>
<th>Whites</th>
<th>Blacks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Percent (95% C.I.)</td>
<td>Percent (95% C.I.)</td>
<td>Percent (95% C.I.)</td>
</tr>
<tr>
<td>Oral Cavity and Pharynx</td>
<td>0.18 (0.18, 0.19)</td>
<td>0.18 (0.18, 0.19)</td>
<td>0.15 (0.13, 0.16)</td>
</tr>
<tr>
<td>Esophagus</td>
<td>0.21 (0.21, 0.22)</td>
<td>0.21 (0.21, 0.22)</td>
<td>0.22 (0.20, 0.23)</td>
</tr>
<tr>
<td>Stomach</td>
<td>0.33 (0.32, 0.33)</td>
<td>0.29 (0.28, 0.29)</td>
<td>0.55 (0.52, 0.57)</td>
</tr>
<tr>
<td>Colon and Rectum</td>
<td>1.85 (1.84, 1.87)</td>
<td>1.81 (1.79, 1.82)</td>
<td>2.21 (2.16, 2.26)</td>
</tr>
<tr>
<td>Liver and Intrahepatic Bile Duct</td>
<td>0.47 (0.46, 0.48)</td>
<td>0.44 (0.44, 0.45)</td>
<td>0.51 (0.49, 0.53)</td>
</tr>
<tr>
<td>Pancreas</td>
<td>1.32 (1.31, 1.33)</td>
<td>1.31 (1.29, 1.32)</td>
<td>1.50 (1.46, 1.54)</td>
</tr>
<tr>
<td>Larynx</td>
<td>0.05 (0.05, 0.05)</td>
<td>0.05 (0.05, 0.05)</td>
<td>0.07 (0.06, 0.07)</td>
</tr>
<tr>
<td>Lung and Bronchus</td>
<td>4.95 (4.93, 4.97)</td>
<td>5.14 (5.11, 5.16)</td>
<td>4.15 (4.09, 4.21)</td>
</tr>
<tr>
<td>Melanoma of the Skin</td>
<td>0.21 (0.21, 0.22)</td>
<td>0.24 (0.24, 0.25)</td>
<td>0.05 (0.04, 0.05)</td>
</tr>
<tr>
<td>Breast</td>
<td>2.72 (2.70, 2.74)</td>
<td>2.69 (2.67, 2.71)</td>
<td>3.26 (3.21, 3.32)</td>
</tr>
<tr>
<td>Cervix Uteri</td>
<td>0.23 (0.22, 0.23)</td>
<td>0.21 (0.20, 0.21)</td>
<td>0.38 (0.37, 0.40)</td>
</tr>
<tr>
<td>Corpus and Uterus, NOS</td>
<td>0.57 (0.56, 0.58)</td>
<td>0.53 (0.53, 0.54)</td>
<td>0.89 (0.86, 0.92)</td>
</tr>
<tr>
<td>Ovary</td>
<td>0.98 (0.97, 0.99)</td>
<td>1.02 (1.01, 1.03)</td>
<td>0.76 (0.73, 0.78)</td>
</tr>
<tr>
<td>Urinary Bladder</td>
<td>0.34 (0.34, 0.35)</td>
<td>0.35 (0.34, 0.35)</td>
<td>0.35 (0.33, 0.37)</td>
</tr>
<tr>
<td>Kidney and Renal Pelvis</td>
<td>0.35 (0.34, 0.35)</td>
<td>0.35 (0.35, 0.36)</td>
<td>0.32 (0.30, 0.34)</td>
</tr>
<tr>
<td>Brain and Other Nervous System</td>
<td>0.40 (0.39, 0.41)</td>
<td>0.43 (0.43, 0.44)</td>
<td>0.22 (0.21, 0.24)</td>
</tr>
<tr>
<td>Thyroid</td>
<td>0.07 (0.07, 0.07)</td>
<td>0.07 (0.07, 0.07)</td>
<td>0.07 (0.06, 0.08)</td>
</tr>
<tr>
<td>Hodgkin Lymphoma</td>
<td>0.03 (0.03, 0.04)</td>
<td>0.04 (0.03, 0.04)</td>
<td>0.03 (0.02, 0.03)</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>0.69 (0.69, 0.70)</td>
<td>0.73 (0.72, 0.74)</td>
<td>0.40 (0.38, 0.42)</td>
</tr>
<tr>
<td>Myeloma</td>
<td>0.38 (0.37, 0.38)</td>
<td>0.35 (0.34, 0.35)</td>
<td>0.64 (0.62, 0.67)</td>
</tr>
<tr>
<td>Leukemia</td>
<td>0.72 (0.72, 0.73)</td>
<td>0.75 (0.74, 0.76)</td>
<td>0.57 (0.55, 0.59)</td>
</tr>
<tr>
<td>Acute Lymphocytic Leukemia</td>
<td>0.04 (0.04, 0.04)</td>
<td>0.04 (0.04, 0.04)</td>
<td>0.02 (0.02, 0.03)</td>
</tr>
<tr>
<td>Chronic Lymphocytic Leukemia</td>
<td>0.15 (0.15, 0.16)</td>
<td>0.16 (0.15, 0.16)</td>
<td>0.12 (0.11, 0.13)</td>
</tr>
<tr>
<td>Acute Myeloid Leukemia</td>
<td>0.28 (0.27, 0.28)</td>
<td>0.29 (0.29, 0.30)</td>
<td>0.19 (0.18, 0.21)</td>
</tr>
<tr>
<td>Chronic Myeloid Leukemia</td>
<td>0.04 (0.03, 0.04)</td>
<td>0.04 (0.03, 0.04)</td>
<td>0.03 (0.03, 0.04)</td>
</tr>
</tbody>
</table>
### Table 1.20 - continued

**Lifetime Risk (Percent) of Dying from Cancer by Site and Race/Ethnicity**

**Females, Total U.S., 2009-2011**

<table>
<thead>
<tr>
<th>Site</th>
<th>Asian/Pacific Islanders</th>
<th>American Indian/Alaska Natives</th>
<th>Hispanics&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Sites</td>
<td>16.84 (16.52, 17.16)</td>
<td>15.93 (15.28, 16.62)</td>
<td>15.81 (15.63, 15.99)</td>
</tr>
<tr>
<td>Oral Cavity and Pharynx</td>
<td>0.20 (0.17, 0.25)</td>
<td>0.16 (0.10, 0.28)</td>
<td>0.14 (0.12, 0.16)</td>
</tr>
<tr>
<td>Esophagus</td>
<td>0.16 (0.13, 0.20)</td>
<td>0.23 (0.15, 0.37)</td>
<td>0.15 (0.13, 0.18)</td>
</tr>
<tr>
<td>Stomach</td>
<td>0.99 (0.90, 1.09)</td>
<td>0.42 (0.31, 0.58)</td>
<td>0.67 (0.63, 0.71)</td>
</tr>
<tr>
<td>Colon and Rectum</td>
<td>1.95 (1.83, 2.09)</td>
<td>1.92 (1.67, 2.21)</td>
<td>1.71 (1.64, 1.78)</td>
</tr>
<tr>
<td>Liver and Intrahepatic Bile Duct</td>
<td>1.15 (1.07, 1.24)</td>
<td>0.71 (0.58, 0.90)</td>
<td>0.89 (0.85, 0.94)</td>
</tr>
<tr>
<td>Pancreas</td>
<td>1.45 (1.36, 1.56)</td>
<td>0.98 (0.80, 1.20)</td>
<td>1.35 (1.30, 1.42)</td>
</tr>
<tr>
<td>Larynx</td>
<td>0.02 (0.01, 0.04)</td>
<td>0.03 (0.01, 0.13)</td>
<td>0.03 (0.02, 0.05)</td>
</tr>
<tr>
<td>Lung and Bronchus</td>
<td>3.39 (3.25, 3.53)</td>
<td>3.70 (3.39, 4.05)</td>
<td>2.23 (2.16, 2.31)</td>
</tr>
<tr>
<td>Melanoma of the Skin</td>
<td>0.05 (0.04, 0.09)</td>
<td>0.06 (0.03, 0.16)</td>
<td>0.10 (0.08, 0.11)</td>
</tr>
<tr>
<td>Breast</td>
<td>1.75 (1.65, 1.87)</td>
<td>1.73 (1.51, 2.00)</td>
<td>2.05 (1.98, 2.12)</td>
</tr>
<tr>
<td>Cervix Uteri</td>
<td>0.24 (0.21, 0.29)</td>
<td>0.31 (0.23, 0.45)</td>
<td>0.31 (0.29, 0.34)</td>
</tr>
<tr>
<td>Corpus and Uterus, NOS</td>
<td>0.46 (0.41, 0.52)</td>
<td>0.39 (0.30, 0.54)</td>
<td>0.51 (0.48, 0.54)</td>
</tr>
<tr>
<td>Ovary</td>
<td>0.69 (0.63, 0.75)</td>
<td>0.83 (0.68, 1.03)</td>
<td>0.82 (0.78, 0.86)</td>
</tr>
<tr>
<td>Urinary Bladder</td>
<td>0.25 (0.20, 0.31)</td>
<td>0.14 (0.09, 0.25)</td>
<td>0.26 (0.24, 0.30)</td>
</tr>
<tr>
<td>Kidney and Renal Pelvis</td>
<td>0.27 (0.22, 0.33)</td>
<td>0.56 (0.43, 0.75)</td>
<td>0.37 (0.35, 0.41)</td>
</tr>
<tr>
<td>Brain and Other Nervous System</td>
<td>0.24 (0.21, 0.28)</td>
<td>0.16 (0.11, 0.26)</td>
<td>0.31 (0.28, 0.33)</td>
</tr>
<tr>
<td>Thyroid</td>
<td>0.16 (0.13, 0.21)</td>
<td>0.06 (0.02, 0.16)</td>
<td>0.11 (0.09, 0.13)</td>
</tr>
<tr>
<td>Hodgkin Lymphoma</td>
<td>0.02 (0.01, 0.05)</td>
<td>0.01 (0.00, 0.10)</td>
<td>0.04 (0.03, 0.05)</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>0.67 (0.61, 0.75)</td>
<td>0.47 (0.36, 0.64)</td>
<td>0.73 (0.69, 0.77)</td>
</tr>
<tr>
<td>Myeloma</td>
<td>0.24 (0.21, 0.28)</td>
<td>0.32 (0.23, 0.47)</td>
<td>0.38 (0.35, 0.41)</td>
</tr>
<tr>
<td>Leukemia</td>
<td>0.57 (0.51, 0.64)</td>
<td>0.36 (0.27, 0.51)</td>
<td>0.60 (0.57, 0.65)</td>
</tr>
<tr>
<td>Acute Lymphocytic Leukemia</td>
<td>0.04 (0.03, 0.06)</td>
<td>0.03 (0.01, 0.12)</td>
<td>0.06 (0.05, 0.07)</td>
</tr>
<tr>
<td>Chronic Lymphocytic Leukemia</td>
<td>0.05 (0.03, 0.08)</td>
<td>0.06 (0.02, 0.18)</td>
<td>0.08 (0.07, 0.11)</td>
</tr>
<tr>
<td>Acute Myeloid Leukemia</td>
<td>0.29 (0.25, 0.34)</td>
<td>0.17 (0.11, 0.28)</td>
<td>0.23 (0.21, 0.25)</td>
</tr>
<tr>
<td>Chronic Myeloid Leukemia</td>
<td>0.04 (0.02, 0.07)</td>
<td>0.01 (0.00, 0.10)</td>
<td>0.03 (0.02, 0.04)</td>
</tr>
</tbody>
</table>

Source: NCHS public use data file for the total US.

<sup>a</sup> Underlying mortality data for American Indian/Alaska Native are based on the CHSDA (Contract Health Service Delivery Area) counties.

<sup>b</sup> Hispanic is not mutually exclusive from whites, blacks, Asian Pacific Islanders, and American Indians/Alaska Natives. A percent or confidence interval value of 0.00 represents a value that is below 0.005.
## Table 1.21

### U.S. and SEER Death Rates by Primary Cancer Site and Race/Ethnicity, 2007-2011

<table>
<thead>
<tr>
<th>Site</th>
<th>Total United States*</th>
<th>SEER 18 Areas**</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total White</td>
<td>Black</td>
</tr>
<tr>
<td>All Sites</td>
<td>173.8</td>
<td>173.3</td>
</tr>
<tr>
<td>Male</td>
<td>211.6</td>
<td>209.8</td>
</tr>
<tr>
<td>Female</td>
<td>147.4</td>
<td>147.5</td>
</tr>
<tr>
<td>Oral Cavity &amp; Pharynx</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>2.5</td>
<td>2.4</td>
</tr>
<tr>
<td>Female</td>
<td>3.8</td>
<td>3.8</td>
</tr>
<tr>
<td>Esophagus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>4.2</td>
<td>4.3</td>
</tr>
<tr>
<td>Female</td>
<td>7.5</td>
<td>7.8</td>
</tr>
<tr>
<td>Stomach</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1.6</td>
<td>1.5</td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colon &amp; Rectum</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>15.9</td>
<td>15.5</td>
</tr>
<tr>
<td>Female</td>
<td>19.1</td>
<td>18.6</td>
</tr>
<tr>
<td>Liver &amp; Intrahepatic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>5.8</td>
<td>5.3</td>
</tr>
<tr>
<td>Female</td>
<td>8.5</td>
<td>7.8</td>
</tr>
<tr>
<td>Bile Duct Female</td>
<td>3.4</td>
<td>3.2</td>
</tr>
<tr>
<td>Pancreas</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>10.9</td>
<td>10.8</td>
</tr>
<tr>
<td>Female</td>
<td>12.5</td>
<td>12.5</td>
</tr>
<tr>
<td>Larynx</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1.1</td>
<td>1.0</td>
</tr>
<tr>
<td>Female</td>
<td>2.0</td>
<td>1.8</td>
</tr>
<tr>
<td>Lung &amp; Bronchus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>48.4</td>
<td>49.1</td>
</tr>
<tr>
<td>Female</td>
<td>61.6</td>
<td>61.4</td>
</tr>
<tr>
<td>Melanoma of the Skin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>2.7</td>
<td>3.1</td>
</tr>
<tr>
<td>Female</td>
<td>4.1</td>
<td>4.6</td>
</tr>
<tr>
<td>Breast</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>22.2</td>
<td>21.7</td>
</tr>
</tbody>
</table>

* US Mortality Files, National Center for Health Statistics, Centers for Disease Control and Prevention. Rates are per 100,000 and are age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1130).

** The SEER 18 areas are San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, Alaska Native Registry, Rural Georgia, California excluding SP/SJM/LA, Kentucky, Louisiana, New Jersey and Georgia excluding ATL/RG.

*** Rates for American Indian/Alaska Native (AI/AN) are based on the CHSDA (Contact Health Service Delivery Area) counties.

**** Asian/Pacific Islander, Hispanic (Hisp) and White Non-Hispanic (W-NHisp) are not mutually exclusive from whites, blacks, Asian/Pacific Islanders, and American Indians/Alaska Natives.

---

The statistic could not be calculated due to less than 16 cases in the time interval.
### Table 1.21 - continued

**U.S. and SEER Death Rates by Primary Cancer Site and Race/Ethnicity, 2007-2011**

<table>
<thead>
<tr>
<th>Site</th>
<th>Total United States</th>
<th>SEER 18 Areas</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>White</td>
</tr>
<tr>
<td>Cervix Female</td>
<td>2.3</td>
<td>2.1</td>
</tr>
<tr>
<td>Corpus &amp; Uterus, NOS Female</td>
<td>4.3</td>
<td>4.0</td>
</tr>
<tr>
<td>Ovary Female</td>
<td>7.9</td>
<td>8.2</td>
</tr>
<tr>
<td>Prostate Male</td>
<td>22.3</td>
<td>20.6</td>
</tr>
<tr>
<td>Testis Male</td>
<td>0.2</td>
<td>0.3</td>
</tr>
<tr>
<td>Urinary Both Sexes</td>
<td>4.4</td>
<td>4.6</td>
</tr>
<tr>
<td>Bladder Male</td>
<td>7.7</td>
<td>8.1</td>
</tr>
<tr>
<td>Female</td>
<td>2.2</td>
<td>2.2</td>
</tr>
<tr>
<td>Kidney &amp; Renal Male</td>
<td>4.0</td>
<td>4.0</td>
</tr>
<tr>
<td>Pelvis Female</td>
<td>5.8</td>
<td>5.9</td>
</tr>
<tr>
<td>Brain &amp; Nervous Male</td>
<td>2.6</td>
<td>2.6</td>
</tr>
<tr>
<td>System Female</td>
<td>3.5</td>
<td>3.8</td>
</tr>
<tr>
<td>Thyroid Both Sexes</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Lymphoma Male</td>
<td>5.5</td>
<td>5.9</td>
</tr>
<tr>
<td>Hodgkin Both Sexes</td>
<td>2.6</td>
<td>2.6</td>
</tr>
<tr>
<td>Hodgkin Male</td>
<td>0.4</td>
<td>0.4</td>
</tr>
<tr>
<td>Lymphoma Female</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Hodgkin Female</td>
<td>0.3</td>
<td>0.3</td>
</tr>
<tr>
<td>Non-Hodgkin Both Sexes</td>
<td>6.3</td>
<td>6.6</td>
</tr>
<tr>
<td>Lymphoma Male</td>
<td>8.1</td>
<td>8.4</td>
</tr>
<tr>
<td>Female</td>
<td>5.0</td>
<td>5.2</td>
</tr>
<tr>
<td>Myeloma Both Sexes</td>
<td>3.4</td>
<td>3.1</td>
</tr>
<tr>
<td>Leukemia Male</td>
<td>7.0</td>
<td>7.3</td>
</tr>
<tr>
<td>Female</td>
<td>9.4</td>
<td>9.7</td>
</tr>
<tr>
<td>Leukemia Male</td>
<td>5.3</td>
<td>5.4</td>
</tr>
</tbody>
</table>

---

*a* US Mortality Files, National Center for Health Statistics, Centers for Disease Control and Prevention. Rates are per 100,000 and are age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1130).

*b* The SEER 18 areas are San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, Alaska Native Registry, Rural Georgia, California excluding SF/SVM/LA, Kentucky, Louisiana, New Jersey and Georgia excluding ATL/KG.

*c* Rates for American Indian/Alaska Native (AI/AN) are based on the CHSDA (County Health Service Delivery Area) counties.

*d* Asian/Pacific Islander.

*e* Hispanic (Hisp) and White Non-Hispanic (W-NHisp) are not mutually exclusive from whites, blacks, Asian/Pacific Islanders, and American Indians/Alaska Natives.

- Statistic could not be calculated due to less than 16 cases in the time interval.
### Table 1.22

U.S. Prevalence Counts, Invasive Cancers Only, January 1, 2011\(^a\)
Using Different Tumor Inclusion Criteria\(^b\)

<table>
<thead>
<tr>
<th>Site</th>
<th>Sex</th>
<th>1st Invasive Tumor Ever(^c)</th>
<th>1st Per Site in Previous 36 Years(^d)</th>
<th>1st Per Site in Previous 5 Years(^e)</th>
<th>1st Invasive Tumor Ever(^c)</th>
<th>36-year Limited Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Sites</td>
<td>Both Sexes</td>
<td>4,594,732</td>
<td>4,684,591</td>
<td>5,152,908</td>
<td>12,998,655</td>
<td>13,213,910</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>2,373,342</td>
<td>2,409,199</td>
<td>2,638,979</td>
<td>6,188,275</td>
<td>6,261,129</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>2,221,390</td>
<td>2,275,392</td>
<td>2,513,929</td>
<td>6,810,390</td>
<td>6,952,781</td>
</tr>
<tr>
<td>Oral Cavity &amp; Pharynx</td>
<td>Both Sexes</td>
<td>104,979</td>
<td>121,403</td>
<td>125,889</td>
<td>272,072</td>
<td>300,609</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>73,503</td>
<td>84,311</td>
<td>87,116</td>
<td>187,087</td>
<td>196,137</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>31,476</td>
<td>37,092</td>
<td>38,773</td>
<td>85,985</td>
<td>104,272</td>
</tr>
<tr>
<td>Esophagus</td>
<td>Both Sexes</td>
<td>21,165</td>
<td>26,055</td>
<td>26,172</td>
<td>34,428</td>
<td>40,593</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>16,662</td>
<td>20,345</td>
<td>20,416</td>
<td>26,846</td>
<td>31,461</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>4,503</td>
<td>5,710</td>
<td>5,756</td>
<td>7,582</td>
<td>9,132</td>
</tr>
<tr>
<td>Stomach</td>
<td>Both Sexes</td>
<td>36,380</td>
<td>43,398</td>
<td>43,779</td>
<td>72,734</td>
<td>83,348</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>21,307</td>
<td>26,023</td>
<td>26,197</td>
<td>41,394</td>
<td>47,992</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>15,073</td>
<td>17,375</td>
<td>17,582</td>
<td>31,340</td>
<td>35,356</td>
</tr>
<tr>
<td>Colon &amp; Rectum</td>
<td>Both Sexes</td>
<td>403,434</td>
<td>465,899</td>
<td>475,547</td>
<td>1,140,625</td>
<td>1,270,460</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>206,233</td>
<td>237,736</td>
<td>242,463</td>
<td>567,872</td>
<td>629,107</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>197,201</td>
<td>228,163</td>
<td>233,084</td>
<td>572,793</td>
<td>641,363</td>
</tr>
<tr>
<td>Liver &amp; Intrahepatic Bile Duct</td>
<td>Both Sexes</td>
<td>33,682</td>
<td>38,427</td>
<td>38,461</td>
<td>45,468</td>
<td>50,961</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>24,973</td>
<td>27,797</td>
<td>27,819</td>
<td>32,312</td>
<td>35,854</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>8,799</td>
<td>10,630</td>
<td>10,642</td>
<td>13,156</td>
<td>15,107</td>
</tr>
<tr>
<td>Pancreas</td>
<td>Both Sexes</td>
<td>32,756</td>
<td>39,642</td>
<td>39,654</td>
<td>43,238</td>
<td>51,264</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>16,110</td>
<td>19,950</td>
<td>19,962</td>
<td>20,679</td>
<td>25,032</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>16,646</td>
<td>19,692</td>
<td>19,692</td>
<td>22,559</td>
<td>26,232</td>
</tr>
<tr>
<td>Larynx</td>
<td>Both Sexes</td>
<td>31,318</td>
<td>37,292</td>
<td>37,636</td>
<td>87,652</td>
<td>98,482</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>25,568</td>
<td>30,391</td>
<td>30,700</td>
<td>70,687</td>
<td>79,142</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>5,750</td>
<td>6,901</td>
<td>6,936</td>
<td>16,965</td>
<td>19,340</td>
</tr>
<tr>
<td>Lung &amp; Bronchus</td>
<td>Both Sexes</td>
<td>231,126</td>
<td>297,286</td>
<td>306,343</td>
<td>395,186</td>
<td>487,438</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>107,276</td>
<td>140,106</td>
<td>143,631</td>
<td>179,129</td>
<td>222,121</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>123,850</td>
<td>157,180</td>
<td>162,712</td>
<td>216,057</td>
<td>265,317</td>
</tr>
<tr>
<td>Melanoma of the Skin</td>
<td>Both Sexes</td>
<td>282,028</td>
<td>320,618</td>
<td>335,149</td>
<td>924,397</td>
<td>998,829</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>151,313</td>
<td>176,923</td>
<td>185,633</td>
<td>489,686</td>
<td>503,903</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>130,715</td>
<td>144,095</td>
<td>149,516</td>
<td>434,711</td>
<td>494,926</td>
</tr>
<tr>
<td>Breast</td>
<td>Female</td>
<td>855,411</td>
<td>924,344</td>
<td>982,776</td>
<td>2,847,146</td>
<td>3,016,451</td>
</tr>
<tr>
<td>Cervix</td>
<td>Female</td>
<td>39,578</td>
<td>41,703</td>
<td>41,825</td>
<td>211,309</td>
<td>217,336</td>
</tr>
<tr>
<td>Corpus &amp; Uterus, NOS</td>
<td>Female</td>
<td>177,109</td>
<td>198,883</td>
<td>199,045</td>
<td>584,180</td>
<td>637,931</td>
</tr>
<tr>
<td>Ovary(^f)</td>
<td>Female</td>
<td>58,762</td>
<td>67,726</td>
<td>67,789</td>
<td>173,192</td>
<td>194,691</td>
</tr>
</tbody>
</table>

\(^a\) U.S. 2011 cancer prevalence counts are based on 2011 cancer prevalence proportions from the SEER 9 registries and 1/1/2011 U.S. population estimates based on the average of 2010 and 2011 population estimates from the U.S. Bureau of the Census.

\(^b\) Prevalence estimates are ambiguous for those with multiple cancers, unless the tumor inclusion criteria are understood. Depending on the application, different inclusion criteria may be appropriate. This table provides three different methods of tumor inclusion:

\(^c\) First invasive tumor ever

\(^d\) First invasive tumor for each cancer site diagnosed during the previous 36 years (1975-2010)

\(^e\) First invasive tumor for each cancer site diagnosed during the previous 5 years (2006-2010)

\(^f\) Ovary excludes borderline cases or histologies 8442, 8451, 8462, 8472, and 8473.
Prevalence estimates are ambiguous for those with multiple cancers, unless the tumor inclusion criteria are understood. Depending on the application, different inclusion criteria may be appropriate. This table provides three different methods of tumor inclusion:

- **(c)** First invasive tumor ever
- **(d)** First invasive tumor for each cancer site diagnosed during the previous 36 years (1975-2010)
- **(e)** First invasive tumor for each cancer site diagnosed during the previous 5 years (2006-2010)

For definitions (d) and (e) all sites is treated as a separate cancer "site".

Consider a woman who had three invasive cancers: Melanoma in 1981; Breast cancer in 2006; Melanoma in 2007.

In method (c) the melanoma is the woman’s first cancer, and is counted for the melanoma and all sites 36-year limited duration prevalence. For 5-year limited duration prevalence, the woman is not counted at all since her first cancer occurred more than 5 years prior to 1/1/2011.

In method (d) the 1981 melanoma is counted for the melanoma and all sites 36-year limited duration prevalence. The 2006 breast cancer is counted for the breast 5-year and 36-year limited duration prevalence.

In method (e) the 2006 breast cancer is counted for the breast cancer and all sites 5-year limited duration prevalence. The 2007 melanoma is counted for 5-year limited duration prevalence for melanoma.
### Table 1.23

**U.S. Complete Prevalence Counts, Invasive Cancers Only, January 1, 2011**

**By Age at Prevalence**

<table>
<thead>
<tr>
<th>Site/Sex</th>
<th>All Ages</th>
<th>0-9</th>
<th>10-19</th>
<th>20-29</th>
<th>30-39</th>
<th>40-49</th>
<th>50-59</th>
<th>60-69</th>
<th>70+</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All Sites</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>6,271,036</td>
<td>19,001</td>
<td>41,846</td>
<td>85,407</td>
<td>155,919</td>
<td>356,211</td>
<td>883,826</td>
<td>1,658,545</td>
<td>3,070,283</td>
</tr>
<tr>
<td>Females</td>
<td>7,126,123</td>
<td>16,447</td>
<td>36,376</td>
<td>88,223</td>
<td>226,162</td>
<td>638,879</td>
<td>1,316,044</td>
<td>1,758,236</td>
<td>3,045,756</td>
</tr>
<tr>
<td><strong>Oral Cavity &amp; Pharynx</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>186,491</td>
<td>62</td>
<td>423</td>
<td>1,548</td>
<td>3,544</td>
<td>14,256</td>
<td>45,288</td>
<td>58,097</td>
<td>63,273</td>
</tr>
<tr>
<td>Females</td>
<td>95,100</td>
<td>90</td>
<td>522</td>
<td>1,483</td>
<td>3,689</td>
<td>8,554</td>
<td>18,160</td>
<td>23,692</td>
<td>38,911</td>
</tr>
<tr>
<td><strong>Esophagus</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>26,909</td>
<td>0</td>
<td>0</td>
<td>22</td>
<td>144</td>
<td>1,109</td>
<td>4,697</td>
<td>9,747</td>
<td>11,190</td>
</tr>
<tr>
<td>Females</td>
<td>7,642</td>
<td>0</td>
<td>0</td>
<td>11</td>
<td>11</td>
<td>240</td>
<td>1,378</td>
<td>1,832</td>
<td>4,170</td>
</tr>
<tr>
<td><strong>Stomach</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>42,127</td>
<td>0</td>
<td>29</td>
<td>62</td>
<td>603</td>
<td>2,502</td>
<td>7,119</td>
<td>11,218</td>
<td>20,593</td>
</tr>
<tr>
<td>Females</td>
<td>31,908</td>
<td>4</td>
<td>23</td>
<td>154</td>
<td>618</td>
<td>2,252</td>
<td>4,650</td>
<td>6,664</td>
<td>17,543</td>
</tr>
<tr>
<td><strong>Colon &amp; Rectum</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>575,457</td>
<td>11</td>
<td>69</td>
<td>1,276</td>
<td>5,758</td>
<td>25,233</td>
<td>82,732</td>
<td>139,236</td>
<td>321,141</td>
</tr>
<tr>
<td>Females</td>
<td>586,969</td>
<td>0</td>
<td>67</td>
<td>1,472</td>
<td>5,551</td>
<td>23,983</td>
<td>70,097</td>
<td>112,784</td>
<td>373,015</td>
</tr>
<tr>
<td><strong>Liver &amp; Intrahep</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>32,389</td>
<td>556</td>
<td>508</td>
<td>616</td>
<td>547</td>
<td>1,590</td>
<td>10,492</td>
<td>11,364</td>
<td>6,716</td>
</tr>
<tr>
<td>Females</td>
<td>13,553</td>
<td>396</td>
<td>521</td>
<td>359</td>
<td>403</td>
<td>889</td>
<td>3,016</td>
<td>3,463</td>
<td>4,506</td>
</tr>
<tr>
<td><strong>Pancreas</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>20,801</td>
<td>23</td>
<td>12</td>
<td>130</td>
<td>276</td>
<td>1,653</td>
<td>4,466</td>
<td>6,626</td>
<td>7,615</td>
</tr>
<tr>
<td>Females</td>
<td>22,737</td>
<td>0</td>
<td>62</td>
<td>212</td>
<td>431</td>
<td>1,446</td>
<td>3,801</td>
<td>6,179</td>
<td>10,604</td>
</tr>
<tr>
<td><strong>Larynx</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>71,999</td>
<td>0</td>
<td>0</td>
<td>90</td>
<td>219</td>
<td>1,822</td>
<td>10,341</td>
<td>21,280</td>
<td>38,207</td>
</tr>
<tr>
<td>Females</td>
<td>17,266</td>
<td>0</td>
<td>0</td>
<td>36</td>
<td>135</td>
<td>841</td>
<td>3,336</td>
<td>4,868</td>
<td>8,051</td>
</tr>
<tr>
<td><strong>Lung &amp; Bronchus</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>183,215</td>
<td>45</td>
<td>110</td>
<td>405</td>
<td>1,195</td>
<td>5,366</td>
<td>24,255</td>
<td>54,762</td>
<td>97,077</td>
</tr>
<tr>
<td>Females</td>
<td>219,111</td>
<td>23</td>
<td>71</td>
<td>367</td>
<td>1,387</td>
<td>7,548</td>
<td>29,898</td>
<td>59,021</td>
<td>120,797</td>
</tr>
<tr>
<td><strong>Melanoma of the Skin</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>471,220</td>
<td>56</td>
<td>594</td>
<td>5,039</td>
<td>17,738</td>
<td>46,603</td>
<td>97,543</td>
<td>130,762</td>
<td>172,885</td>
</tr>
<tr>
<td>Females</td>
<td>489,011</td>
<td>68</td>
<td>878</td>
<td>10,864</td>
<td>34,091</td>
<td>73,459</td>
<td>115,119</td>
<td>113,905</td>
<td>140,628</td>
</tr>
</tbody>
</table>

---

*a* U.S. 2011 cancer prevalence counts are based on 2011 cancer prevalence proportions from the SEER 9 registries (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, and Atlanta) and 1/1/2011 U.S. population estimates based on the average of 2010 and 2011 population estimates from the U.S. Bureau of the Census. Prevalence was calculated using the First Malignant Primary Only for a person.

*b* Cases diagnosed more than 36 years ago were estimated using the completeness index method (Capocaccia et. al. 1997, Merrill et. al. 2000).

*c* Due to rounding, the sum of the age specific estimates may not equal the all ages estimate.
Table 1.23 - continued
U.S. Complete Prevalence Counts, Invasive Cancers Only, January 1, 2011
By Age at Prevalence

<table>
<thead>
<tr>
<th>Site/Sex</th>
<th>All Ages&lt;sup&gt;a&lt;/sup&gt;</th>
<th>0-9</th>
<th>10-19</th>
<th>20-29</th>
<th>30-39</th>
<th>40-49</th>
<th>50-59</th>
<th>60-69</th>
<th>70+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>14,871</td>
<td>0</td>
<td>0</td>
<td>22</td>
<td>112</td>
<td>591</td>
<td>1,838</td>
<td>4,277</td>
<td>8,030</td>
</tr>
<tr>
<td>Females</td>
<td>2,899,726</td>
<td>0</td>
<td>47</td>
<td>2,669</td>
<td>35,679</td>
<td>215,380</td>
<td>550,120</td>
<td>795,921</td>
<td>1,299,910</td>
</tr>
<tr>
<td>Cervix</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Females</td>
<td>249,632</td>
<td>0</td>
<td>57</td>
<td>2,142</td>
<td>15,934</td>
<td>41,969</td>
<td>59,700</td>
<td>57,440</td>
<td>72,389</td>
</tr>
<tr>
<td>Corpus &amp; Uterus, NOS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Females</td>
<td>610,804</td>
<td>12</td>
<td>12</td>
<td>581</td>
<td>5,712</td>
<td>25,316</td>
<td>89,564</td>
<td>165,807</td>
<td>323,801</td>
</tr>
<tr>
<td>Ovary&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Females</td>
<td>188,867</td>
<td>45</td>
<td>1,063</td>
<td>3,475</td>
<td>6,807</td>
<td>18,458</td>
<td>41,719</td>
<td>49,281</td>
<td>68,021</td>
</tr>
<tr>
<td>Prostate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prostate</td>
<td>2,707,821</td>
<td>34</td>
<td>47</td>
<td>113</td>
<td>332</td>
<td>20,758</td>
<td>235,407</td>
<td>776,168</td>
<td>1,674,962</td>
</tr>
<tr>
<td>Urinary Bladder</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>425,722</td>
<td>57</td>
<td>88</td>
<td>567</td>
<td>2,476</td>
<td>10,749</td>
<td>43,060</td>
<td>102,624</td>
<td>266,102</td>
</tr>
<tr>
<td>Females</td>
<td>145,796</td>
<td>56</td>
<td>46</td>
<td>219</td>
<td>1,015</td>
<td>4,094</td>
<td>13,710</td>
<td>30,955</td>
<td>95,700</td>
</tr>
<tr>
<td>Kidney &amp; Renal Pelvis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>212,703</td>
<td>1,458</td>
<td>2,458</td>
<td>2,630</td>
<td>5,254</td>
<td>18,386</td>
<td>41,683</td>
<td>61,520</td>
<td>79,315</td>
</tr>
<tr>
<td>Females</td>
<td>145,900</td>
<td>1,374</td>
<td>2,649</td>
<td>2,922</td>
<td>4,870</td>
<td>12,287</td>
<td>25,458</td>
<td>35,857</td>
<td>60,483</td>
</tr>
<tr>
<td>Hodgkin Lymphoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>96,100</td>
<td>186</td>
<td>2,493</td>
<td>9,242</td>
<td>16,547</td>
<td>23,764</td>
<td>22,436</td>
<td>14,185</td>
<td>7,247</td>
</tr>
<tr>
<td>Females</td>
<td>89,693</td>
<td>67</td>
<td>2,083</td>
<td>9,407</td>
<td>16,399</td>
<td>23,306</td>
<td>19,845</td>
<td>11,219</td>
<td>7,368</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>278,836</td>
<td>842</td>
<td>3,598</td>
<td>7,821</td>
<td>13,627</td>
<td>29,722</td>
<td>54,887</td>
<td>71,106</td>
<td>97,233</td>
</tr>
<tr>
<td>Females</td>
<td>252,083</td>
<td>519</td>
<td>1,758</td>
<td>4,663</td>
<td>8,663</td>
<td>21,422</td>
<td>42,382</td>
<td>60,220</td>
<td>112,455</td>
</tr>
<tr>
<td>Myeloma</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>45,388</td>
<td>0</td>
<td>6</td>
<td>99</td>
<td>490</td>
<td>3,274</td>
<td>8,260</td>
<td>14,917</td>
<td>18,342</td>
</tr>
<tr>
<td>Females</td>
<td>37,979</td>
<td>0</td>
<td>0</td>
<td>28</td>
<td>312</td>
<td>2,325</td>
<td>6,791</td>
<td>11,124</td>
<td>17,399</td>
</tr>
<tr>
<td>Leukemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>170,969</td>
<td>6,686</td>
<td>13,047</td>
<td>12,524</td>
<td>11,179</td>
<td>14,206</td>
<td>23,300</td>
<td>35,001</td>
<td>55,027</td>
</tr>
<tr>
<td>Females</td>
<td>131,831</td>
<td>5,729</td>
<td>10,355</td>
<td>11,342</td>
<td>9,836</td>
<td>10,094</td>
<td>15,793</td>
<td>22,736</td>
<td>45,948</td>
</tr>
<tr>
<td>Acute Lymphocytic Leuk</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>39,514</td>
<td>5,599</td>
<td>11,159</td>
<td>9,649</td>
<td>6,330</td>
<td>3,974</td>
<td>1,505</td>
<td>836</td>
<td>463</td>
</tr>
<tr>
<td>Females</td>
<td>32,723</td>
<td>4,761</td>
<td>8,785</td>
<td>8,138</td>
<td>5,414</td>
<td>3,188</td>
<td>1,137</td>
<td>816</td>
<td>483</td>
</tr>
</tbody>
</table>

<sup>a</sup> U.S. 2011 cancer prevalence counts are based on 2011 cancer prevalence proportions from the SEER 9 registries (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, and Atlanta) and 1/1/2011 U.S. population estimates based on the average of 2010 and 2011 population estimates from the U.S. Bureau of the Census. Prevalence was calculated using the First Malignant Primary Only for a person.

<sup>b</sup> Cases diagnosed more than 38 years ago were estimated using the completeness index method (Capocaccia et. al. 1997, Merrill et. al. 2000).

<sup>c</sup> Due to rounding, the sum of the age specific estimates may not equal the all ages estimate.
### Table 1.24

**Age-Adjusted SEER Incidence Rates and Trends for the Top 15 Cancer Sites\(^a\) by Race/Ethnicity**

<table>
<thead>
<tr>
<th>All Races</th>
<th>White</th>
<th>Black</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rate(^b)</td>
<td>APC(^c)</td>
<td>Rate(^b)</td>
</tr>
<tr>
<td>All Sites</td>
<td>460.4</td>
<td>-0.6(^*)</td>
</tr>
<tr>
<td>Breast</td>
<td>67.1</td>
<td>-0.3</td>
</tr>
<tr>
<td>Prostate(^f)</td>
<td>67.0</td>
<td>-1.3(^*)</td>
</tr>
<tr>
<td>Lung and Bronchus</td>
<td>60.1</td>
<td>-1.7(^*)</td>
</tr>
<tr>
<td>Colon and Rectum</td>
<td>43.7</td>
<td>-2.8(^*)</td>
</tr>
<tr>
<td>Melanoma of the Skin</td>
<td>21.3</td>
<td>1.4(^*)</td>
</tr>
<tr>
<td>Urinary Bladder</td>
<td>20.5</td>
<td>-0.8(^*)</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>19.7</td>
<td>-0.1</td>
</tr>
<tr>
<td>Kidney and Renal Pelvis</td>
<td>15.5</td>
<td>1.9(^*)</td>
</tr>
<tr>
<td>Leukemia</td>
<td>13.1</td>
<td>1.0(^*)</td>
</tr>
<tr>
<td>Thyroid</td>
<td>12.9</td>
<td>5.8(^*)</td>
</tr>
<tr>
<td>Pancreas</td>
<td>12.3</td>
<td>0.7(^*)</td>
</tr>
<tr>
<td>Oral Cavity and Pharynx</td>
<td>11.0</td>
<td>0.4(^*)</td>
</tr>
<tr>
<td>Liver &amp; IBD(^g)</td>
<td>7.9</td>
<td>3.4(^*)</td>
</tr>
<tr>
<td>Stomach</td>
<td>7.5</td>
<td>-1.3(^*)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Asian/Pacific Islander</th>
<th>American Indian/Alaska Native(^d)</th>
<th>Hispanic(^h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rate(^b)</td>
<td>APC(^c)</td>
<td>Rate(^b)</td>
</tr>
<tr>
<td>All Sites</td>
<td>306.7</td>
<td>-0.9(^*)</td>
</tr>
<tr>
<td>Breast</td>
<td>51.6</td>
<td>0.6</td>
</tr>
<tr>
<td>Lung and Bronchus</td>
<td>37.0</td>
<td>-1.4(^*)</td>
</tr>
<tr>
<td>Colon and Rectum</td>
<td>36.9</td>
<td>-2.2(^*)</td>
</tr>
<tr>
<td>Prostate(^f)</td>
<td>34.5</td>
<td>-3.6(^*)</td>
</tr>
<tr>
<td>Liver &amp; IBD(^g)</td>
<td>14.1</td>
<td>0.9</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>13.4</td>
<td>0.0</td>
</tr>
<tr>
<td>Thyroid</td>
<td>12.5</td>
<td>5.5(^*)</td>
</tr>
<tr>
<td>Stomach</td>
<td>11.5</td>
<td>3.7(^*)</td>
</tr>
<tr>
<td>Corpus and Uterus, Nos(^f)</td>
<td>10.5</td>
<td>2.5(^*)</td>
</tr>
<tr>
<td>Pancreas</td>
<td>9.7</td>
<td>0.9</td>
</tr>
<tr>
<td>Urinary Bladder</td>
<td>8.8</td>
<td>1.6(^*)</td>
</tr>
<tr>
<td>Kidney and Renal Pelvis</td>
<td>8.1</td>
<td>2.3(^*)</td>
</tr>
<tr>
<td>Leukemia</td>
<td>7.6</td>
<td>-0.2</td>
</tr>
<tr>
<td>Oral Cavity and Pharynx</td>
<td>7.5</td>
<td>-1.1(^*)</td>
</tr>
<tr>
<td>Ovary(^h)</td>
<td>5.1</td>
<td>-1.5 (^*)</td>
</tr>
</tbody>
</table>

Source: SEER 18 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, Alaska Native Registry, Rural Georgia, California excluding SF/SJM/LA, Kentucky, Louisiana, New Jersey and Georgia excluding AT/RO).  
\(^a\) Top 15 cancer sites selected based on 2007-2011 age-adjusted rates for the race/ethnic group.  
\(^b\) Rates are per 100,000 and age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1130).  
\(^c\) The APC is the Annual Percent Change over the time interval.  
\(^d\) Trends are based on rates age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1130).  
\(^e\) Rates for American Indian/Alaska Native are based on the CHSDA (Contract Health Service Delivery Area) counties.  
\(^f\) Hispanic is not mutually exclusive from whites, blacks, Asian/Pacific Islanders, and American Indians/Alaska Natives.  
\(^g\) Incidence data for Hispanics are based on HNTHA and exclude cases from the Alaska Native Registry.  
\(^h\) The rates for sex-specific cancer sites are calculated using the population for both sexes combined.  
\(^i\) IBD = Intrahepatic Bile Duct. ONS = Other Nervous System.  
\(^j\) Ovary excludes borderline cases or histologies 8442, 8451, 8462, 8472, and 8473.  
\(^k\) The APC is significantly different from zero (p < .05).  
\(^l\) Statistic not shown. Rate based on less than 16 cases for the time interval. Trend based on less than 10 cases for at least one year within the time interval.
Table 1.25
Age-Adjusted SEER Incidence Rates and Trends for the Top 15 Cancer Sites\(^a\) by Race/Ethnicity

### Males

<table>
<thead>
<tr>
<th>Cancer Site</th>
<th>All Races</th>
<th>White</th>
<th>Black</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All Sites</strong></td>
<td>529.4</td>
<td>532.1</td>
<td>600.9</td>
</tr>
<tr>
<td><strong>Prostate</strong></td>
<td>147.8</td>
<td>119.9</td>
<td>223.9</td>
</tr>
<tr>
<td><strong>Lung and Bronchus</strong></td>
<td>72.2</td>
<td>72.4</td>
<td>93.0</td>
</tr>
<tr>
<td><strong>Colon and Rectum</strong></td>
<td>50.6</td>
<td>49.6</td>
<td>62.3</td>
</tr>
<tr>
<td><strong>Urinary Bladder</strong></td>
<td>36.2</td>
<td>39.4</td>
<td>24.7</td>
</tr>
<tr>
<td><strong>Melanoma of the Skin</strong></td>
<td>27.7</td>
<td>32.3</td>
<td>21.3</td>
</tr>
<tr>
<td><strong>Non-Hodgkin Lymphoma</strong></td>
<td>23.0</td>
<td>24.9</td>
<td>17.4</td>
</tr>
<tr>
<td><strong>Kidney and Renal Pelvis</strong></td>
<td>21.2</td>
<td>21.7</td>
<td>21.7</td>
</tr>
<tr>
<td><strong>Leukemia</strong></td>
<td>16.7</td>
<td>17.5</td>
<td>15.6</td>
</tr>
<tr>
<td><strong>Oral Cavity and Pharynx</strong></td>
<td>16.5</td>
<td>17.0</td>
<td>15.3</td>
</tr>
<tr>
<td><strong>Pancreas</strong></td>
<td>14.6</td>
<td>14.0</td>
<td>14.8</td>
</tr>
<tr>
<td><strong>Liver &amp; IBD</strong>f</td>
<td>12.4</td>
<td>10.8</td>
<td>15.6</td>
</tr>
<tr>
<td><strong>Stomach</strong></td>
<td>10.3</td>
<td>9.2</td>
<td>12.9</td>
</tr>
<tr>
<td><strong>Myeloma</strong></td>
<td>7.7</td>
<td>8.0</td>
<td>7.9</td>
</tr>
<tr>
<td><strong>Esophagus</strong></td>
<td>7.6</td>
<td>8.0</td>
<td>7.9</td>
</tr>
</tbody>
</table>

### Asian/Pacific Islander

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prostate</strong></td>
<td>79.3</td>
<td>71.5</td>
<td>121.8</td>
</tr>
<tr>
<td><strong>Lung and Bronchus</strong></td>
<td>49.4</td>
<td>49.5</td>
<td>44.3</td>
</tr>
<tr>
<td><strong>Colon and Rectum</strong></td>
<td>43.1</td>
<td>45.5</td>
<td>39.6</td>
</tr>
<tr>
<td><strong>Liver &amp; IBD</strong>f</td>
<td>21.6</td>
<td>25.3</td>
<td>20.6</td>
</tr>
<tr>
<td><strong>Stomach</strong></td>
<td>16.3</td>
<td>20.7</td>
<td>20.2</td>
</tr>
<tr>
<td><strong>Leukemia</strong></td>
<td>15.5</td>
<td>15.4</td>
<td>20.0</td>
</tr>
<tr>
<td><strong>Pancreas</strong></td>
<td>14.9</td>
<td>14.1</td>
<td>18.7</td>
</tr>
<tr>
<td><strong>Oral Cavity and Pharynx</strong></td>
<td>11.5</td>
<td>12.9</td>
<td>14.8</td>
</tr>
<tr>
<td><strong>Brain and ONSf</strong></td>
<td>10.9</td>
<td>12.6</td>
<td>12.4</td>
</tr>
<tr>
<td><strong>Esophagus</strong></td>
<td>10.7</td>
<td>12.5</td>
<td>12.2</td>
</tr>
</tbody>
</table>

### American Indian/Alaska Native\(^d\)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prostate</strong></td>
<td>331.0</td>
<td>71.5</td>
<td>121.8</td>
</tr>
<tr>
<td><strong>Lung and Bronchus</strong></td>
<td>49.4</td>
<td>49.5</td>
<td>44.3</td>
</tr>
<tr>
<td><strong>Colon and Rectum</strong></td>
<td>43.1</td>
<td>45.5</td>
<td>39.6</td>
</tr>
<tr>
<td><strong>Liver &amp; IBD</strong>f</td>
<td>21.6</td>
<td>25.3</td>
<td>20.6</td>
</tr>
<tr>
<td><strong>Stomach</strong></td>
<td>16.3</td>
<td>20.7</td>
<td>20.2</td>
</tr>
<tr>
<td><strong>Leukemia</strong></td>
<td>15.5</td>
<td>15.4</td>
<td>20.0</td>
</tr>
<tr>
<td><strong>Pancreas</strong></td>
<td>14.9</td>
<td>14.1</td>
<td>18.7</td>
</tr>
<tr>
<td><strong>Oral Cavity and Pharynx</strong></td>
<td>11.5</td>
<td>12.9</td>
<td>14.8</td>
</tr>
<tr>
<td><strong>Brain and ONSf</strong></td>
<td>10.9</td>
<td>12.6</td>
<td>12.4</td>
</tr>
<tr>
<td><strong>Esophagus</strong></td>
<td>10.7</td>
<td>12.5</td>
<td>12.2</td>
</tr>
</tbody>
</table>

### Hispanic\(^e\)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prostate</strong></td>
<td>331.0</td>
<td>71.5</td>
<td>121.8</td>
</tr>
<tr>
<td><strong>Lung and Bronchus</strong></td>
<td>49.4</td>
<td>49.5</td>
<td>44.3</td>
</tr>
<tr>
<td><strong>Colon and Rectum</strong></td>
<td>43.1</td>
<td>45.5</td>
<td>39.6</td>
</tr>
<tr>
<td><strong>Liver &amp; IBD</strong>f</td>
<td>21.6</td>
<td>25.3</td>
<td>20.6</td>
</tr>
<tr>
<td><strong>Stomach</strong></td>
<td>16.3</td>
<td>20.7</td>
<td>20.2</td>
</tr>
<tr>
<td><strong>Leukemia</strong></td>
<td>15.5</td>
<td>15.4</td>
<td>20.0</td>
</tr>
<tr>
<td><strong>Pancreas</strong></td>
<td>14.9</td>
<td>14.1</td>
<td>18.7</td>
</tr>
<tr>
<td><strong>Oral Cavity and Pharynx</strong></td>
<td>11.5</td>
<td>12.9</td>
<td>14.8</td>
</tr>
<tr>
<td><strong>Brain and ONSf</strong></td>
<td>10.9</td>
<td>12.6</td>
<td>12.4</td>
</tr>
<tr>
<td><strong>Esophagus</strong></td>
<td>10.7</td>
<td>12.5</td>
<td>12.2</td>
</tr>
</tbody>
</table>

Source: SEER 18 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, Alaska Native Registry, Rural Georgia, California excluding SF/SJM/LA, Kentucky, Louisiana, New Jersey and Georgia excluding ATL/RC).

\(^{a}\) Top 15 cancer sites selected based on 2007-2011 age-adjusted rates for the race/ethnic group.

\(^{b}\) Rates are per 100,000 and age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1130).

\(^{c}\) The APC is the Annual Percent Change over the time interval.

\(^{d}\) Trends are based on rates age-adjusted to the 2000 US Std Populations (19 age groups - Census P25-1130). Rates for American Indian/Alaska Native are based on the CHSDA (Contract Health Service Delivery Area) counties.

\(^{e}\) Hispanic is not mutually exclusive from whites, blacks, Asian/Pacific Islanders, and American Indians/Alaska Natives.

Incidence data for Hispanics are based on NHIA and exclude cases from the Alaska Native Registry.

\(^{f}\) IBD = Intrahepatic Bile Duct. ONS = Other Nervous System.

* The APC is significantly different from zero (p<.05).

- Statistic not shown. Rate based on less than 16 cases for the time interval. Trend based on less than 10 cases for at least one year within the time interval.
Table 1.26
Age-Adjusted SEER Incidence Rates and Trends for the Top 15 Cancer Sites\(^a\) by Race/Ethnicity

<table>
<thead>
<tr>
<th>Cancer Site</th>
<th>All Races</th>
<th>All Sites</th>
<th>White</th>
<th>Black</th>
<th>Hispanic</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rate(^b)</td>
<td>APC(^c)</td>
<td>Rate(^b)</td>
<td>APC(^c)</td>
<td>Rate(^b)</td>
</tr>
<tr>
<td>All Sites 2007-2011</td>
<td>411.3 -0.2</td>
<td>424.4 0.0</td>
<td>398.8 -0.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast 2007-2011</td>
<td>124.6 -0.2</td>
<td>128.0 0.3</td>
<td>122.8 0.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung and Bronchus 2007-2011</td>
<td>51.1 1.0</td>
<td>53.8 -0.9</td>
<td>51.2 -0.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colon and Rectum 2007-2011</td>
<td>38.2 -2.6</td>
<td>37.3 -2.7</td>
<td>47.5 -2.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corpus and Uterus, NOS 2007-2011</td>
<td>24.6 1.2</td>
<td>25.4 1.1</td>
<td>23.2 2.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thyroid 2007-2011</td>
<td>19.1 6.0</td>
<td>20.4 6.0</td>
<td>14.2 -0.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Melanoma of the Skin 2007-2011</td>
<td>16.7 0.9</td>
<td>20.0 0.9</td>
<td>11.9 -0.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma 2007-2011</td>
<td>16.3 -0.3</td>
<td>17.2 -0.3</td>
<td>11.1 6.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ovary(^g) 2007-2011</td>
<td>13.3 1.7</td>
<td>13.0 1.6</td>
<td>11.3 6.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pancreas 2007-2011</td>
<td>10.9 0.6</td>
<td>11.0 1.7</td>
<td>10.5 0.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kidney and Renal Pelvis 2007-2011</td>
<td>10.7 1.8</td>
<td>10.7 0.7</td>
<td>9.8 -1.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leukemia 2007-2011</td>
<td>10.2 0.1</td>
<td>10.7 0.2</td>
<td>9.4 -3.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary Bladder 2007-2011</td>
<td>8.8 1.2</td>
<td>9.5 1.1</td>
<td>8.5 1.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cervix Uteri 2007-2011</td>
<td>7.8 1.6</td>
<td>7.8 1.2</td>
<td>8.0 0.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral Cavity and Pharynx 2007-2011</td>
<td>6.2 0.1</td>
<td>6.4 0.4</td>
<td>6.9 1.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brain and ONS(^d) 2007-2011</td>
<td>5.4 -0.7</td>
<td>6.0 -0.7</td>
<td>5.3 -1.7</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| Asian/Pacific Islander 2007-2011| 293.0 0.0 | 301.9 0.0 | 320.4 0.0 |
| Breast 2007-2011                | 96.6 0.5  | 79.3 0.2 | 91.3 0.0 |
| Colon and Rectum 2007-2011     | 32.0 -2.1 | 35.5 -3.5 | 30.6 -1.8 |
| Lung and Bronchus 2007-2011     | 28.1 -0.2 | 34.7 2.8  | 25.5 -0.9 |
| Corpus and Uterus, NOS 2007-2011| 19.1 2.5   | 20.0 2.6  | 19.8 1.9 |
| Thyroid 2007-2011               | 18.5 5.3   | 14.5 0.8  | 17.1 5.4 |
| Non-Hodgkin Lymphoma 2007-2011 | 11.2 -0.2 | 11.8 4.7  | 15.4 0.2 |
| Ovary\(^g\) 2007-2011           | 9.3 -1.5   | 10.6 1.3  | 11.2 2.0 |
| Stomach 2007-2011               | 9.0 3.2    | 9.1 -1.4 | 10.9 -1.8 |
| Pancreas 2007-2011              | 8.9 1.0   | 9.1 0.4 | 10.2 -0.5 |
| Liver & IBD\(^f\) 2007-2011     | 8.1 1.3    | 8.1 1.9 | 6.7 1.7 |
| Cervix Uteri 2007-2011          | 6.4 3.5    | 7.3 0.1 | 6.0 0.8 |
| Leukemia 2007-2011              | 6.1 -0.6  | 7.3 -3.6 | 8.7 0.4 |
| Kidney and Renal Pelvis 2007-2011| 5.5 1.8 | 6.5 -0.5 | 8.3 -2.5 |
| Oral Cavity and Pharynx 2007-2011| 4.7 -2.4 | 4.8 - | 5.1 -1.9 |
| Urinary Bladder 2007-2011       | 3.9 -0.5  | 4.0 - | 4.7 -0.6 |

American Indian/Alaska Native 2007-2011 301.9 -0.6 10.2 4.5 6.0 0.8
Breast 2007-2011 79.3 0.2 91.3 0.0
Lung and Bronchus 2007-2011 34.7 2.8 25.5 0.9
Colon and Rectum 2007-2011 20.0 2.5 19.8 1.9
Kidney and Renal Pelvis 2007-2011 14.5 0.8 17.1 5.4
Non-Hodgkin Lymphoma 2007-2011 11.8 4.7 15.4 0.2
Ovary\(^g\) 2007-2011 9.1 0.4 10.9 1.8
Cervix Uteri 2007-2011 7.3 0.1 10.2 1.0
Stomach 2007-2011 7.3 3.6 8.7 0.4
Pancreas 2007-2011 8.0 1.9 8.3 2.5
Liver & IBD\(^f\) 2007-2011 6.7 1.7 5.1 1.9

Source: SEER 18 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, Alaska Native Registry, Rural Georgia, California excluding SF/SJM/LA, Kentucky, Louisiana, New Jersey and Georgia excluding ATL/ROC).

\(^a\) Top 15 cancer sites selected based on 2007-2011 age-adjusted rates for the race/ethnic group.

\(^b\) Rates are per 100,000 and age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1130).

\(^c\) The APC is the Annual Percent Change over the time interval.

\(^d\) Trends are based on rates age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1130).

\(^e\) Hispanic is not mutually exclusive from whites, blacks, Asian/Pacific Islanders, and American Indians/Alaska Natives.

\(^f\) Incident data for Hispanics are based on NHIA and exclude cases from the Alaska Native Registry.

\(^g\) Ovary excludes borderline cases or histologies 8442, 8451, 8462, 8472, and 8473.

\(^*\) The APC is significantly different from zero (p < 0.05).
### Table 1.27

Age-Adjusted U.S. Death Rates and Trends for the Top 15 Cancer Sites<sup>a</sup> by Race/Ethnicity

#### Both Sexes

<table>
<thead>
<tr>
<th>Cancer Site</th>
<th>All Races</th>
<th>White</th>
<th>Black</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rate&lt;sup&gt;b&lt;/sup&gt; 2007-2011</strong></td>
<td><strong>2002-2011</strong></td>
<td><strong>Rate&lt;sup&gt;b&lt;/sup&gt; 2007-2011</strong></td>
<td><strong>2002-2011</strong></td>
</tr>
<tr>
<td>All Sites</td>
<td>173.8</td>
<td>173.3</td>
<td>206.4</td>
</tr>
<tr>
<td>Lung and Bronchus</td>
<td>48.4</td>
<td>49.1</td>
<td>52.0</td>
</tr>
<tr>
<td>Colon and Rectum</td>
<td>15.9</td>
<td>15.5</td>
<td>22.1</td>
</tr>
<tr>
<td>Breast</td>
<td>12.4</td>
<td>12.1</td>
<td>18.0</td>
</tr>
<tr>
<td>Pancreas</td>
<td>10.9</td>
<td>10.8</td>
<td>17.4</td>
</tr>
<tr>
<td>Prostate&lt;sup&gt;f&lt;/sup&gt;</td>
<td>8.8</td>
<td>8.1</td>
<td>13.6</td>
</tr>
<tr>
<td>Leukemia</td>
<td>7.0</td>
<td>7.3</td>
<td>6.5</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>6.3</td>
<td>6.6</td>
<td>6.4</td>
</tr>
<tr>
<td>Liver &amp; IBD&lt;sup&gt;g&lt;/sup&gt;</td>
<td>5.8</td>
<td>5.3</td>
<td>6.2</td>
</tr>
<tr>
<td>Urinary Bladder</td>
<td>4.4</td>
<td>4.6</td>
<td>4.6</td>
</tr>
<tr>
<td>Ovary&lt;sup&gt;f&lt;/sup&gt;</td>
<td>4.4</td>
<td>4.5</td>
<td>4.5</td>
</tr>
<tr>
<td>Brain and ONS&lt;sup&gt;g&lt;/sup&gt;</td>
<td>4.3</td>
<td>4.3</td>
<td>4.5</td>
</tr>
<tr>
<td>Kidney and Renal Pelvis</td>
<td>4.0</td>
<td>4.0</td>
<td>3.9</td>
</tr>
<tr>
<td>Stomach</td>
<td>3.5</td>
<td>3.1</td>
<td>3.6</td>
</tr>
<tr>
<td>Myeloma</td>
<td>3.4</td>
<td>3.1</td>
<td>3.6</td>
</tr>
</tbody>
</table>

#### Asian/Pacific Islander

<table>
<thead>
<tr>
<th>Cancer Site</th>
<th>Rate&lt;sup&gt;b&lt;/sup&gt; 2007-2011</th>
<th>Rate&lt;sup&gt;b&lt;/sup&gt; 2002-2011</th>
<th>Rate&lt;sup&gt;b&lt;/sup&gt; 2007-2011</th>
<th>Rate&lt;sup&gt;b&lt;/sup&gt; 2002-2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Sites</td>
<td>107.8</td>
<td>-1.4*</td>
<td>99.0</td>
<td>-0.8*</td>
</tr>
<tr>
<td>Lung and Bronchus</td>
<td>25.2</td>
<td>-1.1*</td>
<td>20.9</td>
<td>-2.3*</td>
</tr>
<tr>
<td>Colon and Rectum</td>
<td>11.0</td>
<td>-1.6*</td>
<td>12.4</td>
<td>-1.7*</td>
</tr>
<tr>
<td>Liver &amp; IBD&lt;sup&gt;g&lt;/sup&gt;</td>
<td>9.8</td>
<td>-1.2*</td>
<td>8.7</td>
<td>1.5*</td>
</tr>
<tr>
<td>Pancreas</td>
<td>7.7</td>
<td>0.5</td>
<td>8.6</td>
<td>0.3</td>
</tr>
<tr>
<td>Breast</td>
<td>6.4</td>
<td>-1.5*</td>
<td>8.6</td>
<td>-3.0*</td>
</tr>
<tr>
<td>Stomach</td>
<td>6.3</td>
<td>-3.7*</td>
<td>8.4</td>
<td>-0.9*</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>4.1</td>
<td>-1.9*</td>
<td>6.7</td>
<td>-0.5*</td>
</tr>
<tr>
<td>Prostate&lt;sup&gt;f&lt;/sup&gt;</td>
<td>4.0</td>
<td>-2.6*</td>
<td>5.2</td>
<td>-5.5*</td>
</tr>
<tr>
<td>Leukemia</td>
<td>4.0</td>
<td>0.8</td>
<td>4.7</td>
<td>-1.3</td>
</tr>
<tr>
<td>Ovary&lt;sup&gt;f&lt;/sup&gt;</td>
<td>2.6</td>
<td>-1.0</td>
<td>4.6</td>
<td>-1.4</td>
</tr>
<tr>
<td>Kidney and Renal Pelvis</td>
<td>2.0</td>
<td>2.2</td>
<td>3.9</td>
<td>-0.3*</td>
</tr>
<tr>
<td>Oral Cavity and Pharynx</td>
<td>1.9</td>
<td>-2.1*</td>
<td>3.1</td>
<td>-3.1*</td>
</tr>
<tr>
<td>Brain and ONS&lt;sup&gt;g&lt;/sup&gt;</td>
<td>1.9</td>
<td>-0.5</td>
<td>2.7</td>
<td>-5.6*</td>
</tr>
<tr>
<td>Myeloma</td>
<td>1.8</td>
<td>0.6</td>
<td>2.6</td>
<td>2.1*</td>
</tr>
<tr>
<td>Esophagus</td>
<td>1.7</td>
<td>-1.3</td>
<td>2.5</td>
<td>3.4</td>
</tr>
</tbody>
</table>

#### American Indian/Alaska Native<sup>g</sup>

<table>
<thead>
<tr>
<th>Cancer Site</th>
<th>Rate&lt;sup&gt;b&lt;/sup&gt; 2007-2011</th>
<th>Rate&lt;sup&gt;b&lt;/sup&gt; 2002-2011</th>
<th>Rate&lt;sup&gt;b&lt;/sup&gt; 2007-2011</th>
<th>Rate&lt;sup&gt;b&lt;/sup&gt; 2002-2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Sites</td>
<td>158.0</td>
<td>-1.0*</td>
<td>120.3</td>
<td>-1.3*</td>
</tr>
<tr>
<td>Lung and Bronchus</td>
<td>39.9</td>
<td>-1.0</td>
<td>20.9</td>
<td>-2.3*</td>
</tr>
<tr>
<td>Colon and Rectum</td>
<td>17.2</td>
<td>-0.6</td>
<td>12.4</td>
<td>-1.7*</td>
</tr>
<tr>
<td>Liver &amp; IBD&lt;sup&gt;g&lt;/sup&gt;</td>
<td>9.5</td>
<td>2.0</td>
<td>8.7</td>
<td>1.5*</td>
</tr>
<tr>
<td>Pancreas</td>
<td>8.8</td>
<td>1.0</td>
<td>8.6</td>
<td>0.3</td>
</tr>
<tr>
<td>Breast</td>
<td>8.6</td>
<td>-3.0*</td>
<td>8.1</td>
<td>-1.6*</td>
</tr>
<tr>
<td>Prostate&lt;sup&gt;f&lt;/sup&gt;</td>
<td>8.4</td>
<td>-0.9</td>
<td>7.3</td>
<td>-2.4*</td>
</tr>
<tr>
<td>Kidney and Renal Pelvis</td>
<td>6.7</td>
<td>-0.5</td>
<td>5.6</td>
<td>-2.9*</td>
</tr>
<tr>
<td>Stomach</td>
<td>5.2</td>
<td>-5.5*</td>
<td>5.3</td>
<td>-1.4*</td>
</tr>
<tr>
<td>Leukemia</td>
<td>4.7</td>
<td>-1.3</td>
<td>4.8</td>
<td>-0.8*</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>4.6</td>
<td>-1.4</td>
<td>3.6</td>
<td>-1.0</td>
</tr>
<tr>
<td>Ovary&lt;sup&gt;f&lt;/sup&gt;</td>
<td>3.9</td>
<td>-0.3</td>
<td>3.2</td>
<td>-1.7*</td>
</tr>
<tr>
<td>Esophagus</td>
<td>3.3</td>
<td>-3.1*</td>
<td>2.8</td>
<td>-1.4</td>
</tr>
<tr>
<td>Myeloma</td>
<td>2.7</td>
<td>-5.6*</td>
<td>2.8</td>
<td>-0.4</td>
</tr>
<tr>
<td>Brain and ONS&lt;sup&gt;g&lt;/sup&gt;</td>
<td>2.6</td>
<td>2.1*</td>
<td>2.4</td>
<td>-1.2*</td>
</tr>
<tr>
<td>Urinary Bladder</td>
<td>2.5</td>
<td>3.4</td>
<td>2.3</td>
<td>0.0</td>
</tr>
</tbody>
</table>

Source: US Mortality Files, National Center for Health Statistics, Centers for Disease Control and Prevention.

- <sup>a</sup> Top 15 cancer sites selected based on 2007-2011 age-adjusted rates for the race/ethnic group.
- <sup>b</sup> Rates are per 100,000 and age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1130).
- <sup>c</sup> The APC is the Annual Percent Change over the time interval. Trends are based on rates age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1130).
- <sup>d</sup> Rates for American Indian/Alaska Native are based on the CNHSAD (Contract Health Service Delivery Area) counties. Hispanic is not mutually exclusive with whites, blacks, Asian/Pacific Islanders, and American Indians/Alaska Natives.
- <sup>e</sup> The rates for sex-specific cancer sites are calculated using the population for both sexes combined.
- <sup>f</sup> IBD = Intrahepatic Bile Duct. ONS = Other Nervous System.
- <sup>g</sup> The APC is significantly different from zero (p<.05).
- * Statistic not shown. Rate based on less than 16 cases for the time interval. Trend based on less than 10 cases for at least one year within the time interval.
### Table 1.28

Age-Adjusted U.S. Death Rates and Trends for the Top 15 Cancer Sitesa by Race/Ethnicity

#### Males

<table>
<thead>
<tr>
<th>Race</th>
<th>All Races</th>
<th>White</th>
<th>Black</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Sites</td>
<td>211.6</td>
<td>209.8</td>
<td>269.3</td>
</tr>
<tr>
<td>Lung and Bronchus</td>
<td>61.6</td>
<td>61.4</td>
<td>75.7</td>
</tr>
<tr>
<td>Prostate</td>
<td>22.3</td>
<td>20.6</td>
<td>48.9</td>
</tr>
<tr>
<td>Colon and Rectum</td>
<td>19.1</td>
<td>18.5</td>
<td>27.7</td>
</tr>
<tr>
<td>Pancreas</td>
<td>12.5</td>
<td>12.5</td>
<td>15.3</td>
</tr>
<tr>
<td>Leukemia</td>
<td>9.4</td>
<td>9.7</td>
<td>12.1</td>
</tr>
<tr>
<td>Liver &amp; IBDf</td>
<td>8.5</td>
<td>8.4</td>
<td>9.6</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>8.1</td>
<td>8.1</td>
<td>8.0</td>
</tr>
<tr>
<td>Urinary Bladder</td>
<td>7.7</td>
<td>7.8</td>
<td>7.8</td>
</tr>
<tr>
<td>Esophagus</td>
<td>7.5</td>
<td>7.8</td>
<td>7.4</td>
</tr>
<tr>
<td>Kidney and Renal Pelvis</td>
<td>5.8</td>
<td>5.9</td>
<td>5.9</td>
</tr>
<tr>
<td>Stomach</td>
<td>4.7</td>
<td>4.6</td>
<td>5.4</td>
</tr>
<tr>
<td>Myeloma</td>
<td>4.3</td>
<td>4.1</td>
<td>5.1</td>
</tr>
<tr>
<td>Melanoma of the Skin</td>
<td>4.1</td>
<td>4.0</td>
<td>4.1</td>
</tr>
<tr>
<td>Oral Cavity and Pharynx</td>
<td>3.8</td>
<td>3.7</td>
<td>3.8</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Race</th>
<th>Asian/Pacific Islander</th>
<th>American Indian/Alaska Native</th>
<th>Hispanic</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>APC 2002-2011</td>
<td>APC 2002-2011</td>
<td>APC 2002-2011</td>
</tr>
<tr>
<td>All Sites</td>
<td>131.0</td>
<td>190.0</td>
<td>150.1</td>
</tr>
<tr>
<td>Lung and Bronchus</td>
<td>34.7</td>
<td>50.0</td>
<td>30.5</td>
</tr>
<tr>
<td>Liver &amp; IBDf</td>
<td>14.5</td>
<td>21.2</td>
<td>18.5</td>
</tr>
<tr>
<td>Colon and Rectum</td>
<td>13.1</td>
<td>19.2</td>
<td>15.8</td>
</tr>
<tr>
<td>Prostate</td>
<td>10.0</td>
<td>13.8</td>
<td>12.6</td>
</tr>
<tr>
<td>Pancreas</td>
<td>8.5</td>
<td>9.9</td>
<td>9.7</td>
</tr>
<tr>
<td>Stomach</td>
<td>8.3</td>
<td>9.5</td>
<td>7.5</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>5.2</td>
<td>7.0</td>
<td>6.4</td>
</tr>
<tr>
<td>Leukemia</td>
<td>5.0</td>
<td>6.6</td>
<td>6.0</td>
</tr>
<tr>
<td>Esophagus</td>
<td>3.0</td>
<td>6.8</td>
<td>6.8</td>
</tr>
<tr>
<td>Kidney and Renal Pelvis</td>
<td>3.0</td>
<td>5.5</td>
<td>6.1</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>5.3</td>
<td>3.0</td>
<td>0.9</td>
</tr>
<tr>
<td>Urinary Bladder</td>
<td>2.9</td>
<td>2.9</td>
<td>4.4</td>
</tr>
<tr>
<td>Brain and ONSf</td>
<td>2.9</td>
<td>3.4</td>
<td>3.5</td>
</tr>
<tr>
<td>Oral Cavity and Pharynx</td>
<td>2.9</td>
<td>3.4</td>
<td>2.9</td>
</tr>
<tr>
<td>Soft Tissue including Heart</td>
<td>1.0</td>
<td>1.8</td>
<td>1.7</td>
</tr>
</tbody>
</table>

### Source

US Mortality Files, National Center for Health Statistics, Centers for Disease Control and Prevention.

Notes:

- Top 15 cancer sites selected based on 2007-2011 age-adjusted rates for the race/ethnic group.
- Rates are per 100,000 and age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1130).
- Trends are based on rates age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1130).
- Rates for American Indian/Alaska Native are based on the CHSDA (Contract Health Service Delivery Area) counties.
- Hispanic is not mutually exclusive from whites, blacks, Asian/Pacific Islanders, and American Indians/Alaska Natives.
- IBD = Intrahepatic Bile Duct. ONS = Other Nervous System.
- The APC is significantly different from zero (p < .05).
- Statistic not shown. Rate based on less than 16 cases for the time interval. Trend based on less than 10 cases for at least one year within the time interval.
## Table 1.29

Age-Adjusted U.S. Death Rates and Trends for the Top 15 Cancer Sites\(^a\) by Race/Ethnicity

<table>
<thead>
<tr>
<th>Females</th>
<th>All Races</th>
<th>White</th>
<th>Black</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All Sites</strong></td>
<td>147.4 -1.4*</td>
<td>147.5 -1.4*</td>
<td>169.0 -1.7*</td>
</tr>
<tr>
<td>Lung and Bronchus</td>
<td>38.5 -1.2*</td>
<td>39.8 -2.0*</td>
<td>36.5 -1.6*</td>
</tr>
<tr>
<td>Breast</td>
<td>22.2 -2.0*</td>
<td>21.7 -2.0*</td>
<td>30.6 -1.5*</td>
</tr>
<tr>
<td>Colon and Rectum</td>
<td>13.5 -2.9*</td>
<td>13.0 -2.9*</td>
<td>18.5 -3.2*</td>
</tr>
<tr>
<td>Pancreas</td>
<td>9.6 -0.4*</td>
<td>9.4 -0.5*</td>
<td>12.4 -0.2*</td>
</tr>
<tr>
<td>Ovary</td>
<td>7.9 -2.0*</td>
<td>8.2 -2.0*</td>
<td>7.5 1.0*</td>
</tr>
<tr>
<td>Leukemia</td>
<td>5.3 -1.0*</td>
<td>5.4 -0.9*</td>
<td>6.6 1.7*</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>5.0 -3.0*</td>
<td>5.2 -3.0*</td>
<td>5.3 -2.0*</td>
</tr>
<tr>
<td>Corpus and Uterus, NOS</td>
<td>4.3 0.8*</td>
<td>4.0 0.7*</td>
<td>4.8 1.5*</td>
</tr>
<tr>
<td>Brain and ONS(^f)</td>
<td>3.5 -0.5*</td>
<td>3.8 -0.4</td>
<td>4.5 1.5*</td>
</tr>
<tr>
<td>Liver &amp; IBD(^f)</td>
<td>3.4 1.8*</td>
<td>3.2 1.5*</td>
<td>4.2 1.7*</td>
</tr>
<tr>
<td>Myeloma</td>
<td>2.7 -1.9*</td>
<td>2.6 -1.2*</td>
<td>2.3 2.3*</td>
</tr>
<tr>
<td>Kidney and Renal Pelvis</td>
<td>2.6 -1.2*</td>
<td>2.5 -0.9*</td>
<td>2.6 2.9*</td>
</tr>
<tr>
<td>Stomach</td>
<td>2.5 -2.7*</td>
<td>2.2 -0.4</td>
<td>2.6 -0.7</td>
</tr>
<tr>
<td>Cervix Uteri</td>
<td>2.3 -1.1*</td>
<td>2.1 -2.7*</td>
<td>2.4 2.8*</td>
</tr>
<tr>
<td>Urinary Bladder</td>
<td>2.2 -0.6*</td>
<td>2.1 -0.8*</td>
<td>2.1 0.2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Asian/Pacific Islander</th>
<th>All Races</th>
<th>White</th>
<th>Black</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All Sites</strong></td>
<td>91.5 -0.8*</td>
<td>135.2 -1.6*</td>
<td>99.9 -1.2*</td>
</tr>
<tr>
<td>Lung and Bronchus</td>
<td>18.4 -0.1</td>
<td>32.4 -1.5*</td>
<td>14.5 -1.5*</td>
</tr>
<tr>
<td>Breast</td>
<td>11.3 -1.6*</td>
<td>15.6 0.0</td>
<td>14.0 -1.4*</td>
</tr>
<tr>
<td>Colon and Rectum</td>
<td>9.5 -1.3*</td>
<td>15.2 -2.8*</td>
<td>9.9 -2.1*</td>
</tr>
<tr>
<td>Pancreas</td>
<td>7.2 0.5</td>
<td>8.0 0.8</td>
<td>7.7 0.1</td>
</tr>
<tr>
<td>Liver &amp; IBD(^f)</td>
<td>6.0 -1.4</td>
<td>6.9 -0.3</td>
<td>5.6 1.6*</td>
</tr>
<tr>
<td>Stomach</td>
<td>4.8 -4.0*</td>
<td>6.0 -2.4</td>
<td>5.5 0.9*</td>
</tr>
<tr>
<td>Ovary</td>
<td>4.7 -1.0</td>
<td>6.9 -0.3</td>
<td>5.6 1.6*</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>3.4 -2.0*</td>
<td>3.9 -3.2</td>
<td>4.4 1.8*</td>
</tr>
<tr>
<td>Corpus and Uterus, NOS</td>
<td>2.7 1.9*</td>
<td>3.5 3.7</td>
<td>3.4 1.5</td>
</tr>
<tr>
<td>Cervix Uteri</td>
<td>1.8 -3.0*</td>
<td>3.4 -2.2</td>
<td>2.8 2.4*</td>
</tr>
<tr>
<td>Brain and ONS(^f)</td>
<td>1.5 0.0</td>
<td>3.4 3.0</td>
<td>2.4 0.6</td>
</tr>
<tr>
<td>Myeloma</td>
<td>1.4 -1.4</td>
<td>2.3 2.1</td>
<td>2.4 1.1</td>
</tr>
<tr>
<td>Kidney and Renal Pelvis</td>
<td>1.3 1.5</td>
<td>2.2 -5.6</td>
<td>2.2 1.5</td>
</tr>
<tr>
<td>Oral Cavity and Pharynx</td>
<td>1.2 -2.6</td>
<td>1.8 -4.4</td>
<td>1.3 -1.7</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>American Indian/Alaska Native(^d)</th>
<th>All Races</th>
<th>White</th>
<th>Black</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All Sites</strong></td>
<td>135.2 -1.6*</td>
<td>135.5 -1.5*</td>
<td>165.0 -1.6*</td>
</tr>
<tr>
<td>Lung and Bronchus</td>
<td>39.5 -1.1*</td>
<td>39.8 -2.0*</td>
<td>36.5 -1.6*</td>
</tr>
<tr>
<td>Breast</td>
<td>21.7 -2.0*</td>
<td>21.7 -2.0*</td>
<td>30.6 -1.5*</td>
</tr>
<tr>
<td>Colon and Rectum</td>
<td>13.0 -2.9*</td>
<td>13.0 -2.9*</td>
<td>18.5 -3.2*</td>
</tr>
<tr>
<td>Pancreas</td>
<td>9.4 0.5*</td>
<td>9.4 0.5*</td>
<td>12.4 -0.2*</td>
</tr>
<tr>
<td>Ovary</td>
<td>8.2 -2.0*</td>
<td>8.2 -2.0*</td>
<td>7.5 1.0*</td>
</tr>
<tr>
<td>Leukemia</td>
<td>5.4 -0.9*</td>
<td>5.4 -0.9*</td>
<td>6.6 1.7*</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>5.2 -3.0*</td>
<td>5.2 -3.0*</td>
<td>5.3 -2.0*</td>
</tr>
<tr>
<td>Corpus and Uterus, NOS</td>
<td>4.0 0.7*</td>
<td>4.0 0.7*</td>
<td>4.8 -1.5*</td>
</tr>
<tr>
<td>Brain and ONS(^f)</td>
<td>3.8 0.4</td>
<td>3.8 0.4</td>
<td>4.5 1.5*</td>
</tr>
<tr>
<td>Liver &amp; IBD(^f)</td>
<td>3.2 1.5*</td>
<td>3.2 1.5*</td>
<td>4.2 1.7*</td>
</tr>
<tr>
<td>Myeloma</td>
<td>2.7 1.9*</td>
<td>2.6 1.2*</td>
<td>2.3 2.1</td>
</tr>
<tr>
<td>Kidney and Renal Pelvis</td>
<td>2.6 -1.2*</td>
<td>2.5 -0.9*</td>
<td>2.4 2.8*</td>
</tr>
<tr>
<td>Stomach</td>
<td>2.2 -0.4</td>
<td>2.2 -0.4</td>
<td>2.4 0.6</td>
</tr>
<tr>
<td>Cervix Uteri</td>
<td>2.1 -2.7*</td>
<td>2.1 -2.7*</td>
<td>2.4 2.8*</td>
</tr>
<tr>
<td>Urinary Bladder</td>
<td>2.1 0.8*</td>
<td>2.1 0.8*</td>
<td>2.1 0.2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hispanic(^e)</th>
<th>All Races</th>
<th>White</th>
<th>Black</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All Sites</strong></td>
<td>99.9 -1.2*</td>
<td>99.9 -1.2*</td>
<td>99.9 -1.2*</td>
</tr>
<tr>
<td>Lung and Bronchus</td>
<td>32.4 -1.5*</td>
<td>32.4 -1.5*</td>
<td>32.4 -1.5*</td>
</tr>
<tr>
<td>Breast</td>
<td>15.6 0.0</td>
<td>15.6 0.0</td>
<td>15.6 0.0</td>
</tr>
<tr>
<td>Colon and Rectum</td>
<td>15.2 -2.8*</td>
<td>15.2 -2.8*</td>
<td>15.2 -2.8*</td>
</tr>
<tr>
<td>Pancreas</td>
<td>8.0 0.8</td>
<td>8.0 0.8</td>
<td>8.0 0.8</td>
</tr>
<tr>
<td>Ovary</td>
<td>6.9 -0.3</td>
<td>6.9 -0.3</td>
<td>6.9 -0.3</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>3.9 -3.2</td>
<td>3.9 -3.2</td>
<td>3.9 -3.2</td>
</tr>
<tr>
<td>Corpus and Uterus, NOS</td>
<td>3.5 3.7</td>
<td>3.5 3.7</td>
<td>3.5 3.7</td>
</tr>
<tr>
<td>Cervix Uteri</td>
<td>3.4 -2.2</td>
<td>3.4 -2.2</td>
<td>3.4 -2.2</td>
</tr>
<tr>
<td>Brain and ONS(^f)</td>
<td>3.4 3.0</td>
<td>3.4 3.0</td>
<td>3.4 3.0</td>
</tr>
<tr>
<td>Myeloma</td>
<td>2.2 -5.6</td>
<td>2.2 -5.6</td>
<td>2.2 -5.6</td>
</tr>
<tr>
<td>Urinary Bladder</td>
<td>1.8 -4.4</td>
<td>1.8 -4.4</td>
<td>1.8 -4.4</td>
</tr>
</tbody>
</table>

---

Source: US Mortality Files, National Center for Health Statistics, Centers for Disease Control and Prevention.

* Top 15 cancer sites selected based on 2007-2011 age-adjusted rates for the race/ethnic group.

* Rates are per 100,000 and age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1130).

* The APC is the Annual Percent Change over the time interval.

* Trends are based on rates age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1130).

* Rates for American Indian/Alaska Native are based on the CHSDA (Contract Health Service Delivery Area) counties.

* Hispanic is not mutually exclusive from whites, blacks, Asian/Pacific Islanders, and American Indians/Alaska Natives.

* IBD = Intrahepatic Bile Duct. ONS = Other Nervous System.

* The APC is significantly different from zero (p<.05).

* Statistic not shown. Rate based on less than 16 cases for the time interval. Trend based on less than 10 cases for at least one year within the time interval.
Surveillance, Epidemiology, and End Results (SEER) Program: SEER 9, 13, & 18 Geographic Areas
National Cancer Institute, USA

- San Francisco/Oakland, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle/Puget Sound, Utah, Atlanta. SEER 9 is this group.
- San Jose-Monterey, Los Angeles, Alaska Native Registry, Rural Georgia. SEER 13 is this group plus SEER 9.
- California excluding SF/SJM/LA, Georgia excluding AT/RG, Kentucky, Louisiana, New Jersey. SEER 18 is this group plus SEER 13.

http://seer.cancer.gov
Figure 1.2
Leading Causes of Death in US, 1975 vs 2011
Percent of All Causes of Death

1975
- All Malignant Cancers 19.2%
- Heart Disease 37.8%
- Cerebrovascular Diseases 10.3%
- Chronic Lung Disease 2.3%
- Accidents 5.4%
- Pneumonia and Influenza 2.9%
- Other Causes 22.0%

2011
- All Malignant Cancers 22.9%
- Heart Disease 23.7%
- Cerebrovascular Diseases 5.1%
- Chronic Lung Disease 5.7%
- Accidents 5.0%
- Pneumonia and Influenza 2.1%
- Other Causes 35.4%

Source: US Mortality Files, National Center for Health Statistics, Centers for Disease Control and Prevention.
Figure 1.3
Us Death Rates, 1975-2011
Heart Disease compared to Neoplasms, by age at death

Ages Less Than 65

Heart Disease
26% of deaths in 1975

Neoplasms
22% of deaths in 1975

Year of Death

Ages 65 and Over

Heart Disease
18% of deaths in 1975

Neoplasms
26% of deaths in 1975

Rate per 100,000

Year of Death

Source: US Mortality Files, National Center for Health Statistics, Centers for Disease Control and Prevention. Rates are per 100,000 and age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1103).
Figure 1.4
Trends in SEER Incidence and US Death Rates by Primary Cancer Site
2002-2011

<table>
<thead>
<tr>
<th>Trends in SEER Incidence Rates</th>
<th>Trends in US Cancer Death Rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyroid</td>
<td>Liver &amp; Intrahepatic Bile Duct</td>
</tr>
<tr>
<td>Liver &amp; Intrahepatic Bile Duct</td>
<td>Thyroid</td>
</tr>
<tr>
<td>Kidney &amp; Renal Pelvis</td>
<td>Corpus &amp; Uterus, NOS</td>
</tr>
<tr>
<td>Melanoma of the Skin</td>
<td>Pancreas</td>
</tr>
<tr>
<td>Corpus &amp; Uterus, NOS</td>
<td>Melanoma of the Skin</td>
</tr>
<tr>
<td>Pancreas</td>
<td>Urinary Bladder</td>
</tr>
<tr>
<td>Myeloma</td>
<td>Brain &amp; Other Nervous System</td>
</tr>
<tr>
<td>Tests</td>
<td>Esophagus</td>
</tr>
<tr>
<td>Oral Cavity &amp; Pharynx</td>
<td>Kidney &amp; Renal Pelvis</td>
</tr>
<tr>
<td>Leukemia</td>
<td>Leukemia</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>Oral Cavity &amp; Pharynx</td>
</tr>
<tr>
<td>Breast (Female)</td>
<td>Cervix Uteri</td>
</tr>
<tr>
<td>Hodgkin Lymphoma</td>
<td>Lung &amp; Bronchus (Female)</td>
</tr>
<tr>
<td>All Sites Except Lung</td>
<td>All Sites Except Lung</td>
</tr>
<tr>
<td>All Cancer Sites</td>
<td>All Cancer Sites</td>
</tr>
<tr>
<td>Brain &amp; Other Nervous System</td>
<td>Thyroid</td>
</tr>
<tr>
<td>Urinary Bladder</td>
<td>Esophagus</td>
</tr>
<tr>
<td>Ovary</td>
<td>Kidney &amp; Renal Pelvis</td>
</tr>
<tr>
<td>Stomach</td>
<td>Leukemia</td>
</tr>
<tr>
<td>Cervix Uteri</td>
<td>Oral Cavity &amp; Pharynx</td>
</tr>
<tr>
<td>Ovary*</td>
<td>Cervix Uteri</td>
</tr>
<tr>
<td>Larynx</td>
<td>Lung &amp; Bronchus (Female)</td>
</tr>
<tr>
<td>Prostate</td>
<td>All Cancer Sites</td>
</tr>
<tr>
<td>Lung &amp; Bronchus (Male)</td>
<td>Myeloma</td>
</tr>
<tr>
<td>Colon &amp; Rectum</td>
<td>Breast (Female)</td>
</tr>
<tr>
<td></td>
<td>Ovary</td>
</tr>
<tr>
<td></td>
<td>Larynx</td>
</tr>
<tr>
<td></td>
<td>Non-Hodgkin Lymphoma</td>
</tr>
<tr>
<td></td>
<td>Lung &amp; Bronchus (Male)</td>
</tr>
<tr>
<td></td>
<td>Hodgkin Lymphoma</td>
</tr>
<tr>
<td></td>
<td>Stomach</td>
</tr>
<tr>
<td></td>
<td>Colon &amp; Rectum</td>
</tr>
<tr>
<td></td>
<td>Prostate</td>
</tr>
</tbody>
</table>

Source: SEER 18 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, Alaska Native Registry, Rural Georgia, California excluding SF/SJM/LA, Kentucky, Louisiana, New Jersey and Georgia excluding ATL/GRJ) and US Mortality Files, National Center for Health Statistics, Centers for Disease Control and Prevention.

Underlying rates are per 100,000 and age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1103).

For sex-specific cancer sites, the population was limited to the population of the appropriate sex.

* The APC is significantly different from zero (p<.05).

a Ovary excludes borderline cases or histologies 8442, 8451, 8462, 8472, and 8473.
Trends in SEER Incidence Rates by Age Group and Primary Cancer Site 2002-2011

Source: SEER 18 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, Alaska Native Registry, Rural Georgia, California excluding SF/SJM/LA, Kentucky, Louisiana, New Jersey and Georgia excluding ATL/RG).

Underlying rates are per 100,000 and age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1103).

For sex-specific cancer sites, the population was limited to the population of the appropriate sex.

* The APC is significantly different from zero (p<.05).

a Ovary excludes borderline cases or histologies 8442, 8451, 8462, 8472, and 8473.
Figure 1.6
Trends in US Death Rates by Age Group and Primary Cancer Site 2002-2011

Source: US Mortality Files, National Center for Health Statistics, Centers for Disease Control and Prevention.
Underlying rates are per 100,000 and age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1103).
For sex-specific cancer sites, the population was limited to the population of the appropriate sex.
* The APC is significantly different from zero (p<.05).
Figure 1.7
Trends in SEER Incidence Rates by Sex and Primary Cancer Site
2002-2011

Source: SEER 18 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, Alaska Native Registry, Rural Georgia, California excluding SF/SJM/LA, Kentucky, Louisiana, New Jersey and Georgia excluding ATL/RG).
Underlying rates are per 100,000 and age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1103).

For sex-specific cancer sites, the population was limited to the population of the appropriate sex.

* The APC is significantly different from zero (p<.05).
a Ovary excludes borderline cases or histologies 8442, 8451, 8462, 8472, and 8473.
Figure 1.8
Trends in US Death Rates by Sex and Primary Cancer Site 2002-2011

<table>
<thead>
<tr>
<th>Cancer Site</th>
<th>All Races, Males</th>
<th>All Races, Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver &amp; Intrahepatic Bile Duct</td>
<td>2.6*</td>
<td>1.8*</td>
</tr>
<tr>
<td>Thyroid</td>
<td></td>
<td>0.9</td>
</tr>
<tr>
<td>Melanoma of the Skin</td>
<td></td>
<td>0.8*</td>
</tr>
<tr>
<td>Pancreas</td>
<td>-0.7*</td>
<td>0.4*</td>
</tr>
<tr>
<td>Urinary Bladder</td>
<td>-0.3*</td>
<td>-0.3*</td>
</tr>
<tr>
<td>Brain &amp; Other Nervous System</td>
<td>-0.4</td>
<td>-0.5*</td>
</tr>
<tr>
<td>Esophagus</td>
<td>-0.6*</td>
<td>-0.6*</td>
</tr>
<tr>
<td>Testis</td>
<td>-0.6</td>
<td>-0.6*</td>
</tr>
<tr>
<td>Kidney &amp; Renal Pelvis</td>
<td>-0.8*</td>
<td>-0.3*</td>
</tr>
<tr>
<td>Oral Cavity &amp; Pharynx</td>
<td>-0.9*</td>
<td>-0.5*</td>
</tr>
<tr>
<td>Leukemia</td>
<td>-1.0*</td>
<td>-0.6*</td>
</tr>
<tr>
<td>Myeloma</td>
<td>-1.3*</td>
<td>-1.1*</td>
</tr>
<tr>
<td>All Sites Except Lung</td>
<td>-1.4*</td>
<td>-1.2*</td>
</tr>
<tr>
<td>All Cancer Sites</td>
<td>-1.8*</td>
<td>-1.4*</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>-2.3*</td>
<td>-1.4*</td>
</tr>
<tr>
<td>Hodgkin Lymphoma</td>
<td>-2.4*</td>
<td>-1.5*</td>
</tr>
<tr>
<td>Larynx</td>
<td>-2.6*</td>
<td>-1.6*</td>
</tr>
<tr>
<td>Lung &amp; Bronchus</td>
<td>-2.6*</td>
<td>-1.9*</td>
</tr>
<tr>
<td>Colon &amp; Rectum</td>
<td>-3.0*</td>
<td>-2.0*</td>
</tr>
<tr>
<td>Stomach</td>
<td>-3.2*</td>
<td>-2.1*</td>
</tr>
<tr>
<td>Prostate</td>
<td>-3.3*</td>
<td>-2.7*</td>
</tr>
</tbody>
</table>

Source: US Mortality Files, National Center for Health Statistics, Centers for Disease Control and Prevention.

Underlying rates are per 100,000 and age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1103).

For sex-specific cancer sites, the population was limited to the population of the appropriate sex.

* The APC is significantly different from zero (p<.05).
### Figure 1.9

**SEER Incidence\(^a\) and US Death Rates,\(^b\) 2007-2011**

**5-Year Relative Survival,\(^c\) 2004-2010**

**All Cancer Combined, by Race and Sex**

<table>
<thead>
<tr>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SEER Incidence</strong></td>
<td><strong>US Mortality</strong></td>
</tr>
<tr>
<td>Rate per 100,000</td>
<td>Survival Rate, Percent (%)</td>
</tr>
<tr>
<td><img src="image" alt="Graph" /></td>
<td><img src="image" alt="Graph" /></td>
</tr>
</tbody>
</table>

- **Incidence rates** are from the SEER 18 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, Alaska Native Registry, Rural Georgia, California excluding SF/SJM/LA, Kentucky, Louisiana, New Jersey and Georgia excluding ATL/RG) and are age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1103).
- **Death rates** are from the US Mortality Files, National Center for Health Statistics, Centers for Disease Control and Prevention and are age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1103).
- **Survival rates** are from the SEER 18 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, Alaska Native Registry, Rural Georgia, California excluding SF/SJM/LA, Kentucky, Louisiana, New Jersey and Georgia excluding ATL/RG).
Table 1.25
Age-Adjusted SEER Incidence Rates and Trends for the Top 15 Cancer Sites* by Race/Ethnicity

<table>
<thead>
<tr>
<th></th>
<th>All Races</th>
<th>White</th>
<th>Black</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rateb</td>
<td>APCc</td>
<td>Rateb</td>
</tr>
<tr>
<td>All Sites</td>
<td>529.4</td>
<td>-1.2*</td>
<td>532.1</td>
</tr>
<tr>
<td>Prostate</td>
<td>147.8</td>
<td>-2.6*</td>
<td>139.9</td>
</tr>
<tr>
<td>Lung and Bronchus</td>
<td>72.2</td>
<td>-2.4*</td>
<td>72.4</td>
</tr>
<tr>
<td>Colon and Rectum</td>
<td>50.6</td>
<td>-3.0*</td>
<td>49.6</td>
</tr>
<tr>
<td>Urinary Bladder</td>
<td>36.2</td>
<td>-0.8*</td>
<td>39.4</td>
</tr>
<tr>
<td>Melanoma of the Skin</td>
<td>27.7</td>
<td>1.6*</td>
<td>32.3</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>23.9</td>
<td>0.0</td>
<td>24.9</td>
</tr>
<tr>
<td>Kidney and Renal Pelvis</td>
<td>21.2</td>
<td>1.8*</td>
<td>21.7</td>
</tr>
<tr>
<td>Leukemia</td>
<td>16.7</td>
<td>-0.3</td>
<td>17.5</td>
</tr>
<tr>
<td>Oral Cavity and Pharynx</td>
<td>16.5</td>
<td>0.4*</td>
<td>17.0</td>
</tr>
<tr>
<td>Pancreas</td>
<td>14.6</td>
<td>0.2*</td>
<td>14.0</td>
</tr>
<tr>
<td>Stomach</td>
<td>10.3</td>
<td>-1.6*</td>
<td>9.2</td>
</tr>
<tr>
<td>Melanoma</td>
<td>7.7</td>
<td>0.7*</td>
<td>8.0</td>
</tr>
<tr>
<td>Esophagus</td>
<td>7.7</td>
<td>-0.7</td>
<td>7.2</td>
</tr>
</tbody>
</table>

Asian/Pacific Islander

|          | Rateb     | APCc                   | Rateb                  | APCc                   |
| All Sites| 331.0     | -1.8*                  | 331.0                  | -1.8*                  |
| Prostate | 79.3      | -3.8*                  | 71.5                  | -3.9*                  |
| Lung and Bronchus | 49.4     | -2.2*                  | 49.5                  | -2.4*                  |
| Colon and Rectum | 43.1     | -2.4*                  | 45.5                  | 0.2                    |
| Urinary Bladder | 21.6     | -0.7                   | 25.3                  | 2.4                    |
| Non-Hodgkin Lymphoma | 16.3     | 0.0                    | 20.7                  | 5.1                    |
| Stomach  | 14.9      | -4.1*                  | 12.9                  | -4.3*                  |
| Kidney and Renal Pelvis | 11.5     | 2.6*                   | 12.6                  | 0.3                    |
| Oral Cavity and Pharynx | 10.9     | -0.3                   | 12.5                  | 4.1                    |
| Pancreas | 10.7      | 0.8                    | 10.7                  | 0.8                    |
| Leukemia | 9.4       | 0.1                    | 8.6                   | 1.7                    |
| Thyroid  | 5.7       | 5.7*                   | 4.8                   | -0.1                   |
| Myeloma  | 4.5       | 1.8*                   | 4.5                   | -0.5                   |
| Brain and ONSf | 4.2      | 0.8                    | 4.3                   | -1.1                   |
| Esophagus | 3.7       | -1.2                   | 4.3                   | -1.2                   |

American Indian/Alaska Nativef

|          | Rateb     | APCc                   | Rateb                  | APCc                   |
| All Sites| 331.0     | -1.8*                  | 331.0                  | -1.8*                  |
| Prostate | 79.3      | -3.8*                  | 71.5                  | -3.9*                  |
| Lung and Bronchus | 49.4     | -2.2*                  | 49.5                  | -2.4*                  |
| Colon and Rectum | 43.1     | -2.4*                  | 45.5                  | 0.2                    |
| Urinary Bladder | 21.6     | -0.7                   | 25.3                  | 2.4                    |
| Non-Hodgkin Lymphoma | 16.3     | 0.0                    | 20.7                  | 5.1                    |
| Stomach  | 14.9      | -4.1*                  | 12.9                  | -4.3*                  |
| Kidney and Renal Pelvis | 11.5     | 2.6*                   | 12.6                  | 0.3                    |
| Oral Cavity and Pharynx | 10.9     | -0.3                   | 12.5                  | 4.1                    |
| Pancreas | 10.7      | 0.8                    | 10.7                  | 0.8                    |
| Leukemia | 9.4       | 0.1                    | 8.6                   | 1.7                    |
| Thyroid  | 5.7       | 5.7*                   | 4.8                   | -0.1                   |
| Myeloma  | 4.5       | 1.8*                   | 4.5                   | -0.5                   |
| Brain and ONSf | 4.2      | 0.8                    | 4.3                   | -1.1                   |
| Esophagus | 3.7       | -1.2                   | 4.3                   | -1.2                   |

Hispanicf

|          | Rateb     | APCc                   | Rateb                  | APCc                   |
| All Sites| 331.0     | -1.8*                  | 331.0                  | -1.8*                  |
| Prostate | 79.3      | -3.8*                  | 71.5                  | -3.9*                  |
| Lung and Bronchus | 49.4     | -2.2*                  | 49.5                  | -2.4*                  |
| Colon and Rectum | 43.1     | -2.4*                  | 45.5                  | 0.2                    |
| Urinary Bladder | 21.6     | -0.7                   | 25.3                  | 2.4                    |
| Non-Hodgkin Lymphoma | 16.3     | 0.0                    | 20.7                  | 5.1                    |
| Stomach  | 14.9      | -4.1*                  | 12.9                  | -4.3*                  |
| Kidney and Renal Pelvis | 11.5     | 2.6*                   | 12.6                  | 0.3                    |
| Oral Cavity and Pharynx | 10.9     | -0.3                   | 12.5                  | 4.1                    |
| Pancreas | 10.7      | 0.8                    | 10.7                  | 0.8                    |
| Leukemia | 9.4       | 0.1                    | 8.6                   | 1.7                    |
| Thyroid  | 5.7       | 5.7*                   | 4.8                   | -0.1                   |
| Myeloma  | 4.5       | 1.8*                   | 4.5                   | -0.5                   |
| Brain and ONSf | 4.2      | 0.8                    | 4.3                   | -1.1                   |
| Esophagus | 3.7       | -1.2                   | 4.3                   | -1.2                   |

Source: SEER 18 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, Alaska Native Registry, Rural Georgia, California excluding SF/SJSM/LA, Kentucky, Louisiana, New Jersey and Georgia excluding ATL/RG).

* Top 15 cancer sites selected based on 2007-2011 age-adjusted rates for the race/ethnic group.

b Rates are per 100,000 and age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1130).

c The APC is the Annual Percent Change over the time interval.

d Rates for American Indian/Alaska Native are based on the CHSDA (Contract Health Service Delivery Area) counties.

e Hispanic is not mutually exclusive from whites, blacks, Asian/Pacific Islanders, and American Indians/Alaska Natives.

f Incidence data for Hispanics are based on NHIA and exclude cases from the Alaska Native Registry.

f IBD = Intrahepatic Bile Duct. ONS = Other Nervous System.

* The APC is significantly different from zero (p<.05).

- Statistic not shown. Rate based on less than 16 cases for the time interval. Trend based on less than 10 cases for at least one year within the time interval.
Figure 1.11

5-Year Relative Survival (%)
SEER Program, 2004-2010
Both Sexes, by Race and Cancer Site

White Patients | Cancer Site | Black Patients
---|---|---
99 | Prostate | 97
98 | Thyroid | 97
95 | Testis | 91
91 | Melanoma of the Skin | 71
90 | Breast (Female) | 79
86 | Hodgkin Lymphoma | 82
84 | Corpus & Uterus, NOS | 61
78 | Kaposi Sarcoma | 54
78 | Urinary Bladder | 64
73 | Kidney & Renal Pelvis | 71
70 | Non-Hodgkin Lymphoma | 62
69 | Cervix Uteri | 59
66 | Rectum | 62
65 | Colon | 56
64 | Oral Cavity & Pharynx | 44
61 | Larynx | 54
57 | Leukemia | 51
45 | Myeloma | 45
44 | Ovary\(^a\) | 35
32 | Brain & ONS | 40
27 | Stomach | 27
18 | Esophagus | 12
17 | Lung & Bronchus | 14
16 | Liver & IBD | 12
8 | Mesothelioma | 10
7 | Pancreas | 6

Source: SEER 18 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, Alaska Native Registry, Rural Georgia, California excluding SF/SJM/LA, Kentucky, Louisiana, New Jersey and Georgia excluding ATL/RG).

\(^a\) Ovary excludes borderline cases or histologies 8442, 8451, 8462, 8472, and 8473.
By Cancer Site and Race/Ethnicity

<table>
<thead>
<tr>
<th>Incidence</th>
<th>Cancer Site</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lung and Bronchus</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>61.7</td>
<td>White</td>
<td>49.1</td>
</tr>
<tr>
<td>68.0</td>
<td>Black</td>
<td>52</td>
</tr>
<tr>
<td>37.0</td>
<td>Asian/Pacific Islander</td>
<td>25.2</td>
</tr>
<tr>
<td>40.9</td>
<td>Am. Indian/Alaska Nat.</td>
<td>32.5</td>
</tr>
<tr>
<td>31.3</td>
<td>Hispanic</td>
<td>20.9</td>
</tr>
<tr>
<td><strong>Colon and Rectum</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>42.9</td>
<td>White</td>
<td>15.5</td>
</tr>
<tr>
<td>53.6</td>
<td>Black</td>
<td>22.1</td>
</tr>
<tr>
<td>36.9</td>
<td>Asian/Pacific Islander</td>
<td>11</td>
</tr>
<tr>
<td>40.0</td>
<td>Am. Indian/Alaska Nat.</td>
<td>12.7</td>
</tr>
<tr>
<td>36.6</td>
<td>Hispanic</td>
<td>12.4</td>
</tr>
<tr>
<td><strong>Female Breast</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>128.0</td>
<td>White</td>
<td>21.7</td>
</tr>
<tr>
<td>122.8</td>
<td>Black</td>
<td>30.6</td>
</tr>
<tr>
<td>93.6</td>
<td>Asian/Pacific Islander</td>
<td>11.3</td>
</tr>
<tr>
<td>79.3</td>
<td>Am. Indian/Alaska Nat.</td>
<td>12</td>
</tr>
<tr>
<td>91.3</td>
<td>Hispanic</td>
<td>14.5</td>
</tr>
<tr>
<td><strong>Prostate</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>223.9</td>
<td>White</td>
<td>20.6</td>
</tr>
<tr>
<td>79.3</td>
<td>Black</td>
<td>48.9</td>
</tr>
<tr>
<td>121.8</td>
<td>Asian/Pacific Islander</td>
<td>10</td>
</tr>
<tr>
<td>71.5</td>
<td>Am. Indian/Alaska Nat.</td>
<td>16.8</td>
</tr>
<tr>
<td>121.5</td>
<td>Hispanic</td>
<td>18.5</td>
</tr>
</tbody>
</table>

Source: SEER 18 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, Alaska Native Registry, Rural Georgia, California excluding SF/SJM/LA, Kentucky, Louisiana, New Jersey and Georgia excluding ATL/RG) and US Mortality Files,

a National Center for Health Statistics, Centers for Disease Control and Prevention.

Rates for American Indian/Alaska Native are based on the CHSDA (Contract Health Service Delivery Area)

b counties.

Hispanic is not mutually exclusive from whites, blacks, Asian/Pacific Islanders, and American Indians/Alaska Natives.

Incidence data for Hispanics are based on NHIA and exclude cases from the Alaska Native Registry.
Figure 1.13

SEER Incidence 2002-2011
Males by Race/Ethnicity

Source: SEER 18 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, Alaska Native Registry, Rural Georgia, California excluding SF/SJM/LA, Kentucky, Louisiana, New Jersey and Georgia excluding ATL/RG).

Rates are age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1103). Regression lines are calculated using the Joinpoint Regression Program Version 4.1.0, April 2014, National Cancer Institute.

Incidence rates for American Indian/Alaska Native (AI/AN) are based on the CHSDA(Contract Health Service Delivery Area) counties.

Hispanic is not mutually exclusive from whites, blacks, Asian/Pacific Islanders, and American Indians/Alaska Natives.

Incidence data for Hispanics are based on NHIA and exclude cases from the Alaska Native Registry.
Figure 1.14

SEER Incidence 2002-2011
Females by Race/Ethnicity

Breast
Lung and Bronchus
Colon and Rectum

Rate per 100,000
Rate per 100,000
Rate per 100,000

Year of Diagnosis
Year of Diagnosis
Year of Diagnosis

Source: SEER 18 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, Alaska Native Registry, Rural Georgia, California excluding SF/SJM/LA, Kentucky, Louisiana, New Jersey and Georgia excluding ATL/RG). Rates are age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1103). Regression lines are calculated using the Joinpoint Regression Program Version 4.1.0, April 2014, National Cancer Institute.

Incidence rates for American Indian/Alaska Native (AI/AN) are based on the CHSDA(Contract Health Service Delivery Area) counties.

Hispanic is not mutually exclusive from whites, blacks, Asian/Pacific Islanders, and American Indians/Alaska Natives. Incidence data for Hispanics are based on NHIA and exclude cases from the Alaska Native Registry.
Figure 1.15

US Mortality 2001-2010
Males by Race/Ethnicity

Source: US Mortality Files, National Center for Health Statistics, Centers for Disease Control and Prevention.
Rates are age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1103).

Regression lines are calculated using the Joinpoint Regression Program Version 4.1.0, April 2014, National Cancer Institute.

Mortality rates for American Indian/Alaska Native (AI/AN) are based on the CHSDA (Contract Health Service Delivery Area) counties.
Hispanic is not mutually exclusive from whites, blacks, Asian/Pacific Islanders, and American Indians/Alaska Natives.
Figure 1.16

US Mortality 2001-2010
Females by Race/Ethnicity

<table>
<thead>
<tr>
<th>Year of Death</th>
<th>Rate per 100,000</th>
<th>Rate per 100,000</th>
<th>Rate per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>2002</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2005</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2008</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2011</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Source: US Mortality Files, National Center for Health Statistics, Centers for Disease Control and Prevention.
Rates are age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1103).

Regression lines are calculated using the Joinpoint Regression Program Version 4.1.0, April 2014, National Cancer Institute.

Mortality rates for American Indian/Alaska Native (AI/AN) are based on the CHSDA (Contract Health Service Delivery Area) counties.
Hispanic is not mutually exclusive from whites, blacks, Asian/Pacific Islanders, and American Indians/Alaska Natives.
Figure 1.17

Incidence Percent Change between 2002 and 2011
Numbers (burden) vs Rates (risk)
All Races, All Ages, Both Sexes

Source: SEER 18 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, Alaska Native Registry, Rural Georgia, California excluding SF/SJM/LA, Kentucky, Louisiana, New Jersey and Georgia excluding ATL/RG).
Burden is the change in the number of incidence cases between 2002 and 2011.
Risk is the change in the cancer incidence rates between 2002 and 2011.

a Ovary excludes borderline cases or histologies 8442, 8451, 8462, 8472, and 8473.
Figure 1.18

Mortality Percent Change between 2002 and 2011
Numbers (burden) vs Rates (risk)
All Races, All Ages, Both Sexes

Liver & IBD
Corpus & Uterus, NOS
Thyroid
Melanoma of the Skin
Pancreas
Urinary Bladder
Brain & ONS
Esophagus
Kidney & Renal Pelvis
Oral Cavity & Pharynx
Leukemia
Cervix Uteri
Myeloma
Testis
All Cancer Sites
Breast (Female)
Lung & Bronchus
Ovary
Larynx
Non-Hodgkin Lymphoma
Colon & Rectum
Stomach
Hodgkin Lymphoma
Prostate

US Mortality estimates based on US age-specific rates applied to US population.
Burden is the change in the number of deaths between 2002 and 2011.
Risk is the change in the cancer death rates between 2002 and 2011.
Person-Years of Life Lost Due to Cancer
All Races, Both Sexes, 2011

Average Years of Life Lost Per Person Dying of Cancer
All Races, Both Sexes, 2011

Source: US Mortality Files, National Center for Health Statistics, Centers for Disease Control and Prevention and 2009 Life Tables.
Source: US Mortality Files, National Center for Health Statistics, Centers for Disease Control and Prevention and 2009 Life Tables.
Figure 1.21
SEER Observed Incidence and Delay Adjusted Incidence Rates
All Cancer Sites, By Sex

Both Sexes

Male

Female

<table>
<thead>
<tr>
<th>Rate per 100,000</th>
<th>Year of Diagnosis</th>
<th>Rate per 100,000</th>
<th>Year of Diagnosis</th>
<th>Rate per 100,000</th>
<th>Year of Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>350</td>
<td>1975</td>
<td>400</td>
<td>1990</td>
<td>450</td>
<td>2000</td>
</tr>
<tr>
<td>400</td>
<td>1990</td>
<td>450</td>
<td>2000</td>
<td>500</td>
<td>2011</td>
</tr>
<tr>
<td>450</td>
<td>2000</td>
<td>500</td>
<td>2011</td>
<td>550</td>
<td></td>
</tr>
<tr>
<td>500</td>
<td></td>
<td>550</td>
<td></td>
<td>600</td>
<td></td>
</tr>
<tr>
<td>550</td>
<td></td>
<td></td>
<td></td>
<td>650</td>
<td></td>
</tr>
<tr>
<td>600</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>650</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>700</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SEER Incidence APCs
Delay Adj, 1998-11 = -0.4*
Observed, 2009-11 = -2.0

SEER Incidence APCs
Delay Adj, 2000-11 = 0.9*
Observed, 2008-11 = -2.4*

SEER Incidence APCs
Delay Adj, 2003-11 = 0.1
Observed, 1998-11 = -0.2*

* Source: SEER 9 areas. Rates are age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1103). Regression lines and APCs are calculated using the Joinpoint Regression Program Version 4.1.0, April 2014, National Cancer Institute. The APC is the Annual Percent Change for the regression line segments. The APC shown on the graph is for the most recent trend. The APC is significantly different from zero (p < 0.05).
Figure 1.22
SEER Observed Incidence and Delay Adjusted Incidence Rates \( ^a \)
Both Sexes

<table>
<thead>
<tr>
<th>Year of Diagnosis</th>
<th>SEER Incidence APCs</th>
<th>Delay Adj, 2007-11</th>
<th>Observed, 2007-11</th>
</tr>
</thead>
<tbody>
<tr>
<td>1975</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1980</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1985</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1990</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1995</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2000</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2005</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2011</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\( ^a \) Source: SEER 9 areas. Rates are age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1103). Regression lines and APCs are calculated using the Joinpoint Regression Program Version 4.1.0, April 2014, National Cancer Institute. The APC is the Annual Percent Change for the regression line segments. The APC shown on the graph is for the most recent trend. * The APC is significantly different from zero (p < 0.05).
Figure 1.23
SEER Observed Incidence and Delay Adjusted Incidence Rates
Males

Prostate

Lung and Bronchus

Colon and Rectum

Rate per 100,000
Rate per 100,000
Rate per 100,000

Year of Diagnosis
Year of Diagnosis
Year of Diagnosis

SEER Incidence APCs
Delay Adj, 2000-11 = -1.9*
Observed, 2001-11 = -2.4*

SEER Incidence APCs
Delay Adj, 1991-11 = -1.8*
Observed, 2009-11 = -4.3*

SEER Incidence APCs
Delay Adj, 2008-11 = -4.1*
Observed, 2008-11 = -4.4*

Source: SEER 9 areas. Rates are age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1103). Regression lines and APCs are calculated using the Joinpoint Regression Program Version 4.1.0, April 2014, National Cancer Institute. The APC is the Annual percent change for the regression line segments. The APC shown on the graph is for the most recent trend. The APC is significantly different from zero (p < 0.05).
Figure 1.24
SEER Observed Incidence and Delay Adjusted Incidence Rates<sup>a</sup>
Females

<table>
<thead>
<tr>
<th></th>
<th>Year of Diagnosis</th>
<th>Rate per 100,000</th>
<th>SEER Incidence APCs</th>
<th>Delay Adj, 2004-11</th>
<th>Observed, 2004-11</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td></td>
<td></td>
<td></td>
<td>0.3</td>
<td>0.2</td>
</tr>
<tr>
<td>Lung and Bronchus</td>
<td></td>
<td></td>
<td></td>
<td>-2.1&lt;sup&gt;*&lt;/sup&gt;</td>
<td>-2.4&lt;sup&gt;*&lt;/sup&gt;</td>
</tr>
<tr>
<td>Colon and Rectum</td>
<td></td>
<td></td>
<td></td>
<td>-4.5&lt;sup&gt;*&lt;/sup&gt;</td>
<td>-4.8&lt;sup&gt;*&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> Source: SEER 9 areas. Rates are age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1103). Regression lines and APCs are calculated using the Joinpoint Regression Program Version 4.1.0, April 2014, National Cancer Institute. The APC is the Annual Percent Change for the regression line segments. The APC shown on the graph is for the most recent trend.

* The APC is significantly different from zero (p < 0.05).
Abbott, Wallace Calvin, 1:1
Abbott Laboratories (United States), 1:1–2
“ABCDE” (asymmetry, border irregularity, color variations, diameter, evolving), 3:1063, 3:1086–1087
Ablation, 3:1121, 3:1156
Academia Sinia, 3:1138
Açai, 1:33
Accelerating the End of Breast Cancer Act, 3:1223
Access to Medicine Index, 2:842
Accreditation
American Association of Blood Banks, 1:201–202
American Society for Radiation Oncology, 1:69–70
National Accreditation program for Breast Centers, 1:310
National Cancer Registrars Association, 2:805–806
Oncology Nursing Society certification, 2:861
of physical therapies, 2:928–929
Acetaldehyde, 1:344, 1:345–346, 1:346
Acetic acid, 1:357
Acetylsalicylic acid. See Aspirin
Acid copper chromate, 3:1317
Acinar adenocarcinomas, 2:889
Acinic cell carcinoma, 3:1015
ACOR. See Association of Cancer Online Resources
ACRO. See American College of Radiation Oncology
Acrylamide, 2:459
Acrylic rubber and fibers, 1:2–4
acrylonitrile absorption, 1:3
aerospace industry and, 1:10
alkyl acrylate copolymer (ACM), 1:2–3
dyes and pigments in, 1:374
safety issues of, 1:3–4
Actavis, 2:462
Actos, 3:1140
Acupressure, 1:40
Acupuncture, 1:40
Acute myeloid leukemia (AML), 1:303–304, 2:672–675, 2:782
Acute promyelocytic leukemia (APL), 2:522
Adams, Lisa Boncheck, 2:746
Additive flame retardant, 2:451
Adenine (A), 2:488
Adenoatomatic syndromes, 1:307, 1:308
Adenocarcinomas
defined, 1:61
stomach cancer, 3:1104
unknown primary origin and, 1:239
Adenoviruses, 1:146
Adoptive cell transfer, 1:145
Adrenal glands. See Adrenocortical carcinoma
Adrenocortical carcinoma, 1:5–6
Adrenocortical carcinoma, childhood, 1:6–7
Advertising, 1:7–10. See also Pharmaceutical industry
drug marketing, 2:728–729
marketing by hospitals and clinics, 2:729–731
overview, 1:7–10
post-marketing requirements (PMRs), 2:463
smoking and society, 3:1076
tobacco and, 3:1176, 3:1177–1178
Advisory Committee on Immunization Practices
(CDC), 2:563, 2:564
Advisory Group on Non Ionising Radiation, 1:393
Aerospace industry, 1:10–13
radiation risk and, 1:12–13
risks to employees of, 1:11–12
Affordable Care Act (ACA), 1:245, 1:357, 2:587,
   3:1037, 3:1150, 3:1222
Afghanistan, 1:13–14
Aflatoxin, 3:1187
Africa
   Algeria, 1:23–26
   Angola, 1:79–80
   Benin, 1:129–131
   Burkina Faso, 1:192–194
   Burundi, 1:196–197
   Cameroon, 1:204–206
   Central African Republic, 1:253–254
   Chad, 1:258–260
   Congo, Democratic Republic of, 1:311–313
   Côte d’Ivoire, 1:318–320
   Eritrea, 1:410–412
   Ethiopia, 1:418–420
   Ghana, 2:497–499
   Guinea, 2:518–520
   Kenya, 2:646–648
   Libya, 2:683–685
   Madagascar, 2:719–720
   Malawi, 2:721–722
   Mali, 2:724–726
   Morocco, 2:773–775
   Mozambique, 2:775–777
   Niger, 2:830–832
   Nigeria, 2:832–834
   Rwanda, 2:1010–1012
   Senegal, 3:1045–1046
   Sierra Leone, 3:1054–1056
   Somalia, 3:1090–1092
   South Africa, 1:218–220, 3:1092–1093
   Sudan, 3:1111–1113
   Tanzania, 3:1147–1149
   Togo, 3:1182–1184
   Tunisia, 3:1193–1196
   Uganda, 3:1203–1205
   Zambia, 3:1341–1343
   Zimbabwe, 3:1343
   African Organization for Research and Education,
      1:312
   African Women’s Cancer Awareness Association,
      1:205
   AFROC. See Association of Freestanding Radiation Oncology Centers
   Aga Khan Development Network, 3:1139
   Age, 1:14–17. See also Surveillance, Epidemiology,
   latitude and, 2:663–664
   overview, 1:14–17
   as risk factor (See individual cancers)
   young adult cancer prevention, 3:1336–1338
   Agency for Healthcare Research and Quality, 1:383
   Agency for Toxic Substances and Disease Registry (ATSDR), 2:452–453, 2:480
   Agent Orange, 3:1284
   Agriculture. See also Carcinogenic substances;
      Diet and nutrition
      herbicide, 2:544–548
      insecticides, 2:583–586
      pesticides, 2:911–914
      tobacco, 3:1174–1175
   AIDS-related cancers, 1:17–19
   AIDS-defining cancer, 1:17–18
   AIDS-related cancers, 1:18
   Burkitt's lymphoma, 2:701
   Canadian Red Cross and, 1:214
   cancer incidence in developing countries and,
      1:348
   central nervous system lymphoma, primary,
      1:255
   future of cancer and, 2:474
   HIV and Abbott Laboratories, 1:1
   HIV and anal cancer, 1:78
   HIV Vaccine Trials Network, 2:470
   infection and cancer, 2:581–582
   lymphoma, 2:697–700
   penile cancer, 2:905
   treatment for, 1:18
   Air quality
   air pollution, 2:945–947
   Clean Air Act, 1:89, 1:300
   coal and, 1:298, 1:300
   lead in, 2:667
   nickel in, 2:829
   Air Quality, Atmosphere and Health, 1:346
   AkaRx, 1:385
   Albert Einstein Cancer Center, 1:19–20
Alcohol, 1:20–23
Alcohol Use Disorders Identification Test—Consumption, 1:22
beta-carotene and, 1:136
as drug, 1:366
in Japan, 2:628–629
liver cancer and, 2:540
overview, 1:20–23
poverty and, 2:952–953
taxes on, 3:1152–1153
Alcohols, in disinfectants and antiseptics, 1:357–358
Aldehydes, 2:906–908
Alemtuzumab, 2:676
Algeria, 1:23–26
Council of Ministers, anticancer plan, 1:24
Alkalis, 1:358
Alkyl acrylate copolymer (ACM).
See Acrylic rubber and fibers
Alkylating antineoplastic agents, 2:916
Allergan (United States), 1:26
Allspice, 1:33
Aloe, 1:33
Alpha lipoic acid (ALA), 1:46
Alpha particles, radiation and, 2:968–970, 2:971
Alpha-fetoprotein (AFP), 2:690
Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study (ATBC), 1:133, 1:134
Alternative therapy: diet and nutrition, 1:27–32
Asian diet, 1:28
enzyme and metabolism therapies, 1:30
Gerson therapy, 1:30
Gonzalez therapy, 1:30–31
Issel’s Whole Body Therapy, 1:31
Kelley’s metabolic treatment for cancers, 1:31
macrobiotic diet, 1:28–29
Mediterranean diet, 1:29
overview, 1:27
vegetarian diet, 1:29
wheatgrass therapy, 1:29–30
Alternative therapy: herbs, vitamins, and minerals, 1:32–37
herbs, 1:32–35
minerals, 1:36
vitamins, 1:35–36
Alternative therapy: manual healing and physical touch, 1:37–43
acupressure and shiatsu, 1:40
acupuncture, 1:40
applied kinesiology, 1:40
bodywork, 1:40–41
chiropractic, 1:41
craniosacral therapy, 1:41
cupping, 1:41
massage, 1:41
moxibustion, 1:41
myofascial release, 1:41–42
osteopathy, 1:42
overview, 1:38–39
polarity therapy, 1:42
psychic surgery, 1:42
reflexology, 1:42
reiki, 1:43
Rosen method, 1:43
Rubenfeld synergy method, 1:43
summary of manual healing and physical touch, 1:39–40
therapeutic touch, 1:43
Alternative therapy: mind, body, and spirit, 1:38, 1:43–45
Alternative therapy: pharmacological and biological treatment, 1:45–51
alpha lipoic acid, 1:46
cancer clinics abroad, 1:46
chelation therapy, 1:46–47
Coley toxins, 1:47
dichloroacetic acid, 1:47–48
homeopathy, 1:48–49
insulin potentiation therapy, 1:49
low dose naltrexone, 1:49–50
melatonin, 1:50
mistletoe, 1:50–51
714-X, 1:51
Aluminum chlorohydrate, 1:344
Alvear rhabdomyosarcoma, 2:999–1000
Amader Gram (Our Village), 1:120
Amal Center, Al-, 2:641
American Academy for Nutrition and Dietetics, 2:742
American Academy of Ophthalmology, 3:1216
American Academy of Pediatrics, Section on Hematology/Oncology, 1:51–53, 1:75
American Academy of Dermatology, 3:1118
American Association for Cancer Education, 1:382–383
American Association for Cancer Education, 1:53–54
American Association for Cancer Research, 1:55–56
American Association of Blood Banks (AABB), 1:201
American Brain Tumor Association, 1:56–58, 1:162
American Cancer Society, 1:58–60. See also individual names of countries
on alcohol, 1:21
on alternative therapies, 1:39
on aspirin, 1:95
on automobiles, 1:116
background, 1:58–59
on breast cancer detection, 1:176
on coal, 1:299
on cosmetics, 1:313–314
cost of therapy and, 1:315
on diet, 1:92
education resources of, 1:382
on environmental tobacco smoke, 1:406
on mesothelioma, 2:764
Oncology Nursing Society, 2:860
outreach, 1:59–60
on penile cancer, 2:906
on poverty as risk factor for cancer, 2:952
research, 1:59
war on cancer and, 2:834
on women's cancers, 3:1311
American Childhood Cancer Organization
(ACCO), 1:232–234, 1:276, 1:279–280
American College of Gastroenterology, 1:60–62
American College of Radiation Oncology, 1:62–63
American College of Radiology, 1:176, 1:178
American Health Foundation, 3:1327
American Hospital Association (AHA),
2:587–588, 2:736
American Institute for Cancer Research, 1:22,
1:92, 1:381, 3:1306
American Joint Committee on Cancer, 1:63–65,
1:413, 2:478
American Journal of Clinical Oncology, 1:62
American Journal of Gastroenterology, 1:60, 1:61
American Lebanese Syrian Associated Charities
(ALSAC), 3:1099
American Lung Association, 1:65–67
American Medical Association (AMA), 2:587–588
American Nurses Credentialing Center, 2:860
American Oncologic Hospital, 2:463–464
American Psychosocial Oncology Society, 1:67–68
American Society for Radiation Oncology, 1:68–70
American Society of Clinical Oncology, 1:70–72
Canadian Association of Medical Oncologists
and, 1:209
cancer communication, 1:220
Chile and, 1:281
Honduras and, 2:554
hospice care and, 2:559
on infection and cancer, 2:580
overview, 1:70–72
United Kingdom and, 3:1222
American Society of Hematology, 1:72–74
American Society of Pediatric Hematolog/
Oncology, 1:74–75
American University of Beirut Medical Center,
2:641
Americans with Disabilities Act (ADA), 1:355,
1:356
Amgen (United States), 1:75–77, 1:109, 2:749
Amy Strelzer Manasevit Research Program, 2:808
Anal cancer, 1:77–79
HIV and, 1:18
infection and, 2:582
overview, 1:77–79
Anaplastic lymphoma kinase (ALK) inhibitors,
2:841
Anaplastic thyroid cancer, 3:1171, 3:1173
Angola, 1:79–80
National Oncology Center (Luanda), 1:79–80
Anilides, 1:358
Antiangiogenic drugs, in chemotherapy, 1:329–330
Antibiotics, 1:80–84
Antibody drugs, discovery of, 2:551
Anticancer drugs, 1:84–86
Antioxidants, 1:136–138, 2:742, 2:811
Antipsychotics, for nausea, 2:919
Antiseptics. See Disinfectants and antiseptics
Antoni van Leeuwenhoek Hospital, Netherland
Cancer Institute (AvL/NKI), 2:815–817
APHON. See Association of Pediatric
Hematology/Oncology Nurses
APOS. See Association of Pediatric
Psychosocial Oncology Society
Appia, Louis, 2:595
Applied kinesiology, 1:40
Aranesp, 1:76
ARC, 2:617
Arc welding, 3:1213–1214
Argentina, 1:86–87
Aricept, 1:385
Armidex, 1:111
Armstrong, Lance, 1:248
Aromatase inhibitors, 1:438–439, 3:1146
Aromatic amines, 1:374, 2:524
Arsenic, 2:499, 2:884
Arsenicals, 2:545
Arthur G. James Cancer Hospital, 2:856–857
Artificial flavorings, characteristics of, 2:455
Arsenic, 2:545
Asia
Afghanistan, 1:13–14
Azerbaijan, 1:116–118
Bangladesh, 1:119–121
Burma (Myanmar), 1:194–196
Cambodia, 1:202–204
China, 1:282–284
India, 2:576–578
Indonesia, 2:578–579
Kazakhstan, 2:645–646
Kyrgyzstan, 2:655–656
Laos, 2:657–658
Malaysia, 2:722–724
Nepal, 2:812–814
North Korea, 2:837–839
Pakistan, 2:885–886
Philippines, 2:921–923
Singapore, 3:1056–1058
South Korea, 3:1093–1094
Sun exposure in, 3:1113–1115
Sunscreen research by Green in, 2:513–515
Sri Lanka, 3:1097–1099
Taiwan, 3:1137–1139
Tajikistan, 3:1139–1140
Thailand, 3:1165–1167
Turkey, 3:1196–1198
Turkmenistan, 3:1199–1201
Austria, 1:113–115
Automobiles, 1:115–116
diesel exhaust and, 1:350–353
gasoline and, 2:479–481
overview, 1:115–116
Aytub, 2:564
Avion, 2:749
Avon Foundation for Women, 1:248, 1:314–315
Azacytidine, 2:783
Azartias, 2:545
Azasu, 2:913
Azotemia, 2:917
Azorean, 2:917
Azerbaijan, 1:116–118
Azo dyes, 3:1163–1164
Astragalus, 2:565
Asbestos, 1:87–90, 2:764, 2:765, 2:884
Asthma, 2:112–114
Astrocytes, 3:1288
Astrocytomas, 1:163–164, 1:165
Astrazeneca (United Kingdom), 1:110–111
Astrocytomas, 1:165
Astronomy, 1:117
Aspirin, 1:93–96
chemoprevention and, 1:265
overview, 1:93–96
University of Chicago on, 3:1231
Assisted suicide, 1:96–99
Association for International Cancer Research, 1:423
Association for the Cure of Cancer of the Prostate, 1:99–100
Association of Cancer Online Resources, 1:100–102
Association of Community Cancer Centers, 1:102–103
Association of Freestanding Radiation Oncology Centers, 1:103–105
Association of Oncology Social Work, 1:105–107
ASOR and, 1:101
overview, 1:105–107
Association of Pediatric Hematology/Oncology Nurses, 1:107–108
Astellas Pharma (Japan), 1:108–110, 1:332
AstraZeneca (United Kingdom), 1:110–111
Ethiopia and, 1:419
MedImmune and, 2:749
overview, 1:110–111
ASTRO. See American Society for Radiation Oncology
Australia, 1:111–113
Cancer Council Australia, 1:225–227
clothing as skin cancer protection in, 1:226, 1:295
overview, 1:111–113
sun exposure in, 3:1113–1115
sunscreen research by Green in, 2:513–515
Austria, 1:113–115
Austrian Cancer Society, 1:114
history of, 2:565
overview, 1:113–115
Automobiles, 1:115–116
diesel exhaust and, 1:350–353
gasoline and, 2:479–481
overview, 1:115–116
Avicenna, 2:564
Avion, 2:749
Avon Foundation for Women, 1:248, 1:314–315
Axitinib, 2:916
Ayurveda, 1:44–45, 2:813
Ayurveda (Lad), 1:44–45
Azacytidine, 2:783
Azerbaijan, 1:116–118
Azo dyes, 3:1163–1164
Azodicarbonamide, 2:457
Azoles, 3:1317, 3:1318
B vitamins, 1:21, 1:35, 3:1290–1292
Bacteria
antimicrobial treatment for, 1:81–82
experimental cancer drugs, 1:440, 3:1157
in water, 2:948
Bairouni University Cancer Center,
Al (Damascus University), 3:1132–1133
Baltimore, David, 2:551
Bamako Initiative (Guinea), 2:518
Bandura, A., 2:880
Banerji Method, 1:48–49
Bangladesh, 1:119–121
Bao, P. P., 1:416
Barbara Ann Karmanos Cancer Institute,
1:121–122
Barnes-Jewish Hospital, 3:1059–1061
Barrett's esophagus, 3:1065–1066,
3:1086, 3:1119
Basic Science Division (Herbert Irving
Comprehensive Cancer Center), 2:543
Basil, 1:33
Battery acid, 1:122–125
Baylin, Stephen, 3:1223
Beard, John, 1:30–31
Beckman Research Institute (City of Hope), 1:288
Behavioral Risk Factor Surveillance Survey
(NRFSS), 1:220
Belarus, 1:125–127
Belgium, 1:97, 1:127–129
Benin, 1:129–131
Benzene, 1:116, 1:344, 1:345, 2:480–481, 2:550,
2:637, 2:884, 3:1088–1089
Benzidine, 1:375
Benzoic acid, 2:459
Bereavement issues, 1:131–132, 2:557
Berzofsky, Jay, 2:800
Beta particles, radiation and, 2:968–970, 2:971
Beta-carotene, 1:132–138
Beta-Carotene and Retinol Efficacy Trial
(CARET), 1:133, 1:134, 1:266
chemoprevention and, 1:266
Bevacizumab, 1:143, 2:551
BHA, 2:459–460
BHT, 2:459–460
Bichat, Xavier, 2:549
Bicycles, 1:138–140
Bile duct cancer, extrahepatic, 1:140–142
Biliary tract. See Gallbladder cancer
Billroth, Theodore, 3:1123
Bimagrumab, 2:841
Binder, in paint, 2:883
Bioaccumulation, 2:451–452
Bioelectrical impedance, 1:390
Biologic therapy, 1:142–146, 2:482
Biologically closed electric circuits, 1:390
Biologically Closed Electric Circuits
(Nordenstrom), 1:390
Biologically engineered seeds, 2:545
Biostatistics, importance of, 2:544
Biotecnology. See Pharmaceutical industry;
individual names of companies
Bisel, Harry, 1:70–71
Bishop, Michael, 2:551
Bisphenol A (BPA), 2:936
Bis-phenols, 1:358
Bissell, Emily, 1:66
Bituminous coal, 1:297
Black, Shirley Temple, 1:246
Black mold, 3:1187
Black Swan Research Initiative (IMF), 2:598
Bladder cancer, 1:147–148
chlorine and, 1:285
COX-2 inhibitors, 1:323–324
hair dye and, 2:526
overview, 1:147–148
Bladder cancer, childhood, 1:148–150
Bleeding/bleeding disorders
aspirin and, 1:95
Haemophilia Society (United Kingdom), 2:523–524
International Society on Thrombosis and
Haemostasis, 2:609–611
Netherland Hemmophilia Patients Society,
2:817–819
vascular endothelial growth factor (VEGF),
2:551
Blenoxane, 1:185
Blood, 1:74, 1:227
Blood cancer. See also Leukemia; individual types
of leukemia; individual types of lymphoma
mortality statistics, 2:808
multiple myeloma, 2:788–789
myelodysplastic syndromes, 2:782–784
myelodysplastic/myeloproliferative diseases,
2:784–788
myeloproliferative disorders, chronic, 2:789–791
National Marrow Donor Program, 2:807–809
Waldenström’s macroglobulinemia, 3:1297–1298
Blood clots, aspirin and, 1:94
Blood transfusions, hepatitis C and, 2:538
Blood-brain barrier, 1:256
Blue Cross, 2:586
Blue Distinction Center for Complex and Rare Cancers, 2:1007
Blum, Diane, 2:796
Bly, Stanley, 1:26
Body image, sex and, 3:1048–1049
Body mass index (BMI), 2:849, 3:1040
Bodywork, 1:40–41
Boehringer Ingelheim, 2:591
Bolivia, 1:150–151
Bonadonna, Gianni, 1:151–153
Bone cancer, osteosarcoma/malignant fibrous histiocytoma, 1:153–156
Bone health/bone cancer
calculator, 1:199–200
Ewing's family of tumors and, 1:434–436
malignant fibrous histiocytoma of bone/osteosarcoma, 2:726–728
osteoporosis, 2:760–761
osteoporosis and calcium, 1:199–200
Raloxifene and, 2:980
sarcoma, Ewing's family of tumors, 3:1019–1021
Bone marrow. See also individual types of leukemia
chemotherapy and, 1:273
myelosuppression, 2:919
Bone marrow transplants, 1:156–159
bone marrow, historical perspective, 1:212
for chronic myelogenous leukemia, 2:679
in Jordan, 2:641
National Marrow Donor Program, 2:807–809
University of Minnesota and, 3:1240
Book of the O'Hickeys, 2:616
Book of the O'Lees, 2:616
Book of the O'Shiels, 2:616
Boote, Werner, 1:403
Borates, 3:1318
Boron neutron capture therapy, 2:822–823
Borst, Piet, 2:817
Bortezomib, 2:780, 3:1141
Boston Marathon Jimmy Fund Walk, 2:638
Boston Red Sox, Jimmy Fund and, 2:638, 2:639
Botryoid rhabdomyosarcoma, 2:1000
Boudia, Abdelmalek, 1:24
Boyer, Herbert, 2:486
Boyle, Peter, 2:510
Brachytherapy, 2:973–975, 2:977, 3:1122
BRAF gene, 1:164, 2:680
Brain stem glioma, childhood, 1:159–160
Brain tumor, adult, 1:161–162
American Brain Tumor Association, 1:56–58
overview, 1:161–162
Brain tumor, cerebellar astrocytoma, childhood, 1:163–164
Brain tumor, cerebral astrocytoma/malignant glioma, childhood, 1:165
Brain tumor, childhood, 1:165–167
American Brain Tumor Association, 1:56–58
Childhood Brain Tumor Foundation, 1:277–278
overview, 1:165–167
prevalence of, 1:278
Brain tumor, medulloblastoma, childhood, 1:167–169
Brain tumor, supratentorial primitive neuroectodermal, childhood, 1:169–171
Brain tumor, visual pathway and hypothalamic glioma, childhood, 1:171–172
Brain Tumor Center of Excellence, 1:311
Brain tumors, ependymoma and, 1:408–410
Brazil, 1:172–174
Brazillian Association for Supporting Cancer Patients, 1:174
Brazilian Cancer National Institute, 1:173
Brazilian Population-Based Cancer Registry, 1:174
Brazilian Society of Oncology, 1:174
overview, 1:172–174
BRCA 1/2 genes
early menarche and, 2:756
history of cancer and, 2:551
Jewish women and cancer risk, 2:988–990
natural causes of cancer and, 2:810
ovarian low malignant potential tumor and, 2:877
overview of breast cancer and, 1:175–176, 1:179
overview of genetics and, 2:489
Brd4, 1:303–304
Bread making, food additives and, 2:457–458
Breast and Cervical Health Check (Alaska), 3:1037
Breast cancer, 1:174–179. See also BRCA
1/2 genes
advocacy and, 1:178, 3:1223
Asian diet and, 1:91, 1:92
aspirin and, 1:94
Bonadonna and, 1:151–153
chemoprevention for, 1:267
chlorine and, 1:285
cosmetics and, 1:314
COX-2 inhibitors, 1:323
cultural issues of, 2:885–886
diagnosis and prognosis, 1:177
disparities within nations and elimination of cancer, 1:361
ductal carcinoma in situ (DCIS), 1:177, 2:981, 3:1311
Breast cancer, male, 1:179–180, 2:480
Breast cancer, socioeconomic differences and, 1:180–182
Breast cancer and pregnancy, 1:182–184
Breast Cancer Biology Program (Karmanos Institute), 1:122
Breast Cancer Center of Excellence, 1:311
Breast Cancer in Manitoba (Canadian Society of Surgical Oncology), 1:215
Breast Health Day (Europa Donna), 1:421
Breast-feeding
  breast cancer and pregnancy, 1:184
  breast cancer risk and, 1:175
  BREAST-PREDICT (Irish Cancer Society), 2:620
Breitbart, William, 2:995
Brinker, Nancy, 1:248, 2:796
Bristol-Myers Squibb (United States), 1:184–186
British Association of Surgical Oncologists (BASO), 1:433
British Childhood Cancer Survivor Study, 3:1260
British Columbia Cancer Agency (BCCA), 1:216
British Doctors Study, 3:1176
British Medical Journal, 1:211, 1:407, 3:1076
Broad-spectrum ultraviolet (UV) radiation, 1:186–189
  Australia and, 1:226
  overview, 1:186–189
Broder, Samuel, 2:952
Brominated flame retardant (BFR), 2:452–453, 2:936
Bronchial adenomas/carcinoids, childhood, 1:189–190
Bronchoscopes, 1:236
Brook, Itzhak, 3:1339
Brooklyn Institute of Arts and Sciences, 1:303
Brynnor, Yul, 3:1338–1340
Buck, Linda, 2:469
Buddhist meditation/practices, religion and, 2:990–992, 3:1166
Buehrlen, Martina, 2:796
Bulgaria, 1:190–192
Bureaucratic organization, careers and, 1:241
Burg, Gunter, 2:601
Burkina Faso, 1:192–194
Burkitt, Denis Parsons, 2:700
Burkitt’s lymphoma, 2:700–703
Burma (Myanmar), 1:194–196
Burundi, 1:196–197
Bush, G. W., 3:1152
Butaro Cancer Center of Excellence, 2:1011–1012
C, vitamin, 1:35, 3:1292
Caisse, Rene, 1:214
Calcium, 1:199–200
California
  automobiles and cancer risk, 1:115
  bicycles and, 1:139
  California Blood Bank Society, 1:200–202
  California Environmental Protection Agency, 2:903
  Cancer Registry, 2:575
  on detergents, 1:346
  on para-dichlorobenzene, 1:343
  Technical Bulletin 117 (TB 11), 2:451
  Toxic Hot Spots Program, 1:124
California Blood Bank Society, 1:200–202
Caligiuri, Michael, 2:857
Calmette Hospital, 1:204
Caloric intake, 1:353
Cambodia, 1:202–204
Cambridge Antibody Technology, 2:749
Cameron, Ewan, 3:1292
Cameroon, 1:204–206
Campbell, Allan, 3:1292
Canada, 1:206–208. See also individual names of professional organizations
  “Canadian Cancer Statistics 2013,” 1:206
  Canadian Partnership Against Cancer, 1:207
  Canadian Research Data Center Network (CRDCN), 1:207
  Catholics of, on HPV vaccine, 3:1272
  herbicides and, 2:546, 2:547
  insecticides in, 2:585
  overview, 1:206–208
  pesticide study in, 2:913
rise of cancer in, 1:206–207
solvents and, 3:1088
Canadian Association of Medical Oncologists, 1:208–210
Canadian Association of Pharmacy in Oncology, 1:210–211
Canadian Blood Services, 1:214
Canadian Cancer Action Network (CCAN), 1:211
Canadian Cancer Society, 1:211–213
Canadian Medical Association (CMA), 1:212
Canadian Medical Journal, 1:326
Canadian Red Cross, 1:213–215
Canadian Society of Surgical Oncology, 1:215–216
Canadian Urologic Oncology Group, 1:216–218
Canadian Urological Association (CUA), 1:217
Cancer, defined, 1:270, 1:367, 2:488, 2:489, 2:512
Cancer, education about. See Education
Cancer angiogenesis (blood vessel sprouting), 1:395
Cancer antigen 19-9, 2:477
Cancer Association of South Africa, 1:218–220
Cancer centers. See also individual names of cancer centers
Albert Einstein Cancer Center, 1:19–20
Association of Community Cancer Centers, 1:102–103
Chao Family Comprehensive Cancer Center, 1:260–261
Comprehensive Cancer Center of Wake Forest University, 1:310–311
Fox Chase Cancer Center, 2:464–465
Fred & Pamela Buffett Cancer Center, 2:468–469
Herbert Irving Comprehensive Cancer Center, 2:543–544
Holden Comprehensive Cancer Center at the University of Iowa, 2:552–553
Ireland (Ohio) Cancer Center, 2:618–620
Kimmel Cancer Center, 2:653–655
Lombardi Comprehensive Cancer Center, 2:692–694
Massey Cancer Center, 2:733–735
Mayo Clinic Cancer Center, 2:735–736
Mayo Clinic Cancer Center, Jacksonville, 2:736–738
Mayo Clinic Cancer Center, Scottsdale, 2:738–740
Memorial Sloan Kettering Cancer Center, 1:230, 1:1327, 2:754–755
Ohio State University Comprehensive Cancer Center, 2:856–858
Perlmutter Cancer Center, 2:908–910
Salk Institute for Biological Studies, 3:1016–1018
Sanford-Burnham Medical Research Institute, 3:1018–1019
Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, 3:1052–1054
Siteman Cancer Center, 3:1059–1061
University of Alabama at Birmingham Comprehensive Cancer Center, 3:1224–1226
University of California, Davis, Comprehensive Cancer Center, 3:1226–1228
University of California, Los Angeles, Jonsson Comprehensive Cancer Center, 3:1228–1230
University of California, San Francisco, Helen Diller Family Comprehensive Cancer Center, 3:1230–1231
University of Chicago Medicine Comprehensive Cancer Center, 3:1231–1233
University of Colorado Cancer Center, 3:1233–1236
University of Hawai‘i Cancer Center, 3:1236–1237
University of Michigan Comprehensive Cancer Center, 3:1237–1240
University of Minnesota Masonic Cancer Center, 3:1240–1242
University of North Carolina Lineberger Comprehensive Cancer Center, 3:1243–1245
University of Southern California Norris Comprehensive Cancer Center, 3:1248–1249
University of Texas MD Anderson Cancer Center, 3:1249–1251
University of Virginia Cancer Center, 3:1251–1253
University of Wisconsin Carbone Cancer Center, 3:1253–1254
Vanderbilt-Ingram Cancer Center, 3:1278–1280
Vermont Cancer Center, 3:1282–1284
Yale Cancer Center, 3:1333–1335
Cancer communication, 1:220–225. See also Education
for cancer education, 1:381
Health Communication and Informatics Research Branch (HCIRB) (NCI), 1:220, 2:802–803
Healthy People Initiative (U.S. Department of Health and Human Services), 2:533–534
physician communication with aging population, 1:16
sexual partners and, 3:1049
workplace wellness programs and, 3:1319–1321
Cancer Council Australia, 1:112–113, 1:225–227
Cancer Detection and Prevention, 2:604, 2:605
Cancer drugs, costs and benefits of, 1:227–231. See also Pharmaceutical industry
clinical benefits and, 1:229
research costs and, 1:227–229
U.S. prices, 1:227, 1:229–230
Cancer education. See Education
Cancer Epidemiology, Biomarkers & Prevention, 1:224
Cancer Foundation of China, 1:283
Cancer Game, 1:382
Cancer Gold Standard Program (Johnson & Johnson), 2:640
Cancer Incidence in Five Continents (IARC), 2:593
Cancer Information Service (CIS), 1:222, 2:471
Cancer Institute (University of Pittsburgh), 3:1245–1248
Cancer insurance, supplementary, 2:588
Cancer patients. See also Psychosocial care/support; Survivors of cancer; Survivors of cancer, families of; individual names of cancer care centers
childcare and cancer risk issues, 1:276
clothing of, 1:294–296
daily life of, 1:334–335
disability and, 1:355–357
family size and cancer risk, 2:448–449
occupational therapy for, 2:854–856
physical therapy for, 2:927–929
sex and, 3:1048–1049
stress and, 3:1109–1111
Cancer Prevention & Control Research Training Program of Morocco, 2:774
Cancer Prevention Center (Georgia), 2:492
Cancer Prevention Fellowship Program, 2:799
Cancer Program Guidelines (ACCC), 1:103
Cancer registries
disparities within nations (elimination of cancer) and data requirements, 1:360–361
global health issues and data organization, 2:504
Hutch Integrated Data Repository and Archive (HIDRA), 2:470
IARC on, 2:589–590 (See also International Agency for Research on Cancer)
International Association of Cancer Registration, 1:426
International Association of Cancer Registries, 1:426, 2:592–593
lack of, and skin cancer, 3:1065
National Cancer Registrars Association, 2:805–806
need for, 2:511
North American Association of Central Cancer Registries, 2:836–837
Union for International Cancer Control and, 3:1218
Cancer registries, by individual countries
Algeria, 1:25
Belgium, 1:128
Brazil, 1:174
Bulgaria, 1:191
Burma (Myanmar), 1:194–195
Cameroon, 1:205
Canadia, 1:207
Congo, 1:312
Costa Rica, 1:317
Cuba, 1:327
Czech Republic, 1:328
Denmark, 1:341
Finland, 2:450–453453
France, 2:467
Germany, 2:494
Haiti, 2:527
India, 2:576–577
Indonesia, 2:578
Iran, 2:613
Iraq, 2:614–615
Israel, 2:623–624
Japan, 2:630, 2:631
Kyrgyzstan, 2:656
Libya, 2:684
Mexico, 2:767
Morocco, 2:774
Nepal, 2:813
Netherlands, 2:815
New Zealand, 2:825
Niger, 2:831
Nigeria, 2:833
Norway, 2:839, 2:840
Papua New Guinea, 2:894
Peru, 2:911
Philippines, 2:922
Poland, 2:941
Portugal, 2:950
Republic of Ireland, 2:617
Romania, 2:1003
Rwanda, 2:1010
Saudi Arabia, 3:1028, 3:1029
Sierra Leone, 3:1055
South Korea, 3:1094
Spain, 3:1095
Sri Lanka, 3:1098
Sudan, 3:1112
Sweden, 3:1130
Switzerland, 3:1131
Taiwan, 3:1138
Tunisia, 3:1194
Turkey, 3:1197
United Arab Emirates, 3:1219
Vietnam, 3:1285
Zimbabwe, 3:1343
Cancer Research, 1:55
Cancer Research and Treatment Center (University of New Mexico), 3:1242–1243
Cancer Research Institute (New York), 1:47
Cancer Research Institute SAS, 3:1242–1243
Cancer Research Morocco, 2:774
Cancer Research of the Oesophagus and Stomach (CROSS), 2:617
Cancer Science, 2:632
Cancer Staging Manual, The (American Joint Committee on Cancer), 1:63
Cancer Survivor Research Program, 3:1125
Cancer therapy evaluation program, 1:231–232
Cancer Treatment Centers of America (CTCA), 2:731
Cancer World, 1:428
CancerGuide, 1:101
Cancer.Net, 1:71
Candlelighters Childhood Cancer Foundation, 1:232–234
Canon of Medicine, The (Avicenna), 2:564
CaP CURE. See Association for the Cure of Cancer of the Prostate
CAPHO. See Canadian Association of Pharmacy in Oncology
Capital Breast Care Center (CBCC), 2:693
Capsule endoscopy, 3:1104
Caraway, 1:34
Carbamates, 2:545
Carbaryl, 2:545
Carbon dioxide, 2:945–947
Carbone Cancer Center (University of Wisconsin), 3:1253–1254
Carcinoembryonic antigen (CEA), 2:477
Carcinogenic substances. See also individual names of countries
acrylic rubber and fibers, 1:2–4
Agent Orange, 3:1284
air pollution, 2:945–947
asbestos, 1:87–90, 2:764–766
automobiles and, 1:115–116
battery acid, 1:122–125
cell phones and, 1:250–253
chemical industry and, 1:261–264
chlorine, 1:284–286
chloroform, 1:286–287
coil industry and, 1:296–302
from cooking meat, 2:740–743
cosmetics, 1:313–315
daily life and, 1:333–335
DDT, 1:338–341
defined, 1:84
deodorizers, 1:342–345
detergents, 1:345–348
diesel exhaust, 1:350–353
disinfectants and antiseptics, 1:357–360
dyes and pigments, 1:373–378
electrical industry and, 1:388–391
electronics and, 1:391–394
embalming fluid, 1:396–398
environmental justice and cancer, 1:401–405
explosives, 1:441–443
flame retardant, 2:451–454
flavoring agents, 2:454–457
food additives, 2:457–460
Freon, 2:471–474
future of cancer and environment, 2:475
gasoline, 2:479–481
glass industry and, 2:499–502
global health issues, 2:507–508
hair dye, 2:524–527
herbicide, 2:544–547
history of cancer and environmental influences, 2:550
insecticides, 2:583–586
jet and rocket fuels, 2:635–638
lead, 2:665–668
mutation and alteration in genes from, 2:810
nickel compounds, 2:827–830
nuclear industry and, 1:126, 2:844–847, 2:972, 3:1205
paint, 2:883–885
paper industry, 2:892–894
perfume, 2:906–908
plastics industry and, 2:936–939
polishes, 2:942–945
precocious puberty and, 2:757
radiation, overview, 2:967–971
solvents, 3:1088–1090
stainless steel, 3:1100–1101
talcum, 2:874
textile dyes, 3:1162–1165
tobacco, 2:901–904
toxic mold, 3:1186–1188
vinyl, 3:1286–1288
war gases and chemicals, 3:1298–1302
water treatment and, 3:1302–1304
wood dust, 3:1313–1316
wood preserver, 3:1316–1319
Carcinoid, defined, 1:234
Carcinoid Cancer Foundation, 1:234–235
Carcinoid syndrome, 1:189–190
Carcinoid tumor, childhood, 1:235–237
Carcinoid tumor, gastrointestinal, 1:237–239
Carcinoid tumors (pNETs), 2:890
Carcinoma, origin of term, 2:548
Carcinoma in situ, defined, 2:867
Carcinoma of unknown primary, 1:239–240
Cardamom, 1:34
Careers, 1:240–242
Caregivers, 1:242–246
Carfilzomib, 2:780
Caribbean
   Cuba, 1:46, 1:326–328
   Dominican Republic, 1:363–365
   Haiti, 2:527–529
Carnegie Institution for Science, 1:303
Casein, 2:883
Casodex, 1:110
Castro, Fidel, 1:327
Cataracts, 3:1216
Catholics, on HPV vaccine, 3:1272
CBBS Today, 1:201
Cediranib, 1:111
Ceenu, 1:185
Celebrities and cancer, 1:246–249. See also individual names of countries
   celebrity organizations, 1:248
   examples, 1:246–247
Celgene (United States), 1:249–250
Cell phones, 1:250–253
   overview, 1:250–253
   radiofrequency energy from, 1:393
   wireless telecommunication technologies and cancer, 1:388–389
Cell type, staging of cancers and, 1:64
Cellular osmosis, salt and, 2:743
Cellular Pathology (Virchow), 2:549
Center for Advancement in Cancer Education, 1:383
Center for Science in the Public Interest, 1:375
Centers for Disease Control and Prevention
   on common cancers in men, 1:99
   on cooking meat, 2:741
   cost of therapy and, 1:315
   on deodorizers, 1:343
   environmental justice and cancer, 1:403–404
   Healthy People and, 2:534
   on hepatitis, 2:535–536, 2:537, 3:1271
   on HPV vaccinations, 2:563, 2:564
   National Cancer Policy Board and, 2:803–805
   on poverty as risk factor for cancer, 2:853
   on screening, 3:1034
study of town planning and cancer, 3:1185
   on tobacco, 3:1176–1177, 3:1178–1179
Centers for Medicare and Medicaid Services (CMS), 1:104
Centers of Excellence in Cancer Communication Research (CECCR), 1:221
Central African Republic, 1:253–254
Central America
   El Salvador, 1:386–388
   Guatemala, 2:517–518
   Honduras, 2:553–554
   Nicaragua, 2:826–827
   Central nervous system, chemotherapy and, 1:273
Central nervous system lymphoma, primary, 1:254–256
Centre Anti-Cancer de l'Hôpital Frantz Fanon de Blida, Le, 1:24
Cerebellar astrocytomas, 1:163–164, 1:165
Ceresana Research, 2:453
Cerexa, 2:463
Certified nursing assistants, hospice care and, 2:447
Cervarix, 1:257–258, 2:563–564
Cervical cancer, 1:256–258
   AIDS and, 1:17–18
   Chad and, 1:258–259
   immigrant populations and, 2:574
   infection and, 2:582
   overview, 1:256–258, 3:1312
   screening for, 3:1031, 3:1036
Cetuximab, 1:143
Chad, 1:258–260
Chain, Ernst Boris, 1:81
Champalimaud Center for the Unknown, 2:951
Chang classification staging system, 1:168–169
Chao Family Comprehensive Cancer Center, 1:260–261
Chávez, Hugo, 3:1280–1282
Chelation therapy, 1:46–47
Chemical industry, 1:261–264
Chemical Weapons Convention (CWC), 3:1299
Chemoprevention, 1:264–269
Chemotherapy, 1:269–275. See also individual types of cancers
   anticancer drugs, overview, 1:84–86
   Bonnadonna and, 1:152
   cancer definition and, 1:270
   cancer surgery and, 3:1120, 3:1122
   determinants of treatment, 1:270–271
   drug classes, 1:271–272
   drugs for, 1:367–368
   experimental cancer drugs, 1:438–440
   future of cancer and, 2:475
gene therapy and, 2:483–484
megatherapy, 1:435
new classes of chemotherapeutic agents, 1:274
overview, 1:269–270
personalized medicine and, 1:274
pharmaceutical industry overview, 2:916–920
(See also individual names of pharmaceutical companies)
during pregnancy, 1:183–184
side effects, 1:272–274
Skipper and, 3:1068–1070
Chernobyl nuclear accident, 1:126, 2:972, 3:1205
Chewing tobacco, 3:1073–1075
Chicago Tribune, 2:452
Childcare, cancer risk and, 1:275–277
Childcare and cancer risk, 1:275–277
Childhood brain tumor foundation, 1:277–278
Childhood Cancer Foundation, 3:1093
Childhood Cancer Research Group (University of Oxford), 1:393
Childhood cancers, 1:278–280. See also Carcinogenic substances; Maternity care/maternal health;
  Pregnancy; Vaccines; individual types of cancer
acute lymphoblastic leukemia in, 2:670–672
acute lymphoblastic leukeumia (ALL),
acute myeloid leukemia in, 2:673–675
adrenocortical carcinoma in, 1:5, 1:6–7
American Academy of Pediatrics, Section on Hematology/Oncology, 1:51–53
American Society of Pediatric Hematology/Oncology, 1:74–75
assistance, 1:279–280
Association of Pediatric Hematology/Oncology Nurses, 1:107–108
bladder cancer in, 1:148–150
bone cancer in, 1:154
brain stem glioma in, 1:159–160
brain tumors, cerebellar astrocytoma, 1:163–164
brain tumors, cerebellar astrocytoma/
malignant glioma, 1:165
brain tumors, medulloblastoma, 1:167–169
brain tumors, supratentorial primitive neuroectodermal, 1:169–171
brain tumors, visual pathway and hypothalamic glioma, 1:171–172
brain tumors (solid neoplasms, cerebral tumors) in, 1:165–167
bronchial adenomas/carcinoids in, 1:189–190
Candlelighters Childhood Cancer Foundation, 1:232–234
cardinoid tumors in, 1:23–237
cildcare and cancer risk, 1:275–277, 1:275–278
Childhood Brain Tumor Foundation, 1:277–278
Childhood Cancer (UICC) program, 3:1218
childhood cancer rates, 1:52
childhood cancers, generally, 1:278–280
in clinical trials, 1:290
clothing for protection of children’s skin, 1:295–296
colorectal cancer in, 1:308–310
do drug users, 1:370
early pediatric oncology, 2:931–932
ependymoma in, 1:408–410
esophageal cancer in, 1:414–415
Ewing’s family of tumors and, 1:434–436
extracranial germ cell tumors in, 1:443–445
extragonadal germ cell tumors in, 1:445–446
family size and cancer risk, 2:44–449
hepatocellular (liver) cancer in, 2:841–543
Hodgkin’s lymphoma in, 2:705–707
HPV vaccinations for, 2:563–564
hypothalamic and visual pathway glioma in, 2:570–572
International Society of Paediatric Oncology, 2:607–609
juvenile myelomonocytic leukemia, 2:786
kidney cancer in, 2:650–651
laryngeal cancer in, 2:660–662
liver cancer (primary) in, 2:689–692
mesothelioma in, 2:765–766
multiple endocrine neoplasia syndrome in,
  2:777–779
nasopharyngeal cancer in, 2:795–796
National Childhood Cancer Foundation,
  2:806–807
neuroblastoma in, 2:819–821
obesity and, 2:849–854
oral cancer in, 2:864–866
ovarian cancer in, 2:872–873
overview, 1:278
pancreatic cancer in, 2:888–889
pesticide exposure, 2:913
pineoblastoma and supratentorial primitive neuroectodermal, 2:929–931
poverty as risk factor for cancer, 2:961
(See also Psychosocial care/support)
rhabdomyosarcoma, 2:999–1001, 3:1024
salivary gland cancer in, 3:1015–1016
skin cancer in, 3:1061–1062
soft tissue sarcomas in, 3:1023–1025, 3:1027–1028
St. Jude Children’s Research Hospital,
  3:1099–1100
stomach (gastric) cancer in, 3:1106–1109
thymoma in, 3:1167–1168
thyroid cancer in, 3:1172–1174
types of, 1:278–279
unknown primary site cancer of, 3:1254–1256
unusual cancers of, 3:1258–1260
visual pathway and hypothalmic glioma in,
3:1288–1290
Wilms' tumor in, 3:1307–1308
Childhood supratentorial primitive neuroectodermal
tumors (CSPNTs), 2:929–931
Children's Oncology and Hematology National
Center (Belarus), 1:127
Children's Oncology Group (COG). See also
individual cancers affecting children
CureSearch, 2:806–807
staging system of, 2:690
Chile, 1:280–282
Chilean Oncology Foundation, 1:281
overview, 1:280–282
China, 1:282–284
Chinese Anti-Cancer Association, 1:283
Hong Kong Anti-Cancer Society, 2:554–556
overview, 1:282–284
smoking and society, 3:1076
Chinese traditional medicine
as alternative therapy, 1:40, 1:45
Chinese herbal medicines, 1:34
Chini, C. C., 2:736
Chiropractic, 1:41
Chlorhexidine, 1:358
Chlorine, 1:284–286
as disinfectant, 1:358
Freon and, 2:472
in paper making process, 2:893
Chlorofluorocarbons (CFCs), 2:471–474
Chloroform, 1:286–287, 3:1089
Chloromethane, 1:344
Chokunonga, Eric, 3:1343
Cholangiocarcinoma, 2:685, 2:687–688
Chonnam National University, 3:1093
Chopra, Deepak, 1:44–45
Choriocarcinoma, 3:1192–1193
Choroidal melanomas, 2:612–613
Christianity, on preventability versus preordained
risk, 2:993
Christmas Seals, 1:66–67
Chromate, 2:884
Chronic lymphocytic leukemia (CLL), 2:675–677
Chronic myelogenous leukemia (CML),
2:677–680, 2:790
Chronic myeloid leukemia (CML), 1:229
Chronic myelomonocytic leukemia, 2:785
Chronic transfusion therapy, 2:783
Chugai Pharmaceuticals, 2:1002
Church-based health promotion (CBHP)
intervention, 2:993
Cinnamon, 1:34
Cirrhosis, 2:535, 2:537, 2:538, 2:539, 2:540, 2:541
Cisplatan, 2:1004–1006
City of Hope, 1:288–289, 2:486
Clark, John G., 3:1123
Clean Air Act, 1:89, 1:300
Climate change, ozone layer and, 2:473
Clinical Journal of Oncology Nursing, 2:870
Clinical Protocol & Data Management Office (Her-
bert Irving Comprehensive Cancer Center), 2:543
Clinical trials, 1:289–294. See also Pharmaceutical
industry; individual names of pharmaceutical
companies
among aging population, 1:15–16
benefits and drawbacks to, 1:293–294
designing and executing, 1:291–292
ICARE on, 2:594
key players in, 1:289–290
overview, 1:289
trial sites, 1:292–293
types and phases of, 1:290–291
Clinique Al Azhar, 1:24
Clothing, 1:294–296, 1:343
Coagulation factors, hemophilia and, 2:817
Coal industry, 1:296–302
environmental concerns, 1:298–299
health and safety concerns, 1:299
overview, 1:296–297
risk reduction efforts, 1:299–302
types and uses of coal, 1:297
types of mining, 1:298
Cobalt radiation therapy, 1:212
Cochrane Systematic Review, 3:1042–1043
Cognitive impairment, from chemotherapy, 2:920
Coinvestigators (CIs), defined, 1:289
Cold Spring Harbor Laboratory, 1:302–304
Cole, Brenda, 2:995
Coley, William Bradley, 1:47, 1:142, 3:1273, 3:1275
Coley's toxins, 1:47, 1:142, 3:1273
Collaborative Ocular Melanoma Study, 2:612
Colombia, 1:304–306
Colombian League Against Cancer, 1:304
overview, 1:304–306
Colon cancer, 1:306–308
American College of Gastroenterology and, 1:60–62
chemoprevention for, 1:267
ease and, 1:436
overview, 1:306–308
screening, 3:1033
Colonoscopv, 1:60–61
Colorectal cancer, 1:306–308
aspirin and, 1:94
COX-2 inhibitors, 1:321–322
Identification of Colorectal Cancer Opinion Leaders for a Knowledge Transfer Program in Ontario (Canadian Society of Surgical Oncology), 1:215
screening for, 3:1036
University of Colorado on, 3:1235
Colorectal cancer, childhood, 1:308–310
Columbia University, 2:543–544
Columbus, Christopher, 1:363
Complementary medicine (CAM), 1:27
Comprehensive Cancer Center (University of Alabama at Birmingham), 3:1224–1226
Comprehensive Cancer Center (University of California, Davis), 3:1226–1228
Comprehensive Cancer Center (University of Chicago), 3:1231–1233
Comprehensive Cancer Center (University of Michigan), 3:1237–1240
Comprehensive Cancer Center of Wake Forest University, 1:310–311
Comprehensive cancer centers (CCCs), 1:292
Computed tomography (CT) scanning, overview, 2:551, 2:975, 3:1330–1331
Computerized axial tomography (CAT), 3:1330–1331
Conventional external beam radiation therapy (2DXRT), 2:977
Cooking practices, for meat, 2:740–743
Copland, John, 2:736
Copper, 1:47, 3:1317–1318
Cornelius P. Rhoads Memorial Award, 1:55
Cornell University, 3:1304
Corpus uteri cancer, in Belgium, 1:128
Cortisol, 2:832
Cosmetics, 1:313–315
dedorizers in, 1:342
dyes and pigments in, 1:375–376
hair dye, 2:524–527
nail polish, 2:942–945
perfume, 2:906–908
underarm deodorant, 1:344
Cost of therapy, 1:315–316
Costa Rica, 1:316–318
Côte d'Ivoire, 1:318–320
Cotinine, 2:902–903
Coumarin, 2:907–908
Couric, Katie, 1:246, 1:248
Couric Effect, 1:246
Cowen, Ken, 2:468
COX-2 inhibitors, 1:320–325
bladder cancer, 1:323–324
breast cancer, 1:323
colorectal cancer, 1:321–322
esophageal cancer, 1:322–323
gastric cancer, 1:322
lung cancer, 1:323
malignancy and COX-2, 1:321
non-melanoma skin cancer, 1:323
overview, 1:320–321
Cranberry, 1:34
Craniosacral therapy, 1:41
Creamy snuff, 3:1074
Creel, Hugh P., 2:464
Creosote, 3:1316–1317
Crile, George, 3:1123
Crisotinib, 2:915
Croatia, 1:325–326
Croatian League Against Cancer, 1:326
overview, 1:325–326
Cruciferous vegetables, 1:90–91
Cryoprobe, 3:1121
CTR (exams), 2:805
Cuba, 1:46, 1:326–328
Culture of Medicine in Late Medieval Ireland, The, 2:616
CUPID (Cancer in the Under-Privileged Indigent or Disadvantaged) (Sidney Kimmel Comprehensive Cancer Center), 3:1053
Cupping, 1:41
CUPs (cancer of unknown primary site), 1:239–240, 3:1254–1258
CURE, 1:8
Cure for Lymphoma Foundation, 2:716
CureSearch National Childhood Cancer Foundation, 2:806–807
Curie, Marie, 2:467, 2:550, 2:975
Curie, Pierre, 2:467, 2:550
Cushing’s syndrome, 1:5, 1:6, 1:190, 1:237
Cutaneous melanoma, 3:1086
Cyberknife, 1:316, 2:693
Cyclamates, 2:458
Cyclooxygenase isozymes, 1:95
DDT, 3:1223
Cyproconazole, 3:1318
Cyramza, 1:395
Cystoscopy, 3:1296
Cytokines, 1:145
Cytosine (C), 2:488
Cytostatic chemotherapy, defined, 1:269–270
Cytotoxic chemotherapy, defined, 1:269–270
Czech Republic, 1:328–329
D, vitamin, 1:35–36, 1:139, 3:1293
Da Vinci robot-assisted surgery, 2:465
Daffodil Day (Republic of Ireland), 2:542
Deep South Network for Cancer Control, 2:783
Decitabine, 1:335–337
De Ovando, Nicolás, 2:566
De Hevesy, George Charles, 2:783
Decitabine, 2:783
Deep South Network for Cancer Control, 3:1225
Delaney Clause (Food, Drugs and Cosmetic Act of 1938), 2:457
Dell Computer Company, 2:620
DeMatteo, R., 2:937
Demerec, Milislav, 1:303
Denmark, 1:341–342
cancer registry of, 2:592
Danish Cancer Society, 1:337–338
Danish Endometrial Cancer Group, 1:400
H. Lundbeck, 2:521–523
Novo Nordisk, 2:843–844
pain issues in, 2:574
wood dust research in, 3:1315
Dense Inert Metal Explosive (DIME), 1:441, 1:443
Deodorizers, 1:342–345
Depressant drugs, defined, 1:368
Detergents, 1:345–348
Detroit (Michigan), Barbara Ann Karmanos Cancer Institute and, 1:121–122
Developing countries, 1:348–350. See also individual names of developing countries
cancer in, 1:348–349
interventions for cancer control, 1:349–350
Diabetes
cancer and, in Japan, 2:631
insulin, 1:49, 1:440–441, 2:851
Novo Nordisk on, 2:843–844
UN on, 2:843
“Diabetes Attitudes, Wishes, and Needs” (Novo Nordisk), 2:844
Diagnostic tests. See also Screening; Screening, access to; individual names of countries; individual types of cancers
Abbott Laboratories and, 1:1–2
for adrenocorticol carcinoma, 1:5–6
Alcohol Use Disorders Identification Test—Consumption, 1:22
American Academy of Pediatrics on, 1:52–53
American College of Gastroenterology on, 1:60–62
for bladder cancer, 1:149
for bone cancer, 1:155
for brain stem glioma, childhood, 1:160
for brain tumor, medulloblastoma, childhood, 1:167–168
for breast cancer, 1:176–177
colonoscopy, 1:60–61, 1:306
cystoscopy, 3:1296
in developing countries, 1:349–350
for extrahepatic bile duct cancer, 1:141
GeneSearch Breast Lymph Node Assay, 2:639
for hepatitis B, 2:535
history of cancer and, 2:550–552
imaging technology, overview, 3:1154–1156
Medicare and Medicaid allowances, 2:748
Pap tests, 1:18, 1:212, 1:349, 3:1137, 3:1277
prostate-specific antigen (PSA), 1:99, 2:955
staging of cancer and, 1:63–65, 1:141–142,
Daily life, 1:333–335
disability and, 1:355–357
health-related quality of life (HRQoL), 2:995
occupational therapy and activities of daily living (ADL), 2:855
overview, 1:333–335
quality of life (QoL) and head and neck cancer, 2:529–530
Damascus University Al Bairouni University Cancer Center, 3:1132–1133
Dana-Farber Cancer Institute, 1:335–337
Jimmy Fund, 1:335, 1:336, 2:638–639
overview, 1:335–337
Pfizer and, 2:915
Danhauer, Suzanne, 2:669–670
Danish Cancer Society, 1:337–338
Darragh, Austin, 2:620
Dauksa, Albertas, 2:622
David H. Koch Institute for Integrative Cancer Research, 2:769–771
DDT, 1:338–341
history of, 2:912, 2:913
insecticide hazards, 2:583–586
in paper processing, 2:893
De Hevesy, George Charles, 2:566
De Ovando, Nicolás, 1:363–364
Decitabine, 2:783
Deep South Network for Cancer Control, 3:1225
Delaney Clause (Food, Drugs and Cosmetic Act of 1938), 2:457
INDEX
staging of cancers and, 1:64–65
surgery for diagnosis, 3:1120
Diaminoanisole, 1:375
Diaminotoulene, 1:375
Dibutyl phthalate (DBP), 2:944
Dichloroacetic acid (DCA), 1:47–48
Dichlorodiphenyltrichloroethane. See DDT
Diesel exhaust, 1:115–116, 1:350–353

Diet and nutrition, 1:353–355. See also individual alternative therapies; individual names of countries; individual names of vitamins
alternative therapy and, 1:32–37
alternative therapy and diets, 1:27–32
Asian diet, 1:28, 1:90–93
banana plantations, 1:317
barbecue risks and, 1:13–14
beta-carotene, 1:132–138
calcium, 1:199–200
cancer incidence in developing countries and, 1:348
cancer incidence in Chile and, 1:280–281
as cause of cancer, statistics, 2:809
chemoprevention, 1:268–269
daily life and cancer prevention, 1:334
early menarche and, 2:756–758
education about, 1:381
flavoring agents, 2:454–457
food additives, 2:457–460
food dyes, 1:374–375
herbicide and food, 2:544–547
in Japan, 2:627–628
meat, cooking, 2:740–743
meat processing, 2:743–744
obesity and, 2:851
overview, 1:353
phytochemicals as chemoprevention, 1:266
poverty and, 2:953
for preventing natural causes of cancer, 2:811
selenium, 1:36, 3:1041–1044
special populations and, 1:354
specific nutrients and other dietary constituents, 1:353–354
study of, 1:354–355
total caloric intake, 1:353
U.S. regulatory authorities, 2:460
vitamins, overview, 3:1290–1295
Western diet, 1:304–1307
Diffusion tensor imaging (DTI), 1:163
Digital Divide Pilot Projects (NCI), 1:221
Digital mammography, 1:212
Dignity therapy, 2:995
DiMasi, Joseph, 1:227

Dinshah Health Society, 2:927
Dioxane, 1:344, 1:345–346, 1:347
Dioxins, 2:893
Dipping tobacco, 3:1074
Direct-to-consumer advertising, 2:728–729

Disability, 1:355–357
attitudes toward, 1:356
disabling barriers, 1:356–357
education about, 1:381
overview, 1:355
problems with health system and insurance, 1:357
protection under legislation, 1:356
Disease-Specific Division (Herbert Irving Comprehensive Cancer Center), 2:543
Disinfectants and antiseptics, 1:357–360
disinfection by-products (DBPs), 1:359
overview, 1:357
types of, 1:357–359

Disparities within nations (elimination of cancer), 1:360–363. See also Economic issues; Ethnicity; Health care access; Race; individual names of countries
data requirements, 1:360–361
endometrial cancer, 3:1264–1265
existing disparities, 1:361–362
future directions, 1:362–363
overview, 1:360
Program for the Elimination of Cancer Disparities (PECaD), 3:1060
women’s cancers and, 3:1310

DNA. See Genetics
Do not resuscitate (DNR) order, 1:97
Doctors of osteopath (DO), 1:42
Doh, Anderson S., 1:205
Doll, Richard, 1:353, 3:1176

Dominican Republic, 1:363–365
Dominican League Against Cancer Inc., 1:364–365
Dominican Society of Hematology and Oncology, 1:365
Donnell-Thomas, E., 2:469

Donor programs
bone marrow transplants, 1:156–159
California Blood Bank Society, 1:200–202
Canadian Red Cross, 1:214
LifebankUSA, 1:249
National Marrow Donor Program, 2:807–809
Doshas, 1:45
Drake, Edwin, 2:479
Drug Enforcement Administration, 1:123
Drugs, 1:366–371. See also Pharmaceutical industry
cancer-related drugs, 1:366–367
cost of chemotherapy, 1:367–368
drug abuse or drug misuse, 1:369
drug marketing, 2:728–729
experimental cancer drugs, 1:438–441
impact of, on society, 1:370–371
for pain control, 1:368
rational use of, 1:369–370
regulatory authorities, 1:371
types of, 1:368–369
FDA role and, (See also Food and Drug Administration)
Druker, Brian, 2:859
Ductal adenocarcinomas, 2:888–889
Ductal carcinoma in situ (DCIS), 1:177, 2:981, 3:1311
Dufour, Guillaume-Henry, 2:595
Duke Cancer Institute, 1:372–373
Duke University Medical Center, 1:440
Dulbecco, Renato, 2:551
Dunant, Jean Henry, 1:213, 2:595
Dunn, Steve, 1:101
DuPont Corporation, 2:472–474
Durie, G. M., 2:597
Durkheim, E., 2:987
Dutch Hemophilia Patients Association.
See Netherlands Hemophilia Patients Society
Dye couplers, 2:524
Dyes and pigments, 1:373–378
in cosmetics, 1:375–376
in food, 1:374–375
in hair dye, 2:524–527
occupational exposure to, 1:377
overview, 1:373–374
in paint, 2:883–885
in tattoo inks, 1:376
textile dyes, 3:1162–1165
Dysplasias, 2:864
E, vitamin, 1:36, 3:1293–1294
Eagle, Harry, 1:19
Eastern Cooperative Oncology Group (ECOG), 1:15
Ebola virus, 2:519
Ecancermedicalscience, 1:425
ECCO, See European CanCer Organisation
Ecological and Toxicological Association of Dyes and Organic Pigment Manufacturers (ETADOPM), 3:1163
Economic issues. See also Disparities within nations (elimination of cancer); Poverty; individual names of countries
cancer drugs, costs and benefits of, 1:227–231
cost of therapy, 1:315–316
cost-effectiveness of treatments, pancreatic cancer, 2:888
doing of drugs, 1:370–371
doing of proton therapy, 2:960
smoking and society, 3:1077
of tobacco usage, 2:904
Ecuador, 1:379–380
Edge technique, 2:951
Edison, Thomas, 1:388
Educating the Child with Cancer (Candlelighters Childhood Cancer Foundation), 1:233
Education, 1:380–383. See also Psychosocial care/support; individual names of educational and research organizations; individual names of non-profit organizations
about physical activity and diet, 1:381
about proton therapy, 2:960
about sun exposure, 1:381
about tobacco use, 1:381
American Association for Cancer Research, 1:55–56
American Psychosocial Oncology Society resources, 1:67–68
American Society for Radiation Oncology resources, 1:70
American Society of Clinical Oncology resources, 1:71
Association of Cancer Online Resources, 1:100–102
cancer communication, 1:220–225
cancer disparities and, 1:382
diet and, 1:92
disparities within nations and elimination of cancer, 1:362
education levels (See individual names of countries)
future of cancer education, 1:382–383
medical education in Cuba, 1:327
NABCO Breast Cancer Resource list, 2:797
NCI programs, 2:802
Oncology Nursing Society materials, 2:860–861
overview, 1:380–381
patient-centered, 1:381–382
patient-provider communication, 1:382
poverty as risk factor for cancer, 2:853
promoting screening tests, 3:1034
purpose and importance of cancer education, 1:381
sun exposure in Australia and, 3:1114–1115
workplace wellness programs and, 3:1319–1321
young adult cancer prevention, 3:1338
Edwards, Margaret Hay, 1:54
Egypt, 1:383–385
Ehrlich, Paul, 1:81, 1:143
Eisai (Japan), 1:385–386
El Salvador, 1:386–388
Electrical industry, 1:388–391
Electromagnetic fields (EMF), 1:388
Electronic Surveillance System for the Early Notification of Community-Based Epidemics (ESSENCE), 1:394
Electronics, 1:391–394
Eli Lilly & Company (United States), 1:394–396, 2:591
Elion, Gertrude, 2:674
**Embalming fluids**, 1:396–398
Embryonal rhabdomyosarcoma, 2:1000
Emend, 2:761, 2:863
EMI, 3:1330
Emmerich, Rudolf, 1:81
Employee safety. See Occupational hazards
Enbrel, 1:76
Endocrine pancreas, 2:621–623
**Endometrial cancer**, 1:398–401
exercise and, 1:437
health disparities, 3:1264–1265
overview, 1:399–401, 3:1263–1264, 3:1312
screening for, 3:1036
treatment options, 3:1264
Endometrioid adenocarcinoma, 1:400
Endoscopic surgery, 3:1121
Endoscopy, 1:60–61
Energy industry
coil, 1:296–302
diesel exhaust and, 1:350–353
gasoline, 1:115–116, 2:479–481, 2:668
nuclear, 2:844–847
**Ensuring Quality Cancer Care** (National Cancer Policy Board), 2:804
Environmental Defense Fund, 1:285
**Environmental Health**, 3:1304
**Environmental justice and cancer**, 1:401–405.
See also Carcinogenic substances; Environmental Protection Agency (EPA); Environmental tobacco smoke; Natural causes of cancer; Occupational hazards; Passive smoking
automobiles and, 1:115–116
Azerbaijan and cancer risk, 1:118
carcinogenic ingredients in domestic products, 1:403–405
environment, defined, 1:402
environmentally attributable risk (EAR), 1:402
first correlation between cancer and environment, 3:1123
global health issues, 2:507–508
nature versus environment, 2:809–811 (See also Carcinogenic substances; Natural causes of cancer)
occupational risk and, 1:402–403
overview, 1:401–402
**Silent Spring** (Carson), 1:338–339, 2:893, 2:912–913
Environmental Protection Agency (EPA)
air pollution, 2:946
asbestos, 1:89, 2:766
automobiles, 1:116
chemical industry, 1:263
chlorine, 1:285
coil, 1:299
DDT banned by, 1:340
detergents, 1:345, 1:346
disinfectants and antiseptics, 1:359
dyes and pigments, 1:374
environmental tobacco smoke, 1:406
explores, 1:441
flame retardants, 2:452, 2:453
gasoline, 2:479–480
herbicides, 2:545
insecticides, 2:584, 2:585
jet and rocket fuels, 2:636
lead, 2:667
nickel compounds, 2:829
passive smoking, 2:903
pesticides, 2:911
role of, 2:460
solvents, 3:1088
water treatment, 3:1302–1303
Environmental Protection Group, 3:1303
**Environmental Science & Technology**, 1:347, 3:1303
**Environmental tobacco smoke**, 1:405–408
as cause of cancer, 1:407
overview, 1:405–407
tobacco companies on, 1:407–408
Environmental Working Group, 1:404, 2:636, 2:913–914
Enzymes
d enzyme and metabolism therapies, 1:30, 2:736
experimental cancer drugs, 1:438–439
Ependymoma, childhood, 1:408–410
Ependymomas, 1:166
Epidemiology of cancer, Trichopoulos and, 3:1190–1192
Epidermal growth factor receptor (EGFR), 1:111
Epidermoid cancer, 1:117–118
Epidermoid carcinoma, 2:905
Epigenetics, 3:1043
EPO, 1:76–77
Epogen, 1:76, 1:77
Epstein-Barr, future of cancer and, 2:474
Erhart, Charles, 2:914
Eritrea, 1:410–412
ESO. See European School of Oncology
Esophageal cancer, 1:412–414
aspirin and, 1:94
COX-2 inhibitors, 1:322–323
esophageal adenocarcinoma (EAC), 1:414
esophageal squamous cell carcinoma (ESCC), 1:414
Esophageal cancer, childhood, 1:414–415
ESSO. See European Society of Surgical Oncology
Estrada-Claudio, Sylvia, 3:1310
ESTRO. See European Society for Therapeutic Radiology and Oncology
Estrogen, steroidal, 1:415–418
Ethics, of assisted suicide, 1:96, 1:98
Ethiopia, 1:418–420
Ethnicity. See also Surveillance, Epidemiology, and End Results (SEER) Cancer Statistics Review, 1975–2011; individual names of countries
care and cancer risk, 1:275–276
disparities within nations and elimination of cancer, 1:362
immigrant populations, 2:573–576
Mayo Clinic trials and, 2:735
passive smoking and, 2:903
precocious puberty, 2:757
screening access and, 3:1036–1038
stomach cancer and, 3:1103
testicular cancer and, 3:1162
women's cancers and, 3:1312
Ethoxylation, 1:347
Ethylene diamine tetracetic acid (EDTA), 1:46–47
Ethylenediaminetetraacetic acid (EDTA), 2:893
Eurocancercoms, 1:423
Europa Donna, the European Breast Cancer Coalition, 1:420–422
education by, 1:421
goals of, 1:420–421
overview, 1:420
public affairs, 1:421–422
Europe. See also individual names of European countries
alternative therapies in, 1:46
Austria, 1:113–115, 2:565
Azerbaijan, 1:116–118
Belarus, 1:125–127
Belgium, 1:97, 1:127–129
Bulgaria, 1:190–192
Croatia, 1:325–326
Czech Republic, 1:328–329
Denmark, 1:341–342
Finland, 2:449–451
France, 2:465–468
Georgia, 2:492–493
Germany, 2:493–495
Hungary, 2:565–567
Italy, 2:625–626
Moldova, 2:771–773
Netherlands, 2:814–815
Norway, 2:839–841
Organisation of European Cancer Institutes, 2:868–870
Poland, 2:940–942
Portugal, 2:950–951
Republic of Ireland, 2:615–618
Romania, 2:1003–1004
Russia, 2:1008–1010
Serbia, 3:1046–1048
Slovakia, 3:1070–1071
Spain, 3:1095–1096
Sweden, 3:1130–1131
Switzerland, 3:1131–1132
Turkey, 3:1196–1198
Ukraine, 3:1205–1206
United Kingdom, 3:1220–1221
Europe Against Cancer (European School of Oncology), 1:428
European Association for Cancer Research, 1:422–423
European CanCer Organisation, 1:424–425, 1:433
European Cancer Prevention, 1:425–427
European Economic Interest Grouping (EEIG) designation, 2:869
European Federation of Pharmaceutical Industries and Association (EFPIA), 2:843, 2:1002
European Food Safety Authority (EFSA), 2:458
European Institute of Oncology, 2:626
European Journal of Cancer, 1:422, 1:425, 1:431
European Journal of Cancer Prevention, 1:426
European Journal of Surgical Oncology, 1:433
European Medicines Agency, 2:482
European National Toxicology Program, 2:501
European Network of Cancer Registries (ENCR), 2:504
European Organisation for Research and Treatment of Cancer (EORTC), 1:421, 2:951
European Ramazzini Foundation (ERF), 2:458
European Randomized Study of Screening for Prostate Cancer, 2:955
European School of Oncology, 1:427–429
European Society for Therapeutic Radiology and Oncology, 1:429–431
European Society of Breast Specialists (EUSOMA), 1:421, 1:428
European Society of Mastology, 1:431–432
European Society of Surgical Oncology, 1:432–434
European Society of Thoracic Surgeons, 3:1169
Euthanasia. See Assisted suicide
Evista, 1:394
Ewing, James Stephen, 3:1084
Ewing's family of tumors, 1:434–436, 3:1019–1021
Exercise, 1:436–438
   bicycles and, 1:138–140
   breast cancer and, 1:436–437
   colon cancer and, 1:436
   education about, 1:381
   endometrial cancer and, 1:437
   global health issues, 2:506
   Healthy People Initiative, 2:534
   lung cancer and, 1:437
   obesity and, 2:851–852
   ovarian cancer and, 1:437
   overview, 1:436
   poverty and, 2:953
   prostate cancer and, 1:437
   recommendations, 1:438
   sedentary occupations, 3:1039–1041
Experimental cancer drugs, 1:438–441
   Experimental Hematology, 2:603, 2:604
   Exploratory surgery, 3:1121
Explosives, 1:441–443
   External beam radiation therapy, 2:970, 2:975, 2:976–977
   Extracranial germ cell tumor, childhood, 1:443–445
   Extragonadal extracranial germ cell tumors, 1:444
   Extragonadal germ cell tumor, 1:445–446
   Extrahepatic duct, cancer of, 1:140–142
   Extraosseous Ewing tumors, 3:1019
   Extremely low frequency (ELF) electromagnetic fields, 1:389
   Eye health
   intraocular melanoma, 2:611–613, 2:752–754
   optic gliomas, 1:171–172
   retinoblastoma, 2:997–999
   sunbed/sunlamp exposure and, 3:1116
   UV exposure and cataracts, 3:1216
   visual pathway and hypothalamic glioma, childhood, 3:1286–1288
F. Hoffman-La Roche Ltd., 2:1001
Familial adenomatous polyposis (FAP), 1:306–307, 1:308
Familial cancer path, 2:488
Family and Medical Leave Act (1993), 1:245
Family size, 2:447–449
   Hinkula on, 2:450–451
   overview, 2:447–449
   social trends in Japan, 2:628
Fanon, Frantz, 1:24
Farber, Sidney, 1:335, 1:336, 2:550, 2:671, 2:674
Faslodex, 1:111
Fast neutron therapy, 2:822, 2:823
Fatalism, about cancer, 2:992–994
Fatigue, from chemotherapy, 1:272
Federal Aviation Administration (FAA), 1:11
Federation of European Cancer Societies, 1:424
Fee-for-service plans, 2:587
Feldenkrais Method, 1:40
Ferenczi, Alexander, 2:566
Fermented wheat germ extract (FWGE), 2:566
Fifth Annual Cancer Control Congress (El Salvador), 1:386
Financial costs, of cancer. See Cost of therapy
Finland, 2:449–451, 3:1315
First National Cancer Nursing Conference (1973), 2:860
First Nations population (Canada), cancer control programs for, 1:208
Fishman, Lillian Waterman, 3:1018
Fishman, William H., 3:1018
5-HT3 inhibitors, 2:919
Flame retardant, 2:451–454, 3:1318
Flavoring agents, 2:454–457
Fleming, Alexander, 1:81
Flocculants, 2:948
Florey, Howard, 1:81
Fluorescence in situ hybridization (FISH), 1:2, 2:935
Fluoridated water, 2:949, 3:1303
Folate/folic acid, 1:21, 1:36
FOLFIRINOX, 2:887
Folk medicine. See Traditional medicines
Follicular cancer (thyroid), 3:1173
Follicular lymphoma, 2:525
Food. See Diet and nutrition
Food, Drugs and Cosmetic Act of 1938, 2:457
Food additives, 2:457–460
Food and Drug Administration, 2:460–462. See also Pharmaceutical industry; Technology, new therapies
on advertising, 1:8, 1:9, 2:729
on alternative therapies, 1:39
Association of Community Cancer Centers on, 1:102–103
on biologic therapy, 1:142
cancer research and, 2:460–461
clinical trials and, 1:290
current issues of, 2:462
on DDT, 1:340
drug regulation, overview, 1:371
on dyes and pigments, 1:374, 1:375, 1:376
on flavoring agents, 2:454, 2:455
on food additives, 2:457–460
generally recognized as safe (GRAS) designation of, 2:455, 2:457
on hair dye, 2:525
history of, 2:461
history of cancer and, 2:550
on lead, 2:668
on multiple myeloma treatment, 2:780
on nail polish, 2:943
overview, 2:460
on plastics, 2:938
smoking cessation products and, 3:1077–1081
on tobacco, 3:1177
Food Guide Pyramid, 3:1306
Food Safety and Modernization Act (FSMA) (2011), 2:462
Ford, Betty, 1:246, 2:835
Forefront, 2:736
Foreign free rider argument, drug costs and, 1:230
Forest Labs (United States), 2:462–464
Cerexa, 2:463
Forest Pharmaceuticals, Inc., 2:463
Forest Research Institute, 2:463
Formaldehyde, 1:397, 2:944, 3:1089, 3:1317
Fosamax, 2:760
Foster, George, 2:510
4-methoxy-m-phenylenediamine, 1:375–376
Fox, Terry, 1:212
Fox Chase Cancer Center, 2:464–465
France, 2:465–468
Algeria colonization and, 1:24
Pierre and Marie Curie, 2:467
smoking and society, 3:1076
Fred Hutchinson Cancer Research Center, 2:469–471, 2:516
Fred & Pamela Buffet Cancer Center, 2:468–469
Frederick Cancer Research and Development Center, 2:835
Free Dive (video game), 2:881
Free radicals, 1:268
Frei, Emil, 2:675, 2:931
Freireich, Emil J., 2:675, 2:931
Freon, 2:471–474
Freundlich, Barbara, 2:716
Freudlich, Jerry, 2:716
Frontiers, 2:857
Fuchs, Ernst, 2:549–550
Fungi, antimicrobial treatment for, 1:81–83
Furniture Flame Retardancy Partnership (FFRP), 2:452
Fushimiya, Ichibei, 2:862
Future of cancer, 2:474–475. See also Prevention of cancer overview, 2:474
prevention and, 2:474–475
treatment and, 2:475
“Future of Nuclear Power” (MIT), 2:847
Galen, 2:512, 2:663, 3:1119
Gallbladder cancer, 2:477–479
Gamma radiation. See Radiation, gamma
Garcia, Donato Perez, 1:49
Garlic, 1:34
Gasoline, 2:479–481
automobiles and, 1:115–116
lead and, 2:668
taxes on, 3:1153–1154
Gastrinomas, 2:890
Gastrointestinal tract. See also Colon cancer;
Colorectal cancer; Esophageal cancer;
Gallbladder cancer; Stomach (gastric) cancer; Stomach (gastric) cancer, childhood
American College of Gastroenterology, 1:60–62
bile duct cancer and, 1:140
carcinoid tumors, childhood, 1:235–237
COX-2 inhibitors, 1:322
gastroesophageal reflux disease (GERD), 1:414–415
Japanese Gastric Cancer Association, 2:632–634
small intestine cancer, 3:1071–1073
stomach (gastric) cancer, 3:1103–1106
stomach (gastric) cancer, childhood, 3:1106–1109
Gel manicures, 2:944–945
Gelsinger, Jesse, 2:485
Gemcitabine, 2:886–887
Gender issues. See also Breast-feeding;
  Maternity care/maternal health; Pregnancy;
  Surveillance, Epidemiology, and End Results (SEER) Cancer Statistics Review, 1975–2011;
  Women’s cancers; individual types of cancer
Bangladesh and women’s health, 1:120
cultural obstacles to women’s health, 2:885
global trend of female and male cancer rates, 1:386
Gender Issues in Cancer Care (Estrada-Claudio), 3:1310
Gendicine, 2:482
Gendron, Claude Deshais, 2:466
Gene therapy, 2:482–485
  biologic therapy, 1:146
  experimental cancer drugs, 1:440–441
technology and, 3:1158
Genentech, 2:486–487
  City of Hope and, 1:288
  overview, 2:486–487
  Roche Group and, 2:1002
Generally recognized as safe (GRAS) (FDA), 2:455
GeneSearch Breast Lymph Node Assay, 2:639
Genetically modified seeds, 2:545
Genetics, 2:487–490
  alcohol and carcinogenic effects, 1:21
  anticancer drugs and, 1:84, 1:85
  beta-carotene and, 1:132–138
  BRAF gene, 2:680
  brain tumor, cerebellar astrocytoma, 1:163–164
  breast cancer and, 1:175–176
  breast cancer in men and, 1:179
  chemoprevention and, 1:266
  chemotherapy and personalized medicine, 1:274
  Cold Spring Harbor Laboratory and, 1:302–303
  colon cancer and, 1:306–307
  colorectal cancer, childhood, 1:309
  Ewing’s family of tumors, 1:434–436
  gene therapy compared to, 2:484
  Genome Institute (Washington University) and, 3:1060
  global health issues and cancer, 2:508
  history of cancer and, 2:551
human migration and, 2:574
medulloblastomas in children, 1:166
Merkel cell carcinoma, 2:762–763
multiple endocrine neoplasia syndrome, 1:777–779
natural causes of cancer and, 2:809–811
neuroblastoma, 2:819–821
ovarian cancer and, 2:873–875
overview, 2:487–490
P53 gene, 1:268
pituitary tumors, 2:933
plasma cell neoplasm/multiple myeloma and, 2:934
pleuropulmonary blastoma, 2:940
primary central nervous system lymphoma and, 2:714–716
prostate cancer and, 2:955
R337H mutation, 1:6–7
radiation damage to, 1:11
Ras Association Domain Family 1 (RASSF1) gene, 2:622
retinoblastoma, 2:997
selenium and, 3:1043
unusual cancers of childhood, 3:1259
uterine sarcoma, 3:1266–1267
Genetics Institute, 1:76
Geneva Cross, 1:213
Geneva Protocol, 3:1298
Genome Institute, Washington University, 3:1060
Genzyme (United States), 2:490–492
Geography, latitude and, 2:662–665
Georgetown University Medical Center, 2:692–694
Georgia, 2:492–493
  Georgia National Screening Center, 2:493
  overview, 2:492–493
Gerhardt, Charles Frederic, 1:93
Germany, 2:493–495, 2:758–759
Germicidal irradiation, 3:1213
Gersh, Max, 1:30
Gerson Therapy, 1:30, 2:566
Gestational trophoblastic tumor, 2:495–497
Ghadiali, Dinshah, 2:927
Ghana, 2:497–499
Giuliano, Armando, 3:1123
Glass industry, 2:499–502
GlaxoSmithKline (United Kingdom), 2:502–503
cancer drugs, costs and benefits, 1:229
Cervarix, 1:257–258, 2:563–564
Pfizer and, 2:915
Glial cells, 1:159
Global health issues and cancer, 2:503–509.

See also individual names of countries
cancer control and, 2:504–505
cancer control, 2:504–505
data organization, 2:504
future of, 2:508–509
genetics and risk factor analysis, 2:508
interdisciplinary nature of, 2:503–504
latitude and, 2:662–665
prevention policies and risk factor analysis, 2:508–509
worldwide cancer burden, 2:505–506

“Global Health Observatory Data Repository” (WHO), 1:80

Global Strategy for Health for All by the Year 2000 (WHO), 1:111

Global Task Force on Expanded Access to Cancer Care and Control in Developing Countries Innovation (GTF.CCC), 2:528

Global Vaccine Action Plan (GVAP), 2:536

GLOBOCAN (database). See also individual names of countries
on esophageal cancer, 1:412
overview of, 2:794
on rectal cancer, 2:986
on stomach cancer, 3:1103

Glybera, 2:482

Godfrey, Kathryn, 2:606
Goldstein, Linda Gene, 1:56
Golter, Samuel, 1:288
Gonadal extracranial germ cell tumors, 1:444
Gonadotropin-releasing hormones, 2:917
Gonzalez Therapy, 1:30–31
Good, Robert A., 3:1240

Government, 2:509–511. See also individual names of countries
cancer prevention and, 2:510
cure, care, and alleviating suffering, 2:510–511
government-sponsored health insurance plans, 2:587–588
obesity issues and, 2:854
overview, 2:509–510
research and surveillance, 2:511
Grade, staging of cancers and, 1:64
Graft-versus-host disease (GVHD), 1:157–158
Grant programs, of NCI, 2:799–801
Greece, 2:512–513
Green, Adele, 2:513–515
Green Journal, 1:429
Greenpeace International, 3:1164
Gregoire, Christine, 2:515–516

Gregoire, Mike, 2:516
Grimmer, Arthur, 1:48
Groundwater water pollution, 2:948–949
Group psychotherapy, 2:995
Grubbe, Emil, 2:975, 3:1329
Guanine (G), 2:488
Guatemala, 2:517–518
Guards, careers and, 1:241
Guinea, 2:518–520

Gynecological cancers. See also Breast cancer;
Pregnancy; Screening; individual names of countries
cervical cancer, 1:256–258
endometrial cancer, 1:398–401, 1:437, 3:1263–1266
ovarian cancer, 1:94, 1:324, 1:437
ovarian cancer, childhood, 2:872–873
ovarian epithelial cancer, 2:873–875
ovarian germ cell tumor, 2:875–877
ovarian low malignant potential tumor, 2:877–878
Society of Gynecologic Oncology, 3:1082–1084
uterine sarcoma, 3:1025–1027, 3:1266–1267
vaginal cancer, 3:1276–1278
vulvar cancer, 3:1295–1296
women’s cancers, overview, 3:1310–1313

H. Lundbeck (Denmark), 2:521–523
Habibi, Abdollah, 2:613

Haemophilia Society (United Kingdom), 2:523–524

Hair dye, 1:375–376, 2:524–527
Hair loss, from chemotherapy, 1:272
Hairy cell leukemia, 2:680–682
Haiti, 2:527–529

Halaven’s eribulin, 1:385
Hallucinogenic drugs, defined, 1:369
Haloacetic acids (HAAs), 1:359
Halogen-releasing agents, 1:358
Halsted, William Stewart, 2:549, 3:1120
Hamartomatous syndromes, 1:306–307
Hamartomous syndromes, 1:307, 1:309
HAMLET (Human Alpha-lactalbumin Made LETHal to Tumor cells), 2:918, 3:1157
Hanaoka, Seishū, 2:549
Hanon, Gregory, 1:303
Haredi Jewish populations, cancer risk and, 2:989–990
Harlow, Edward, 1:303
Hartwell, Lee, 2:469
Harvard Medical School, 1:335, 1:337
Harvey, Samuel C., 1:54
Harvey, William, 2:549
“Hashtag mamming,” 2:745
Hazard Communication Standard (NTP), 2:480
Head and neck cancer, 2:529–530
  hypopharyngeal cancer, 2:568–570
  oral cancer in children and, 2:865
  oropharyngeal cancer, 2:870–872
  squamous neck cancer with occult primary, metastatic, 3:1096–1097
Heald, Perter, 2:601
Health advocacy, 2:530–533. See also Cancer communication; Education; Psychosocial care/support
  health communication advocacy model, 2:531–532
  by International Myeloma Foundation, 2:598–599
  medical students and, 2:732
  in U.S., 3:1223–1224
Health care access. See also Insurance
  Access to Medicine Index, 2:842
  cancer drugs, costs and benefits of, 1:227–231
  cost of therapy and, 1:315–316
  in developing countries, 1:348–349
  disability and, 1:357
  poverty and disparities in, 2:953–954
  screening access, 3:1035–1039
Health care personnel. See also Cancer centers; Hospitals; individual names of professional associations
  careers of, 1:240–242
  certified nursing assistants, 2:447
  doctors of osteopath (DO), 1:42
  occupational therapists, 2:854–856
  pharmacists, 1:241, 1:290 (See also Pharmaceutical industry)
  physician therapist, 2:927–929
  social workers, 2:557
Health Cluster (WHO), 1:254
Health Communication and Informatics Research Branch (HCIRB) (NCI), 1:220, 2:802–803
Health Economics in Radiation Oncology (HERO), 1:430
Health equity, 1:360
Health Information National Trends Survey (HINTS) (NCI), 1:220–221, 2:803
Health information privacy rights (HIPAA), 1:291
Health insurance. See Insurance
Health maintenance organization (HMO) plans, 2:587
HealthDesign, 1:251
HealthNet, 1:419
Healthy People, 2:533–534
  goals of, 2:533–534
  Healthy People 2020, 2:533, 3:1310
Heat, for disinfection, 1:359
HeLa cells, 3:1310
Helen Diller Family Comprehensive Cancer Center (University of California, San Francisco), 3:1230–1231
HELP (Canadian Red Cross), 1:214
Héma-Québec, 1:214
Hematologist, The, 1:74
Hematology, ASH Education Program, 1:74
Hematology associations
  American Academy of Pediatrics, Section on Hematology/Oncology, 1:51–53, 1:75
  American Society of Hematology, 1:72–74
  Association of Pediatric Hematology/Oncology Nurses, 1:107–108
  Dominican Society of Hematology and Oncology, 1:365
  International Society for Experimental Hematology, 2:602–604
Hematopoietic stem cell transplants (HCSTs), 1:156–158
Hematuria, 1:149
Hemophilia
  Haemophilia Society (United Kingdom), 2:523–524
  Netherland Hemophilia Patients Society, 2:817–819
  overview, 2:523–524
  Pan-Thames Haemophilia Consortium, 2:523
Hepatitis B, 2:534–536
  biologic therapy, 1:144
  future of cancer and, 2:474
  liver cancer and, 2:540
Hepatitis C, 2:536–539
  future of cancer and, 2:474
  liver cancer and, 2:540
  vaccine workers, 3:1271–1272
Hepatoblastoma, 2:689–692
Hepatocellular (liver) cancer, adult (primary), 2:539–541
Hepatocellular (liver) cancer, childhood (primary), 2:541–543
Hepatocellular carcinoma (HCC), 2:685–687, 2:691–692
Herbert, Gavin, 1:26
Herbert Irving Comprehensive Cancer Center, 2:543–544
Herbicide, 2:544–548, 3:1299
Herbs/herbal plants, as alternative therapy, 1:32–37
Herceptin, 2:487
Hereditary cancer path, 2:488
Heredity. See Genetics
Herman, James, 3:1223
Heterocyclic amines, 2:742
Hidvegi, Mate, 2:566
Highly active antiretroviral therapy (HAART), 1:18, 2:581–582
High-voltage overhead power lines (HVOLs), 1:388
Hill, John, 2:550
Hinkula, Marianne, 2:450–451
Hippocrates, 2:512, 2:548
Hippocratic oath, 2:512
History of cancer, 2:548–552
History of cancer and its treatment, 2:550–552
first cancer hospital, 2:464
first magnetic resonance imaging (MRI), 2:465
insights into environmental influences, 2:550
19th and early-20th century breakthroughs, 2:549–550
before 19th century, 2:548–549
overview, 2:548
HIV Vaccine Trials Network, 2:470
HIV/AIDS. See also AIDS-related cancers
Hemophilia, 1:93
Hoffman, Dietrich, 3:1327
Hoffman, Felix, 1:93
Holden Comprehensive Cancer Center at the University of Iowa, 2:552–553
Holistic medicine. See Alternative therapy: mind, body, and spirit
Holland, James, 2:931
Homeopathy, 1:48–49
Honduras, 2:553–554
Hong Kong Anti-Cancer Society, 2:554–556
Hope Lab, 1:382
Hormones. See also Insulin; individual names of hormone replacement drugs
adrenocortical carcinoma, 1:5–6
adrenocortical carcinoma, childhood, 1:6–7
antiestrogens (SERMs), 3:1143, 3:1146
breast cancer and pregnancy, 1:182–184
chemotherapy and, 1:271
daily life and cancer risks, 1:333
deodorizers and, 1:342–343
early menarche and, 2:756–758
endocrine pancreas, 2:621–623
endometrial cancer and, 1:398–399
estrogen, 1:415–418
experimental cancer drugs, 1:438–439
hypothalamic and visual pathway glioma in children and, 2:571
multiple endocrine neoplasia syndrome, childhood, 2:777–779
non-Hodgkin’s lymphoma during, 2:712–714
obesity and, 2:851, 2:852
pancreatic cancer, 2:886–888
pancreatic cancer, childhood, 2:888–889
pancreatic cancer, islet cell, 2:890–892
pharmaceutical industry overview, 2:917
pituitary tumors, 2:932–934
sunscreen and estrogenizing effects, 3:1119
Hospice care, 2:556–561
brief history of, 2:558
core services, 2:556–558
end-of-life care, 1:16
misconceptions about, 2:559–560
oncology and, 2:559
overview, 2:556
palliative care compared to, 2:558–559
(See also Palliative care)
Singapore Cancer Society and, 3:1058–1059
Hospital Outpatient Prospective Payment System (HOPPS) (CMS), 1:104
Hospitals, 2:561–563. See also individual names of hospitals
American Hospital Association (AHA), 2:587–588
current concept of, 2:562
eye cancer hospitals, 2:940
history of, 2:561
history of cancer hospitals, 2:562
marketing by, 2:729–731
in modern times, 2:561–562
overview, 2:561
Hounsfie, Geoffrey N., 2:550, 2:975, 3:1330
Household exposure, hepatitis C and, 2:538
How I Treat—A Compendium for the Practicing Hematologist, 1:74
HPV vaccination, 2:563–565
background, 2:563
barriers to, 2:563–564
biologic therapy, 1:144
cervical cancer and, 1:256–258
effectiveness of, 2:564
human papillomavirus and risks of daily life, 1:333
Merck and, 2:761
public controversy, 2:564
vaccine workers, 3:1271–1272
H3 Biomedicine Inc., 1:385
Human herpes virus 8 (HHV8), 2:643. See also
Kaposi’s sarcoma
Human papillomavirus. See also HPV vaccination
cancer incidence in developing countries and, 1:348
future of cancer and, 2:474
head and neck cancer, 2:529
infection and cancer, 2:582
MedImmune and HPV technology rights, 2:749
oropharyngeal cancer and, 2:870
penile cancer and, 2:905
Human studies, animal studies versus, 1:262
“Hundreds of Places in China With High Carcinogenic Risk” (Phoenix Weekly), 1:283
Hungary, 2:565–567
Hunter, John, 2:549, 3:1119
Hunter-gatherer diet, 3:1306
Huntsman, Jon M., 2:567
Huntsman Cancer Institute, 2:567–568
Hussein (king of Jordan), 2:641
Hutch Integrated Data Repository and Archive (HIDRA), 2:470
Hybrid automobiles, 1:116
Hydatidiform mole, 3:1192, 3:1193
Hydrocarbons, 2:948
Hydrocyanic acid, 3:1298
Hydrogen peroxide, 1:358
Hypercalcemia, 1:199
Hyperparathyroidism, parathyroid cancer and, 2:899
Hyperthermia, local, 3:1158
Hyperthermic intraperitoneal chemotherapy, 3:1122
Hypopharyngeal cancer, 2:568–570
Hypothalamic and visual pathway glioma, childhood, 2:570–572
Hypothalamus, 2:932
I QUIT! Smokers’ Helpline, 1:212
Ibritumomab tiuxetan, 1:143
ICARE. See International Cancer Alliance for Research and Education
Ice industry, history of, 2:471
Ichikawa, Koichi, 2:550
Identification of Colorectal Cancer Opinion Leaders for a Knowledge Transfer Program in Ontario (Canadian Society of Surgical Oncology), 1:215
If You Are the One (movie), 1:283
Imaging technology. See Radiation therapy;
Technology, imaging; individual types of cancer; individual types of imaging technology
ImClone Systems, Inc., 1:185
IMF. See International Myeloma Foundation
Immigrant populations, 2:573–576. See also
Ethnicity overview, 2:573
patterns of cancer trends, 2:573–575
Immortal Life of Henrietta Lacks, 3:1310
Immune system
care and cancer risk, 1:275–277, 1:275–278
care, generally, 1:279
Kaposi’s sarcoma and, 2:644
side effects of cancer and cancer treatments, 2:919–920
vaccines and, 3:1274
weakened, as cause of cancer, 2:810
Immune-mediated therapies, 2:750
Immunoglobulin M (IgM) molecules, 3:1297
Immunology
AstraZeneca and, 1:111
biologic therapy and, 1:142
Cancer Society Symposium on the Immunotherapy of Cancer (Danish Cancer Society), 1:338
Coley’s toxins and, 1:47
experimental cancer drugs, 1:440
psychoneuroimmunology, 2:665
Immunotoxins, 2:750
ImPACT (International Atomic Energy Agency), 1:130
INCAN (Guatemala), 2:517–518
Incidence rates, of cancer. See also Surveillance, Epidemiology, and End Results (SEER)
Cancer Statistics Review, 1975–2011; individual names of countries in Denmark, 1:341
in developing countries, 1:348
disparities within nations, 1:360–363
future of, 2:474
statistics on, 3:1101–1103
India, 2:576–578
causes of cancer in, 2:576
challenges to, 2:577
disparities within nations and elimination of cancer, 1:361
impact of cancer in, 2:576
Novartis and, 2:842
overview, 2:576
policies and interventions, 2:576–577
Indoles, 1:90–91
Indonesia, 2:578–579
Indoor air pollution, 2:946–947
Infantile choriocarcinoma of the liver, 2:692
Infection, 2:579–583. See also Viruses
anal cancer and, 2:582
cancer incidence in developing countries and, 1:348
cancer risk and daily life, 1:333
as cause of cancer, statistics, 2:810–811
cervical cancer and, 2:582
global health issues, 2:506–507
HIV and, 2:581–582
HPV and, 2:582
Kaposi’s sarcoma and non-Hodgkin’s lymphoma, 2:580–581
latitude and cancer, 2:664–665
overview, 2:579–580
STI-related cancers, 2:583
Insecticides, 2:583–586
Institute for Cancer Research, 2:551
Institute of Cancer Biology (Danish Cancer Society), 1:337
Institute of Cancer Epidemiology (Danish Cancer Society), 1:337–338
Institute of Medicine, 1:181, 2:559, 2:693, 2:803–805
Instituto Nacional de Enfermedades Neoplasicas (Peru), 2:910
Insulin. See also Pharmaceutical industry
experimental cancer drugs, 1:440–441
insulin potentiation therapy (IPT), 1:49
obesity and, 2:851
Insulinomas, 2:890
Insurance, 2:586–588. See also individual names of countries
Association of Community Cancer Centers on, 1:102–103
cancer drug costs in U.S. and, 1:227
daily life issues and, 1:334–335
disability and, 1:357
fee-for-service and preferred provider organization (PPO) plans, 2:587
government-sponsored health insurance plans, 2:587–588
history of, in U.S., 2:586–587
hospice care and, 2:556
managed care and health maintenance organization (HMO) plans, 2:587
overview, 2:586
supplementary cancer insurance, 2:588
Integrated gasification combined cycle (IGCC), 1:300
Integrated pest management (IPM), 2:585
Integrated Risk Information System (IRIS), 1:442
Intensity-modulated radiotherapy (IMRT), 2:795–796
Interferon-alfa, 2:679, 2:761
Interleukins, 1:440
Intermountain Healthcare, 2:567
Internal-beam radiation therapy, 2:970, 2:977
International Agency for Research on Cancer, 2:588–590
acrylic rubber and fibers, 1:3
aerospace industry, 1:12
air pollution, 2:947
alcohol, 1:20–21
asbestos, 1:89
battery acid, 1:123–124
chemical industry, 1:262–263
coal, 1:299
diet and nutrition, 1:354
disinfectants and antiseptics, 1:359
environmental justice and cancer, 1:403
estrogen, steroidal, 1:416
exercise, 1:436
food additives, 2:458
formaldehyde, 1:397
gasoline, 2:480–481
GLOBOCAN overview and, 2:794
hair dye, 2:526
herbicide, 2:547
inception of, 2:793
Monograph Program, 2:480
nickel compounds, 2:829
para-dichlorobenzene, 1:343
pesticides, 2:913
rectal cancer, 2:985
solvents, 3:1088
stomach cancer, 3:1103
viruses as cause of cancer, 2:810–811
wood preserver, 3:1316
International Agency of Cancer Registration, 1:426
International Association for the Study of Lung Cancer, 2:590–592, 3:1038
International Association of Cancer Registries, 2:592–593. See also Cancer registries
history of, 2:592–593
overview, 2:592
role of cancer registries, 2:593
International Association of Cancer Registries (IACR), 2:504
International Association of Cancer Victims and Friends (IACVF), 1:38
International Association to Combat Cancer (Netherlands), 2:815
International Atomic Energy Agency (IAEA), 1:130, 1:197, 2:959
International Cancer Alliance for Research and Education, 2:593–595
International Cancer Nursing News, 2:607
International Classification of Childhood Cancer, 3:1259
International Code of Conduct on Pesticide Management, 2:913
International Commission on Radiation Units and Measurements, 2:949
International Committee of the Red Cross, 2:595–597
International Gastric Cancer Association, 2:633
International Journal of Cancer, 2:527, 3:1217
International Journal of Radiation Oncology, Biology, Physics (IJROBP), 2:595–597
International Myeloma Foundation, 2:597–599
International Neuroblastoma Risk Group (INRG), 2:820
International Neuroblastoma Staging System (INSS), 2:820
International Psycho-Oncology Society, 2:599–601
International Society for Cutaneous Lymphomas, 2:601–602
International Society for Experimental Hematology, 2:602–604
International Society for Preventive Oncology, 2:604–605
International Society of Nurses in Cancer Care, 2:605–607
International Society of Oncology Pharmacy Practitioners (ISOPP), 1:210
International Society of Paediatric Oncology, 2:607–609
International Society on Thrombosis and Haemostasis, 2:609–611
International Statistical Classification of Diseases, 3:1102
International Union Against Cancer. See Union for International Cancer Control
Intervention, religious use of, 2:994–997
Intraocular melanoma, 2:611–613, 2:752–754
Intron A, 2:761
Inverted papilloma (IP), 2:897–899
Investigational drug (IND) studies, 1:291
Iodine-based disinfectants, 1:358
Ionizing radiation, 2:969, 2:973–975, 3:1331
Ipilimumab, 1:143
IQ
ependymoma treatment and, 1:409, 1:410
radiation therapy and, 2:980
Iran, 2:613–614
Iraq, 2:614–615
Ireland, Republic of, 2:615–618, 2:620–621
Ireland (Ohio) Cancer Center, 2:618–620
Irell & Manella Graduate School of Biomedical Sciences, 1:289
Iressa, 1:111
Irish Cancer Society, 2:620–621
Iron, 1:36, 1:47
Irrational drug use, 1:370
Islam, on preventability versus preordained risk, 2:993
Islet Cell Carcinoma (Endocrine Pancreas), 2:621–623
Islet cell carcinomas, 2:889
Islet cell tumors, 2:890–892
Isozymes, 1:95
Israel, 2:623–625
Issels, John, 1:31
ISTH. See International Society on Thrombosis and Haemostasis
Istituto di Candiolo, 2:626
Italian Information System on Occupational Exposure to Carcinogens, 3:1315
Italy, 2:625–626
Ixazomib, 2:890
James, Arthur G., 2:856
James Cancer Hospital, 2:856–857
Japan, 2:627–629
beliefs and attitudes, 2:629
Daiichi Sankyo, 1:331–332
diet in, 2:627–628
Eisai, 1:385–386
on hair dye, 2:525
health behaviors, 2:628–629
Japanese Cancer Association, 2:631–632
Japanese Diabetes Society, 2:631
Japanese Gastric Cancer Association, 2:632–634
Japanese Lung Cancer Society, 2:629–631
Japanese Society for Therapeutic Radiology and Oncology, 2:634–635
Ono Pharmaceutical, 1:185, 2:862–864
overview, 2:627
<table>
<thead>
<tr>
<th>Entry</th>
<th>Volume/Issue/Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>social trends</td>
<td>2:628</td>
</tr>
<tr>
<td>Taisho Pharmaceutical</td>
<td>3:1135–1136</td>
</tr>
<tr>
<td>Takeda Pharmaceutical</td>
<td>3:1140–1142</td>
</tr>
<tr>
<td>Japan Lung Cancer Society</td>
<td>2:629–631</td>
</tr>
<tr>
<td>Japanese Association</td>
<td>2:631–632</td>
</tr>
<tr>
<td>Japanese Gastric Cancer Association</td>
<td>2:632–634</td>
</tr>
<tr>
<td>Japanese Journal of Clinical Oncology</td>
<td>3:1165</td>
</tr>
<tr>
<td>Japanese Society for Therapeutic Radiology and Oncology</td>
<td>2:634–635</td>
</tr>
<tr>
<td>Jaundice</td>
<td>1:140</td>
</tr>
<tr>
<td>Jenner, Edward</td>
<td>3:1272–1273</td>
</tr>
<tr>
<td>Jerne, Niels Kaj</td>
<td>1:143</td>
</tr>
<tr>
<td>Jet and rocket fuels</td>
<td>2:635–638</td>
</tr>
<tr>
<td>Jewish Consumptive Relief Association</td>
<td>1:288</td>
</tr>
<tr>
<td>Jewish women, cancer risk</td>
<td>2:988–990</td>
</tr>
<tr>
<td>Jimmy Fund</td>
<td>1:335, 1:336, 2:638–639</td>
</tr>
<tr>
<td>Jobs, Steve</td>
<td>1:247</td>
</tr>
<tr>
<td>Johns, Harold</td>
<td>1:212</td>
</tr>
<tr>
<td>Johnson, Edward Mead</td>
<td>2:639</td>
</tr>
<tr>
<td>Johnson, James Wood</td>
<td>2:639</td>
</tr>
<tr>
<td>Johnson, Lyndon B.</td>
<td>2:588</td>
</tr>
<tr>
<td>Johnson, Robert Wood</td>
<td>2:639</td>
</tr>
<tr>
<td>Johnson &amp; Johnson (United States)</td>
<td>2:639–640</td>
</tr>
<tr>
<td>Jolie, Angelina</td>
<td>1:247</td>
</tr>
<tr>
<td>Jonsson Comprehensive Cancer Center (University of California, Los Angeles)</td>
<td>3:1228–1230</td>
</tr>
<tr>
<td>Jordan</td>
<td>2:641–642</td>
</tr>
<tr>
<td>Jordan Breast Cancer Program</td>
<td>2:641</td>
</tr>
<tr>
<td>overview</td>
<td>2:641–642</td>
</tr>
<tr>
<td>José Alencar Gomes da Silva National Cancer Institute (INCA)</td>
<td>1:174</td>
</tr>
<tr>
<td>Journal Citation Reports</td>
<td>2:632</td>
</tr>
<tr>
<td>Journal of Cancer Education (JCE)</td>
<td>1:53–54</td>
</tr>
<tr>
<td>Journal of Clinical Oncology (JCO)</td>
<td>1:71, 2:474</td>
</tr>
<tr>
<td>Journal of Gastric Cancer</td>
<td>2:633</td>
</tr>
<tr>
<td>Journal of JASTRO</td>
<td>2:634</td>
</tr>
<tr>
<td>Journal of National Cancer Institute</td>
<td>1:408</td>
</tr>
<tr>
<td>Journal of Oncology Practice (JOP)</td>
<td>1:71</td>
</tr>
<tr>
<td>Journal of Practical Radiation Oncology</td>
<td>1:70</td>
</tr>
<tr>
<td>Journal of Psychosocial Oncology</td>
<td>1:106</td>
</tr>
<tr>
<td>Journal of the Association of Pediatric Hematology/Oncology Nursing (JOPON)</td>
<td>1:107</td>
</tr>
<tr>
<td>Journal of Thoracic Oncology</td>
<td>2:591</td>
</tr>
<tr>
<td>Journal of Thrombosis and Haemostasis</td>
<td>2:610</td>
</tr>
<tr>
<td>Journal Watch</td>
<td>2:731</td>
</tr>
<tr>
<td>Judaism</td>
<td></td>
</tr>
<tr>
<td>Jewish women and cancer risk</td>
<td>2:988–990</td>
</tr>
<tr>
<td>on preventability versus preordained risk</td>
<td>2:993</td>
</tr>
<tr>
<td>Juvenile Polyposis Coli (JPC)</td>
<td>1:309</td>
</tr>
<tr>
<td>Juvenile myelomonocytic leukemia</td>
<td>2:786</td>
</tr>
<tr>
<td>K, vitamin</td>
<td>3:1294</td>
</tr>
<tr>
<td>Kahn, Louis</td>
<td>3:1016, 3:1017</td>
</tr>
<tr>
<td>Kantarjian, Hagop</td>
<td>2:672</td>
</tr>
<tr>
<td>Kapha</td>
<td>1:45</td>
</tr>
<tr>
<td>Kaposi’s sarcoma</td>
<td>2:643–645</td>
</tr>
<tr>
<td>AIDS and</td>
<td>1:17–18</td>
</tr>
<tr>
<td>in developing countries</td>
<td>1:348</td>
</tr>
<tr>
<td>future of cancer and</td>
<td>2:474</td>
</tr>
<tr>
<td>infection and</td>
<td>2:580–581</td>
</tr>
<tr>
<td>Karmanos, Barbara Ann</td>
<td>1:122</td>
</tr>
<tr>
<td>Karnofsky performance status (KPS)</td>
<td>1:15</td>
</tr>
<tr>
<td>Katin, Michael J.</td>
<td>1:104</td>
</tr>
<tr>
<td>Kava</td>
<td>1:261</td>
</tr>
<tr>
<td>Kayula Childhood Cancer Foundation</td>
<td>3:1342</td>
</tr>
<tr>
<td>Kazakhstan</td>
<td>2:645–646</td>
</tr>
<tr>
<td>Kefauver-Harris Act</td>
<td>1:8</td>
</tr>
<tr>
<td>Keller, Bill</td>
<td>2:746</td>
</tr>
<tr>
<td>Kelley, William</td>
<td>1:30–31</td>
</tr>
<tr>
<td>Kennedy, Edward</td>
<td>2:834</td>
</tr>
<tr>
<td>Kennedy, John</td>
<td>3:1159</td>
</tr>
<tr>
<td>Kent, James Tyler</td>
<td>1:48</td>
</tr>
<tr>
<td>Kenya</td>
<td>2:646–648</td>
</tr>
<tr>
<td>Keratin, nail polish and</td>
<td>2:943</td>
</tr>
<tr>
<td>Keratin filaments</td>
<td>2:762</td>
</tr>
<tr>
<td>Kerr-Mills Act (1960)</td>
<td>2:588</td>
</tr>
<tr>
<td>Kettering, Charles F.</td>
<td>2:754</td>
</tr>
<tr>
<td>Keytruda</td>
<td>2:761</td>
</tr>
<tr>
<td>Khorog General Hospital</td>
<td>3:1139–1140</td>
</tr>
<tr>
<td>Kidney (renal cell) cancer</td>
<td>2:648–650, 2:652</td>
</tr>
<tr>
<td>Kidney cancer, childhood</td>
<td>2:650–651</td>
</tr>
<tr>
<td>Kidney Cancer Association</td>
<td>2:652–653</td>
</tr>
<tr>
<td>Kimmel, Sidney</td>
<td>3:1052</td>
</tr>
<tr>
<td>Kimmel Cancer Center</td>
<td>2:653–655</td>
</tr>
<tr>
<td>King Hussein Cancer Center (KHCC)</td>
<td>2:641–642</td>
</tr>
<tr>
<td>Kizner, Kenneth</td>
<td>3:1223</td>
</tr>
<tr>
<td>Knight Cancer Institute (Oregon Health Science University)</td>
<td>2:858–860</td>
</tr>
<tr>
<td>Koch Institute (David H. Koch Institute for Integrative Cancer Research)</td>
<td>2:769–771</td>
</tr>
<tr>
<td>Kohler, Georges</td>
<td>1:143, 2:551</td>
</tr>
<tr>
<td>Koirala, Bishweshwar Prasad</td>
<td>2:813</td>
</tr>
<tr>
<td>Kongnakorn, Thitima</td>
<td>2:676</td>
</tr>
<tr>
<td>Kotler, Philip</td>
<td>2:532</td>
</tr>
<tr>
<td>Krag, David</td>
<td>3:1123</td>
</tr>
<tr>
<td>Kramer, Susan Netchin</td>
<td>1:56</td>
</tr>
<tr>
<td>Krivit, Bill</td>
<td>1:74</td>
</tr>
<tr>
<td>Kuhlthau, Karen</td>
<td>1:409</td>
</tr>
<tr>
<td>Kun, Viktória</td>
<td>2:566</td>
</tr>
<tr>
<td>Kushi, Michio</td>
<td>1:28</td>
</tr>
<tr>
<td>Kushner, Rose</td>
<td>2:796</td>
</tr>
<tr>
<td>Kuten, Abraham</td>
<td>2:624</td>
</tr>
<tr>
<td>Kyrgyzstan</td>
<td>2:655–656</td>
</tr>
</tbody>
</table>
Labeling, of flavoring agents, 2:454–455
Lacks, Henrietta, 3:1310
Lad, Vasant, 1:44
Laetrile, 1:38–39
Lahey, Frank, 3:1123
Lalla Salma Foundation, 2:774
Lance Armstrong Foundation, 2:859
Lancet, 1:428
Lancet Oncology, 3:1133
Langer, Amy, 2:798
Langone Medical Center (NYU), 2:908–910
Laos, 2:657–658
Laparoscopic surgery, 3:1121
Larisch, Sarit, 2:624
Laron syndrome, 1:380
Laryngeal cancer, 2:658–660
Laryngeal cancer, childhood, 2:660–662
Laser surgery, 3:1121
Lasker, Mary, 2:834
Latex rubber, 3:1286
Latitude, 2:662–665
infection and cancer, 2:664–665
life history evolution and, 2:664
special case of cancer and, 2:662–664
Laura and Isaac Perlmutter Cancer Center, 2:908–910
Lawrence, Ernest Orlando, 3:1223
LDK378, 2:741
Lead, 2:665–668, 2:883, 2:884
League Against Cancer, 2:554
Leather Souq (Morocco), 2:774
Lee, Kang Hyun, 3:1094
Leeds Cancer Centre, 2:641
Lenalidomide, 2:783
Lenatinib, 1:385
Lennox, Tom, 2:857
Leukemia. See also individual types of leukemia
acute lymphoblastic leukemia, childcare, and cancer risk, 1:275
acute myeloid leukemia (AML), 1:303–304, 2:672–675, 2:782
anticancer drugs and, 1:85
atypical chronic myeloid leukemia, 2:785–786, 2:787
blood cell comparison, 1:73
childhood cancers, generally, 1:278–280
in children, 1:278
exercise and, 1:437–438
hair dye and, 2:525–526
Leukemia, acute myeloid, adult, 2:668–670
Leukemia, acute lymphoblastic, childhood, 2:670–672
Leukemia, acute myeloid, adult, 2:672–673
Leukemia, acute myeloid, childhood, 2:673–675
Leukemia, chronic lymphocytic, 2:675–677
Leukemia, chronic myelogenous, 2:677–680, 2:790
Leukemia, hairy cell, 2:680–682
Leukemia & Lymphoma Society, 2:682–683
Libya, 2:683–685
LifebankUSA, 1:249
Lifetime risk, calculating, 3:1102–1103
Light, Donald, 1:227
Light boxes, 2:927
Light therapy, 2:923–927
Lighting, cancer risk and, 1:389–390
Lignite coal, 1:297
Lignite Energy Council, 1:297
Living, 3:1242–1245
Lip, cancer of. See Oral cavity cancer, lip and
Liposomal therapy, 1:274, 2:580
Listening Hand, 1:43
Lister, Joseph, 2:549
Liver cancer, adult (primary), 2:685–689
alcohol and, 1:20–23
cholangiocarcinoma, 2:685, 2:687–688
hepatocellular carcinoma (HCC), 2:685–687
hepatitis B, 2:534–536
hepatitis C, 2:536–539, 3:1271–1272
hepatocellular (liver) cancer, childhood (primary); Liver cancer, adult (primary); Liver cancer, childhood (primary)
bile duct cancer and (See Bile duct cancer, extrahepatic)
cirrhosis of, 2:535, 2:537, 2:538, 2:539, 2:540, 2:541
hepatitis B, 2:534–536
hepatitis C, 2:536–539, 3:1271–1272
hepatocellular (liver) cancer, childhood (primary), 2:541–543
hepatocellular carcinoma (HCC) (liver cancer), 2:539–541
Trichopoulos and, 3:1191
Livestrong Foundation, 1:248
Lobbyists, 2:531
Lobular carcinoma in situ (LCIS), 2:983
Lombardi Comprehensive Cancer Center, 2:692–694
Longevity, aging population and, 1:16
Lopes, Lygia Viera, 1:79–80
Low, Oscar, 1:81
Low dose naltrexone (LDN), 1:49–50
Lowe, Scott, 1:303
Low-intensity electric fields, as cancer treatment, 1:394
Lugo, Fernando, 2:896
Lundbeck, Hans, 2:521
Lung cancer
COX-2 inhibitors, 1:323
diesel exhaust and, 1:350–353
environmental tobacco smoke and, 1:405–408
electricity and, 1:437
International Association for the Study of Lung Cancer, 2:590–592
Japan Lung Cancer Society, 2:629–631
screening for, 3:1036, 3:1038
Lungs
American Lung Association on respiratory diseases, 1:65–67
asbestos and, 1:87–90
bronchial adenomas/carcinoids, childhood, 1:189–190
carcinoid bronchial tumors, 1:236
electrode inhalation, 2:480
mediastinum, 1:166, 2:712, 3:1168
mesothelioma, 2:763–766
pleuropulmonary blastoma, 2:939–940
Luo Jing, 1:284
Luria, Salvador, 2:770, 3:1223
Lusitani, Zacutus, 2:548–549
Luxembourg, assisted suicide in, 1:97
Lymphatic system/lymph nodes
Aselli on, 2:466
bone marrow transplants, 1:156
central nervous system lymphoma, primary, 1:254–256
eyphopharyngeal cancer, 2:568–570
sentinel lymph node biopsy, 3:1123
sentinel lymph nodes (SLNs), 1:177
staging of cancers, 1:64
tumor stage and chemotherapy, 1:270
Lymphedema, 1:178, 3:1043
Lymphoma, AIDS-related, 2:697–700
Lymphoma, Burkitt’s, 2:700–703
Lymphoma, Hodgkin’s, adult, 2:703–705
Bonadonna on, 1:152
electrode and, 1:437–438
overview, 2:703–705
Lymphoma, Hodgkin’s, childhood, 1:278, 2:705–707
Lymphoma, Hodgkin’s, during pregnancy, 2:707–708
Lymphoma, non-Hodgkin’s, adult, 2:709–710
AIDS and, 1:17–18
dyes and pigments, 1:375–376
electrode and, 1:437–438
infection and, 2:580–581
mycosis fungoides, 2:781–782
Lymphoma, non-Hodgkin’s, childhood, 2:710–712
Lymphoma, non-Hodgkin’s, during pregnancy, 2:712–714
Lymphoma, primary central nervous system, 2:714–716
Lymphoma Research Foundation of America, 2:716–718
Lynch syndrome, 1:306, 1:309
Macrobiotic diet, 1:28–29
Macrocyclic musk, 2:907
Macrophage subpopulations, tumor progression and, 1:19–20
Madagascar, 2:719–720
Magic Cancer Bullet (Vasella), 1:229
Magnetic fields, 1:388
Magnetic hyperthermia, 2:926
Magnetic resonance imaging (MRI), 2:465, 3:1155
Major life activities, defined, 1:356
Malaria, 1:83, 1:338, 1:340, 2:504
Malawi, 2:721–722
Malaysia, 2:722–724
Maley, Carlo, 3:1231
Mali, 2:724–726
Malignant fibrous histiocytoma of bone/osteosarcoma, 2:726–728
Malignant fibrous histiocytoma (MFH-B), 1:153–156
Malignant tumors, defined, 2:489
Malpeli, Giorgio, 2:622
Mammography
digital, 1:212
early detection with, 1:176
Gregoire and, 2:515–516
media awareness about, 2:745–746
Managed care, 2:587
Man-made vitreous fibers, 2:500
Manual healing, as alternative therapy, 1:37–43
Māori tribes, 2:824–826
Marathon of Hope, 1:212
Margaret Hay Edwards Achievement Medal, 1:54
Mafran Mattson’s Health Communication Advocacy Model, 2:531–532
Marketing, drug, 2:728–729
Marketing, hospitals and clinics, 2:729–731
Martin, Hayes, 3:1123
Mary and Al Schneider Healing Garden, 2:619
Mason, Margie, 2:838
Masonic Cancer Center (University of Minnesota), 3:1240–1242
Massachusetts Institute of Technology, 2:769–771, 2:847
Massachusetts Medical Society, 2:731–733
Massage, 1:41
Massey Cancer Center, 2:733–735
Mastectomy, 1:177, 1:178, 1:180, 2:515–516
Maternity care/maternal health breast cancer and pregnancy, 1:182–184
breast-feeding and breast cancer risk, 1:175
ey early menarche and, 2:756
gestational trophoblastic tumor, 2:495–497
rocket fuel exposure and, 2:636
Maunoir, Théodore, 2:595
Maxillary sinuses, cancer of, 2:898
Maxwell, James Laidlaw, 3:1137
Maya population (Guatemala), 2:517–518
Mayo Clinic Cancer Center, 2:735–736, 3:1312
Mayo Clinic Cancer Center, Jacksonville, 2:736–738
Mayo Clinic Cancer Center, Scottsdale, 2:738–740
McCulloch, Ernest, 1:212
MD Anderson Cancer Center (University of Texas), 1:8, 1:9, 3:1249–1251
Meaning-Centered Group Psychotherapy (MCGP), 2:995
Meat, cooking, 2:740–743
Meat processing, 2:743–744
MED1-4736, 1:111
Media, 2:744–746
community and social media, 2:745–746
(See also Social media)
exposure and attention, 2:744–745
information seeking about cancer, 2:745
obesity issues and, 2:852–853
overview, 2:744
studies and impact, 2:746
video games for exercise, 2:854
video games for pain management, 2:879–883
Mediastinum, 1:166, 2:712, 3:1168
Medical Mission of Hope, 1:205
Medicare and Medicaid, 2:746–748
Association of Community Cancer Centers on, 1:102–103
Association of Freestanding Radiation Oncology Centers and, 1:104
cancer coverage by, 2:748
cancer drugs, costs and benefits, 1:230
fraud and, 2:747–748
government-sponsored health insurance plans, generally, 2:587–588 (See also Insurance)
hospice care and, 2:556
Hospital Outpatient Prospective Payment System (HOPPS), 1:104
inception of, 2:587
Medicaid, explained, 2:747
Medicare, explained, 2:747
Medicare Hospice Benefit, 2:558
overview, 2:746–747
Medication. See Antibiotics; Anticancer drugs;
Cancer drugs, costs and benefits of; Cost of therapy; Drugs; Pharmaceutical industry
Medicinal plants, used in Angola, 1:79–80
MedImmune (United States), 1:111, 2:749–750
Meditation, religion and, 2:990–992
Mediterranean diet, 1:29, 3:1306
Medullary thyroid cancer, 2:778
Megatherapy, 1:435
Meir, Golda, 2:624
Melanoma, 2:750–752
broad-spectrum ultraviolet (UV) radiation and, 1:186–189
family size and, 2:447
follow-up for, 2:752
intraocular, 2:611–613
malignant melanoma in children, 3:1061–1062
overview, 2:750–751
screen research by Green and, 2:513–515
treatment, 2:751–752
types of, 2:751
Melanoma, intraocular (eye), 2:752–754
Melatonin, 1:50
Memorial Sloan Kettering Cancer Center, 2:754–755
cancer drugs, costs and benefits, 1:230
overview, 2:754–755
Wynder and, 3:1327
Memories of Solferino (Dunant), 2:595
Menarche, early, 2:756–758
Merck (Germany), 2:758–760
  Merck Serono, 2:758–759
  Pfizer and, 2:915–916
Merck, Friedrich Jacob, 2:758
Merck & Co. (United States), 2:760–762
Merck Manual of Diagnosis and Therapy (Merck), 2:760
Merck Manuals (Merck), 2:760
Merck Sharp and Dohme, 2:760
Mesenchymal cells, 3:1021
Mesothelioma, adult malignant, 2:763–765
Mesothelioma, asbestos and, 1:89
Mesothelioma, childhood, 2:765–766
Messaging process, for health advocacy, 2:531–532
Metabolic equivalent (MET)-hours, of physical activity, 1:139
Metabolic treatment for cancers, 1:31
Metabolism, of beta-carotene, 1:135–136
Metabolism therapy, enzyme supplements for, 1:30
Metallothionein, 1:84
Metastasis
  defined, 2:489
  staging of cancers, 1:64
Metastectomy, 3:1121
Methamphetamine, 1:371
Methanol, 1:398
Methicillin-resistant Staphylococcus aureus (MRSA), 1:83
Methods in Clinical Cancer Research (European CanCer Organisation), 1:424
Methylation, pancreas and, 2:622–623
Methylene chloride, 3:1089
Mexico, 1:46, 2:767–769
MG1 Pharma, 1:385
Michael and Mauritia Patcha Foundation, 1:205
Michelangelo Foundation, 1:152–153
Microbicidal antimicrobials, 1:81–82
Microbiostatic antimicrobials, 1:81–82
Micronutrients, study of, 1:354
MicroRNAs, 1:303
Micspheres, glass, 2:501
Microwave popcorn, flavoring agents in, 2:455–456
Middle East
  Egypt, 1:383–385
  Iran, 2:613–616
  Iraq, 2:614–615
  Israel, 2:623–625
  Jordan, 2:641–642
  Saudi Arabia, 3:1028–1030
  Syria, 3:1132–1133
United Arab Emirates, 3:1218–1220
Yemen, 3:1335–1336
Milken, Michael, 1:99
Millennium Pharmaceuticals, 3:1141
Miller, Anthony, 1:212
Milstein, Cesar, 1:143, 2:551
Mimpara, 1:77
Mind-body connection, alternative therapy and, 1:43–45
Mindfulness, 2:990–992
Mine Safety and Health Administration, 1:301
Minerals. See also Diet and nutrition
  calcium, 1:199–200
  selenium, 1:36, 3:1041–1044
Mining
  asbestos and, 2:764–766
  of coal, 1:298–299
  diesel exhaust and, 1:351
  of uranium, 2:845
Ministry of Health, Labor, and Welfare (Japan), 2:525
Mirza, Fahmida, 2:885–886
Mismatch-repair genes, defined, 2:489
Missions, in Cameroon, 1:205–206
Mistletoe, 1:50–51
MIT Center for Cancer Research, 2:769–771
Mobile phones, 1:250–253
Modifiers (dye couplers), 2:524
Mohammed, Sulma, 3:1112–1113
Mohs micrographic surgery, 3:1086
Moldova, 2:771–773
Molds, 3:1186–1188
Monaco, Kathleen, 1:233
Monel, 2:828
Monoclonal antibody drugs, discovery of, 2:551
Monoclonal antibodies (“mabs”), 1:143–144
Monograph Program (IARC), 2:480
Monro, Alexander, 3:1119
Montana, assisted suicide in, 1:97
Montefiore Medical Center, 1:20
Montreal Protocol, 1:286
Morgagni, Giovanni, 2:549
Morocco, 2:773–775
Morphine, hospice and, 2:560
Morphotek, 1:385
Mortality rate. See also Surveillance, Epidemiology, and End Results (SEER)
  from childhood cancers, 1:278
  disparities within nations and elimination of cancer, 1:361–362
  statistics on, 3:1101–1103
Morton, Donald, 3:1123
Morton, William T. G., 2:549
Mouth, alcohol carcinogenic effect and, 1:21
Mouth, cancers of. See Oral cancer, childhood; Oral cavity cancer, lip and; Oropharyngeal cancer
Moxibustion, 1:41
Moynier, Gustave, 2:595
Mozambique, 2:775–777
Mucinous cystadenocarcinomas, 2:888
Mucositis, 2:919–920
Mukherjee, Siddhartha, 2:550
Muller, Johannes, 2:494
Multidisciplinary Cancer Management Course (MCMC), 1:281
Multi-leaf collimator (MLC), 2:958, 3:1329–1330
Multiple endocrine neoplasia syndrome, childhood, 2:777–779
Multiple endocrineneoplasia type 1, 2:889
Multiple myeloma. See International Myeloma Foundation; Multiple myeloma/plasma cell neoplasm; Myeloma, multiple; Plasma cell neoplasm/multiple myeloma
Multiple myeloma/plasma cell neoplasm, 2:779–781. See also Plasma cell neoplasm/multiple myeloma
Music therapy programs, 1:261
Musk xylene, 2:907
Mutamycin, 1:185
Mutations, as cause of cancer, 2:489
Mutuelles de Santé, 2:1011
My Voice (Brook), 3:1339
Myanmar. See Burma (Myanmar)
Myasthenia gravis (MG), 3:1167–1168
Mycosis fungoides, 2:781–782
Mycotoxins, 3:1186–1187
Myelodysplastic syndromes, 2:782–784
Myelodysplastic/myeloproliferative diseases, 2:784–788
Myelodysplastic/myeloproliferative neoplasms - unclassifiable (MDS/MPN-U), 2:786, 2:787
Myeloma, multiple, 2:597–599, 2:788–789
Myeloproliferative disorders, chronic, 2:789–791
Myelosuppression, 2:679, 2:919
MYH-associated polyposis (MAP), 1:306–307
Myofascial release, 1:41–42
MyPlate, 3:1306
Mysticism, meditation and, 2:990–992

NAACCR. See North American Association of Central Cancer Registries
NABCO. See National Alliance of Breast Cancer Organizations
NaCenter for International Blood and Marrow Transplant Program (CIBMTR), 2:808
Nail polish, 2:942–945
Naito, Toyoji, 1:385
Naloxone, 2:781
Nampt, 2:736
Nanoparticles, pigments, 1:376
Naphthalene, 1:343
Narratives, pain management and, 2:880
Nasal cavity cancer. See Paranasal sinus and nasal cavity cancer; Wood dust
Nasopharyngeal cancer, 2:793–795
Nasopharyngeal cancer, childhood, 2:795–796
Nathanson, Martha, 1:233
National Accreditation program for Breast Centers, 1:310
National Aeronautics and Space Administration (NASA), 1:12. See also Aerospace industry
National Alliance of Breast Cancer Organizations, 2:796–798
National Anti-Cancer Corporation, 3:1335
National Association for Proton Therapy, 2:960
National Ayurvedic Medical Association, 1:45
National Breast and Cervical Cancer Early Detection Program (NBCCEDP), 3:1037
National Breast Cancer Coalition (NBCC), 3:1223
National Cancer Act (1937), 2:799
National Cancer Advisory Board, 1:102
National Cancer Center (Georgia), 2:492
National Cancer Center, BP Koirala Memorial Cancer Hospital (Nepal), 2:812–813
National Cancer Centre Singapore (NCCS), 3:1057
National Cancer Control Committee (NCCC) (Cameroon), 1:205
National Cancer Control Program Plan (Morocco), 2:773
National Cancer Control Program (India), 2:576–577
National Cancer Control Program (Turkey), 3:1197
National Cancer Control Program (Vietnam), 3:1285
National Cancer Control Programme (Republic of Ireland), 2:617
National Cancer Control Programme (Sri Lanka), 3:1098
acute myeloid leukemia, 2:675
anal cancer, 1:78
automobiles, 1:115
bladder cancer in childhood, 1:148
bone cancer, 1:154
breast cancer, sociocultural issues, 1:180–182
cancer care centers and, 1:260 (See also
individual names of cancer care centers)
cancer communication by, 1:220–225
Cancer Information Service, 2:471
Cancer Therapy Evaluation Program (CTEP),
1:231–232
chemoprevention, 1:265, 1:266
chlorine, 1:285–286
cisplatan, 2:1006
City of Hope and, 1:288
clinical trials, 1:290–291, 1:292, 1:293
collaboration of, 2:801–802
education by, 1:381, 1:383, 2:802
funding by, 2:799–801
goals of, 2:799
International Association for the Study of Lung
Cancer, 2:590
National Cancer Policy Board and, 2:803–804
National Clinical Trials Network and NCI
Community Oncology Research Program,
3:1230
organization of, 2:802–803
overview, 2:798–799
prostate cancer, 1:99
women’s cancers, defined, 3:1310
National Cancer Institute (Argentina), 1:86
National Cancer Institute (Libya), 2:684
National Cancer Institute of Canada (NCIC), 1:210
National Cancer Policy Board, 2:803–805
National Cancer Policy Forum (NCPF), 2:803–805
National Cancer Prevention and Control
Strategy (Zimbabwe), 3:1344
National Cancer Prevention Policy (Australia),
1:112, 1:225
National Cancer Registrars Association, 2:805–806
National Care Institute (Oran, Algeria), 1:25
National Center for Toxicological Research, 1:376
National Center of Cancerology (Mexico),
2:768–769
National Childhood Cancer Foundation, 2:806–807
National Comprehensive Cancer Network, 1:288,
2:468, 2:735
National Council for Scientific Research (Zambia),
3:1342
National Council of Sciences and Technology
(Mexico), 2:769
National Council of Scientific and Technical
Research (Argentina), 1:87
National Department of Public Health (Brazil),
1:173
National Guideline Clearinghouse (Agency for
Healthcare Research and Quality), 1:383
National Health and Nutrition Examination
Survey (NHANES), 1:220–221
National Health Insurance Fund (Serbia),
3:1046–1047
National Health Insurance Scheme (NHIS)
(Ghana), 2:498
National Health Interview Survey (NHIS), 1:220
National Health Service (United Kingdom), 2:523,
2:811
National Healthcare Career Network, 1:108
National Initiative on Cancer Care Quality
(NICCQ), 1:71
National Institute for Health and Welfare
(Finland), 2:451
National Institute for Occupational Safety and
Health (NIOSH), 1:115, 1:124, 1:300, 1:301,
National Institute of Cancer Research and
Hospital (Bangladesh), 1:120
National Institute of Cancerology (Colombia),
1:305
National Institute of Cancerology (Mexico), 2:767
National Institute of Oncology (Hungary), 2:565
National Institute of Statistics and Geography
(Mexico), 2:767
National Institutes of Health
alternative therapies, 1:39
breast cancer, sociocultural issues, 1:180–182
Chao Family Comprehensive Cancer Center,
1:260
Childhood Brain Tumor Foundation and, 1:277
cost of therapy and, 1:315–316
genre therapy and, 2:484–485
NCI relationship to, 2:798 (See also National
Cancer Institute)
non-Hodgkin’s lymphoma, 2:709
war on cancer, 2:835
women’s cancers, 3:1311
National Marrow Donor Program, 1:158,
2:807–809
National Oceanic and Atmospheric
Administration (NOAA), 1:11, 1:115
National Program for Prevention and Control of
Cancer, Diabetes, Cardiovascular Diseases, and
Stroke (India), 2:576–577
National Research Council, 2:803
National Resources Defense Council, 1:342
National Rural Health Mission (India), 2:576–577
National Strategy on Cancer Control (Tunisia), 3:1194
National Surgical Adjuvant Breast and Bowel Project (NSABP), 3:1142
National Toxicology Program, 1:343, 2:667
National University Cancer Institute (Singapore), 3:1057
Natural causes of cancer, 2:809–812
   nature versus environment, 2:809–811
   overview, 2:809
   prevention versus treatment, 2:811
   unusual cancers of childhood, 3:1259
Nature, 2:1006
Nausea, from chemotherapy, 1:272, 2:918–919
Naylor Dana Institute, 3:1327
NCI. See National Cancer Institute
Neoplasm, defined, 1:84
Neopogen, 1:76
Nepal, 2:812–814
Netherlands, 1:97, 2:814–815
Netherlands Cancer Institute, 2:815–817
Netherlands Hemophilia Patients Society, 2:817–819
Netson, Kelli, 1:76
Nevada, 1:8, 1:76
Neuroblastoma, 2:819–821
Neuroendocrine tumors (NETs), 2:890
Neuroendocrine tumors, catecholamine-producing. See Pheochromocytoma
Neurofibromatosis type 1 (NF-1), 3:1289
Neutriepigenetics, selenium, 3:1043
Neuton-rich radioisotopes, 2:823, 2:824
Neutrons, 2:821–824. See also Radiation therapy
   boron neutron capture therapy, 2:822–823
   fast neutron therapy, 2:822, 2:823
   neutron-rich radioisotopes, 2:823, 2:824
   nuclear reactors, 2:822, 2:845–846
   overview, 2:821–822, 2:968–970
   particle accelerators, 2:822
   radioisotopes, 2:823, 2:824
   “New American Plate” (American Institute for Cancer Research), 3:1306
New England Journal of Medicine, 2:671, 2:674, 2:731, 2:732
New England Sports Network (NESN), 2:638
New York Times, 2:746
New York University Cancer Institute (NYUCI), 2:908–910
New Zealand, 2:824–826
   immigrant populations in, 2:574
   overview, 2:824–826
   plastics study in, 2:938
NHL. See Lymphoma, non-Hodgkin’s, adult;
   Lymphoma, non-Hodgkin’s, childhood;
   Mycosis fungoides
Nicaragua, 2:826–827
Nickel compounds, 2:827–830
Nieburgs, H. E., 2:604–605
Niger, 2:830–832
Nigeria, 1:370, 1:371, 2:832–834
Nitrate/nitrite, 2:458–459, 2:743, 2:744
Nitrogen compounds, in water, 2:948
Nitrogen dioxide, 2:635
Nitrogen oxide, 2:945–947
Nitrosamines, 2:744, 3:1303
Nivolumab, 2:863
Nixon, Richard (war on cancer), 2:834–836,
   2:1004–1005
NK1 inhibitors, 2:919
N,N-Diethyl-meta-Toluamide (DEET), 2:584
N-nitrosodimethylamine (NDMA), 1:347
Nobel, Alfred, 1:441
Novadex, 1:110–111
Nonmelanoma skin cancer, 3:1062, 3:1064–1066
Non-small cell lung cancer (NSCLC), 2:694–696
Nonsteroidal, anti-inflammatory drugs (NSAID), 1:95, 1:265, 1:266, 1:320–325
Nordenstrom, Bjorn E. W., 1:390
Norris Comprehensive Cancer Center (University of Southern California), 3:1248–1249
North America. See also Canada; Caribbean;
   United States
   Canada, 1:206–208
   Mexico, 1:46, 2:767–769
   United States, 3:1222–1224
North American Association of Central Cancer Registries, 2:836–837
North Korea, 2:837–839
Norway, 2:839–841
Novartis Group (Switzerland), 2:797, 2:841–843
Novis, Brian, 2:597
Novis, Susie, 2:597
Novo Nordisk (Denmark), 2:524, 2:843–844
Nowell, Peter C., 2:464
Nuclear industry, 2:844–847. See also Radiation
   Chernobyl nuclear accident, 1:126, 2:972, 3:1205
   overview, 2:844–845
   protection and industry’s future, 2:846–847
   radiation, overview, 2:972, 2:973
studies of, 2:846
uranium mining, 2:845

Nuclear Medicine Molecular Biology and Oncology (Sudan), 3:1112

Nurses
Association of Pediatric Hematology/Oncology Nurses, 1:107–108
careers of, 1:241
hospice care and, 2:557
International Conference on Cancer Nursing (CCN), 2:606
International Society of Nurses in Cancer Care, 2:605–607
Oncology Nursing Society, 2:860–862
Nurses’ Health Study Research Group, 1:139
Nutrients. See Diet and nutrition; Minerals; Vitamins; Water supply
Nutritional Prevention of Cancer Trial, 3:1043
NY-ESO-1 (vaccine), 3:1274–1275

Obama, Barack, 2:587

Obesity, 2:849–854
causes and consequences, 2:850
definition and measurements, 2:849–850
diet and nutrition issues, 2:851
esophageal cancer and, 1:415
exercise and, 2:851–852
mood control and, 2:852
overview, 2:849
phthalates and, 1:343
preventive strategies, 2:851
role of mass media in, 2:852–853
roles of government and policy makers, 2:854
roles of parents and schools, 2:854
sedentary occupations, 3:1039–1041
sleep and, 2:852
technology and, 2:853–854
Obligatory Medical Program (Argentina), 1:86
Occult causes, defined, 3:1102
Occupational hazards. See also Carcinogenic substances; Occupational Safety and Health Administration (OSHA)
aerospace industry, 1:11–12
asbestos, 2:764–766
chemical industry and, 1:262, 1:263
coal and, 1:299–302
diesel exhaust nd, 1:350–353
disability and employment, 1:356
from dyes and pigments, 1:377
embalming fluid, 1:396–398
environmental justice and, 1:402–403
flavoring agents, 2:455–456
glass industry and, 2:499
global health issues, 2:507
hair dye, 2:524–527
herbicide, 2:544–548
insecticides, 2:583–586
lead, 2:667
nickel compounds, 2:827–830
passive smoking and, 2:903
perfume and, 2:908
from pesticides, 2:912–913
plastics industry, 2:936
sedentary occupations, 3:1039–1041
solvents, 3:1088
stainless steel, 3:1101
tobacco-related exposures, 3:1181
wastewater workers, 3:1303–1304
wood dust, 3:1313–1315
wood preserver, 3:1318
workplace wellness programs and, 3:1319–1321
Occupational Safety and Health Administration (OSHA)
acrylic rubber and fibers, 1:3–4
asbestos, 1:89, 2:766
battery acid, 1:124
dyes and pigments, 1:374
explosives, 1:442
gasoline, 2:480
lead, 2:668
nail polish, 2:943
passive smoking, 2:903–904
Occupational therapy, 2:854–856
Ochratoxins, 3:1187
OECD. See Organisation of European Cancer Institutes
Ofatumumab, 1:143
Office of Cancer Survivorship (OCS), 2:803
Office of Management and Budget (OMB), 2:808–809
Ohio State University Comprehensive Cancer Center, 2:856–858
OHSU Knight Cancer Institute, 2:858–860
Olive oil, in Mediterranean diet, 1:29
Oncochat.org, 1:101
Oncogenes, 2:483, 2:489
Oncologist Assisted Spiritual Intervention Study (OASIS), 2:995–996
OncoMBOLogists
American Society of Clinical Oncology, 1:70–72
Canadian Association of Medical Oncologists, 1:208–210
Canadian Association of Pharmacy in Oncology, 1:210–211
Canadian Society of Surgical Oncology, 1:215–216
Pinkel, 2:931–932
Oncology, defined, 1:438
Oncology Institute of Moldova, 2:772
Oncology Nursing Forum, 2:860, 2:861
Oncology Nursing Society, 2:860–862
“Oncology Personalized Medicine” (Novartis Oncology), 2:842
Oncology Research Information Exchange Network (ORIEN), 2:857
Oncolytic viruses, 1:145–146
Oncoplastic Hospital Registry (Argentina), 1:86
Oncopolicy (European CanCer Organisation), 1:424
1,4-dioxane, 1:345–346, 1:347
Ono Pharmaceutical (Japan), 1:185, 2:862–864
Ontak, 2:781
Ontario Ministry of Food, Agriculture, and Rural Affairs, 2:546
Operation Enduring Freedom, 1:13
OPI Products, Inc., 2:943–944
Optic gliomas, 1:171–172
Oral cancer, childhood, 2:864–866
Oral cavity cancer, lip and, 2:866–868
Oregon, assisted suicide in, 1:97
Oregon Breast and Cervical Cancer Program, 3:1037
Oregon Health and Science University (OHSU), 2:858–860, 3:1037
Oregon State University, 1:115
Organ donors, 1:397
Organisation of European Cancer Institutes, 2:868–870
Organophosphates, 2:545, 2:585
Oropharyngeal cancer, 2:870–872
Orphan Drug Act, 2:490, 2:491
Osteopathy, 1:42
Osteosarcoma, 1:153–156, 2:726–728
O*Tinnri, Maelodar, 2:616
Ovarian cancer
aspirin and, 1:94
COX-2 inhibitors, 1:324
exercise and, 1:437
overview, 3:1312
Ovarian cancer, childhood, 2:872–873
Ovarian epithelial cancer, 2:873–875
Ovarian germ cell tumor, 2:875–877
Ovarian low malignant potential tumor, 2:877–878
Ovulation, 2:756–758
Oxidation, 2:741
Oxidative hair dye, 2:524–527
Oxidative stress, 2:925
Oz, Mehmet, 1:247
Ozone layer, 1:188, 2:471–474
P53 gene, 1:268
Pacific island countries
New Zealand, 2:824–826
Papua New Guinea, 2:894–896
Paget, Stephen, 2:549, 2:550, 3:1123
Pain and pain management, 2:879–883
government’s role in, 2:510–511
overview, 2:879
pain control from drugs, 1:368
pain issues of immigrant populations, 2:574
palliative surgery, 3:1122–1123
video games used for pain management, 2:879–883
WHO on, 3:1323
Paine, Cecil George, 1:81
Paint, 2:883–885
Pakistan, 2:885–886
Palbociclib, 2:915
Palliative care
aging population and, 1:16
as alternative therapy, 1:38
government’s role and, 2:510
hospice care compared to, 2:558–559 (See also Hospice care)
physical therapy and, 2:928
surgery and, 3:1122–1123
Pan American Health Organization (PAHO), 1:150, 1:327, 2:517, 3:1282
Pan Arab Human Genetics Conference, 3:1219
Pancreatic cancer, 2:886–888
Pancreatic cancer, childhood, 2:888–889
Pancreatic cancer, islet cell, 2:621–623, 2:890–892
Pancreatic Cancer Action, 1:8
Pancreatic endocrine tumors (PETs), 2:890
Pancreatic neuroendocrine tumors (pNETs), 2:890–892
Pancreatoblastoma, 2:892
Pancreatoblastoma, 2:889
Panitumumab, 1:143
Pan-Thames Haemophilia Consortium, 2:523
Pap tests, 1:18, 1:212, 1:349, 3:1137, 3:1277
Papanicalauo, Georgios, 3:1137
Paper industry, 2:892–894
Papillary thyroid cancer, 3:1173
Papua New Guinea, 2:894–896
Para-aminobenzoic acid (PABA), 1:189
Para-dichlorobenzene, 1:343–344
Paraguay, 2:896–897
Paramanov, Viktor, 3:1206
Paranasal sinus and nasal cavity cancer, 2:897–899
Paraplatin, 1:185
Parasites, antimicrobial treatment for, 1:81–83
Parathyroid cancer, 2:899–901
Pargament, Kenneth, 2:995
Park, Roswell, 2:1006, 3:1123
Parotid glands, 3:1013, 3:1014, 3:1015
Paroxetine, 3:1145
Particle accelerators, 2:822, 3:1223
Particle therapy, 2:975–976
Particleboard, 3:1314
Passive smoking, 2:901–904, 3:1075–1076,
  3:1178, 3:1180–1181
Pasteur, Louis, 1:81, 2:549
Patient Resource Publishing
Patient Resource Lung Cancer Guide (IALSC
Pauling, Linus, 3:1292
Pediatric Blood and Cancer, 1:75
Pelotonia, 2:857
Penicillin, 1:81
Penile cancer, 2:905–906
Peracetic acid, 2:635–636
Peretz, Tamar, 2:624
Perfume, 2:906–908
Peripheral nervous system, chemotherapy
  and, 1:273
Peripheral neuropathy, treating, 2:919
Peripheral primitive neuroectodermal tumors
  (pPNET), 3:1019–1020
Perlmutter, Isaac, 2:909
Perlmutter, Laura, 2:909
Perlmutter Cancer Center, 2:908–910
Permanent hair dye, 2:524–527
Perry, Rick, 2:761, 3:1272
Personal health records (PHRs), 1:251
Peru, 1:285, 2:910–911
Pesticides, 2:911–914
DDT, 1:338–341
herbicides, 2:544–548
history of development and use, 2:912
human exposure from, 2:912–913
insecticides, 2:583–586
overview, 2:911–912
regulation and exposure prevention, 2:913–914
Peto, Richard, 1:353
Petrochemical industry, nickel used in, 2:828
Peutz-Jeghers syndrome, 1:307, 1:309
Pfizer (United States), 1:385, 2:914–916
Pfizer, Charles, 2:914
Phage Course, 1:303
Pharmaceutical industry, 2:916–920. See also
  Chemoprevention; Chemotherapy; Gene therapy
Abbott Laboratories (United States), 1:1–2
advertising by, 1:7–10
Allergan (United States), 1:26
alternative therapies: pharmacological and
  biological treatment, 1:45–51
Amgen (United States), 1:75–77
Astellas Pharma (Japan), 1:108–110
AstraZeneca (United Kingdom), 1:110–111
Bristol-Myers Squibb (United States), 1:184–186
Canadian Association of Pharmacy in
  Oncology, 1:210–211
cancer drugs, costs and benefits of, 1:227–231
Celgene (United States), 1:249–250
chemoprevention and, 1:264–269
daiichi Sankyo (Japan), 1:331–332
drug marketing, 2:728–729
drugs and, 1:366–371
Eisai (Japan), 1:385–386
Eli Lilly & Company (United States), 1:394–396
experimental cancer drugs, 1:438–441
experimental cancer treatments, 2:918
Forest Labs (United States), 2:462–464
Genentech, 2:486–487
Genzyme (United States), 2:490–492
GlaxoSmithKline (United Kingdom), 2:502–503
H. Lundbeck (Denmark), 2:521–523
Johnson & Johnson (United States), 2:639–640
major companies in oncology field, 2:920
MedImmune (United States), 2:749
Merck (Germany), 2:758–759
monoclonal antibody drugs, discovery of, 2:551
Novartis Group (Switzerland), 2:841–843
Novo Nordisk (Denmark), 2:843–844
Ono Pharmaceutical (Japan), 1:185, 2:862–864
overview, 2:916
Pfizer (United States), 2:914–916
pharmacists and clinical trials, 1:290
Roche Group (Switzerland), 2:1001–1003
Rosenberg and, 2:1004–1106
History of development and use, 2:912
human exposure from, 2:912–913
insecticides, 2:583–586
overview, 2:911–912
regulation and exposure prevention, 2:913–914
Peto, Richard, 1:353
Petrochemical industry, nickel used in, 2:828
Peutz-Jeghers syndrome, 1:307, 1:309
Pfizer (United States), 1:385, 2:914–916
Pfizer, Charles, 2:914
Phage Course, 1:303
Pharmaceutical industry, 2:916–920. See also
  Chemoprevention; Chemotherapy; Gene therapy
Abbott Laboratories (United States), 1:1–2
advertising by, 1:7–10
Allergan (United States), 1:26
alternative therapies: pharmacological and
  biological treatment, 1:45–51
Amgen (United States), 1:75–77
Astellas Pharma (Japan), 1:108–110
AstraZeneca (United Kingdom), 1:110–111
Bristol-Myers Squibb (United States), 1:184–186
Canadian Association of Pharmacy in
  Oncology, 1:210–211
cancer drugs, costs and benefits of, 1:227–231
Celgene (United States), 1:249–250
chemoprevention and, 1:264–269
daiichi Sankyo (Japan), 1:331–332
drug marketing, 2:728–729
drugs and, 1:366–371
Eisai (Japan), 1:385–386
Eli Lilly & Company (United States), 1:394–396
experimental cancer drugs, 1:438–441
experimental cancer treatments, 2:918
Forest Labs (United States), 2:462–464
Genentech, 2:486–487
Genzyme (United States), 2:490–492
GlaxoSmithKline (United Kingdom), 2:502–503
H. Lundbeck (Denmark), 2:521–523
Johnson & Johnson (United States), 2:639–640
major companies in oncology field, 2:920
MedImmune (United States), 2:749
Merck (Germany), 2:758–759
monoclonal antibody drugs, discovery of, 2:551
Novartis Group (Switzerland), 2:841–843
Novo Nordisk (Denmark), 2:843–844
Ono Pharmaceutical (Japan), 1:185, 2:862–864
overview, 2:916
Pfizer (United States), 2:914–916
pharmacists and clinical trials, 1:290
Roche Group (Switzerland), 2:1001–1003
Rosenberg and, 2:1004–1106

selenium interaction with pharmaceutical agents, 3:1043–1044
Shire UK, 3:1051–1052
standard modalities of cancer treatment, 2:916–918
Taisho Pharmaceutical (Japan), 3:1135–1136
Takeda Pharmaceutical (Japan), 3:1140–1142
treating side effects of cancer and cancer treatments, 2:918–920
Pharmaceutical Research and Manufacturers of America (PhRMA), 2:728, 2:918, 3:1157
Pharmacists, careers of, 1:241
Pharynx, 2:568–570
Phenolic-type microbial agents, 1:359
Phenoxyis, 2:545
Phenylendiamines, 1:375
Pheochromocytoma, 2:778–779
Pheochromocytoma, 2:920–921
Philadelphia (Ph) chromosome, 2:677, 2:678
Philip Morris, 3:1327
Philippines, 2:921–923
overview, 2:921–923
Philippine Cancer Society, 2:922
Philippine Society of Medical Oncology, Inc., 2:922
Phoenix Weekly (China), 1:283
Photodynamic therapy, 2:923–927, 3:1158
Phthalates, 1:343, 2:934, 2:938, 2:944,
   3:1286–1288
Physical therapy, 2:927–929
Physical touch, as alternative therapy, 1:37–43
Physician-assisted suicide. See Assisted suicide
Physicians
cancer institute employment and, 2:816
careers of, 1:241–242
communication with aging population, 1:16
hospice care and, 2:556–557
Massachusetts Medical Society, 2:731–733
Massachusetts Medical Society, 2:731–733
Massachusetts Medical Society, 2:731–733
Massachusetts Medical Society, 2:731–733
Massachusetts Medical Society, 2:731–733
Massachusetts Medical Society, 2:731–733
Massachusetts Medical Society, 2:731–733
Physician’s Health Study (PHS), 1:133–134
Physician’s Weekly, 1:103
Phytochemicals, 1:343
Phytochemicals, 1:343
Phytochemicals, 1:343
Phytochemicals, 1:343
Phytochemicals, 1:343
Pigments. See Dyes and pigments
Pilocytic astrocytoma (PA), 1:166
Pineoblastoma and supratentorial primitive neuroectodermal, childhood, 2:929–931
Pinkel, Donald, 2:671, 2:931–932
Pitta, 1:45
Pituitary tumor, 2:932–934
Placental-site trophoblastic tumors (PSTT), 2:495
Planning
   transportation and, 3:1189–1190
   urban planning, 3:1184–1186
Plasma cell neoplasm/multiple myeloma, 2:934–936. See also Multiple myeloma/plasma cell neoplasm
Plastic Planet (documentary), 1:403
Plastic surgery, 3:1122, 3:1226
Plastics industry, 2:936–939
chemical industry and risk to workers, 1:262
deodorizers and, 1:343
vinyl, 3:1286–1288
water pollution and, 2:948
Platinol, 1:185
Pleuropulmonary blastoma, 2:939–940
Plewes, Donald, 1:212
Plexxikon, 1:332
Plowman, Nick, 2:907
Polishes, 2:942–945
Pollution, air, 2:945–947
Pollution, water, 2:948–950
Polychlorinated biphenyl (PCB), 1:389, 1:390,
   2:452–453, 3:1303
Polycyclic aromatic hydrocarbons (PAH), 1:115,
   2:636–637, 2:742, 2:938
Polymerase chain reaction (PCR) technique, 2:1002
Polymeric biguanides, 1:359
Polyomavirus, 2:862
Polyvinyl chloride (PVC), 3:1286–1288
Poon, Y. F., 2:555
Population Science Division (Herbert Irving Comprehensive Cancer Center), 2:543
Portugal, 2:950–951
Positron emission tomography (PET) scan, 2:824,
   3:1155. See also individual types of cancer
Post-marketing requirements (PMRs), 2:463
Potassium bromate, 2:458
Potassium nitrate, 2:743
Pott, Percivall, 2:550, 3:1123
Poverty, 2:951–954
Access to Medicine Index, 2:842
Albert Einstein Cancer Center’s work and, 1:20
alcohol use and, 2:952–953
defined, 2:951–952
diet and exercise, 2:953
economic issues, 1:227–231, 1:315–316,
health care access disparities, 2:953–954
mortality rate from childhood cancers, 1:278
Program for the Elimination of Cancer Disparities (PECaD), 3:1060
as risk factor for cancer, 2:952
sacrifice zones and chemical industry, 1:264
tobacco use and, 2:953
Powers, Scott, 1:303
Precocious puberty, 2:757
Preferred provider organization (PPO) plans, 2:587
Pregnancy. See also Maternity care/maternal health
breast cancer and, 1:182–184
gestational trophoblastic tumor, 2:495–497,
3:1192–1193
Hodgkin’s lymphoma during, 2:707–708
liver cancers in fetuses, 1:296, 2:690
neuroblastoma and, 2:819
non-Hodgkin’s lymphoma during, 2:712–714
pheochromocytoma and, 2:921
rocket fuel exposure during, 2:636
Preston Robert Tisch Brain Tumor Center (Duke Cancer Institute), 1:372–373
Prevalence statistics, defined, 3:1102
Prevention of cancer. See also Education
aspirin for, 1:93–96
Austria on, 1:113–114
beta-carotene and, 1:137
Chad and, 1:259
chemoprevention and, 1:264–269
daily life risks and, 1:333–335
in developing countries, 1:349–350
future of, 2:474–475
global intervention, 2:506–508
government’s role and, 2:510
International Society for Preventive Oncology, 2:604–605
media and information seeking, 2:745
preventability versus preordained risk, 2:992–994
screening access, 3:1035–1039
screening and, 3:1030–1035
Preventive Medicine, 3:1327–1328
Primary central nervous system lymphoma, 2:699–700, 2:714–716
Primary effusion lymphoma, 2:700
Primitive neuroectodermal tumors (PNETs), 1:169–171
Principal investigators (PIs), defined, 1:289
Prison populations, hepatitis C and, 2:538
Probiotics, 1:31
Processed meats, 2:743–744
Procter & Gamble, 1:346
Profession, organizational career versus, 1:241
Progestin therapy, 1:416
Prostate cancer, 2:954–956
aging and, 1:15
aspirin and, 1:94
Association for the Cure of Cancer of the Prostate, 1:99–100
Astellas Pharma products, 1:108–109
Canadian Urologic Oncology Group on, 1:217–218
chemoprevention for, 1:267
disparities within nations and elimination of cancer, 1:361
exercise and, 1:437
screening for, 3:1036
Prostate Cancer Foundation (PCF), 1:99–100
Proteases and Cancer Program (Karmanos Institute), 1:122
Proteasome inhibitors, 2:779–780
Proton therapy, 2:956–961
clinical experience and perspectives, 2:959
dosimetry and quality assurance, 2:959
economic issues of, 2:960
future of, 2:960–961
history of, 2:956–957
Mayo Clinic (Scottsdale) proton-beam therapy, 2:740
patient education for, 2:960
physics of, 2:957
radiobiology of, 2:958
relative biological effectiveness (RBE) and, 2:956, 2:958
side effects of, 2:959–960
technology, 2:957–958
treatment planning for, 2:958–959
Protozoa, 2:948
Protropin, 2:487
Psoralen UVA (PUVA) therapy, 2:926
Psoriasis, penile cancer and, 2:905
Psychic surgery, 1:42
Psychoneuroimmunology, 2:665
Psycho-Oncology, 1:67
Psychosocial care/support, 2:961–964. See also Hospice care; individual topics on religion
American Psychosocial Oncology Society, 1:67–68
Association of Oncology Social Work, 1:105–107
barriers to, 2:963
bereavement issues, 1:131–132, 2:557
breast cancer and, 1:178
caregivers and, 1:243–244, 1:245
Chao Family Comprehensive Cancer Center and, 1:261
International Psycho-Oncology Society, 2:599–600
leukemia and, 2:669
obesity issues and, 2:852
overview, 2:961–962
provision of care for, 2:962–963
psychoneuroimmunology, 2:665
sex and, 3:1048–1049
stress and, 3:1109–1111
stress and early menarche, 2:756
video games for pain management, 2:879–883
Puberty, early menarche and, 2:756–758
Public health, town planning and, 3:1184–1186
Purdue University Center for Cancer Research, 2:964–965
Pyrimidine dimers, 1:188
Qi gong, 1:45
Quality Oncology Practice Initiative (QOPI), 1:71
R337H mutation, 1:6–7
Race. See also Surveillance, Epidemiology, and End Results (SEER) Cancer Statistics Review, 1975–2011
beliefs about preventability versus preordained risk, 2:993
breast cancer, sociocultural issues, 1:181, 1:182
childcare and cancer risk, 1:275–276
disparities within nations and elimination of cancer, 1:361–362
esophageal cancer and, 1:412
health disparities, 3:1264–1265
laryngeal cancer and, 2:659
Mayo Clinic trials and, 2:735
osteosarcoma and, 2:726–727
passive smoking and, 2:903
poverty as risk factor for cancer and, 2:952
precocious puberty, 2:757
prostate cancer and, 2:955–956
screening access and, 3:1036–1038
stomach cancer and, 3:1103
testicular cancer and, 3:1162
UC Davis on, 3:1227
in U.S., 3:1222
Race for the Cure, 1:248
Radiation, 2:967–971
aerospace industry and, 1:12–13
alpha and beta particles, gamma and X-rays, and neutrons, 2:968–970, 2:971–973 (See also Neutrons; Radiation, gamma; X-rays)
electromagnetic radiation (EMR), 1:392–393 (See also Electronics)
exposure as risk factor, 2:677
global health issues, 2:508
overview, 2:967
radiation therapy, overview, 2:970–971 (See also Radiation therapy)
radioactivity, 2:967–968
Radiation, gamma, 2:968–970, 2:971–973
Radiation, ionizing, 2:969, 2:973–975
Radiation and Isotope Center in Kartoum, 3:1112
Radiation oncology societies
Advisory Group on Non Ionising Radiation, 1:393
American College of Radiation Oncology, 1:62–63
American Society for Radiation Oncology, 1:68–70
Association of Freestanding Radiation Oncology Centers, 1:103–105
Radiation therapy, 2:975–980. See also individual types of cancer
among aging population, 1:16
anticancer drugs, overview, 1:84–86
Association of Freestanding Radiation Oncology Centers, 1:103–105
cancer surgery and, 3:1120, 3:1122
Cobalt radiation therapy, 1:212
costs of, 1:316
Cyberknife, 1:316, 2:693
European Society for Therapeutic Radiology and Oncology, 1:429–432
external-beam radiation therapy (EBRT), 1:400
image guided radiography, overview, 3:1331
intensity-modulated radiotheraphy (IMRT), 2:795–796
for intraocular melanoma, 2:611–612
methods for, 2:976–978
neutrons and, 2:821–824
overview, 1:238, 2:975–976
Pierre and Marie Curie on radiation, 2:467
during pregnancy, 1:183–184
radiography, overview, 3:1154
side effects from, 2:978–980
three-dimensional conformal radiation therapy (3D-CRT), 2:465
X-rays, overview, 3:1329–1332

Puberty, early menarche and, 2:756
video games for pain management, 2:879–883

R337H mutation, 1:6–7
Race. See also Surveillance, Epidemiology, and End Results (SEER) Cancer Statistics Review, 1975–2011
beliefs about preventability versus preordained risk, 2:993
breast cancer, sociocultural issues, 1:181, 1:182
childcare and cancer risk, 1:275–276
disparities within nations and elimination of cancer, 1:361–362
esophageal cancer and, 1:412
health disparities, 3:1264–1265
laryngeal cancer and, 2:659
Mayo Clinic trials and, 2:735
osteosarcoma and, 2:726–727
passive smoking and, 2:903
poverty as risk factor for cancer and, 2:952
precocious puberty, 2:757
prostate cancer and, 2:955–956
screening access and, 3:1036–1038
stomach cancer and, 3:1103
testicular cancer and, 3:1162
UC Davis on, 3:1227
in U.S., 3:1222
Race for the Cure, 1:248
Radiation, 2:967–971
aerospace industry and, 1:12–13
alpha and beta particles, gamma and X-rays, and neutrons, 2:968–970, 2:971–973 (See also Neutrons; Radiation, gamma; X-rays)
electromagnetic radiation (EMR), 1:392–393 (See also Electronics)
exposure as risk factor, 2:677
global health issues, 2:508
overview, 2:967
radiation therapy, overview, 2:970–971 (See also Radiation therapy)
radioactivity, 2:967–968
Radiation, gamma, 2:968–970, 2:971–973
Radiation, ionizing, 2:969, 2:973–975
Radiation and Isotope Center in Kartoum, 3:1112
Radiation oncology societies
Advisory Group on Non Ionising Radiation, 1:393
American College of Radiation Oncology, 1:62–63
American Society for Radiation Oncology, 1:68–70
Association of Freestanding Radiation Oncology Centers, 1:103–105
Radiation therapy, 2:975–980. See also individual types of cancer
among aging population, 1:16
anticancer drugs, overview, 1:84–86
Association of Freestanding Radiation Oncology Centers, 1:103–105
cancer surgery and, 3:1120, 3:1122
Cobalt radiation therapy, 1:212
costs of, 1:316
Cyberknife, 1:316, 2:693
European Society for Therapeutic Radiology and Oncology, 1:429–432
external-beam radiation therapy (EBRT), 1:400
image guided radiography, overview, 3:1331
intensity-modulated radiotheraphy (IMRT), 2:795–796
for intraocular melanoma, 2:611–612
methods for, 2:976–978
neutrons and, 2:821–824
overview, 1:238, 2:975–976
Pierre and Marie Curie on radiation, 2:467
during pregnancy, 1:183–184
radiography, overview, 3:1154
side effects from, 2:978–980
three-dimensional conformal radiation therapy (3D-CRT), 2:465
X-rays, overview, 3:1329–1332
Radiobiology, of proton therapy, 2:958
Radiofrequency ablation, 3:1121
Radiofrequency electromagnetic field (RF-EMF), 1:388–389
Radiofrequency energy, from cell phones, 1:393
Radioisotopes, 2:823, 2:824
Radiotrophic fungus, 2:972–973
Radium, 2:550, 2:975
RAG model, 2:934–935
Raloxifene, 1:394, 2:980–985, 3:1146
Ramakrishnan Method, 1:48
Ras Association Domain Family 1 (RASSF1) gene, 2:622
Rational drug use, 1:369–370
Reactive flame retardant, 2:451
Reactive oxygen species, 2:924–925
Readers Digest, 3:1176
Recenitin, 1:111
Recommended exposure limit (IARC), 2:481
Reconstructive surgery, 3:1122
Rectal cancer, 2:985–986
Rectal Cancer Outcomes Are Affected by Referral Patterns of General Surgeons (Canadian Society of Surgical Oncology), 1:215
Reed-Sternberg Cells, 2:700
Reflexology, 1:42
Refrigeration, Freon and, 2:471–474
Regional cancer centers, in India, 2:577
Regulation. See also Carcinogenic substances; Food and Drug Administration; individual names of legislation
chemical industry and, 1:263–264
drug regulatory authorities, 1:371 (See also individual names of agencies)
on environmental tobacco smoke, 1:408
hair dye and, 2:525
of herbicide, 2:547
insecticides and, 2:585 (See also Pesticides)
pesticides, 2:913–914
smoking in public places, 2:902
Reiki, 1:43
Relative biological effectiveness (RBE), of proton therapy, 2:956, 2:958
Relative value units (RVUs), 1:104
Relay for Life (American Cancer Society), 1:59–60
Religion, 2:986–988. See also individual names of countries
Religion: Jewish women and cancer risk, 2:988–990
Religion: meditation and risk, 2:990–992
Religion: preventability versus preordained, 2:992–994
Religion: use of interventions, 2:994–997
Re-Mission (video game), 2:881–882
Remission, defined, 1:238
Renal cancer
kidney cancer, childhood, 2:650–651
Kidney Cancer Association, 2:652–653
renal cell carcinoma (RCC), 2:648–650, 2:652
ureter and renal pelvis, transitional cell cancer, 3:1260–1261
Wilms’ tumor, 3:1307–1308
Republic of Ireland. See Ireland, Republic of
Research costs, cancer drug prices and, 1:227–229
RespiGam, 2:749
Retinoblastoma, 2:997–999
Retinoic acid, 1:135
Revlimid, 1:249
Revlon, 1:314–315, 2:942
Rhabdoid tumor, 2:651
Rhabdomyosarcoma, childhood, 2:999–1001, 3:1024
Rheims, first cancer hospital in, 2:562
Rhoads, Cornelius P., 1:55
RhoGam, 2:639
Right-to-die legislation, 1:97
Ringed sideroblasts and thrombocytosis (RARS-T), 2:786, 2:787
Rituxan, 2:487
RNA interference therapy, 2:485
Roberts, Robin, 1:247
Roche Group (Switzerland), 2:486–487, 2:1001–1003
Rocket fuel, 2:635–638
Rodin, Gary, 2:669
Roemer, Ruth, 3:1324
Roentgen, Wilhelm Conrad, 3:1329
Rolfing, 1:40
Romania, 2:1003–1004
Röntgen, Wilhelm Conrad, 2:550, 2:975
Rosemary, 1:34–35
Rosen Method, 1:43
Rosenberg, Barnett, 2:1004–1006
Ross, Elizabeth Kubler, 1:233
Roswell Park Cancer Institute, 2:931, 2:1006–1008
Rous, Peyton, 3:1223, 3:1327
Royal College of Physicians and Surgeons of Canada, 1:208
Royal Demolition eXplosive (RDX), 1:441, 1:442
Rubenfeld Synergy Method, 1:43
Russia, 2:1008–1010
Rwanda, 2:1010–1012
Ryerson, George Sterling, 1:214
Saccharin, 2:458
Sacrifice zones, chemical industry and, 1:264
Sacrococcygeal teratomas, 1:445–446
Sakuragaoka Research Laboratory, 1:385
Salivary gland cancer, 2:865, 3:1013–1015
Salivary gland cancer, childhood, 3:1015–1016
Salk, Jonas, 3:1016
Salk Institute for Biological Studies, 3:1016–1018
Salmonella typhimurium mutagenicity assay, 2:525
Salt, in meat processing, 2:743–754
Sambrook, Joseph, 1:303
Samuel C. Harvey Memorial Lecture award, 1:54
San Raffaele Telethon Institute for Gene Therapy, 2:484
Sanford Health, 3:1018
Sanford-Burnham Medical Research Institute, 3:1018–1019
Sankyo. See Daiichi Sankyo (Japan)
Sanofi, 2:490–491
Santos, George, 1:156
Santos, Juan Manuel, 1:305
Sarcoma, Ewing’s family of tumors, 3:1019–1021
Sarcoma, soft tissue, adult, 3:1021–1023
Sarcoma, soft tissue, childhood, 3:1023–1025
Sarcoma, uterine, 3:1025–1027, 3:1266–1267
Sarcoma Foundation of America, 3:1027–1028
Sarhan, Mahmoud, 2:641
Sarin, 3:1299
Saudi Arabia, 3:1028–1030
Saunders, Dame Cicely, 2:558
Scaffold-Based Drug Discovery Platform (Plexxikon), 1:332
Scented detergents, 1:346–347
Scientific Committee on Cosmetic Products and Non-Food Products Intended for Consumers (SCCNFP), 2:525
Screening, 3:1030–1035. See also Diagnostic tests
breast cancer, 3:1032–1033
cervical cancer, 3:1031
colon cancer, 3:1033
evidence-based recommendations and implications for care, 3:1030–1031
promoting use of screening tests, 3:1034
Screening, access to, 3:1035–1039
ACS recommendations, 3:1037–1038
need for, 3:1040
state guideline examples, 3:1039–1040
U.S. Congress on, 3:1038–1039
U.S. Preventive Services Task Force recommendations, 3:1038–1039
WHO on, 3:1037
Seattle Cancer Care Alliance (SCCA), 2:471
Seattle Post-Intelligencer, 1:116
Secondary organic aerosols (SOAs), 1:115
Secondhand smoke, 2:901–904
Section on Hematology/Oncology (AAP). See American Academy of Pediatrics, Section on Hematology/Oncology
Sedentary occupations, 3:1039–1041
Seidman Cancer Center, 2:618–619
Selective estrogen receptor modulators (SERMs), 1:438–439, 2:980–985
Selenium, 1:36, 3:1041–1044
Self-examination, breast, 1:176, 1:420
Semipermanent hair dye, 2:524–527
Semmelweis, Ignaz Philipp, 2:566
Senegal, 3:1045–1046
Sensipar, 1:77
Sentinel lymph node biopsy, 3:1123
Sentinel lymph nodes (SLNs), 1:177
Seoul National University Hospital, 3:1094
Serbia, 3:1046–1048
Serelaxin, 2:841
Servizio Sanitario Nazionale (Italy), 2:625 714-X, 1:51
Seventh-Day Adventists, 1:354
Sewer authority workers, 3:1303–1304
Sex, 1:273, 3:1048–1049. See also Hormones
Sézary, Albert, 3:1050
Sézary Syndrome, 3:1049–1051
Shah, Nihal, 3:1221
Sharon, Ariel, 2:624
Sharp, Phillip, 1:303
Sheele, Karl Wilhelm, 1:284
Shiatsu, 1:40
Shih, Chun-Jen, 3:1137–1138
Shire UK, 3:1051–1052
“Sick building syndrome,” 2:884
Sidestream smoke, 1:406
Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, 3:1052–1054
Sidransky, David, 3:1223
Sierra Leone, 3:1054–1056
Sigma Aldrich, 2:759
Sigmoidoscopy, 1:60–61
Silent Spring (Carson), 1:338–339, 2:893, 2:912–913
Silver compounds, 1:359
Singapore, 3:1056–1058
Sinus cancer. See Paranasal sinus and nasal cavity cancer; Wood dust
SIOP. See International Society of Paediatric Oncology
Sisson, George, 3:1338
Siteman, Alvin J., 3:1060
Siteman Cancer Center, 3:1059–1061
Skin cancer. See also Melanoma; Skin cancer, melanoma; Skin cancer, non-melanoma
individual entries for ultraviolet radiation
aspirin and, 1:94
chemoprevention for, 1:267
childhood, 3:1061–1062
clothing as protection from, 1:294–296
glass protection from, 2:501
nonmelanoma, 3:1062, 3:1064–1066
Sézary syndrome, 3:1049–1051
sunscreen and, 3:1117–1119
types, 3:1085–1088
Skin cancer, childhood, 3:1061–1062
Skin cancer, melanoma, 3:1062–1064
broad-spectrum ultraviolet (UV) radiation and, 1:186–189
overview, 3:1062–1064
stages of, 3:1087
sunscreen and, 3:1117–1119, 3:1210
sunscreen research by Green and, 2:513–515
Skin cancer, non-melanoma, 3:1064–1066
COX-2 inhibitors, 1:323
sunscreen and, 3:1119
types, 3:1085–1086
Skin carcinoma, Merkel cell, 2:762–763, 3:1067–1068
Skin problems, from chemotherapy, 1:272–273
Skipper, Howard E., 3:1068–1070
Sleep, need for, 2:852
Sloan, Alfred P., 2:754
Slovakia, 3:1070–1071
Small cell lung cancer (NSCLC), 2:696–697
Small intestine cancer, 3:1071–1073
Small molecule kinase inhibitor, 2:918
Smartphones, 1:250–253
Smilow Cancer Hospital (Yale), 3:1333–1335
Smokeless tobacco, 3:1073–1075
See also Tobacco in history
Smoking cessation, 3:1077–1082
expectations for, 3:1081–1082
gum, 3:1079
inhalers, 3:1080–1081
lozenges, 3:1081
nasal spray, 3:1080–1081
nicotine replacement therapy, overview, 3:1077–1078
nicotine replacement therapy, side effects, 3:1078–1079
patch, 3:1079–1080
Smoothened protein inhibitor (SMO), 2:915
Snow, John, 1:284
Snow World (video game), 2:880–881
Snuff, 3:1074
Snus, 3:1074
Social cognitive theory, pain management and, 2:880
Social media. See also Education; Psychosocial care/support; individual names of professional organizations
Association of Cancer Online Resources, 1:100–102
health advocacy through, 2:532
Massey Cancer Center, 2:734
Oncology Nursing Society, 2:861
overview, 2:745–746
psychosocial issues of cancer and, 1:68
Social Security Act, 2:588
Social Work Toolbox, 1:106
Social workers, 2:557
Society of Gynecologic Oncology, 3:1082–1083
Society of Surgical Oncology, 3:1084–1085, 3:1124
Sociocultural issues. See individual names of countries
Sodium benzoate, 2:459
Sodium nitrate/sodium nitrite, 2:458–459, 2:743, 2:744
Sofosbuvir, 2:539
Soft tissue sarcoma, adult, 3:1021–1023, 3:1027–1028
Soft tissue sarcoma, childhood, 3:1023–1025, 3:1027–1028
Solar radiation, 3:1085–1088. See also Melanoma; Melanoma, intraocular (eye); Skin cancer; Skin cancer, childhood; Skin cancer, melanoma; Skin cancer, non-melanoma; Skin carcinoma, Merkel cell
broad-spectrum ultraviolet (UV) radiation and, 1:186–189
clothing as protection from, 1:294–296
education about sun exposure, 1:381
Finland and cancer rates, 2:451
overview, 3:1085
types of skin cancer, 3:1085–1088
vitamin D and, 1:36, 3:1040
Solar Radiation Alert (FAA), 1:11
Solid Tumor Translational Research (STTR), 2:470–471
Solvents, 3:1088–1090
Somalia, 3:1090–1092
Soman, 3:1299
Somatostatinomas, 2:890
Somers, Suzanne, 1:246–247
Sonoporation, 2:484
South Africa, 1:218–220, 3:1092–1093
South America
Argentina, 1:86–87
Bolivia, 1:150–151
Brazil, 1:172–174
Chile, 1:280–282
Colombia, 1:304–306
Costa Rica, 1:316–318
Ecuador, 1:379–380
Paraguay, 2:896–897
Peru, 2:910–911
Venezuela, 3:1280–1282
South Korea, 3:1093–1094
Southern Research Institute, 3:1068
Soy products, 1:28, 1:91–92
Spain, 3:1095–1096
chlorine use and, 1:285–286
Dominican Republic and, 1:364
overview, 3:1095–1096
Spear, Ruth, 2:796
Spindle cell rhabdomyosarcoma, 2:1000
Spirituality. See also individual topics on religion
alternative therapy and, 1:43–45
spiritual care workers and hospice care, 2:557
spirituality-centered intervention, 2:994–997
Sporadic cancer path, 2:488
Squamous neck cancer with occult primary, metastatic, 3:1096–1097
Squibb Corporation, 1:185
Sri Lanka, 3:1097–1099
St. Jude Children’s Research Hospital, 3:1099–1100
Stachybotrys chartarum, 3:1187
Stages, of cancer. See also individual types of cancer
American Joint Committee on Cancer, 1:63–65
of brain tumor, medulloblastoma, childhood, 1:168–169
for childhood cancers, 2:864
Children’s Oncology Group (COG) staging system of, 2:690
of extrahepatic bile duct cancer, 1:141–142
of melanoma, 3:1087
as prognostic factor, 2:478
surgery and, 3:1120–1121
Stainless steel, 3:1100–1103
Staph infection, antibiotic resistance and, 1:83
State taxes. See Taxation
Statistics, 3:1101–1103. See also Surveillance,
Epidemiology, and End Results (SEER)
Stearoyl-CoA, 2:736
Stem cell research
Albert Einstein Cancer Center, 1:19–20
bone marrow transplants, 1:156, 1:157
brain tumor, medulloblastoma, childhood, 1:169
Celgene (United States), 1:249
transplants, 2:679
Wistar Institute and, 3:1309
Witte and, 3:1227
Stigma, disability and, 1:356–357
Stimulant drugs, defined, 1:368–369
STI-related cancers, 2:583
Stockholm Convention, 2:585
Stomach (gastric) cancer, 3:1103–1106
aspirin and, 1:94
family size and, 2:447–448
Stomach (gastric) cancer, childhood, 3:1106–1109
Stone, Reverend Edward, 1:93
Stress, 3:1109–1111. See also Psychosocial care/
support
factors that exacerbate and ameliorate cancer stress, 3:1111
focus on long-term survivors, 3:1110–1111
overview, 3:1109–1110
studies on cancer stress, 3:1110
Stroma, 1:156–157
Structured Clinical Interview for DSM IV Axis I Disorders, The, 3:1117
Styrene, 3:1089–1090
Subbarow, Yellapragada, 2:550
Subbituminous coal, 1:297
Sublingual glands, 3:1013, 3:1014
Submandular glands, 3:1013, 3:1014, 3:1015
Substance abuse
Canadian Red Cross, 1:214
drug abuse or drug misuse, 1:369
irrational drug use, 1:370
Sudan, 3:1111–1113
Sugden, William, 1:303
Suicide, assisted. See Assisted suicide
Sulfur (brimstone), 2:583
Sulfur dioxide, 2:945–947
Sulfuric acid, 1:125
Sulmasy test, 1:96
Sun exposure (Australia), 1:112, 1:226, 1:295, 3:1113–1115
Sunlamps or sunbeds, exposure to, 1:189, 3:1115–1117
Sunscreen, 3:1117–1119
Supernova events, 1:11
Supplementary cancer insurance, 2:588
Supplements. See Diet and nutrition; individual alternative therapies
Support systems. See Cancer patients; Survivors of cancer; Survivors of cancer, families of
Supratentorial primitive neuroectodermal brain tumors, in children, 1:169–171
Surface Mining Control and Reclamation Act of 1977, 1:299–300
Surgery, 3:1119–1124. See also individual types of cancer
diagnostic, 3:1120
as first line therapy, 3:1120–1121
future of cancer surgery, 3:1124
minimally invasive, 3:1121
other treatment modalities with, 3:1122
overview, 3:1119–1120
palliation and, 3:1122–1123
reconstructive, 3:1122
surgeons and cancer, 3:1123–1124
Surgical oncology societies. See also Surgery
British Association of Surgical Oncologists (BASO), 1:433
Canadian Society of Surgical Oncology, 1:215–216
European Society of Surgical Oncology, 1:432–434
Society of Surgical Oncology, 3:1084–1085, 3:1124
age, overview, 1:14, 3:1124
age distribution of deaths by site (2007–2011), all races, both sexes, 3:1430–1431
age distribution of incidence cases by site (2007–2011), all races, both sexes, 3:1426–1427
age-adjusted SEER incidence and U.S. death rates and five-year relative survival, by primary cancer site, sex and time period, Blacks, 3:1418–1419
age-adjusted SEER incidence and U.S. death rates and five-year relative survival, by primary cancer site, sex and time period, Whites, 3:1416–1417
age-adjusted SEER incidence and U.S. death rates and five-year survival, by primary cancer site, sex and time period, 3:1414–1415
age-adjusted SEER incidence rates and trends for the top 15 cancer sites by race/ethnicity, both sexes, 3:1452
age-adjusted SEER incidence rates and trends for the top 15 cancer sites by race/ethnicity, females, 3:1454
age-adjusted SEER incidence rates and trends for the top 15 cancer sites by race/ethnicity, males, 3:1453, 3:1467
age-adjusted U.S. death rates and trends for the top 15 cancer sites by race/ethnicity, both sexes, 3:1455
age-adjusted U.S. death rates and trends for the top 15 cancer sites by race/ethnicity, females, 3:1457
age-adjusted U.S. death rates and trends for the top 15 cancer sites by race/ethnicity, males, 3:1456
average years of life lost per person due to major causes of death in U.S., all races, both sexes (2011), 3:1476
average years of life lost per person dying of cancer, all races, both sexes (2011), 3:1476
data sources, 3:1388–1391
definitions, 3:1402–1406
estimated new cancer cases and deaths for 2014, all races, by sex, 3:1411
five-year relative survival SEER program (2004–2010), both sexes, by race and cancer site, 3:1468
immigrant populations and, 2:574, 2:575
incidence percent change between 2002 and 2011, numbers (burden) versus rates (risk, all races, all ages, both sexes, 3:1474
interpretation of cancer statistics, 3:1381–1385
introduction, 3:1380–1381
leading causes of death in U.S., 1975 versus
2011, percent of all causes of death, 3:1459
lifetime risk of being diagnosed with cancer by
site and race/ethnicity, 18 SEER areas, both
lifetime risk of being diagnosed with cancer by
site and race/ethnicity, females, 18 SEER
lifetime risk of dying from cancer by site and
race/ethnicity, both sexes, total U.S.
lifetime risk of dying from cancer by site and
race/ethnicity, females, total U.S.
lifetime risk of dying from cancer by site and
race/ethnicity, males, total U.S.
media age of cancer patients at death
(2007–2011), by primary cancer site, race
and sex, 3:1432–1433
median age of cancer patients at diagnosis
(2007–2011), by primary cancer site, race
and sex, 3:1428–1429
mortality percent change between 2002 and
2011, numbers (burden) versus rates (risk,
al races, all ages, both sexes, 3:1475
on osteosarcoma, 2:726–727
person-years of life lost due to cancer, all races,
both sexes (2011), 3:1476
person-years of life lost due to major causes of
death in U.S., all races, both sexes (2011),
3:1477
SEER 9, 13, & 18 geographic areas, 3:1458
SEER cancer incidence and U.S. death rates
(2007–2011), by cancer site and race/ethnicity, 3:1469
SEER incidence (2002–2011), females by race/
ethnicity, 3:1471
SEER incidence (2002–2011), males by race-ethnicity, 3:1470
SEER incidence and U.S. death rates
(2007–2011), five-year relative survival
(2004–2010), all cancer combined by race
and sex, 3:1466
SEER incidence and U.S. mortality trends by
primary cancer site and sex, all races
SEER observed incidence and delay adjusted
incidence rates, all cancer sites, by sex, 3:1478
SEER observed incidence and delay adjusted
incidence rates, both sexes, 3:1479
SEER observed incidence and delay adjusted
incidence rates, females, 3:1481
SEER observed incidence and delay adjusted
incidence rates, males, 3:1480
SEER Program, 3:1387–1388
software used for, 3:1406
standard errors of rates, 3:1402
statistical methods, 3:1391–1400
statistical significance, 3:1400–1402
summary of changes in cancer mortality
(1950–2011) and five-year relative
survival, males and females, by primary
cancer site, 3:1413
technical notes, 3:1387
trends in SEER incidence and U.S. death rates by
trends in SEER incidence rates by age group and
trends in SEER incidence rates by sex and
trends in U.S. death rates by age group and
trends in U.S. death rates by sex and primary
U.S. and SEER death rates by primary
cancer site and race/ethnicity
U.S. cancer death rates, 62-year trends, all races,
males and females, 3:1412
U.S. complete prevalence counts, invasive cancers
only, January 1, 2011, by age at prevalence,
3:1450–1451
U.S. death rates (1975–2011), heart disease
compared to neoplasms, by age of death,
3:1460
U.S. mortality (2001–2010), females by race/
ethnicity, 3:1473
U.S. mortality (2001–2010), males by race/
ethnicity, 3:1472
U.S. prevalence counts, invasive cancers only,
January 1, 2011, using different tumor
inclusion criteria, 3:1448–1449
Survivors of cancer, 3:1124–1126. See also
Psychosocial care/support
cancer communication and statistics of, 1:224
daily life and, 1:334–335
future of, 3:1126
long-term survivorship, 3:1125–1126
Office of Cancer Survivorship (OCS), 2:803
overview, 3:1124–1125
stress and long-term survivorship, 3:1110–1111
UCLA on, 3:1229
Survivors of cancer, families of, 3:1126–1129. See also Psychosocial care/support
American Childhood Cancer Organization (ACCO), 1:279–280
challenges faced by, 3:1127–1128
childcare and cancer risk issues, 1:276
confusion about death, 3:1128–1129
diagnosis of cancer and, 3:1127
family roles, 3:1129
overview, 3:1126–1127
planning for future, 3:1128
support system, 3:1128
Susan G. Komen Foundation, 1:178, 1:248
Tamoxifen, 3:1142–1147
alternatives to, 3:1146
contraindications, 3:1145
effectiveness of, 3:1143–1144
historical background, 3:1142–1143
negative interactions with other drugs, 3:1144–1145
neutral interactions with other drugs, 3:1145
prognostic biomarkers for resistance, 3:1144
resistance to, 3:1145–1146
side effects, 3:1144
Tan, Winston, 2:736
Tanning beds/lamps, 1:189, 3:1115–1117, 3:1150, 3:1208
Tanzania, 3:1147–1149
Targeted alpha therapy (TAT), 2:823
Targeted therapy, defined, 2:917
Tattoos, dyes/pigments in, 1:376–377
Taxation, 3:1149–1154
Affordable Care Act and, 3:1150
on alcohol, 3:1152–1153
on gasoline, 3:1153–1154
on indoor tanning, 3:1150
overview, 3:1149
on tobacco, 3:1150–1152
Taxol, 1:185
Taylor, Allyn, 3:1324
T-cells, 1:440, 2:781
Tea, in Asian diet, 1:28
Technology, imaging, 3:1154–1157
cancer imaging for diagnosis and detection, 3:1154–1156
cancer imaging in treatment, 3:1156
future of, 3:1156
overview, 3:1154
Technology, new therapies, 3:1157–1158
overview, 3:1157
types, 3:1157–1158
Technology use
human health and, 1:393–394
obesity and, 2:853–854
Tehran University, 2:613
Teletherapy, 2:975
Telework, 1:393–394
Telomerase, 1:439
Temel, Jennifer, 2:559
Temin, Howard M., 2:551
Temodar, 2:761
Temporary hair dye, 2:524–527
Terabe, Musaki, 2:800
Teratomas, 1:445–446
Terpenes, 1:344
Terry, Luther, 3:1159–1161
Testicular cancer, 3:1161–1162
barriers to early detection, 3:1161–1162
overview, 3:1161
psychosocial concerns, 3:1161
racial and ethnic disparities, 3:1162
Testicular germ cell tumors, 1:444
Tetrachloroethylene, 3:1090
Texaco, 1:379
Texas, on Gardasil, 2:761, 3:1274
Textile dyes, 3:1162–1165
Thailand, 3:1165–1167
Therapeutic touch, 1:43
Thiersch, Karl, 2:549, 3:1123
Thomas, Danny, 3:1099
Thomas, Don, 2:603
Thomas Jefferson University, 2:653–655
Thomson Reuters, 2:861
Thornton, Mark, 3:1027
Thornton, Patricia, 3:1027
Three-dimensional conformal radiation therapy (3D-CRT), 2:465
Thymine (T), 2:488
Thymoma, childhood, 3:1167–1168
Thymoma and thymic carcinoma, 3:1168–1170
Thyroid cancer, 3:1170–1172
overview, 3:1170
risk, prevalence, outcomes, 3:1171
symptoms and detection, 3:1171–1172
treatment, 3:1172
types, 3:1171
Thyroid cancer, childhood, 3:1172–1174
multiple endocrine neoplasia syndrome, childhood, 2:778
overview, 3:1172
risk, prevalence, outcomes, 3:1172
treatment, 3:1173
types, 3:1172–1173
Tide, 1:346
Tikur Anbessa Hospital, 1:419
Till, James, 1:212
Time, 1:343
Tobacco in history, 3:1174–1176
chewing tobacco, 3:1073–1075
eye awareness of health concerns, 3:1175–1176
Framework Convention on Tobacco Control (WHO), 2:903, 3:1123, 3:1324–1326
future of cancer and, 2:475
growth era, 3:1175
Massachusetts Medical Society on, 2:732
overview, 3:1174–1175
tobacco tax and, 3:1150–1152
Wynder and, 3:1326–1328
Tobacco smoking, 3:1176–1179
alcohol and, 1:21
in Algeria, 1:25
American Cancer Society on, 1:59
American Lung Association on, 1:65–67
asbestos, 1:89
in Bangladesh, 1:120
beta-carotene and, 1:136
in Burma (Myanmar), 1:195
cancer incidence in developing countries and, 1:348, 1:349
as cause of cancer, statistics, 2:809
chemicals in smoke, 3:1178
daily life and, 1:333
education about tobacco use, 1:381
environmental tobacco smoke, 1:405–408
facts about, 3:1178–1179
global health issues, 2:506
laryngeal cancer and, 2:659
misconceptions of, 3:1177–1178
overview, 3:1176–1177
passive smoking and, 2:901–904
poverty and, 2:953
secondhand smoke and, 3:1178 (See also Passive smoking)
smoking cessation and screening, 3:1038
smoking cessation in Canada, 1:212
water pipe smoking, 3:1132
WHO on, 1:113
Tobacco-related exposures, 3:1179–1182
epidemiology, 3:1179–1180
forms of tobacco consumption, 3:1180
prevention, 3:1182
secondhand smoke, 3:1180–1181 (See also Passive smoking)
symptoms, 3:1181
treatment, 3:1182–1183
workplace exposure, 3:1181
Togo, 3:1182–1184
Toluene, 2:944
Total therapy, leukemia and, 2:671, 2:932
Town plans, 3:1184–1186
Toxic Hot Spots Program (California), 1:124
Toxic mold, 3:1186–1188
Toxic Substance Control Act, 1:89
Traditional medicines
Angola, 1:79–80
Burkina Faso, 1:192–193
Cambodia, 1:202
Canadian Red Cross history and, 1:214
Cote d’Ivoire, 1:318–319
Eritrea, 1:411
herbs/medicinal plants, as alternative therapy, 1:32–37, 1:40, 1:45
historical perspective, 1:44–45
kava, 1:261
Kenya, 2:647
Mali, 2:724
Paraguay, 2:896
Peru, 2:910
Philippines, 2:922
Republic of Ireland, 2:616
Senegal, 3:1045
Sierra Leone, 3:1055
Somalia, 3:1090–1091
Sri Lanka, 3:1098
Tanzania, 3:1147–1148
Thailand, 3:1165
Togo, 3:1183
Uganda, 3:1203

Trait inheritance. See Genetics

Transcutaneous electrical nerve stimulation (TENS), 1:394

Transgenic plants, 2:584
Transitional cell cancer (TCC), 3:1260–1261
Translational Oncology Research International (TORI), 3:1228

Translational research, 3:1224–1225
Transplants, bone marrow, 1:156–159

Transportation, 3:1188–1190
automobiles, 1:115–116
bicycles, 1:138–140
diesel exhaust and, 1:350–353
disability and barriers, 1:356–357
gasoline and, 2:479–481
ejet and rocket fuels, 2:635–638
overview, 3:1188–1189
role of policy makers, planners, and architects, 3:1189–1190

“Transportation into a narrative world,” 2:880

Trastuzumab, 1:143
Treanda, 2:522
Treatment centers, advertising by, 1:7–10
Tresiba, 2:844
Triazines, 2:545
Trichloroethylene (TCE), 1:10, 3:1090

Trichopoulos, Dimitrios, 3:1190–1192


Trinitrotoluene (TNT), 1:441, 1:442
Tris(1,3-dichloro-2-propyl) phosphate, 2:453
Trisenox, 2:522
Trophoblast glycoprotein (TPBG), 1:146

Trophoblastic tumor, gestational, 3:1192–1193

Truman, Harry, 2:587–588
Truxel, 2:521
Tsuei, Julia J., 3:1137
Tsukuba Research Institute, 2:863
Tuberculosis, 1:83, 1:288
Tufts Center for the Study of Drug Development, 1:227
Tulp, Nicholas, 2:549

Trumans, bone marrow, 1:156–159

“Transportation into a narrative world,” 2:880

Uehara Memorial Foundation, 3:1136
Uganda, 3:1203–1205
Ukraine, 3:1205–1206

Ultraviolet A radiation, 3:1206–1209
characteristics of, 3:1207–1208
effects of, 3:1207
factors influencing levels of, 3:1208–1209
overview, 3:1206–1207
sunscreen and, 3:1118
UV index, 3:1207

Ultraviolet B radiation, 3:1209–1211
characteristics of, 3:1210
effects of, 3:1209–1210
factors influencing levels of, 3:1211
overview, 3:1209
sun exposure and, 3:1210–1211
sunscreen for, 3:1118, 3:1210
UV index, 3:1210

Ultraviolet C radiation, 3:1211–1214
arc welding, 3:1213–1214
characteristics of, 3:1212–1213
germicidal irradiation, 3:1213
overview, 3:1211–1212

Ultraviolet radiation related exposures, 3:1214–1217
broad spectrum UV, 1:186–189
clothing as protection from, 1:294–296
disinfectants and, 1:359
effects of, 3:1215
exposure to, 3:1216
overview, 3:1214, 3:1215
sun exposure in Australia, 1:112, 1:226, 1:295, 3:1113–1115 (See also Australia)
sunlamps and sunbeds, 1:189, 3:1115–1117
sunscreen for, 3:1117–1119, 3:1210, 3:1216–1217
tanning beds/lamps, 1:189, 3:1115–1117, 3:1150, 3:1208
UV index, 3:1215–1216
Underarm deodorant, 1:344
Undifferentiated pleomorphic sarcoma, 1:154
Unified Program (Moldova), 2:772
Union for International Cancer Control, 3:1217–1218
Danish Cancer Society and, 1:337
International Association of Cancer Registries, 2:592
International Society of Nurses in Cancer Care and, 2:605
Organisation of European Cancer Institutes and, 2:869
work of, 3:1217–1218
United Arab Emirates, 3:1218–1220
United Kingdom, 3:1220–1221
on battery acid, 1:124
GlaxoSmithKline, 2:502–503, 2:563–564
Haemophilia Society, 2:523–524
obesity in, 2:849
overview, 3:1220–1221
Shire UK, 3:1051–1052
United Nations. See also individual names of countries
Children’s Fund (UNICEF), 2:776
Convention Against Illicit Traffic in Narcotic Drugs and Psychotropic Substances, 1:123, 1:193
on diabetes, 2:843
UN Convention against the Illicit Traffic in Narcotic Drugs, 1:319
UNITAID, 2:518
WHO Framework Convention on Tobacco Control, 2:903, 3:1152, 3:1324–1326
WHO relationship to, 2:838
United States, 3:1222–1224. See also Affordable Care Act (ACA); individual names of cancer centers; individual names of U.S. government agencies
Abbott Laboratories, 1:1–2
Allergan, 1:26
Amgen, 1:75–77, 1:109, 2:749
Bristol-Myers Squibb, 1:184–186
cancer drug costs in, 1:227, 1:229–2330
cancer mortality rate, 1:260
cancer scientists of, 3:1222–1223
Celgene, 1:249–250
Eli Lilly & Company, 1:394–396, 2:591
Family and Medical Leave Act (1993), 1:245
Forest Labs, 2:462–464
Genzyme, 2:490–492
health care as percentage of GDP, 2:838
history of health insurance in, 2:586–587
(See also Insurance)
Johnson & Johnson, 2:639–640
MedImmune, 1:111, 2:749–750
Merck & Co., 2:760–762
Nixon and war on cancer, 2:834–836, 2:1004–1005
overview, 3:1222
Pfizer, 1:385, 2:914–916
research and advocacy organizations of, 3:1223–1224
WHO Framework Convention on Tobacco Control and, 3:1152
Unity of Prevention and Control of Cancer (Brazil), 1:173
University at Buffalo, 2:1007
University Clinical Center of Kosovo, 3:1047
University Hospital (Haiti), 2:528
University Hospitals Cleveland, 2:618–620
University of Alabama at Birmingham Comprehensive Cancer Center, 3:1224–1226
University of California, Berkeley, 2:551
University of California, Davis, Comprehensive Cancer Center, 3:1226–1228
University of California, Irvine, 1:260
University of California, Los Angeles, 1:115, 2:475
University of California, Los Angeles, Jonsson Comprehensive Cancer Center, 3:1228–1230
University of California, San Diego, 3:1017
University of California, San Francisco, 1:440, 2:486–487
University of California, San Francisco, Helen Diller Family Comprehensive Cancer Center, 3:1230–1231
University of Chicago Medicine Comprehensive Cancer Center, 3:1231–1233
University of Colorado Cancer Center, 3:1233–1236
University of Hawai‘i Cancer Center, 3:1236–1237
University of Iowa, 2:552
University of Maryland, 1:9, 2:881
University of Michigan Comprehensive Cancer Center, 3:1237–1240
University of Minnesota, 2:551
University of Minnesota Masonic Cancer Center, 3:1240–1242
University of New Mexico Cancer Research and Treatment Center, 3:1242–1243
University of North Carolina Lineberger Comprehensive Cancer Center, 3:1243–1245
University of Oxford, 1:393
University of Pittsburgh Cancer Institute, 3:1245–1248
University of Rochester, 2:749
University of Southern California Norris Comprehensive Cancer Center, 3:1248–1249
University of Texas MD Anderson Cancer Center, 1:8, 1:9, 3:1249–1251
University of Utah, 2:551, 2:567–568
University of Vermont, 3:1282–1284
University of Virginia Cancer Center, 3:1251–1253
University of Washington Cancer Consortium, 2:470
University of Wisconsin Carbone Cancer Center, 3:1253–1254
Unknown primary site, cancer of, childhood, 3:1254–1256
Unknown primary site, carcinoma of, adult, 3:1257–1258
Unusual cancers of childhood, 3:1258–1260
overview, 3:1258
prevalence of, 3:1259–1260
Upper endoscopy, 1:60–61, 3:1104
Urachal carcinoma, 1:149
Urban planning, 3:1184–1186
Ureter and renal pelvis, transitional cell cancer, 3:1260–1261
Urethral cancer, 3:1261–1263
Urinal cakes, 1:344
U.S. Agricultural Health Study, 2:547
U.S. Bioscience, 2:749
U.S. Code of Federal Regulations, 2:455
U.S. Department of Agriculture, 2:460, 2:741, 2:742, 3:1306
U.S. Department of Health and Human Services
asbestos, 1:89
cancer communication by, 1:220
coal, 1:299
DDT, 1:339
Healthy People Initiative, 2:533–534, 3:1310
nickel compounds, 2:829
screening, 3:1034
solvents, 3:1088
U.S. Department of Justice, 2:463
U.S. Department of Labor, 3:1039
U.S. Environmental Protection Agency. See Environmental Protection Agency (EPA)
U.S. National Cancer Program, 2:799
U.S. National Institute of Environmental Health Sciences, 1:404
U.S. National Toxicological Program (NTP), 2:458, 2:459, 2:480
U.S. Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial, 2:955
U.S. Surgeon General, on smoking, 1:406, 2:901, 3:1159–1161, 3:1327
Utah Population Database (UPDB), 2:567
Uterine embryonal sarcoma of the liver (UESL), 2:692
Uterine sarcoma, 3:1025–1027, 3:1266–1267
Uveal melanomas, 2:611, 2:752
Uzbekistan, 3:1267–1269
V600E (BRAF gene), 2:680
Vaccine Adverse Event Reporting System (VAERS), 2:563, 2:564
Vaccine workers, HPV and HCV, 3:1271–1272
Vaccines, 3:1272–1276. See also HPV vaccination biologic therapy, 1:144
bladder cancer and, 1:147
Coley and, 3:1273, 3:1275
experimental cancer drugs, 1:440
future of cancer vaccines, 3:1275–1276
Healthy People Initiative on, 2:534
hepatitis B, 2:535–536, 2:542
hepatitis C, 2:536, 3:1271–1272
immune system and, 3:1274
liver cancer and, 2:540
by Merck, 2:760
NY-ESO-1 example, 3:1274–1275
overview, 3:1272–1273
pathogen-associate molecular patterns (PAMPs), 3:1273–1274
University of Alabama on, 3:1225
vaccine-preventable diseases, generally, 2:536
V-agents, 3:1299–1301
Vaginal cancer, 3:1276–1278, 3:1312
Vaginal cuff brachytherapy, 1:400
Vakoc, Chris, 1:303
Vanderbilt-Ingram Cancer Center, 3:1278–1280
Vapor-phase sterilants, 1:359
Varmus, Harold E., 2:551
Vascular endothelial growth factor (VEGF), 2:551
Vasella, Daniel, 1:229
Vata, 1:45
Vector development, in gene therapy research, 2:483
Vegetarian diet, 1:29, 1:354
Venezuela, 3:1280–1282
Ventana, 2:1002
Vepesid, 1:185
Vermont, assisted suicide in, 1:97
Vermont Cancer Center, 3:1282–1284
Victoza, 2:844
Video games
  for exercise, 2:854
  for pain management, 2:879–883
Video news releases (VNRs), 2:730
Vietnam, 3:1284–1286
Vineland Adaptive Behavior Scales (VABS), 1:409
Vinyl, 2:937–938, 3:1286–1288
VIPomas, 2:890
Virchow, Rudolph, 2:494, 2:549, 2:550
Virginia Commonwealth University Medical Center, 2:733–735
Viruses
  experimental cancer drugs, 1:440
  future of cancer and, 2:474
  gene therapy and, 2:482, 2:483
  hepatitis B, 2:534–536
  hepatitis C, 2:536–539, 3:1271–1272
  polyomavirus, 2:862
  in water, 2:948
Visual inspection with acetic acid (VIA) method, 2:993
Visual pathway and hypothalamic glioma,
  childhood, 1:171–172, 3:1288–1290
Vital statistics, defined, 3:1101–1103
Vitamins, 3:1290–1295. See also Diet and nutrition; specific vitamins
  as alternative therapy, 1:32–37
  B vitamins, 1:21, 1:35
  beta-carotene, 1:132–138
  exercise and, 1:139
  future research, 3:1294
  overview, 3:1290
  for preventing natural causes of cancer, 2:811
  sedentary occupations and, 3:1040
  types of, 3:1290–1294
Vitriol, 1:123
Vogelstein, Bert, 3:1223
Volatile organic compounds (VOCs), 1:347, 2:884
Volunteers, in hospice care, 2:557
Vomiting, from chemotherapy, 1:272
Von Drais, Baron, 1:138
Von Hippel-Lindau (VHL) disease, 2:649
Von Hoff, Katja, 1:410
Von Mikulicz, Jan, 3:1123
Von Wasserman, August, 3:1041
Vonderheid, Eric, 2:601
Vulvar cancer, 3:1295–1296, 3:1312–1313
Wake Forest University. See Comprehensive Cancer Center of Wake Forest University
Waldenström's macroglobulinemia, 3:1297–1298
Walshe, Walter Hayle, 3:1220
War gases and chemicals, 3:1298–1302
War on cancer. See Nixon, Richard (war on cancer)
Warburg, Otto H., 2:551
Warburton, Rebecca, 1:227
Warren, John Collins, 1:124, 2:549, 3:1120
Washington, assisted suicide in, 1:97
Washington University, 3:1059, 3:1060, 3:1100
Wat Kampramong, 3:1166
Water pipe smoking, 3:1132
Water supply
  chlorine in, 1:284–286
  chloroform in, 1:286–287
  coal and, 1:298
  disinfectants and antiseptics, 1:359
  lead in, 2:666–667
  paper industry and, 2:893
  perfume ingredients in, 2:907
  water pollution, 2:948–950
Water treatment, 3:1302–1304
Watson, James, 1:303
Wayne State University, 1:121–122
We Have Kidney Cancer (Kidney Cancer Association), 2:653
Web sites. See Social media
Weber, Max, 1:240
Weed removal, herbicides and, 2:544–547
WEEN, 2:638
Weisburger, John, 3:1327
Weismann Barrier, 2:663
Wertheim, Ernst, 3:1123
Western diet, 3:1304–1307
Whang-Ped, Jacqueline, 3:1138
Wheatgrass therapy, 1:29–30
Whole Body Therapy, 1:31
Whorton, James, 1:44
Wigler, Michael, 1:303
Wigmore, Ann, 1:29–30
Wildlife, pesticides and, 1:340
Wilms’ tumor, 2:650–651, 3:1307–1308
Wilson, Rita, 1:247–248
Wilson, Robert, 2:956
Wireless telecommunication technologies, 1:388–389
Wistar, Caspar, 3:1308–1309
Wistar Institute, 3:1308–1310
Women’s cancers, 3:1310–1313. See also individual types of cancer
Women’s Empowerment Cancer Advocacy Network (WE CAN) (Georgia), 2:493
Women’s Health Initiative, 1:416
Women’s Health Study (WHS), 1:134
Wong, Chi-Huey, 3:1138
Wood, paper industry and, 2:892
Wood dust, 3:1313–1316
insecticides and, 2:584
overview, 3:1313–1315
research, 3:1315
WOODEX database, 3:1314
Wood preserver, 3:1316–1319
Workplace Wellness Alliance, 3:1320
Workplace wellness programs, 3:1319–1321
World Cancer Declaration, 2:509, 2:510, 2:511
World Cancer Research Fund, 1:22, 2:662, 3:1221
World Cancer Research Institute, 2:742
World Coal Association, 1:297
World Diabetes Foundation, 2:843
World Health Organization, 3:1321–1324. See also individual names of countries
alcohol, 1:21
battery acid, 1:123–124
brain stem glioma in children, 1:159
Burkitt’s lymphoma, 2:701
cancer incidence in developing countries and, 1:349
cancer prevention and, 3:1322
cancer vaccines, 1:144
chlorine, 1:285
cost-effectiveness of treatments and, 2:888
on drug marketing, 2:728
on drugs, 1:366, 1:368
early detection and, 3:1322
electronics, 1:393
exercise recommendations by, 1:438
Framework Convention on Tobacco Control, 2:903, 3:1152, 3:1324–1326
on future of cancer, 2:474
glass industry, 2:499, 2:500
global health issues and cancer, 2:503–509
Global Strategy for Health for All by the Year 2000, 1:111
Global Vaccine Action Plan (GVAP), 2:536
GLOBOCAN (database), 1:305, 1:326, 1:412
Health Cluster, 1:254
IARC established by, 2:793 (See also International Agency for Research on Cancer)
International Association of Cancer Registries, 2:592
International Society for Preventive Oncology and, 2:604
latitude and, 2:662
medulloblastomas in children, 1:166
obesity, 2:849
overview, 3:1321–1322
palliative care, 3:1323
on poverty as risk factor for cancer, 2:952
rectal cancer, 2:986
research by, 3:1323 (See also individual types of cancer)
salivary gland cancer, 3:1013
on smoking, 1:113, 1:120, 3:1075–1076
tamoxifen, 1:110–111
on treatment, 3:1322–1323
UN relationship of, 2:838
World Health Organization Framework Convention on Tobacco Control, 3:1324–1326
World Oncology Forum, 1:428
World Trade Center syndrome, 2:766
Worms, in water, 2:948
Wright, Jane, 1:70, 1:71
Wu, Cheng-Wen, 3:1138
Wynder, Ernst, 3:1326–1328
Xalkori, 2:915
Xenoestrogens, 1:343
Xgeva, 1:77
X-rays, 3:1329–1331
CAT/CT, 3:1330–1331
Germany and, 2:494
history of, 2:975, 3:1329 (See also Radiation therapy)
image guided radiotherapy, 3:1331
ionization, 3:1331
linear accelerators, 3:1329–1330
overview, 2:968–970
society and, 3:1331
Yaffe, Martin, 1:212
Yale Cancer Center, 3:1333–1335
Yamagiwa, Katsusaburo, 2:550
Yarborough, Ralph, 2:835
<table>
<thead>
<tr>
<th>Term</th>
<th>Page(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yarborough Commission</td>
<td>2:835</td>
</tr>
<tr>
<td>Yemen</td>
<td>3:1335–1336</td>
</tr>
<tr>
<td>Yeshiva University</td>
<td>1:19–20</td>
</tr>
<tr>
<td>You Are Not Alone (Nathanson)</td>
<td>1:233</td>
</tr>
<tr>
<td>Young adult cancer prevention</td>
<td>3:1336–1338</td>
</tr>
<tr>
<td>Young Investigator (CureSearch)</td>
<td>2:807</td>
</tr>
<tr>
<td>Yul Brynner Head and Neck Cancer Foundation (Head and Neck Cancer Alliance)</td>
<td>3:1338–1340</td>
</tr>
<tr>
<td>Zaltman, Gerald</td>
<td>2:532</td>
</tr>
<tr>
<td>Zambia</td>
<td>3:1341–1343</td>
</tr>
<tr>
<td>Zanmi Lasante</td>
<td>2:528</td>
</tr>
<tr>
<td>Zimbabwe</td>
<td>3:1343–1344</td>
</tr>
<tr>
<td>Zinc</td>
<td>1:36</td>
</tr>
<tr>
<td>ZL Sociomedical Complex (Haiti)</td>
<td>2:528</td>
</tr>
<tr>
<td>Zoladex</td>
<td>1:110</td>
</tr>
<tr>
<td>Zolindan</td>
<td>2:761</td>
</tr>
<tr>
<td>Zykadia</td>
<td>2:841</td>
</tr>
</tbody>
</table>