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The opinions and assertions contained herein are the private views of the authors and are not to be construed as official views representing the views of the Department of Defense.
To my parents
who were so very proud of me. No kid could have been loved or supported more. They would have considered
this a coffee table book and looted it upon all their unsuspecting friends.

PJW

To my parents
for giving me opportunities that they never had and to my wonderful family Neel, Jay, Tara and Lisaeric for
looking after each other while I looked after “the book”.

AK

To my husband
David R. Boston and my wonderful children, Haley and Brett, who mean everything to me. Thank you for your
patience, enthusiasm and support. I promise you the same for your adventures.

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We at Amiryx and Elsevier are proud to present Diagnostic Imaging: Obstetrics, the sixth volume in our acclaimed Diagnostic Imaging series. This present-setting, image- and graphic-packed series began with David Stoller’s Diagnostic Imaging: Orthopedics. The next four volumes: Diagnostic Imaging: Brain, Head & Neck, Diagnostic Imaging: Abdomen and Diagnostic Imaging: Airway are now joined by Paula Woodrow, one of the world’s premier authorities in obstetrical imaging and her co-leads Drs. Arline Kennedy and Rosa Salmay, along with their team of experts, have compiled an engaging mixture of highly refined color graphics, ultrasound, MRI, clinical and gross pathology photos of obstetrical diseases the likes of which has not been seen before.

Again, the unique bulleted format of the Diagnostic Imaging series allows our authors to present approximately twice the information and four times the images per diagnosis compared to the old-fashioned traditional prose textbook. All the Diagnostic Imaging books follow the same format, which means the same information is in the same place every time. In every organ system. The innovative visual differential diagnosis “thumbnail” that provides an at-a-glance look at entities that can mimic the diagnosis in question has been highly popular. “Key Facts” boxes provide a succinct summary for quick, easy review.

In summary, Diagnostic Imaging: Obstetrics is a product designed with you, the reader, in mind. Today’s typical practice settings demand efficiency in both image interpretation and learning. We think you’ll find this new Dh Obstetrics volume a highly efficient and wonderfully rich resource that will significantly enhance your practice. Enjoy!

Anne G. Oshorn, MD
Executive Vice President & Editor-in-Chief, Amiryx Inc.

R. Bis Harokepeter, MD
CIO & Chairman, Amiryx Inc.
FOREWORD

What a great book! I have long felt that most textbooks were unattractive, boring, and out of date by the time they were published. However, Dr. Paula Woodward and her colleagues have succeeded in organizing an innovative, up-to-date, and fascinating book on fetal and perinatal ultrasound. It is obvious that a great deal of careful planning has gone into this book. The format is concise, efficient, and the illustrations are magnificent.

I knew Dr. Woodward very well from her days at the University of Utah and that she has devoted her professional life to medical education. She has assembled an impressive team of co-authors who are experts in radiology, high-risk obstetrics, genetics, prenatal diagnosis, pediatric cardiology, and perinatal pathology who all have extensive experience in fetal imaging, disease processes, and patient care.

This is a book of differential diagnoses and actual cases that both experts and those of us with less expertise will find useful. Each image has been selected to illustrate an important point. The standardised format for rapid access to multiple examples has resulted in a comprehensive and clinically useful resource. I know of no other textbook on this topic that is as authoritative and rich in illustrations. Diagnostic Imaging: Obstetrics is surely destined to become a "must have" for anyone performing obstetric ultrasound.

James R. Scott, MD, Editor
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I said I would never write a textbook. Why would I want to? There are a lot of textbooks out there on OB ultrasound; do we really need another one? Also, quite frankly, I don't like to write prose (I know that is a sacrilege for someone who has chosen an academic career, but it is the truth). There are those long, mandatory introductory paragraphs that prattle on but deliver little actual usable information. There are strict restrictions on the number of images (which is the most important part) and you can forget most of those color photographs. The writing/editing process is seemingly endless, and by the time it finally gets to print, it is out-of-date. I definitely didn't want to do that.

Although I have never enjoyed writing, I do love to lecture and can spend hours on the perfect weed slide. The lecture format, by its very nature, has to be compacted. The information is concise, bulleted, heavily illustrated, and with the right finesse, will flow seamlessly.

No, I never wanted to write a textbook, and was on record as such, with all my friends. My life changed when Anne Osborn and Ric Hammerroeder approached me about participating in the FocherRadiologist series. Their enthusiasm for this new template concept of writing was infectious (much like my process for producing a lecture they said) and so I somewhat reluctantly came on board. As it turns out, it is one of the most gratifying things I have done.

The Amiys Diagnostic Imaging series uses a highly structured, information dense, bulleted style that yields more "pears per pound" than a standard prose style textbook. Each diagnosis is richly illustrated including graphics, fetal MRI, 3D ultrasound as well as conventional grayscale and Doppler imaging. Many diagnoses include pathologic and/or clinical correlation. The end result is something unique and very different than any other OB ultrasound textbook.

The true joy for me in doing this book was the opportunity to put together an extraordinary team of fetal imagers from across the country. I have long believed patients are best served when a multidisciplinary team works in concert. I took that approach to assembling my team, which includes experts in radiology, perinatology, cardiology, pathology and genetics. We have collectively poured over thousands of images, selecting each one to illustrate an important clinical point.

I am indebted to everyone on the team for their hard work. I, especially, want to thank my two co-leads (and dear friends) Anne Kennedy and Roja Schayer, without whom I would have never undertaken this project. It is always a kick when we are together. I also want to acknowledge Rich Coombs, the gifted illustrator, and the extraordinarily helpful staff at Amiys for all their assistance. Finally, on behalf of all of the authors, I want to thank all the sonographers who helped us to so richly illustrate this book.

I hope you enjoy this textbook I said I would never write, or as I like to think of it, the world's longest word slide.

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XXIV
DIAGNOSTIC IMAGING
OBSTETRICS
# SECTION 1: First Trimester

**Introduction and Overview**

Normal Early Pregnancy & Imaging ........................................... 1-2

**First Trimester**

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NORMAL EARLY PREGNANCY & IMAGING

Terminology

Definitions
- First trimester: From fertilization of ovum to end of 13th post-menstrual week

Anatomy-Based Imaging Issues

Key Concepts or Questions
- Sonographic signs of intrauterine pregnancy (IUP) important to recognize
  - Intraduodenal sac sign (IDDS), earliest sign of IUP
    - Seen by 4-4.5 weeks after last menstrual period (LMP) by endovaginal ultrasound
    - Fertilized ovum implants into decidua basalis
    - Gestational sac: "burrows" into endometrium
    - Echogenic ring is seen eccentric to linear interface of endometrial surfaces
  - Double decidua sac sign (DDSS)
    - Described as earlier transabdominal sign of IUP
    - Two echogenic rings seen within endometrial cavity
    - Decidua parietalis
    - Outer ring: decidual lining of uterine cavity
    - Decidua vera:
      - Inner ring, covering free margin of gestational sac
    - Decidua basalis
    - Endometrial "base" of sac
    - Decidua basalis + chorionic trophoblastic forms placenta
  - Development of yolk sac
    - Presence of a yolk sac within a gestational sac confirms IUP
    - Seen by 5-5.5 weeks after LMP
    - Round and echogenic:
    - Amnion develops embryologically before yolk sac, but yolk sac is easier to see
    - Number of yolk sacs = number of amnions
    - In multiple gestations, count yolk sacs to determine amniotically
    - Embryo

- First seen as focal thickening on yolk sac
  - "Diamond ring" sign
  - Embryo appears as echogenic "diamond" on top of yolk sac
  - "Double bubble" sign
  - Yolk sac and amniotic sac
  - Embryo is in amniotic sac, immediately adjacent to yolk sac
  - Distinct embryo with cardiac activity seen by 6-6.5 weeks
  - 5 mm is discriminatory value for presence of heart beat
  - "5 alive" rule: If heartbeat not present by 5 mm → demise

Imaging Approaches
- Endovaginal ultrasound is mainstay of early pregnancy imaging
  - Well-established developmental stages, excellent resolution
  - Transabdominal ultrasound
    - Used in trials of first trimester screening
    - Excellent for rapid confirmation of live IUP
  - Doppler
    - Use of pulsatile Doppler avoided in first trimester
    - Concerns regarding heating/embryonic damage
    - Limited color Doppler may be used
    - "Ring of fire" appearance described as circle of increased flow on color Doppler
    - Non-specific finding
  - Seen in normal trophoblastic tissue around embryo
  - Seen with ectopic gestation (lack of flow does not rule out ectopic)
  - Seen in ovary, surrounding normal corpus luteum
  - M-mode: Used to document cardiac activity in embryo
  - MRI: Current recommendations are to avoid MRI during first trimester, especially with developing embryo unknown
  - CT: for feting evaluation
    - May still use depending on clinical circumstance (e.g. trauma)
Normal Early Pregnancy Milestones
- Biweekly fetal sac sign (DSD): 4-4.5 weeks
- Yolk sac: 5-5.5 weeks
- Embryo with heart beat: 6-6.5 weeks
- Double bubble sign: Yolk sac + amniotic sac
- Embryo forms within amnion
- May determine chorioangioma/amnioticity in multiple gestation care; not to include yolk sac
- Number of yolk sacs = number of amnions

Failed 1st Trimester Pregnancy
- Normal milestones are clear and may be met for normal pregnancy development
- Mean sac diameter ≥ 10 mm: Must see yolk sac
- Mean sac diameter ≥ 18 mm: Must see embryo
- If embryo ≥ 5 mm: Cardiac activity must be seen

- Even with fetus in head, radiation dose below threshold for concern
- In author's institution, amniocentesis CT dose approximates 14 mGy; threshold for concern is > 106 mGy

Imaging Protocols
- Measure mean sac diameter (MSD)
  - Mean sonographic area only, do not include echogenic chorionic rim
- Measure diameter in 3 planes, average of these measurements = MSD
- Measure crown-rump length (CRL)
  - Most accurate method to date pregnancy from 6-10 weeks
- Use CRL as soon as embryo is visible
- Measure longest axis of embryo
  - Be careful not to include yolk sac
- Biological variation does not become significant until > 12 weeks
- Evaluate yolk sac
  - Look for sac outside amnion
  - Shape should be spherical, diameter ≤ 6 mm
  - Thin-walled
  - Cerebella, calcified or thick wall abnormal
  - Becomes obliterated as amnion fuses with chorion at ≤ 14 weeks
- Do not just measure IUP, look at anatomy
  - Many anomalies may be detected in 1st trimester
  - Anencephaly, spina bifida, holoprosencephaly
  - Cystic hygroma
  - Dorsal meniscal wall defects; be cautious about omphalocele before 12 weeks

Normal Measurements
- MSD increases by about 1 mm per day
- Sac diameter should be about 3 cm longer than CRL
- Cord length approximates embryo length
- Nuchal translucency < 3 mm (11-14 weeks)
- Embryonic heart rate ≤ 5 weeks, 110-115 beats/min
- By 6 weeks, 144-159 beats/min
- By 9 weeks, 137-144 beats/min

- Rate ≤ 90 bpm = embryonic bradycardia
- Screening for aneuploidy
  - Nuchal translucency
    - ≤ 3 mm by strict standardized measuring techniques
  - Ductus venosus
  - Should be continuous forward flow throughout cardiac cycle
  - Tricuspid valve
  - Nails/bone
  - Should see nail bone separate from skin

Pathology-Based Imaging Issues

Key Concepts or Questions
- Is there an intrauterine gestation?
- Is there an ectopic gestation?
- How many gestational sacs are there?
- If multiple sacs, what is chromosomally, amniotically?
- Is there a yolk sac?
- Is there a normal embryo?

Embryology

Embryologic Events
- Embryo
  - Fission of ovum + sperm = zygote
- Cleavage of zygote = formation of morula
  - Central fluid-filled space is morula = blastocystic cavity, which separates trophoblast from inner cell mass
- Trophoblast = embryonic part of placenta
- Inner cell mass (embryoblast) = primordium of embryo
- Embryoblast = bilaminar embryonic disc
  - Embryonic disc = three dimensional, C-shaped embryo by beginning of 6th post-menstrual week
- Undergoes cranial, caudal, lateral folding
  - Neural tube closure
  - Caudal neuropore closes embryonic day 26
    (5th-6th post-menstrual week)
NORMAL EARLY PREGNANCY & IMAGING

- Heart partitioned by end of 8th post-menstrual week
- Cardiac activity seen before partitioning complete
- Cardiac activity should be present once embryo = 5 mm in length
- Limb buds
- Visible by 8-9 post-menstrual weeks
- Movements seen by 9-10 post-menstrual weeks
- Embryo is recognizable "human" by end of 10th week
- Placenta
  - Anoxic arrangements for maternal-fetal exchange are present by end of 50 post-menstrual week
  - Cord fully formed with established coiling of vessels by 9 weeks
  - Cord formed by fusion of vitelline duct, body stalk, yolk sac, allantois
- Bowel herniation:
  - Bowel grows rightwards, volume greater than embryo therefore herniates into base of cord
  - Bowel undergoes rotation within cord, then returns to abdominal cavity
  - Liver never herniates normally
- Multiple gestations: Type of twinning depends on number of zygotes and timing of division
  - Dichorionic/diamniotic
  - Monochorionic/diamniotic and monoamniotic determined by timing of zygote division
  - Before 3rd day postconception = dichorionic, diamniotic
  - After 4th-6th days postconception = monochorionic, diamniotic
  - Cannulation of inner cell mass of blastocyst after 8th day post conception = monochorionic, monoamniotic
  - Incomplete cleavage of embryonic disc after 13th day post conception = conjoined twins

Practical Implications
- Rhombencephalon is normal
  - Lumen in back of head where hindbrain is forming
  - Not to be confused with intracranial eye, posterior fossa mass

- Physiologic bowel herniation is normal < 12 weeks
  - Do not confuse with omphalocele
  - Presence of herniated liver is never normal, and if seen, indicates an omphalocele
  - Do not confuse normal umbilical hernia for skin when performing nuchal thickness measurements

Clinical Implications
- Human chorionic gonadotropin (hCG)
  - Normal pregnancy results in hCG
  - Discriminatory level of hCG can be very useful in triage of pain and bleeding in early pregnancy
  - If hCG > 2,000 IU/L (mid-trimester reference preparation) expect to see IUP
  - Triage decision points:
    - Empty uterus with hCG > 2,000
    - Differential diagnosis is ectopic pregnancy vs. spontaneous abortion
    - If signs of ectopic pregnancy = methotrexate vs. surgery
      - If patient is stable, with no sonographic features of ectopic pregnancy, follow with serial hCG, US
      - Empty uterus with hCG < 2,000
        - Differential diagnosis = ectopic pregnancy vs. spontaneous abortion vs. normal early pregnancy
        - Look for signs of ectopic if present treat accordingly
        - If no signs = ectopic follow with serial hCG, US
        - In a normal entity 1st trimester pregnancy hCG should double every 2-3 days

- Hydatidiform mole has markedly elevated hCG

Related References
NORMAL EARLY PREGNANCY & IMAGING

IMAGE GALLERY

(B) Endovaginal ultrasound shows the embryonic disc (curved arrows) between the yolk sac (arrow) and amniotic (open arrows). All of these structures are within the chorionic sac. (C) Endovaginal ultrasound shows the same with which chorionicity and amnioncity can be determined in the first trimester. There are 2 chorionic sacs and 3 yolk sacs (implying 1 amnion), therefore this is a dichorionic, triamniotic triplet gestation.

(E) Endovaginal ultrasound shows an 8 week embryo inside the amniotic (curved arrow), with the yolk sac (arrow) being obliterated as the amnion approaches the chorion. The fluid in the extra amniotic space (open arrow) is echogenic. (F) Color Doppler ultrasound shows normal pulsation of umbilical cord vessels in a 9 week gestation.

(G) Transabdominal ultrasound shows a normal nuchal translucency measurement (curved arrow) and normal ductus venous waveform (open arrows) in the first trimester. (H) 3D ultrasound clearly shows the "fernlike" appearance of the amnion at the end of the first trimester. The nose (arrow), limbs (curved arrows) and biparietal head (open arrows) are easily identified.
ANEMBRYONIC PREGNANCY

**TERMINOLOGY**

**Abbreviations and Synonyms**
- Anembryonic pregnancy (AP)
- Blighted ovum

**Definitions**
- Anembryonic pregnancy
  - Gestational sac without visible embryo
  - Failure of embryo to develop
  - Early demise and resorption of embryonic pole
- Embryonic demise
  - Gestational sac with visible dead embryo
- Consider term "failed first trimester pregnancy"
  - Avoid confusion
  - Simplifies terminology
- Why "blame" the ovum with tetras such as blighted ovum

**IMAGING FINDINGS**

**General Features**
- Gestational sac without identifiable embryo
- Discriminatory criteria for anembryonic pregnancy by endovaginal (EV) ultrasound
  - Mean sac diameter > 10 mm without a yolk sac

**Ultrasonographic Findings**
- Grayscale Ultrasound
  - Empty amnion
  - Specific sign of anembryonic gestation
- Amniotic sac without an embryo
- Yolk sac may be visible: Outside amnion
- Yolk sac forms after amnion but is easier to see
- Embryo first seen as focal thickening on yolk sac
- Amnion then becomes visible
- Amnion enlarges rapidly and envelops embryo
- Yolk sac eventually obliterated as amnion fuses with chorion
- Signs of abnormal pregnancy
  - Irregular sac shape, may be "teardrop" shaped
  - Poor decidual reaction
  - Sac position low in uterus

**DDx: Uterine Finding With Pain Or Bleeding In First Trimester**

- Ectopic, Cornual
- GTD-Invasive Mole
- GTD-Complete Mole
- Postmolar Bleed
ANEMBRYONIC PREGNANCY

Terminology
- Gestational sac without visible embryo
- Consider term “failed first trimester pregnancy”

Imaging Findings
- Sac size must have reached discriminatory threshold
- Mean sac diameter > 18 mm without an embryo
- Empty amnion
- Poor color Doppler signal around sac

Top Differential Diagnoses
- Normal early intrauterine pregnancy (IUP)
- Retained products of conception (RPOC)
- Gestational trophoblastic disease (GTD)

Key Facts
- 60% of spontaneous abortions < 12 weeks due to abnormal chromosomes

Clinical Issues
- No specific recurrence risk
- Most will spontaneously abort without treatment

Diagnosis Checklist
- Abnormality common in early pregnancy
- Diagnosis depends on knowledge of normal early pregnancy milestones
- If in doubt, wait and see
- “Empty amnion sign” is a specific indicator of anembryonic gestation

Imaging Recommendations
- Use TV sonography
- Better resolution
- More confidence in diagnosis
- Be sure to scan through entire uterus in longitudinal and transverse planes
- Must load carefully the yolk sac, embryo
- Avoids missing multiple gestations
- Measure sac diameter in 3 planes
- Measurement does not include choioic reaction
- Mean sac diameter = average of these three measurements
- Followed by: evaluate normal early pregnancy
- Check menstrual history
- Verify date of last menstrual period (LMP)
- Is cycle regular?
- What is cycle length?
- Know anatomy and developmental stages
- “Double bleb”: Embryonic disc between amnion and yolk sac
- Yolk sac and amnion should be visible by 7 weeks post-LMP
- Embryo lies inside amniotic cavity
- Yolk sac lies outside amniotic cavity
- Normal yolk sac round in shape
- Normal yolk sac ≤ 6 mm diameter

Pseudosac of ectopic pregnancy
- Sac central in endometrial cavity
- No IUP
- Doppler: Absent or low velocity flow
- Peak systolic velocity < 8 cm/sec

Retained products of conception (RPOC)
- Degraded material in uterine cavity
- Echogenic material with flow on color Doppler most likely RPOC
- Retained clot is usually hypoechoic, non-perfused
- No recognizable gestation sac

Gestational trophoblastic disease (GTD)
- Classic hydatidiform mole has “cheese” appearance
- May see abnormal appearing gestational sac
- Can mimic anembryonic sac
- May see associated ovarian theca lutein cysts

Perigestational hemorrhage
- Usually crescentic around periphery of gestational sac
- +/- Living embryo

DIFFERENTIAL DIAGNOSIS

Normal early intrauterine pregnancy (IUP)
- Double decidual sac sign (DDS)
- Thick echogenic decidual reaction
- Yolk sac may not be seen if MSD < 10 mm EV
- > 10 mm + no yolk sac = failed IUP
- Prominent color flow around sac
- Low resistance, high-velocity flow on spectral analysis of chorion
- Remember to use Doppler sparingly in early gestation

PATHOLOGY

General Features
- General path comments
- 60% of spontaneous abortions < 12 weeks due to abnormal chromosomes
- Trisomies
- Trophoblastic tetraploid
- 45 XO
- Translocations
- Moles
- Teratomas
- Malignancy
- Endometriosis
ANEMBRYONIC PREGNANCY

- 30-60% documented elevations of beta human chorionic gonadotrophin end as failed pregnancy
- Pregnancy "abortion" biochemical not clinical
- Up to 20% confirmed first trimester pregnancies end in spontaneous abortion
- Pathology series of abnormal early pregnancies
  - 35% aneembryonic
  - 54% early loss (cause not specified)
  - 11% molar (partial or complete)
- Groups with increased incidence of early pregnancy failure
  - Advanced maternal age
  - History: recurrent abortions
  - Poor diabetic control

Microscopic Features
- Chorionic villi present in uterine curettings
- Significant reduction in number of vessels per chorionic villus when compared to normal pregnancy
- Vessel abnormally located within chorionic villi: Remnia as central cords
- Thought to relate to inadequate vasculogenesis, abnormal development of vasculosynthetic membrane
- Vessels marginalize to periphery of villus in normal pregnancy
- Nuclear DNA abnormal in high proportion (up to 40%)
- Suggests chromosomal aberrations → abnormal embryogenesis → anembryonic gestation

CLINICAL ISSUES

Presentation
- May be asymptomatic with diagnosis made during routine first trimester scan
- If spontaneous miscarriage iatrogenic
  - Vaginal bleeding
  - Pelvic pain
  - Uterine contractions
- Patient perception
  - Diminished breast tenderness
  - Decrease of nausea/vomiting
  - "Doesn't feel like other pregnancies"

Natural History & Prognosis
- Random event
- No specific recurrence risk
- Threatened abortion occurs in 25% first trimester pregnancies
- Presents with pain and bleeding after missed menstrual period

Treatment
- "Wait and see"
  - Most will spontaneously abort without treatment
- Vaginal misoprostol
  - Successful evacuation of uterus in majority of patients
  - Many patients prefer definitive treatment to expectant management
  - Some will require curettage but overall expect 50% reduction in need for surgical management
- Suction curettage
  - Small associated risk of excessive bleeding, uterine rupture, Asherman syndrome

DIAGNOSTIC CHECKLIST

Consider
- Aneembryonic pregnancy often due to chromosomal aberration
- Diagnosis depends on knowledge of normal early pregnancy milestones
- B in doubt, wait and see
  - Normal pregnancies grow at predictable manner
  - MSD increases by 1 mm per day
  - Schedule follow-up for a time when gestational sac should have reached discriminatory threshold

Image Interpretation Pearls
- "Empty amniotic sac" is a specific indicator of anembryonic gestation
- Gestational sac with amnion but no visible embryo
  - YS may be visible

SELECTED REFERENCES

ANEMBRYONIC PREGNANCY

IMAGE GALLERY

Typical

(Left) Endovaginal ultrasound shows an empty gestational sac with poor decidual reaction (arrows). The sac is also irregular in shape. (Right) Endovaginal ultrasound in a normal pregnancy shows the double decidual sac sign created by the apposition of the decidua capsularis (curved arrow) and decidua parietalis (arrows). The open arrow marks the decidual basalis.

Typical

(Left) Endovaginal ultrasound shows the empty amniotic sac. The amniotic cavity is seen within the gestational sac (curved arrow) but there is no evidence of an identifiable yolk sac. (Right) Endovaginal ultrasound shows another example of an empty amniotic sac (arrow). In this case, a yolk can be seen (curved arrow).

Typical

(Left) Endovaginal ultrasound shows a "live-drop" shaped gestational sac (curved arrow), with surrounding hemorrhage (arrows). The patient had a spontaneous abortion the next day. (Right) Transabdominal ultrasound shows a large gestational sac with poor decidual reaction and internal debris (arrows) but no embryo. A sac of this size would be expected to contain an embryo with a crown-rump length of approximately 1 cm.
PERIGESTATIONAL HEMORRHAGE

Terminology

Abbreviations and Synonyms
- Perigestational hemorrhage (PGH)
- Subchorionic hematoma
- Intrauterine hematoma
- Abortion
- Term more often reserved for 2nd/3rd trimester
- Massive PGH

Definitions
- Hematoma adjacent to gestational sac in first trimester (first 13 wks of gestation)
  - Bleeding often from chorionic frondosum (CF)
  - CF is early placenta

Imaging Findings

General Features
- Best diagnostic clue: Intrauterine fluid collection separate from and adjacent to gestational sac (GS)
- Location: Often near CF
- Size: Variable
- Morphology: Depends on size and age of hemorrhage

DX: Intrauterine Fluid Collection

Ultrasoundographic Findings
- Hematoma appearance depends on age of bleed
  - Acute hematoma
  - Isoechoic to CF
  - Subacute hematoma
  - More hyperechoic than acute
  - Complex fluid collection
  - Fibrin strands resemble septations
  - Resolving hematoma
  - Sonolucent
  - May see fluid-fluid level
  - Hematoma size + with time
  - Eventually resolves
  - Curvilinear shape often seen
  - Follows contour of uterus
  - May extend completely around GS
  - Blood in subchorionic space
  - Can often be traced to edge of CF
  - May see edge of placenta lifted
  - Mass-like hematoma
  - May significantly compress GS
  - Distorted GS
  - PGH may be larger than GS
  - Difficult to find GS
  - Mimic anembryonic sac
  - May mimic > second GS
  - PGH may extend beyond subchorionic space
PERIGESTATIONAL HEMORRHAGE

Key Facts
- Pseudogestational sac (ectopic pregnancy)

Pathology
- 3.1% of all first trimester cases have PGH
- 20% of patients with vaginal bleeding have PGH

Clinical Issues
- PGH may be an incidental finding
- 10-15% spontaneous abortion rate with PGH

Diagnostic Checklist
- Use transvaginal ultrasound to carefully assess morphology of PGH and GS
- High-risk of pregnancy failure if GS < 16 mm at time of diagnosis
- Beware of twins mimicking PGH and vice versa
- 1st trimester PGH ⇒ 1 fetal/maternal morbidity later in pregnancy

Terminology
- Subchorionic hematoma

Imaging Findings
- Best diagnostic clue: Intraperitoneal fluid collection separate from and adjacent to gestational sac (GS)
- Hematoma appearance depends on age of bleed
- Curvilinear shape often seen
- May see edge of placenta lifted
- Distorted GS
- 90-95% have good outcomes when living embryo present
- PGH may mimic GS or twin gestation

Top Differential Diagnoses
- Chorioamniotic (CA) separation
- Diaphragmatic twinning

- May extend into placenta
- Large intraplacental hematoma
- Appears as placentation thickening when acute
- Blood in amniotic cavity
- Floating echogenicities in amniotic fluid
- Often present with large PGH
- Fetus swallows blood ⇒ echogenic bowel

Findings associated with poor prognosis
- Large hematoma
- > 50% CF detached
- GS apparent floating in uterine cavity
- Mishapen GS
- GS located in lower uterine segment
- GS detached completely
- Cervical os dilatation ⇒ miscarriage
- GS without: normal intrasac anatomy
- No yolk sac when GS > 8-10 mm
- No embryo when GS > 16-18 mm
- Anembryonic GS
- Bradycardia
- Embryo heart rate ≤ 90 beats/minute

- Most PGH resolves, with delivery of a normal infant
- 90-95% have good outcomes when living embryo present

Role of color Doppler
- Helps show inchootic PGH
- PGH without flow
- CF has block flow
- Helps identify detached CF
- Subplacental veins show areas of attachment

Imaging Recommendations
- Best imaging tool: Transvaginal ultrasound with color Doppler
- Protocol advice
- Look carefully at GS size and morphology
- PGH may mimic GS or twin gestation
- Short term follow-up helpful
- Normal GS grows 1 mm/day
- Hematoma should ↑ in size
- Hematoma will become less echogenic

DIFFERENTIAL DIAGNOSIS

Chorioamniotic (CA) separation
- Amnion seen separate from uterine wall
- Normal before 14 wks
- Membranes should fuse by 16 wks
- Chorionic fluid more echogenic than amniotic fluid
- Fluid less complex than PGH
- Causes of CA separation ⇒ 16 wks
- Invasive procedure (amniocentesis)
- Delayed CA fusion
- Associated with pre eclampsia
- Trisomy 21 most common
- Placental edge well attached
- Placental edge often lifted with PGH

Diaphragmatic twinning
- Second GS can mimic PGH
- Dichorionic
  - 2 GS with 2 distinct cords
  - "Thick" separating tissue
- PGH without distinct twinning
- Monozygotic twin less likely to mimic PGH
- Only one chorionic sac
- Thin separating membrane
- GS round while PGH often curvilinear
- Follow-up to see yolk sac/embryo development in sac

Pseudogestational sac (ectopic pregnancy)
- Endometrial blood
- Centrally located in endometrium
- No associated intratue-placental sac
- Adnexal mass
- Ectopic ring
- Hematoma
- Cut-sac echogenic fluid
- Intraperitoneal hemorrhage

PATHOLOGY

General Features
- General path comments
PERIGESTATIONAL HEMORRHAGE

- Blood usually collects in subchorionic space
- Potential space between chorion and uterus
- Can extend freely around GS in this space
- Large PGIH
- Blood may extend into chooroamniotic space
- Blood may extend into amniotic space
- Pregnancy failure associated with CF detachment
- Blood draws under placenta
- May detach GS completely

- Biology
  - Bleeding from CF
  - Most common
  - Loss from subamniotic vesical
  - Self-limited process

- Epidemiology
  - 3% of all first trimester cases have PGIH
  - 20% of patients with vaginal bleeding have PGIH
  - Associated abnormalities: Abnormal placenta

CLINICAL ISSUES

Presentation
- Threatened abortion
  - Bleeding
  - Uterine cramping
  - Closed cervical os
- Abortion in progress
  - Open cervical os + bleeding/pain
- PGIH may be an incidental finding
- Pattern: without symptoms
  - Elevated maternal serum alpha-fetoprotein (AFP)
  - Mixing of fetal and maternal blood at time of PGIH
- May see residual of PGIH at screen for AFP

Natural History & Prognosis
- 15-18% spontaneous abortion rate with PGIH
  - Severity of symptoms do not necessarily correlate with outcome
- Excellent prognosis if living embryo + small PGIH
  - > 90% miscarriage rate
- Guarded prognosis if early PGIH
  - GS < 16 mm + PGIH
  - 34% loss rate
  - Short-term follow-up
- Guarded prognosis with large PGIH
  - 20% loss rate even if living embryo present
- Poor prognosis if fetoplacental hematoma
  - > 50% of CF detachment greatest loss rate
- Poor prognosis if associated embryo hirudinlecia
  - 80% loss rate
  - Cervical os dilatation => near 100% loss rate
  - Cervical os dilatation in clinical diagnosis
- PGIH associated with maternal/fetal morbidity
  - 2nd trimester abruption (5.6% 1 risk)
  - Preclampsia (4.0X 1 risk)
  - Fetal growth restriction (2.4X 1 risk)
  - Preterm delivery (2.3X 1 risk)
  - Pregnancy induced hypertension (2.1X 1 risk)
  - Cesarean section (1.4X 1 risk)

Treatment
- Follow-up ultrasound
  - Look for normal first trimester landmarks

- Advise patient to seek care if bleeding worsens
- Most often self-limited process
- Follow-up 2nd/3rd trimester scan
- Follow human chorionic gonadotropin (hCG) levels
- Normally doubles every 48 hours in first trimester
- Should see GS when hCG levels are > 2,000 mIU/mL
- Epe (international reference preparation)
- Pregnancy failure
  - Diagnosis
  - Embryonic demise
  - Falling HCG levels
  - Anembryonic GS
- Treatment
  - Expectant management and miscarriage
  - Dilatation and evacuation of uterus

DIAGNOSTIC CHECKLIST

Consider
- Use transvaginal ultrasound to carefully assess morphology of FSH and GS

Image Interpretation Pearls
- Presence of a living embryo is most reassuring sign when PGIH seen
  - ≥ 90% pregnancy success rate if PGIH not large
- Follow-up ultrasound in 5-7 days helps in early cases
- Blood resolves quickly
- GS grows 1 mm/day
- Uterine pregnancy failure if GS < 16 mm at time of diagnosis
- Beware of twins mimicking PGIH and vice versa
- Careful pregnancy assessment in 2nd/3rd trimester
  - 1st trimester PGIH → 1 fetal/maternity ativity later in pregnancy
  - Associated with abnormal placenta

SELECTED REFERENCES

**IMAGE GALLERY**

**Typical**

(Detail) Axial ultrasound shows PCMs and an echogenic CS. The large anechoic CS (open arrow) is empty and the cystic, echogenic fluid collection (arrow) is blood. (Right) Axial ultrasound shows a large, circumferential PCM (arrow) and a small CS (curved arrow). Color Doppler shows a living embryo (open arrow). Large PCMs have a poor prognosis especially when the sac is < 16 mm. The patient miscarried 2 days later.

**Typical**

(Detail) Sagittal color Doppler ultrasound shows a hypoechoic cysticulous PCM (arrow) in a 12 wk pregnancy presenting with bleeding. The placenta (open arrow) is well attached. (Right) Ultrasound performed at 16 weeks in the same case shows residual PCM (arrow) at the base of the cervix (calipers). Echogenic dots in the amniotic fluid (open arrow) and echogenic bowel (curved arrow) from maternal blood.

**Variant**

(Detail) Ultrasound images from a transabdominal scan show 2 fluid collections (arrows) within the uterus mimicking the appearance of a twin gestation. (Right) Sagittal endovaginal ultrasound shows that the smaller fluid collection (arrow) is actually a PCM adjacent to an adherent normal appearing CS with a living embryo (curved arrow). The PCM is thin-walled and lies the edge of the chorionic membrane (open arrow).
**TUBAL ECTOPIC**

**TERMINOLOGY**

**Abbreviations and Synonyms**
- Ectopic pregnancy (EP)
- Tubal pregnancy

**Definitions**
- Ectopic gestation developing in fallopian tube

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue: No intrauterine pregnancy (IUP)
- Tubal mass + echogenic cut-de-sac fluid
- Location: Separate from ovary
- Morphology
  - Complex adnexal mass
  - From hemorrhage
  - Tubal ring
  - Similar to IUP gestational sac (GS)

**Ultrasoundographic Findings**
- Uterine findings vary
  - Thin endometrium
  - Empty uterus
  - Thick echogenic endometrium
  - Decidual reaction of pregnancy

- Adnexal mass in pregnancy
  - Endometrial cysts
    - Often small and multiple
    - Large cyst may mimic early IUP
  - "Pseudogestational sac" sign
  - Decidual cast
  - Ectometrial fluid (blood)
  - Lacks double-decimal sac sign of normal IUP
  - Heterotopic pregnancy (rare)
  - IUP + EP
  - Tubal findings
    - Adnexal abnormality in 80-95%
    - Tubal hematoma (40-60%)
    - Nonspecific mass
    - Heterogeneous echotexture
  - Tubal ring (50%)
    - Echogenic ring separate from ovary
    - +/- Yolk sac
    - +/- Embryonic cardiac activity
    - Tubal ring "lights up" with color Doppler
    - "Ring of fire"
    - May show small EP missed otherwise
  - Pulsed Doppler findings
    - High-velocity, low-resistance flow
    - Trophoblastic flow velocity > ovarian velocity
    - > 2.4 kHz common for trophoblastic flow
  - Ovary findings
    - Identify which ovary contains corpus luteum (CL)
    - 83% of ectopics on same side as CL
Key Facts

**Terminology**
- Ectopic gestation developing in fallopian tube

**Imaging Findings**
- Best diagnostic clue: No intrauterine pregnancy (IUP) + tubal mass + echogenic cul-de-sac fluid
- "Pseudogestational sac" sign
- Adnexal abnormality in 80-95%
- Tubal hematoma (40-60%)
- Tubal ring (50%)
- "Ring of fire"
- 85% of ectopics on same side as CL
- Ultrasound completely negative in 5-10% of cases
- 91% of EP accurately diagnosed
- Suspect EP if no IUP and hCG > 2,000 mIU/mL IRP
- Use endovaginal probe as a palpation tool

- Corpus luteum appearance is variable
  - Echogenic ring
  - Hypoechoic cyst
  - Anechoic cyst
  - Complex cyst from hemorrhage
  - Corpus luteum can mimic EP
    - CL is within ovary and tubal EP is outside of ovary
    - Corpus luteum Doppler findings
      - Similar to "ring of fire" but in ovary
    - CL flow velocity < trophoblastic tissue velocity
    - Low-reactive flow-like EP flow
    - Echogenic fluid in cul-de-sac
    - Blood within peritoneal space
    - Between uterus and rectum
    - Echogenic fluid
    - May need 1 gain settings to see echoes
    - Small amount of anechoic fluid considered physiologic
    - Clotted blood may be mass-like and complex
  - Blood may be an isolated finding
    - 42% will have EP if small amount of fluid seen
    - 73% will have EP if large amount of fluid seen
  - Role of transabdominal ultrasound
    - Look for upper abdomen fluid
    - Paracolic gasses
    - Morrison pouch (between liver and kidney)
  - Ultrasound completely negative in 5-10% of cases
  - No IUP, normal adnexa, no cul-de-sac fluid

**Imaging Recommendations**
- Best imaging tool
  - Transvaginal ultrasound + color Doppler
  - 91% of EP accurately diagnosed
- Protocol advice
  - Correlate findings with human chorionic gonadotropin (hCG) levels
    - Should see IUP when hCG levels are > 2,000 mIU/mL IRP (International reference preparation)
    - Suspect EP if no IUP and hCG > 2,000 mIU/mL IRP
  - Lack of IUP at low hCG levels does not rule out EP
  - EP's beta lower hCG levels/gestational age
  - Obtain sagittal cul-de-sac view in every case

**Top Differential Diagnoses**
- IUP
- Cervical pregnancy
- Incidental adnexal mass

**Pathology**
- 1.4% of all pregnancies are ectopic
- 95% of all ectopics are tubal

**Clinical Issues**
- Medical treatment with methotrexate preferred

**Diagnostic Checklist**
- Presence of IUP is best negative predictor of EP
- Can often find EP with hCG levels < 2,000 mIU/mL
- CL can mimic EP

**Differential Diagnosis**

**IUP**
- Gestational sac
  - Double decidual sac sign
- Perigestational hemorrhage common
  - Resembles pseudosac
  - CL appearance variable
  - Hemorrhagic CL
  - Echogenic cul-de-sac fluid if ruptured
  - Presence of IUP makes EP less likely

**Cornual pregnancy**
- Pregnancy in interstitial (cornual) portion of tube
  - Ectotopic gestational sac
    - Incomplete myometrial coverage
    - Sac within 5 mm of uterine serosa
  - At risk for rupture
  - Often later than EP
  - Can cause massive intraperitoneal hemorrhage
  - Treatment
    - Ultrasonoguided injection preferable to surgery
    - Methotrexate or potassium chloride

**Incidental adnexal mass**
- Parovarian cyst
- Unciliated and anechoic
TUBAL ECTOPIC

PATHOLOGY

General Features
- **Etiology**: Normal blastocyst implantation
- **Within uterine cavity on day 7 after ovulation**
- **Abnormal blastocyst implantation in tube**
- **Delayed transport = tubal implantation**
- **Abnormal tube is a risk factor for EP**
- **Chronic salpingitis**
- **Salpingitis-infermia medica**
- **Tubal surgery**
- **Prior IP**
- **Epidemiology**
  - 5.4% of all pregnancies are ectopic
  - 95% of all ectopic are tubal
  - 10-40% risk in fertility patients
  - 5-20% incidence if patient presents with pain/bleeding

CLINICAL ISSUES

Presentation
- **Most common signs/symptoms**: First trimester pain/bleeding
- **Other signs/symptoms**
  - Palpable adnexal mass
  - Cardiovascular shock
  - Incident diagnosis
  - No RUP and HCg < 2,000 mIU/mL
  - EP vs. fallag IUP
  - Low HCg level and negative ultrasound
  - EP vs. early IUP vs. failed IUP
  - Maternal serum progesterone levels
    - Helps predict normal IUP vs. EP/failing IUP
    - Can not differentiate EP from failed IUP
  - Serum progesterone and/or hCG levels with 95% sensitivity

Natural History & Prognosis
- **Delayed diagnosis = morbidity and death**
- **Case fatality rate has from 3.5 to 1,400**
- **2% to 4% of all pregnancy with ultrasound**
- **Prognois for future pregnancies**
  - 80% will have future IUP
  - 15-20% will have future EP
- **EP may resolve on own**
- **More likely if HCg levels are < 1,000 mIU/mL IR**
- **Most follow drop in HCg levels very carefully**
- **20% of all EP may spontaneously resolve**

Treatment
- **Medical treatment with methotrexate preferred**
  - Patient must be hemodynamically stable
  - No evidence for tubal rupture
  - Little or no peritoneal fluid
- **Early, unruptured, small ectopic**
  - 90%-50% success rate
- **EP < 4 cm**
- **HCg levels < 5,000 mIU/mL**
- **≤ 8 ws gestation**
- **70%-50% success rate if living embryo**
- **Multiple doses may be necessary**
- **Ultrasound after treatment is often confusing**
  - **Hemorrhage around EP**
  - **Size of EP**
  - **Use only if suspect tubal rupture**
- **Surgical therapy**
  - **Salpingectomy**
    - **Segment of tube removed**
    - Ends reconstituted if possible
    - **Only choioic for ruptured EP**
  - **Salpingectomy**
  - **Small lengthwise incision in tube**
  - **Removal of EP**
  - **Ultrasound guided local injection**
  - **Methotrexate or potassium chloride (KCl)**
  - **Injected directly into GS**
  - **Live ectopic + unruptured tube**
  - **30% fail systemic treatment**
  - **Preferred method for cornual and cervical ectopics**

DIAGNOSTIC CHECKLIST

Consider
- **Seal hCG levels in indeterminate cases**
  - Levels double every 2 days with normal IUP
  - Repeat ultrasound if hCG levels are rising
  - **Drop in hCG levels suggest failing pregnancy**

Image Interpretation Pearls
- **Presence of EP is best negative predictor of EP**
- **Can often first EP with hCG levels < 2,000 mIU/mL**
- **Do not delay ultrasound**
- **Look for “ring of fire” in alimenation color Doppler**
  - May detect a small EP when gray-scale findings are negitave
- **Be aware and beware of corpus luteum**
  - **CL can mimic EP**
  - **Offers on same side as EP**
  - **Can be cause of pain**

SELECTED REFERENCES

TUBAL ECTOPIC

IMAGE GALLERY

Typical

(Right) Septal endovaginal ultrasound shows a gestational sac (arrows). Only one layer of decidua (theca-luteal cist) surrounds the fluid. Complex calde-sac fluid (curved arrow) is also seen. (Right) Endovaginal ultrasound of the right adnexa in the same case shows a heterogenous adnexal mass (arrows) adjacent to the müllerian topography. Nonaccidental adnexal mass is common with tubal EP.

Typical

(Right) Endovaginal ultrasound images of a living embryo in a tubal ectopic. The tubal ring (arrows) is adjacent to the müllerian (open arrow) and contains a distinguishable embryo (calipers) and with sac (scared arrow). Minor or confirmed cardiac activity. (Right) Gross pathology from the same case shows a well-formed embryo (arrows) within the tubal gestational sac. Note the presence of extensive trophoblastic tissue around arrows.

Typical

(Right) Endovaginal ultrasound shows an echogenic ring (arrows) next to the müllerian (curved arrow). This ring “lights up” with power Doppler and inhibits the typical high-velocity, low-resistance flow of an EP. (Right) Endovaginal ultrasound of the right adnexa shows a CT scan with the arrow (open arrows), but no other obvious findings. Color Doppler shows a “ring of fire” from an EP. Color Doppler may aid in defining a small EP that might otherwise be missed.
INTERSTITIAL ECTOPIC

TERMINOLOGY

Abbreviations and Synonyms
- Interstitial ectopic pregnancy
  - Preferred term
- Cornual ectopic pregnancy
  - Often used interchangeably
  - More appropriately applied to pregnancies in a rudimentary horn
- Intramural ectopic pregnancy
- Angular pregnancy
- Pregnancy implanted at lateral angle of uterine cavity by isthmus
- Medial to interstitial portion of tube and round ligament

Definitions
- Pregnancy occurring in interstitial portion of fallopian tube

IMAGING FINDINGS

General Features
- Best diagnostic clue
  - Combination of findings
  - Interstitial line sign: Echogenic line from endometrium to ectopic sac

- Myometrium thinned to < 5 mm
- Location
  - Intertitial (interrunual) portion of fallopian tube
  - Connects uterine cavity to isthmus (extratubal portion of tube)
- 1 cm in length, 1 mm in diameter
- Size: Covered by myometrium so can grow to larger size than tubal ectopics
- Early interstitial pregnancy often difficult to diagnose
  - 12% of cases missed in other large series

Ultrasonographic Findings
- Gestational sac located high in fundus
  - Ectomically located with respect to endometrial cavity
- Appearance of sac contents quite variable
  - Gestational sac +/- yolk sac, embryo
    - Gestational sac and embryo can be quite large
  - May appear as echogenic mass within cavity
  - Combination of trophoblastic tissue, hematoma
  - No definable sac
  - Thinned myometrium
  - < 5 mm of surrounding myometrium very suggestive
  - May have areas where no definable myometrium is seen
  - Normal myometrium may be seen early and does not exclude an interstitial ectopic

DDx: Uterine Duplication Anomalies

- Uterus Didelphys
- Bicornuate
- Septate
- Septate
INTERSTITIAL ECTOPIC

Key Facts

**Terminology**
- Pregnancy occurring in interstitial portion of fallopian tube

**Imaging Findings**
- Intestinal line sign: Echogenic line from endometrium to ectopic sac
- Gestational sac located high in fundus
- Eccentrically located with respect to endometrial cavity
- Gestational sac and embryo can be quite large
- May appear as echogenic mass within normal
- < 5 mm of surrounding myometrium very suggestive
- Normal myometrium may be seen early and does not exclude an interstitial ectopic
- Intestinal line sign has reported sensitivity of 80% and specificity of 98%

**MR Findings**
- Has been shown accurate in diagnosis
- Ectopic sac separated from endometrium by junctional zone
- Generally not necessary
- Consider when ultrasound finding are equivocal or pre-operative planning for large ectopics
- Generally avoided in first trimester unless clinical situation warrants

**Imaging Recommendations**
- Always document location of sac with respect to endometrium in both transverse and longitudinal views
- Measure surrounding myometrium if it appears thin
- Look for echogenic line leading to myometrium (interstitial line sign)
- Use 3D ultrasound if available
- If unclear, short term follow-up with careful instructions to patient to return immediately if symptoms occur
- May consider MRI if still unclear

**Top Differential Diagnoses**
- Normal intrauterine pregnancy
- Uterine duplications

**Pathology**
- 2-4% of ectopic pregnancies are interstitial
- Mortality rate 2-2.5%

**Clinical Issues**
- Hyperesthesia and shock if presenting with rupture
- Significantly greater morbidity and mortality than for tubal ectopic
- Uterine rupture most commonly occurs at 9-12 weeks

**Diagnostic Checklist**
- Despite technical advances, diagnosis of interstitial ectopic pregnancy remains difficult

**DIFFERENTIAL DIAGNOSIS**

**Normal intrauterine pregnancy**
- High, eccentric implantation may be confusing
- Should always have normal myometrial coverage
- Follow-up scan shows normal development

**Uterine duplications**
- Duplication of endometrial cavity
- Implantation within one horn gives eccentric appearance
- Myometrium will completely surround gestational sac in all types
- May give false appearance of interstitial line sign
- Can follow an echogenic line to main cavity
- Close evaluation shows it is curved, rather than straight
- Classification system based on external contour
  - Uterus didelphys
  - Two separate uteri
  - Easiest to distinguish from interstitial ectopic
- Bicornuate
- External contour of uterus is concave
- Must obtain views of uterine fundus to adequately evaluate contour
- Septate
- External uterine contour is normal
- Most likely congenital anomaly to be confused with interstitial ectopic
- Septum extends for variable lengths (subseptate vs. complete)

**Tubal ectopic**
- Can occasionally be confusing if adjacent to cornual of uterus
- Use ultrasound probe to gently separate structures

**PATHOLOGY**

**General Features**
- Ectopic
- Risk factors
INTERSTITIAL ECTOPIC

• History of prior tubal surgery, especially salpingectomy
• Prior ectopic pregnancy
• Assisted reproductive technology (ART) pregnancies
• May see heterotopic pregnancy with ART with one sac in common
  - Intrauterine contraceptive devices (IUD) are not associated with interstitial ectopies
• Ectopic pregnancies more likely to be in tube when IUD present
• Epidemiology
  - 2.4% of ectopic pregnancies are interstitials
  - Mortality rate 2-2.5%
• Microscopic Features
  - Intestinal portion of tube composed of multiple layers
  - Endosalpinx (mucusa)
  - Myometrium
  - 3 layers of muscle
  - Highly vasculonized
  - Serosa is directly continuous with peritoneum

CLINICAL ISSUES

Presentation
• Most common signs/symptoms
  - Pelvic/abdominal pain
  - Vaginal bleeding
• Other signs/symptoms
  - Hypotension: monitor blood pressure
  - Shock: monitor heart rate
• May be an incidental finding, routine 1st trimester scan
  - Easier to diagnose early scan

Natural History & Prognosis
• Significantly greater morbidity and mortality than for tubal ectopic
• Surrounding mesovarium is distensible, allowing for greater gestational sac size
• Ultrasound gestation most commonly occurs at 7-12 weeks
• May occur earlier
• Potential ex dangium
• Large accurate vessels run in outer third of placenta
• Good outcome, with preserved future fertility, with appropriate treatment

Treatment
• Systemic methotrexate
  - Follow human chorionic gonadotropins (hCG) after initial dose
  - May require second dose if levels do not fall appropriately
• Failed treatment goes to surgery
• SAC injection
  - Generally with methotrexate
  - Via laparoscopy or ultrasound guidance
• Potassium chloride, etoposide also used
• Emergencies with sac excision
  - May be done with laparoscope or laparotomy
  - Expectant management

• Considered only if small sac and no living embryo
• Rupture may require hysterectomy
• May consider uterine artery embolization prior to surgery

DIAGNOSTIC CHECKLIST

Consider
• 3D ultrasound for improved spatial orientation of sac to endometrial cavity

Image Interpretation Pearls
• Despite technical advances, diagnosis of interstitial ectopic pregnancy remains difficult
• Must have a high degree of suspicion, especially in a high-risk patient
• Short term follow-up for any sac which appears high and eccentric

SELECTED REFERENCES
INTERSTITIAL ECTOPIC

IMAGE GALLERY

Typical

(Left) Axial endovaginal ultrasound shows the interstitial line type (arrow), which extends from the endometrium to the ectopic gestational sac (curved arrow). The surrounding myometrium is thinned.

(Right) Axial color Doppler ultrasound in another case shows flow around the interstitial ectopic (arrow=endometrium). Prominent arcuate vessels (open arrow) are seen in the outer third of the myometrium. Exaggeration may occur if the uterus ruptures.

Typical

(Left) Ultrasound of a 13.5 week interstitial ectopic with questionable myometrial coverage around the lateral aspect of the sac (arrow).

(Right) Axial T1W MRI was likewise concerning for areas of absent myometrium (arrow).

Typical

(Left) Sagittal T2W MRI in the same case shows the normal myometrium rapidly thinning (arrow) and becoming a thin membrane (curved arrow) around the large ectopic sac. Blood (open arrow) is seen in the sub-serum. (Right) Coronal T2W photograph at the right cornus shows two areas of rupture (arrow). Catastrophic hemorrhage may occur without prompt medical treatment.
CERVICAL ECTOPIC

TERMINOLOGY

Definitions
- Implantation of gestational sac within cervical stroma

IMAGING FINDINGS

General Features
- Best diagnostic clue: Gestational sac within cervical stroma with live embryo
- Morphology:
  - Gestational sac usually round
  - Similar appearance to normal pregnancy
  - Can be elliptical or flattened making diagnosis more difficult

Ultrasonographic Findings
- Gray scale Ultrasound:
  - Eccentric sac within cervical stroma
  - Endometrial/cervical canal visualized separately, adjacent to sac
  - "Hourglass" shaped uterus
  - Secondary to cervical dilation from pregnancy
- Embryo with heartbeat often present
- Internal or closed
- Decidual reaction of endometrium
- Color Doppler

- Marked peripheroblastic flow around sac
- Can be deceiving as early demise can also have some persistent vasculatized tissue

Imaging Recommendations
- Transabdominal ultrasound aids in identifying anatomic landmarks:
  - Uterine shape
  - Uterine position
  - Intestinal loops
  - Bladder and bladder wall
- Transvaginal ultrasound helpful to characterize early gestational sac
  - Aids in evaluating uterine cavity to differentiate from abortion in progress
  - Can also better evaluate adnexa
- Rare, but should exclude heterotopic pregnancy:
  - Especially in the setting of assisted reproductive technology or hormonal stimulation
- Ultrasound localization for medical treatment:
  - Used for guidance of needle into sac
  - Subsequent injection for termination
  - Methotrexate
  - Potassium chloride

DDx: Cervical Mass

- Spontaneous Menstr
- Prolapsed Polyp
- Cervical Adenoma
- Tubo-ovarian Mass
CERVICAL ECTOPIC

Imaging Findings
- Eccentric sac within cervical stroma
- "Hourglass" shaped uterus
- Internal os closed
- Masked posttrophoblastic flow around sac

Top Differential Diagnoses
- Normal pregnancy with low uterine implantation
- Spontaneous abortion
- Cesarean section (C-section) scar ectopic
- Nabothian cyst

Pathology
- Prior instrumentation key risk factor
- Endometrium is injured, adversely impacting implantation of pregnancy
- Epidemiology: 4% of ectopic pregnancies

Key Facts
- Cervical mucosa vulnerable to trophoblast proliferation

Clinical Issues
- Potentially fatal if unrecognized
- Preservation of fertility usually successful when treated conservatively
- Medical management advisable if possible
- Hysterectomy, if conservative therapy fails

Diagnostic Checklist
- Always consider if gestational sac has a low implantation
- Be suspicious of a cervical ectopic if gestational sac is in or near the cervix is round instead of flattened
- A living embryo within a cervical sac is highly suspicious for an ectopic pregnancy

Differential Diagnosis

Normal pregnancy with low uterine implantation
- Sac will be show internal os
- Eccentric location in decidualized endometrium
- Normal pregnancy milestones should be identified
  - Early sac correlates with serial human chorionic gonadotropin (hCG) levels
  - Should double every 48 hours in early pregnancy
  - Look for normal yolk sac
  - Should be seen by mean sac diameter of 20 mm
  - Normal diameter ≤ 6 mm
  - Located outside amnion
  - Identify presence of embryo
  - Should be seen by mean sac diameter of 18 mm
  - Must have a heart beat if ≥ 5 mm

Spontaneous abortion
- Irregular, deformed, flattened sac
  - Centered in cervical canal
  - Mobile with gentle pressure ("sliding sign")
- Use transvaginal probe to visualize
- Lacks surrounding edematous ring
- May see spontaneous movement of sac through endocervical canal
- Repeat scan in a few hours may show complete passage
- No embryo/fetal heart beat
- Enlarged globular uterus
  - Typical hourglass shape of cervical ectopic not seen
- Internal os open
- Externally may or may not be open at time of clinical exam
- Correlate with serial hCG
- Should be decreasing with miscarriage

Cesarean section (C-section) scar ectopic
- Can be difficult to distinguish from cervical ectopic
- Correlate with prior history of C-section
- Look for thinned or absent myometrium at scar

- Trophoblastic tissue may invade into adjacent bladder
- Medical treatment is similar to cervical ectopic
  - Helpful to distinguish if surgery planned
  - May require scar revision

Nabothian cyst
- Obstructed mucous secreting endocervical glands
- Thought to result from prior inflammation
- Asymptomatic, incidentally noted on pelvic ultrasound
- Eccentric within cervical stroma
- Anechoic or low-level echoes
- May be single or multiple
- Usually 2-10 mm but may be larger
- No surrounding increased vascularity on Doppler evaluation
- Generally follows fluid signal intensity on MRI
  - Low signal T1WI, high signal T2WI
- Occasionally mucin causes high signal on T1WI

Cervical mass
- Cervical fibroid
  - Hypoechoic cervical mass
  - Can be documented from myometrium
  - If passes into cervix can present with pain
  - Can protrude into vagina
  - MRI
  - Intermediate signal T1WI, low signal T2WI
- Cervical polyp
  - Either from cervix or prolapsed from endometrium
  - Solid lesion in cervical canal
  - Polyps may have cystic areas
  - Vascularity seen with color Doppler ultrasound
  - May have dominant feeding vessel
- Cervical carcinomas
  - Irregular cervical mass
  - Better evaluated with pelvic MR
  - Intermediate signal mass invading cervical stroma
CERVICAL ECTOPIC

PATHOLOGY

General Features
- Etiology
  o Prior instrumentation key risk factor
  o Endometritis is injured, adversely impacting implantation of pregnancy
- Multiple etiologies of endometrial injury
  o Dilatations and curettage
  o In vitro fertilization with embryo transfer
  o Previous cervical procedure: Loop electrosurgical excision procedure (LEEP), conization, cryosurgery
  o Prior C-section
  o Previous uterine surgery
  o Atheromas syndrome
  o Epidemiology: ~1-4% of ectopic pregnancies

Gross Pathologic & Surgical Features
- Trophoblastic invasion into cervical stroma
- Insufficient vascularization within cervix to support gestation

Microscopic Features
- Cervical miomata vulnerable to trophoblast proliferation
- Allows deep penetration of chorionic villi

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  o Bleeding
    o Usually painless
  o Other signs/symptoms
    o May be incidental finding on early viability scan
    o Often larger and presents later than tubal ectopic
    o Abdominal/pelvic pain
    o Hypotension and shock if ruptured
    o Urinary problems
    o Dissected cervix
    o Endometrial dilatation

Natural History & Prognosis
- Potentially fatal if unrecognized
  o May rupture
  o Uncontrolled hemorrhage can result
  o Good with appropriate treatment
- Preservation of fertility usually successful when treated conservatively

Treatment
- Medical management advisable if possible
  o Methotrexate
  o Injected into sac
  o Systemic administration
  o Potassium chloride injection into sac
  - May use combined approach of sac injection followed by systemic methotrexate
  - Close follow-up required to document regression of pregnancy
- Follow-up ultrasound to show centrometric descent and/or sac resorption
- Serial hCG should show declining levels

- Uterine artery embolization
  - Can be used to attempt hemostasis if significant bleeding occurs
  - May be required even if medical therapy initiated
- Hysterectomy, if conservative therapy fails
- Require in setting of uncontrolled, massive hemorrhage
  - Large ectopic
  - Other methods also reported
  - Caretage of ectopic cervical remnants of pregnancy
  - Following injection of sac
  - Hysteroscopic resorption of sac and tissue

DIAGNOSTIC CHECKLIST

Consider
- Always consider if gestational sac has a low implantation

Image Interpretation Pearls
- Be suspicious, of a cervical ectopic if a gestational sac in
  or near the cervix is round instead of flattened
- A living embryo within a cervical sac is highly suspicious for an ectopic pregnancy
- A follow-up scan in a few hours will show change or passage of the sac if a spontaneous abortion

SELECTED REFERENCES

CERVICAL ECTOPIC

IMAGE GALLERY

Typical

Variant

Variant

(Left) Color Doppler ultrasound of the uterus shows mild vascularity, surrounding a gestational sac in the cervical canal (panel). The sac has a fetiform appearance, suggestive of a spontaneous abortion.

(Right) Monochorionic ultrasound shows a heartbeat but no embryo, making a cervical ectopic more likely. A manual evacuation 3.5 hours later confirmed the diagnosis. The heartbeat would be gone and we either change or passed with a spontaneous abortion.

(Left) Sagittal ultrasound of a large cervical ectopic shows a 3.5 week living fetus (sacoidal arrow) and placenta (arrows) implanted within the cervical canal — open arrow.

(Right) Coronal 11/17 MRI shows the fetus (arrow) within the cervix. Open arrow shows the zygote. The uterus is out of the plane of section, the patient underwent intervention.

(Left) Cross-pathology from the case above shows marked enlargement of the cervix (arrows) with an associated myometrial fibromyoma. Sagittal axial (arrows) — open arrow.

(Right) Sagittal 1/17 MRI from a different case shows intramural extension into the cervical area. Arrows near a cervical ectopic indicate a curvilinear aspect. There is also blood within the endometrial cavity (open arrow).
**ABDOMINAL ECTOPIC**

![Image of ultrasound scans showing abdominal ectopic pregnancy]

**TERMINOLOGY**

Definitions
- Pregnancy outside of the uterus and within the peritoneal cavity

**IMAGING FINDINGS**

General Features
- Best diagnostic clue
  - Gestational sac with embryo or fetus in abdomen
  - Uterus identified separately

Ultrasoundographic Findings
- Lack of normal, hypoechoic rim of myometrium surrounding gestational sac
- Most often in pouch of Douglas or posterior uterine wall
- Implantation sites also include various abdominal structures
  - Omentum, mesentery, bowel
  - Liver, spleen
  - May implant on multiple sites
- Echogenic free fluid (hemorrhage) may be present

Imaging Recommendations
- Abdominal MRI useful

**DIFFERENTIAL DIAGNOSIS**

Tubal ectopic pregnancy
- Less likely to see a true embryofetus
- Echogenic tubal ring or hemorrhage most common findings

Intrauterine pregnancy
- Hypoechoic endometrium surrounds gestational sac

**PATHOLOGY**

General Features
- Epidemiology: Approximately 1% of all ectopic pregnancies

Gross Pathologic & Surgical Features
- Primary abdominal pregnancy
  - Extremely uncommon

**Dx: Other Ectopic Pregnancies**

- Heterotopic Pregnancy
- Liver Tubal Ectopic
- Ruptured Ectopic
- Endometrial Ectopic
ABDOMINAL ECTOPIC

**Imaging Findings**
- Gestational sac with embryo or fetus in abdomen
- Lack of normal, hypercohesive rim of myometrium surrounding gestational sac
- Most often in pouch of Douglas or posterior uterine wall

**Top Differential Diagnoses**
- Tubal ectopic pregnancy
- Intrauterine pregnancy

**Key Facts**
- **Pathology**
  - Ectopic pregnancy: Approximately 1% of all ectopic pregnancies

**Clinical Issues**
- Significant rate of maternal morbidity and mortality
- Placental embolization reported to be successful in decreasing placental mass

**CLINICAL ISSUES**

**Presentation**
- Most common signs/symptoms
  - Abdominal pain
  - Hypotension
  - Hypovolemic shock may occur secondary to massive hemorrage
  - Incidentally noted on routine ultrasound or anatomic survey

**Natural History & Prognosis**
- Significant rate of maternal morbidity and mortality
- Higher maternal mortality rate than with other types of ectopic pregnancy
- Most will cause intraperitoneal bleeding
- Spontaneous demise of embryo/fetus occurs when blood supply becomes insufficient
- Insuficient blood supply to carry pregnancy to viability

**Treatment**
- First trimester
  - Potassium chloride injection into sac or embroyo
  - Methotrexate
  - Systemic or injection into sac
  - Surgical evacuation of pregnancy may be necessary if bleeding persists
- Second trimester
  - Consider presurgical embolization of placental vessels
  - Surgical evacuation of fetus
  - Third trimester (rare)
  - Consider watchful waiting if near viability
  - Immediate delivery of signs of bleeding
  - Surgical delivery of fetus
  - Placenta not necessarily removed surgically

- Placental embolization reported to be successful in decreasing placental mass
- CT used to follow regression of residual placental tissue in abdomen
- Serial beta-hCG after evacuation to document appropriately declining levels

**DIAGNOSTIC CHECKLIST**

**Image Interpretation Pearls**
- Always assess for hypercohesive myometrium around developing pregnancy to prove intrauterine location

**SELECTED REFERENCES**
5. Debrococo E et al: Laparoscopic pregnancy; sonography and CT findings. JBR-BTR. 17(6):577-8, 1999

**IMAGE GALLERY**

*Left*: Axial T2W MRI of a second trimester abdominal pregnancy shows the fetal head and a placental mass above the uterus. Note the no other apparent myometrial signal. *Right*: Axial CT scan shows a large residual placental mass at the level of the umbilicus. Both images demonstrate the abdominal location of the pregnancy. (Images courtesy of Dr. F. Chestnutt)
C-SECTION SCAR ECTOPIC

TERMINOLOGY

Definitions
- Ectopic pregnancy developing at the cesarean section (C-section) scar

IMAGING FINDINGS

General Features
- Best diagnostic clue:
  - Eccentric gestational sac within anterior myometrium at site of cesarean section scar
  - Empty uterine cavity and cervical canal
  - Thinned or absent myometrium at scar between sac and bladder
  - Color Doppler shows marked peritrophoblastic flow around sac
- Generally: low-impedance, high-velocity flow
- Useful to detect invasion into bladder

Imaging Recommendations
- Assess for other associated complications of prior C-section
  - Placenta accreta, increta or percreta
  - Placenta previa
  - Placental abruption

DIFFERENTIAL DIAGNOSIS

Cervical ectopic
- Located within cervical stroma
- Can be difficult to distinguish from C-section scar ectopic, especially if sac is large
- May be lateral or posterior, not just anterior as with C-section scar ectopic

Prominent C-section scar
- Varied appearance
  - Wedge-shaped anechoic defect in anterior myometrium
  - Cystic fluid collection within incision site
- Consider evaluation of C-section scar and uterine wall integrity prior to conception in patients at high risk of complications
  - In vitro fertilization patients
  - Multiple prior C-sections

Adenomyosis
- Well-defined, hypoechoic, thickened junctional zone
- Ectopic glands create small cysts, which could be confused with C-section ectopic
  - Most cysts are 2-3 mm but can be as large as 4 cm

DDx: C-Section Scar Variations And Ectopic Mimes
C-SECTION SCAR ECTOPIC

KEY FACTS

- Can be asymptomatic initially
- Massive bleeding usually occurs by late first trimester if not treated
- High risk of uterine rupture
- Avoid isolated dilatation and curettage

DIAGNOSTIC CHECKLIST

- Prominent, cystic C-section scar can mimic early ectopic gestational sac
- Revision/resection of C-section scar
- Avoid isolated dilatation and curettage
- Trophoblastic tissue invading myometrium unlikely to be fully removed
- Risk of perforating uterine wall and/or damaging bladder
- May lead to massive bleeding

SELECTED REFERENCES


IMAGE GALLERY

(left) Sagittal endovaginal ultrasound shows the gestational sac located within the wall of the lower uterine segment at 7 weeks gestation with a fetus of 1st trimester外形 seen within the gestational sac, Figure 1 shows the contrast of the uterine wall and the gestational sac, Figure 2 shows the contrast of the uterine wall and the gestational sac.
**TERMINOLOGY**

**Definitions**
- Two concurrent pregnancies, at least one of which is ectopic in location
  - Tubal, cervical, cornual, abdominal, cesarean section scar
  - Usually one intrauterine pregnancy with tubal ectopic pregnancy
  - Triplet heterotopic pregnancies reported

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue: intrauterine embryo/fetus with second ectopic pregnancy

**Imaging Recommendations**
- Identify intrauterine pregnancy
- Look for echogenic free fluid or adnexal mass/ring
- Use color Doppler whenever ectopic is suspected
  - Increased trophoblastic flow creates "ring of fire"
- Helpful for identifying small ectopic pregnancies, which might otherwise be missed

**DIFFERENTIAL DIAGNOSIS**

**Ectopic pregnancy**
- Much more common
- Pseudosac may mimic a true gestational sac simulating a heterotopic pregnancy
  - Centrally fluid collection
  - Normal sac is eccentric to endometrial cavity
  - No double decidual sac sign

**Uterine duplication**
- May appear as heterotopic pregnancy
  - Twins with one sac in each horn
  - Single sac with fluid in other horn
  - Myometrium completely surrounds each sac
  - No adnexal masses
  - Types of anomalies
    - Didelphys: 2 separate uteri
    - Bicornuate: Concave fundal contour
    - Septate: Normal fundal contour

**PATHOLOGY**

**General Features**
- Epidemiology
  - < 1:30,000 naturally conceived pregnancies
  - Incidence is increasing

**DDx: Two Sacs Simulating Heterotopic Pregnancy**

- Ectopic, Pseudosac
- Ectopic, Adnexas
- Bicornuate Twins
- Bicornuate Twins
HETEROTOPIC PREGNANCY

Terminology
- Two concurrent pregnancies, at least one of which is ectopic in location

Top Differential Diagnoses
- Ectopic pregnancy
- Uterine duplications

Pathology
- < 1:30,000 naturally conceived pregnancies

○ 1:100-500 following assisted reproductive technology (ART) pregnancies
○ Damage to endometrium or fallopian tubes predisposes to ectopic pregnancy implantation
○ Tubal damage
○ Prior ectopic pregnancy
○ Endometriosis
○ Prior salpingectomy
○ Pelvic inflammatory disease
○ History of pelvic surgery
○ Intrauterine contraceptive device
○ Uterine anomalies

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  ○ Abdominal pain
  ○ Adnexal mass
  ○ Vaginal bleeding
  ○ Hypovolemic shock if ruptured

Natural History & Prognosis
- Depends on size and location of ectopic
- Approximately 60% of treated heterotopic pregnancies deliver live fetus

Treatment
- Surgical management treatment of choice, to preserve intrauterine pregnancy
  ○ Salpingectomy
  ○ Small longitudinal incision in tube
  ○ Removal of ectopic pregnancy
  ○ Salpingectomy
  ○ Segment of tube removed
  ○ Ends reconnected if possible
  ○ Only choice if ruptured ectopic

Medical treatment
- Potassium chloride (KCl) injection into ectopic sac
- Methotrexate injection into sac
- Slows trophoblastic tissue growth
- Less favored due to potential risk of toxicity to intrauterine embryo
- Combination of KCl and methotrexate injection

- Serial beta hCG measurements
- May be misleading, as normal pregnancy placental production will be high

Key Facts
- 1:100-500 following assisted reproductive technology (ART) pregnancies
- Damage to endometrium or fallopian tubes predisposes to ectopic pregnancy implantation

Clinical Issues
- Approximately 60% of treated heterotopic pregnancies deliver live fetus
- Surgical management treatment of choice, to preserve intrauterine pregnancy

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls
- Careful evaluation of high-risk patients warranted to exclude heterotopic pregnancy
  ○ Always carefully check adnexa, even if intrauterine pregnancy identified
  ○ Especially important if patient presents with pelvic pain

SELECTED REFERENCES

IMAGE GALLERY

(left) Sagittal ultrasound Views an eccentric gestational sac located within the uterus. A closed membrane is present. Junctional trophoblastic tissue or embryo is identified, consistent with a heterotopic pregnancy. (right) Transverse ultrasound reveals an eccentric gestational site in the right adnexa, adjacent to the intrauterine gestation. This is consistent with a heterotopic pregnancy.
TERMINOLOGY

Abbreviations and Synonyms
- Increased nuchal translucency (1 NT)
- Increased nuchal lucency
- Thickened nuchal fold

Definitions
- Fluid under skin in back of fetal neck
  - Measurement performed at 11-14 wks menstrual age
  - Marker for aneuploidy
  - Trisomy 21 (T21) most common
  - Marker for congenital heart defect (CHD)

IMAGING FINDINGS

General Features
- Best diagnostic clue
  - NT > 95th percentile for menstrual age (MA)
  - NT ≥ 3 mm always abnormal (11-14 wks MA)
- Location
  - Fluid is underneath skin
  - May extend beyond neck
  - Inferiorly to back
  - Superiorly to scalp
  - Anteriorly to abdomen
- Size

DDx: Pitfalls In NT Measurements
- Amniotic
- Barred fetal position
- Large cystic hygroma
- Amnion

Variable
- Most often NT is minimal
- Morphology: Usually simple fluid without septations

Ultrasoundographic Findings
- NT measurement technique
  - Transabdominal ultrasound often adequate
  - 95% success rate
  - 5% require transvaginal exam
  - Success rate for obtaining accurate NT near 100%
  - Takes time and patience
- Small window of opportunity for NT screening
  - 11-14 wks MA
  - Crown-rump length (CRL) of 45-64 mm
  - Biparietal diameter < 27 mm
- Mid sagittal plane
  - Beam perpendicular to skin
  - Maximizes ability to discern skin
- Image magnification crucial
  - Head, neck, upper chest occupies ≥ 75% of image
  - Fetal head in neutral position
  - Flexion minimizes NT
  - Extension falsely minimizes NT
  - Beware of amnion
  - Gravity dependent; fetus may lie on amnion
  - Wait for fetus to move away
  - Show amnion and skin on same image
  - Correct caliper alignment critical
INCREASED NUCHAL TRANSLUCENCY

Terminology
- Increased nuchal translucency (1 NT)
- Fluid under skin in back of fetal neck
- Measurements performed at 11-14 wks menstrual age
- Marker for aneuploidy
- Trisomy 21 (T21) most common
- Marker for congenital heart defect (CHD)

Imaging Findings
- Success rate for obtaining accurate NT near 100%
- Correct caliper placement critical
- NT associated with hydrops
- Ultrasound testing: NT + maternal serum screen
- 90% detection rate for aneuploidy

Top Differential Diagnoses
- Choiorriamnionic separation

Key Facts
- Poor measurement technique
- Cystic hygroma

Pathology
- Abnormal lymphatic drainage
- Early heart failure

Clinical Issues
- 90% normal outcome if no aneuploidy
- Larger NT has worse prognosis

Diagnostic Checklist
- Perform NT screening only in certified lab
- Fetal echocardiography if NT and normal chromosomes
- Amniotic membrane is a potential pitfall in measuring NT

- Use "+" calipers only
- Can not use "-" calipers
- Caliper border anechoic space
- Transverse caliper line excluded skin
- True measurement of fluid only
- Measure largest fluid depth
- Accurate and sensitive calibration necessary
- Incremental increase in calipers of 0.1 mm
- Example: Can measure 2.1 - 2.2 mm
- Machine must have cine-loop ability
- 1st trimester fetal movement is "static"
- Abrupt flexion and extension common
- Cine to appropriate neutral position

Measurement criteria for 1 NT
- NT measurement + 95% percentile for MA
- Certified labs have software to calculate percentile
  - NT > 3 mm always abnormal
  - NT < 3 mm may be normal

1 NT and chromosome abnormalities
- Trisomies 13, 18, 21
- Most common
- 1 NT leads to m. nuchal fold in 2nd trimester
- Trisomy 18 (T18)
- Early intrauterine growth restriction may be present
- Trisomy 21 (T21)
- Other anomalies are detectable in 1st trimester
- CARD defects
- Intracardiac echogenic focus
- Echopleocephaly
- Severe facial anomaly
- Turner syndrome
- Diarrhea with largest NT
- Septations may be seen
- Associated hydrops

1 NT and non-chromosome abnormalities
- CHD
- 2X NT if NT > 99th percentile (normal chromosome)  
- Cardiac defect rarely obvious at 11-14 wks
- Syndromes and 1 NT
- Nuchal edema
- Myotonic dystrophy
- Many other syndromes

- 1 NT associated with hydrops
  - T13 + skin edema
  - T13, 18, 21, 13 + pleural effusion
  - More common with Turner syndrome
  - Can be seen regardless of cause of 1 NT

- Pitfalls
  - Amniotic edema
  - Gravity dependent fetus lies on amnion
  - Can mimic fetal skin
  - Wait for fetus to move away from amnion
  - Nuchal cord
  - 5-10% incidence in 1st trimester
  - Presence makes NT measurement difficult
  - Measure below and above nuchal cord
  - Report smallest NT number

Imaging Recommendations
- Ret imaging tool: NT measurement by certified sonographers/sonologist
- Protocol advice
  - Fetal medicine foundation (FMF) certification should be obtained before performing
  -Certifies individuals to perform NT measurement
  - Education course required
  - Ultrasound and video tape review required
  - Ultrasound testing: NT + maternal serum screen
  - Obligatory FMF certification
  - First trimester maternal serum screen
  - Free E-human chorionic gonadotropin (β-hCG)
  - Prenatal landscape of pregnancy-associated plasma protein A (PAPP-A)
  - 1 β-hCG, 1 PAPP-A with 121
  - Can aid nasal bone assessment
  - Look for absence of nasal bone
  - Part of ultrasound program now
  - Improves detection rates for aneuploidy
  - Aneuploidy detection rates using NT alone:
    - 82% for 121
    - 82% for 116
    - 80% for 113
  - 80% for Turner syndrome
INCREASED NUCHAL TRANSLUCENCY

Differential Diagnosis

- Chorionicamniotic separation
  - Normal at 11-14 wk MA
  - Amnion confused for fetal skin
  - Fetus less supine upon amnion
  - Measurement taken from fetus to amnion
  - NT measurement requires patience
  - Wait to see fetus move away from amnion

- Poor measurement technique
  - Image not adequately magnified
  - Calipers not correctly placed
  - Incorrect orientation of fetus
  - Measurement performed late (> 14 wks)

- Cystic hygroma
  - Large fluid collection behind fetal neck
  - Septations common
  - Can mimic amniotic fluid
  - Often with associated hydroxy
  - More often second trimester diagnosis
  - 2/3 with chromosomal abnormality
  - Turner syndrome most common
  - Trisomy 21

PATHOLOGY

General Features

- Genetics
  - Trisomy 21
  - Trisomy 18
  - Trisomy 13
  - Turner syndrome
  - Most often normal chromosomes

- Biology
  - Abnormal lymphatic drainage
  - Delayed lymphatic development
  - Reduction lymphatic channels
  - Genetic abnormality
  - Movement disorder
  - Early heart failure
  - Congenital infection
  - Fetal anemia
  - Abnormal extracellular matrix
  - Proteins encoded on chromosomes 21, 18, 13
  - Associated abnormalities
    - Non-chromosomal structural abnormalities
    - Cardiac defects
    - Musculoskeletal dysplasia
    - Skeletal dysplasia
    - Hydrops fetalis
    - Ophthalmologic

- VACTERL association

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
  - Incidentally seen during first trimester ultrasound
  - Detected during ultrasounds test

Demographics

- Age
  - Associated with advanced maternal age (AMA)
  - AMA > 35 yr old at time of delivery
  - Trisomies associated with AMA
  - Turner not associated with AMA

Natural History & Prognosis

- Variable prognosis dependent upon chromosome results and presence of other abnormalities
  - 98% normal outcome if no aneuploidy
  - 8% with CHD
  - 2% with other anomalies/syndrome

- Larger NT has worse prognosis
  - CHD: 3% if NT 3.5-5 mm vs 15% if NT > 5.5 mm
  - Largest NT associated with Turner syndrome

- NT natural history
  - Often resolve spontaneously
  - Progress to 2nd trimester fetal fold
  - Progress to 2nd trimester cystic hygroma
  - Progress to hydroxy

Treatment

- Chorionic villus sampling (CVS)
- Amniocentesis

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls

- Perform NT screening only in certified lab
- Should be able to offer CVS
- Should be able to offer genetic counseling
- Fetal echocardiography if NT > 3.5 mm and normal chromosomes
- Amniotic fluid-birefringence is a potential pitfall in measuring NT

SELECTED REFERENCES

Increased Nuchal Translucency

Image Gallery

Typical

**Left**: Sagittal ultrasound shows a NT (open arrows) in a fetus with trisomy 21. The amniotic fluid (curved arrows) is not included in this NT measurement. The nasal bone is absent (open arrows).

**Right**: Sagittal ultrasound shows a markedly thickened NT (curved arrow) in a fetus with Turner syndrome. Very large NT and hypoplasia are often seen with Turner syndrome.

Typical

**Left**: Sagittal ultrasound shows a 13 wk fetus with a thickened bladder (curved arrows). **Right**: Ultrasound performed pre-1995 shows a nuchal fold (curved arrows) and club foot (curved arrow pointing to toes and open arrow pointing to shaft). This fetus has multiple aneuploidies and trisomy 18.

Typical

**Left**: Sagittal ultrasound shows a NT (curved arrows) and fetal wall edema (open arrows). Chromosomes were normal and echocardiography was performed in the second trimester. **Right**: Axial ultrasound shows a severe hypoplastic left heart. Only the right atrium (open arrows) and right ventricle (curved arrows) are visible. 1 NT is associated with cardiac defects, with or without chromosomal abnormalities.
**TERMINOLOGY**

**Abbreviations and Synonyms**
- Ductus venosus (DV)

**Definitions**
- Fetal vascular connection from portal vein (PV) to inferior vena cava (IVC)
  - Brings oxygenated blood from placenta to heart
  - Shunts oxygenated stream to fetal venae cavae to left atrium → ascending aorta

**IMAGING FINDINGS**

**General Features**
- **Size**
  - Maximum length DV 3 mm in first trimester
  - Diameter at umbilus (narrow portion of inlet) ≤ 2 mm throughout pregnancy
- **Morphology**
  - PV is funnel-shaped
  - Focal narrowing creates a "jet effect" → at least 50% of UV blood shunted toward foramen ovale
  - Enteras blood with higher oxygen saturation goes to ascending aorta → coronary/cerebral circulations
- **Applications of DV ultrasound**
  - First trimester screening for aneuploidy
  - 2nd/3rd trimester
  - Evaluation of cardiac function
  - Information on fetal response to hostile environment with growth restriction
  - Normal waveform is triphasic, with continuous forward flow
  - S wave: Ventricular systole
  - D wave: Early ventricular diastole
  - A wave: Atrial contraction

**Physiology**
- Waveform reflects pressure gradient between right atrium and umbilical vein
- Ventricular contraction = maximum atrial filling = S wave
- Early ventricular diastole = atria empty into ventricles = atrial inflow increases → D wave
- Atrial contraction = highest atrial pressure = lowest atrial inflow → A wave
- **Abnormal waveform**
  - Reduction of forward flow during A wave
  - Reversed flow during A wave
  - Abnormal indices: Normative data available
    - Tensility index (PI), S/A ratio, peak velocity index

**Imaging Recommendations**
- Best imaging tool: Pulsed Doppler
- **First trimester**

**DDx: Conditions Associated With Abnormal DV Flow**

- Enlarged PV
- Hypoleakage IVC
- CHD (atrioventricular)
- Hypoplastic ductus
**Termi

nology**

- Fetal vascular connection from portal vein (PV) to inferior vena cava (IVC)
- Brings oxygenated blood from placenta to heart

**Imaging Findings**

- DV is funnel-shaped
- Focal narrowing creates a "jet effect" — at least 50% of UV blood shunted toward foramen ovale
- Ensures blood with higher oxygen saturation goes to ascending aorta — coronary/cerebral circulations
- Normal waveform is triphasic, with continuous forward flow
- Beware of pitfalls in Doppler evaluation of DV
- Incorrect placement of sample volume may give spurious results

**Key Facts**

**Top Differential Diagnoses**

- Absence of ductus venosus

**Clinical Issues**

- Published incidence of aneuploidy associated with abnormal DV flow varies from 65-90%

**Diagnostic Checklist**

- Published data is based on study of high-risk populations
- Value of DV assessment in fetuses with normal NT, normal growth is unclear
- Changes so DV flow in 2nd/3rd trimester imply severe fetal compromise and imminent demise
- In first trimester, abnormal DV flow is associated with aneuploidy and increased risk for adverse outcome, even if chromosomes are normal

**DIFFERENTIAL DIAGNOSIS**

**Absence of ductus venosus**

- Very rare but 3 subtypes described
  - UV connects directly to right atrium, bypassing liver
  - Color Doppler shows aberrant vessel crossing diaphragm
- Courses between liver and right abdominal wall
- UV connects to IVC via iliac or renal vein (bypasses liver)
- UV courses inferiorly if connected to iliac vein
  - IVC enlarged
- UV connects to PV without development of DV
  - Color Doppler fails to identify DV
  - Hepatic veins may be distorted
- Strong association with aneuploidy (25%)
- Trisomy 21, 18, Turner syndrome
- Strong association with adverse outcome
  - Hydrops 33%
  - Polyhydramnios
  - Surviving infants: 10% have absent portal veins

**PATHOLOGY**

**General Features**

- Epidemiology
  - DV waveform abnormal in 7.7% of series 1, 217
  - Unselected patients presenting for first trimester screening
  - Maternal age > 15 yrs in 45% of group
  - Nuchal translucency (NT) > 95th percentile for > 1 EL in 48% of cases with abnormal DV flow
  - First trimester
DUCTS VENOSUS

- Cardiac impairment thought to be cause of abnormal NT and abnormal DV flow
- Significant correlation observed between DV PI and NT measurement
- 2nd/3rd trimester condition that affect DV flow
  - Diminished cardiac contractility
  - Severe placental insufficiency; arrhythmia, aspergillus
  - Hypoxia
  - Intracardiac or pericardial/pleural fluid
  - Increased afterload
  - Abnormal placental resistance
  - Obstruction to cardiac outflow (e.g., pulmonary atresia with intact ventricular septum)
  - Increased preload (increased venous return)
  - Shunt lesions: Vascular tumors, arteriovenous malformation
  - Recipient twin in twin-twin transfusion syndrome
- Physiology of abnormal placental resistance
  - Increased cardiac work, required to perfuse abnormally resistive placenta
  - Right ventricle (RV) is systemic ventricle in fetus
  - RV decompensation, tricuspid regurgitation
  - Tricuspid regurgitation = increased right atrial pressure
  - Increased right atrial (RA) pressure transmitted to venous structure
  - Eventually RA pressure prevent forward flow from RV
  - A wave (RV) tracing reaches baseline, with further decompensation causing flow reversal

CLINICAL ISSUES

Presentation
- First trimester screening for aneuploidy
- Second/third trimester evaluation of abnormal growth, cardiac function

Natural History & Prognosis
- Published incidence of aneuploidy associated with abnormal DV flow varies from 65-90%
- Abnormal NT but normal chromosomes in unscreened group presenting for first trimester screening
  - Abnormal DV flow = 77% live birth
  - Normal DV flow = 94% live birth
- Abnormal NT + normal chromosomes + abnormal DV flow
  - 27-44% congenital heart disease (CHD)
- Early trimester high-risk fetuses with abnormal NT + abnormal DV but normal chromosomes
  - 9 fold risk of adverse outcome compared to those with abnormal NT + normal chromosomes + normal DV

Treatment
- First trimester
  - Offer karyotype
  - Chronic villus sampling or early amniocentesis
- If normal chromosomes
  - Normal fetal echocardiography at 16-18 weeks
  - Consider repeat echo later, in third trimester
  - Monitor closely for increased risk of adverse outcome
  - Second/third trimester

- Management of growth restriction depend on gestational age at diagnosis
  - > 32 weeks, consider delivery
  - < 32 weeks, risk associated with severe prematurity are considerable

DIAGNOSTIC CHECKLIST

Consider
- TV Doppler adds additional physiologic information to anatomic survey
  - First trimester
    - Detection of aneuploidy
    - Fetuses at risk for adverse outcome including congenital heart disease
  - Second/third trimester
    - Fetal response to adverse intrauterine environment in placental insufficiency
    - Cardiac compromise/suspending hydrodrops
- Published data is based on study of high-risk populations
- First trimester with abnormal NT
- 2nd/3rd trimester fetuses with growth restriction, cardiac compromise
- Value of IV assessment in fetuses with normal NT, normal growth is unclear

Image Interpretation Pearls
- LV has characteristic triphasic waveform
  - Ratios of flow velocities have less interserver variability than direct velocity measurements
  - Changes in DV flow in 2nd/3rd trimester imply severe fetal compromise and imminent demise
  - In first trimester, abnormal DV flow is associated with aneuploidy and increased risk for adverse outcome, even if chromosomes are normal

SELECTED REFERENCES
Typical

(Left) Pulsed Doppler ultrasound shows the normal triphasic waveform seen in the ductus venosus. The S wave (upper arrow) occurs during ventricular systole, the D wave (lower arrow) occurs during ventricular diastole, and the A wave (arrowhead) occurs during atrial contraction.

(Right) Pulsed Doppler ultrasound shows an abnormal ductus venosus waveform with reversed flow (arrows) during the A wave.

Typical

(Left) Pulsed Doppler ultrasound shows reversed flow (arrows) during the A wave in a 3-week 3-day embryo. This pregnancy was considered high-risk due to a history of previous abnormal pregnancies.

(Right) Follow-up ultrasound at 13 weeks in the same case shows an increased cordal translucency observed by the examiner. The amnion seen separately (arrows) farther afield showed short limbs, the fetus was born with mild short-limbed dysplasia.

Variant

(Left) Sagittal ultrasound shows an abnormal normal waveform (arrows).

(Right) Pulsed Doppler ultrasound in the same case shows forward flow during the A wave (arrows) but apparent flow reversal (arrowheads) is also seen. The normal triphasic waveform contaminates the tracing with aliasing visible beneath the baseline (arrowhead and open arrows).

Examination of the AV can determine whether a ductus venosus is present or whether it should be considered.
SECTION 2: Brain

Introduction and Overview

Brain Development & Imaging

Brain

Cranial Anomalies

Ectoencephaly, Anencephaly 2-6

Acrania 2-10

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Agenesia of the Corpus Callosum 2-36

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**Imaging Anatomy**

**Ultrasound**
- Brain parenchyma
  - Cerebral hemispheres
  - Hypoechoic parenchyma
  - Increasing gyration/indentation visible with maturation
- Cerebellum
  - Bilobed structure
  - Linear echogenic folia
- Midline cerebellar vermis
- Most echogenic intracranial structure
- With increasing gestational age, visible anatomic detail increases
- Thalamus, brainstem, corpus callosum
- Ventricles
  - Anechoic cerebral spinal fluid (CSF)
  - Homogeneous echogenic choroid plexus fills lateral ventricles
- Cavernous venous sinus (CVS)
- CSF-filled structure between frontal horns
- Important marker of normal brain development
- Cisterna magna
- CSF-filled space behind cerebellum
- May see dual folds in subarachnoid space
- Linear echogenic structures extending from cerebellum to inner table of skull
- May represent inferior attachment of falx cerebri
- Normal anatomic finding
- Skull
  - Echogenic with posterior acoustic shadowing
  - Evaluation of skull shape
- Orbit
- Nasal bone
- Osseous palate
- Tooth buds

**Doppler Ultrasound**
- Identify Circle of Willis
- Can be used to identify callosomarginal and pericallosal arteries in sagittal phase
- Used to confirm presence of corpus callosum

**MRI**
- Helpful for optimal visualization of anatomy
- Consider when screening ultrasound shows abnormality
- Can uncover additional anomalies or clarify ultrasound diagnosis
- May affect prognosis of fetus
- Rapid acquisition techniques with T2WI are most useful
- Gray matter
  - Low signal on T2WI
  - White matter
  - High signal on T2WI
- May use T1WI as well
- Helpful to identify blood products
- High signal material in ventricles or parenchyma
- Myelination documented by high signal on T1WI
- Can help show evidence of fetal brain maturation
- More helpful as pregnancy/myelination progresses
- Survival, growth, and myelination progress with increasing gestational age
- Cortical appear relatively smooth at 22 weeks
- Do not mistake for lissencephaly
- Interhemispheric fissure should be visible
- Sylvian fissure widely open at 22 weeks
- Opeculorization occurs back - front from 22-38 weeks
- Closure complete at 46 weeks gestation

**Anatomy-Based Imaging Issues**

**Imaging Protocols**
- American Institute of Ultrasound in Medicine (AIUM) evaluation
  - Head and neck
**BRAIN DEVELOPMENT & IMAGING**

### Imaging Issues
- **AIUM requirements**
  - Measure BPD and HC at level of thalami and cavum septi pellucidum
  - Fetal anatomic survey must include:
    - Head and neck
    - Cerebellum
    - Choroid plexus
    - Cisterna magna
    - Lateral cerebral ventricles
    - Midline falx
    - Cavum septi pellucidum
  - **Normal lateral ventricles < 10 mm**
  - **Normal cisterna magna ≤ 10 mm**
  - **Cavum septi pellucidum important marker for normal brain development**
- **Brain**: Cerebellum, Choroid plexus, Cisterna magna, Lateral cerebral ventricles, Midline falx, Cavum septi pellucidum
- **Fetal profile useful to document**
  - Nasal bone, micrognathia, frontal bossing

### Imaging Pitfalls
- **Normally developing rhombencephalon**
  - Seen in first trimester
  - Sonolucent area in dorsal cranial end of embryo
  - Should not be mistaken for hydrocephalus or cystic mass
- **Posterior fossa**
  - Imaging in steep oblique axial plane
  - May simulate mega cisterna magna or Dandy-Walker variant
  - Dural folds in subarachnoid space of cisterna magna
  - Normal finding, do not mistake for cystic mass
  - Cerebellar vermis is not complete until 18 weeks
  - Caution in diagnosing Dandy-Walker continuum before formation complete
- **Skull**
  - Unilateral petrous ridge seen in axial plane
  - Can mimic echogenic mass in fetal brain
  - Caused by angling slightly oblique in axial plane
  - Posterior acoustic shadowing from skull in occipital region
  - Can mimic ossous defect in axial plane due to dropout
  - Change transducer angle to verify

### Normal Measurements
- **Routine measurements required by AIUM**
  - Biparietal diameter (BPD)
  - Measure at level of thalami and CSP
  - Cerebellar hemispheres should not be visible
  - Measurement taken from outer edge proximal skull to inner edge distal skull
  - Head circumference (HC)

### Key Facts
- Consider fetal MRI for detailed visualization of anatomy

### Clinical Issues
- **BPD may underestimate gestational age in dolichocephaly**
- **HC less affected by skull shape**

### Avoid Imaging Pitfalls
- **Normal developing rhombencephalon appears cystic**
- **Sleep oblique imaging simulates posterior fossa abnormalities**
- **Be cautious diagnosing Dandy-Walker continuum before vermis is fully formed (18 weeks)**
- **Cortex appears relatively smooth until late 2nd trimester on fetal MRI**
  - Do not mistake for lissencephaly

### Pathology-Based Imaging Issues
- **Measure at same level as BPD**
  - Circumference taken along outer edge of skull
  - BPD and HC used in calculation of gestational age (GA) and estimated fetal weight (EFW)
- **Lateral ventricles**
  - Normal < 10 mm
  - Measured inner edge to inner edge
  - At level of glomus of choroid plexus
  - Measure perpendicular to long axis of ventricle (cor midline)
  - Generally stable measurement between 14-40 weeks gestation
  - Male fetuses have slightly larger ventricle measurements than female fetuses
  - Cisterna magna
  - Normal ≤ 10 mm
  - Size varies slightly with gestational age

### Imaging Protocols
- **Head shape has greater effect on BPD than HC**
  - Dolichocephaly
    - Relative flattened appearance of fetal skull
    - BPD tends to underestimate gestational age
    - Can be seen in normal fetuses, breech presentation, oligohydramnios, myelomeningocele
  - Brachycephaly
    - Rounded appearance of fetal skull
    - Relatively shortened anteroposterior diameter
    - BPD may overestimate fetal age
    - Can be seen in normal fetuses, trisomy 21
  - HC more reliable in calculating GA and EFW in these conditions

### Embryology

#### Embryologic Events
- 3rd-4th week
  - Neural plate and folds appear
**Clinical Implications**

**Clinical Importance**
- Brain abnormalities have significant impact on intellect and developmental growth postnatally
- Pregnancy management may be affected by results
  - Termination may be considered based on prognosis
  - Karyotyping may be offered
  - Consider neonatology or pediatric neurosurgery consultation if pregnancy continues
- Delivery issues
  - Massive hydrocephalus
  - Requires close monitoring of BPD
  - BPD > 10 cm inhibits vaginal delivery
  - May require immediate resuscitation/intervention at birth
  - Delivery at tertiary medical center optimal
  - Supportive care for lethal malformations

**Related References**
(Left) Axial ultrasound corresponding to plane A shows the normal thalamus (open arrow) and corpus callosum (solid arrow). This is the plane in which HC and BPD are measured. Note the cingulum is not in focus.
(Right) Axial oblique ultrasound corresponding to plane B shows a normal choroid plexus. Vascular echoes are present in the cisterna magna (arrows), representing normal fetal vessels in the subarachnoid space.

(Lefl) Sagittal ultrasound of a live fetus. Arrows show the corpus callosum (arrow) forming. Hypochoic band above the cisterna magna (small arrow). (Right) Sagittal color Doppler ultrasound shows flow in the pericallosal artery, which interconnects the corpus callosum.
GENERAL FEATURES

• Best diagnostic clue
  ○ No calvarium, with absence of neural tissue above orbits
  ○ Diagnosis should never be missed with routine views

• Morphology
  ○ Encephaly/Anencephaly sequence
  ○ Neural tissue "wears away" during gestation
  ○ Result of fetal movement and exposure to amniotic fluid
  ○ Small amounts of dysmorphic tissue may still be present in 2nd trimester
  ○ Encephaly

IMAGING FINDINGS

• Neural tissue present
• Remaining tissue abnormal with an irregular contour
• Typically seen in first trimester
• Encephaly
• No organized neural tissue remaining
• Cranial defect is covered by amnionatous stroma (area cerebrovasculara)

ULTRASONOGRAPHIC FINDINGS

• First trimester
  ○ Neural tissue is still present (encephaly)
  ○ Normal head contour is absent
  ○ Headplan is irregular, flattened, splayed appearance
• Second and third trimester
  ○ Exposed brain has a lobulated ("Mickey Mouse") or spiked ("Bart Simpson") appearance
  ○ Crown-rump length (CRL) less than expected

• Second and third trimester
  ○ Neural tissue not dissolves
  ○ No soft tissue above orbits
  ○ Remaining surface is irregular
  ○ Area cerebrovasculara

• Face
  ○ Protruberant eyes
  • Secondary to shallow orbits
  • Eyes themselves normally formed
  • "Frog-like" appearance when face viewed in coronal plane

DDx: Abnormal Calvarium
EXENCEPHALY, ANENCEPHALY

Terminology
- Exencephaly/anencephaly sequence
- Abnormal cranial vault and varying amounts of supratentorial brain

Imaging Findings
- Cranial defect is covered by angiomatous stroma (area cerebrovascularis)
- Crown-rump length (CRL) less than expected
- Proptosis or enophthalmos
- Often contiguous with cervical spine defect
- Polyhydramnios common
- Amniotic fluid often echogenic secondary to dissolved neural tissue
- Should be able to pick up routinely 10-14 weeks
- Routine 2nd trimester cranial views detect 100% of cases

- Cleft lip/palate may be seen
- Often have other open neural tube defects (ONTD)
- Often contiguous with cervical spine defect
- Lumbar myelomeningocele
- Polyhydramnios common
- Secondary to impaired swallowing
- Amniotic fluid often echogenic secondary to dissolved neural tissue
- 3D ultrasound
- More detailed depiction of cranial contour
- May potentially increase accuracy in first trimester

MR Findings
- Not generally needed for diagnosis
- May be useful if ultrasound is compromised or equivocal
- Obvious cranial defect
- Little or no supratentorial brain remains
- Brainstem and cerebellum often aplastic

Imaging Recommendations
- Endovaginal scanning in 1st trimester for earlier diagnosis
- Often difficult before 10 weeks
- Should be able to pick up routinely 10-14 weeks
- Examine cranial contour carefully
  - Splayed
  - Flattened
  - Lobular
  - Spiked
- Can measure crown-heel length (CCL)
  - 77% of anencephaly < 5th percentile
  - CCL/CRL ratio
  - 62% of anencephaly < 5th percentile
- Show transabdominal scan to follow-up if any suspicions
- Cord insertion with maternal serum alpha-fetoprotein
- Routine 2nd trimester cranial views detect 100% of cases

Key Facts

Top Differential Diagnoses
- Acrania
- Encephalocoele
- Anomalous band syndrome
- Atelencephaly/aprosencephaly

Pathology
- Multifactorial disorder that likely results from a combination of etiologic agents

Clinical Issues
- Lethal malformation
- Preconception folic acid should be given for future pregnancies

Diagnostic Checklist
- CRL < expected is not always incorrect dates

DIFFERENTIAL DIAGNOSIS

Acralia
- Defined neural tissue still present
- Brain better seen than normal
  - Secondary to absent skull
- Considered part of anencephaly spectrum
- Lethal

Encephalocoele
- Cranial present
- Neural tissue protrudes through defect
  - Most commonly occipital
  - May be difficult to differentiate in 1st trimester
  - Becomes obvious with advancing gestational age

Anomalous band syndrome
- Defect is symmetric
- Soft tissue defects
- Other body parts often affected
- Bands may be visible

Atelencephaly/aprosencephaly
- Severe microcephaly with or without limb abnormalities
  - No normal cerebral structures
  - Facial anomalies
    - Micrognathia
  - Midline malformations including cyclopia
  - Cleft lip/palate
  - Cranium intact

Severe microcephaly
- Cranial intact
- Sloped forehead
- Cerebrum present

PATHOLOGY

General Features
- General pathologic comments
EXENCEPHALY, ANENCEPHALY

- Multicifatorial disorder that likely results from a combination of etiologic agents
  - Genetic
  - Environmental
  - Metabolic
  - Nutritional
- Genetics
  - Multifactorial
  - Risk of recurrence increased if positive family history
  - Greater risk if first degree relative
- Etiology
  - Risk factors
    - Folic acid deficiency
    - Insulin-dependent diabetes
    - Hypertension
    - Malignancies, valproic acid, carbamazepine, aminopterin (folate acid antagonist)
- Embryology
  - Anterior neuropore closes on day 23
  - Failure of closure results in cranial defects including anencephaly, encephaloceles and menencephaly
  - Skull complete by 10 weeks
- Epidemiology
  - 1/1,000
  - United Kingdom greatest incidence
  - M/F = 1.4
- Associated abnormalities
  - Reported in 41% but lack importance given lethality of condition
    - Spina bifida: 27%
    - Cleft lip/cleft palate: 6%
    - Most commonly involves cervical spine
    - Genito-rinary: 16%
    - Other: Cleft palate: 10%
    - Cardio-vascular: 6%
    - Cardiac: 4%

Gross Pathological & Surgical Features
- Absent calvarium and telercephalon
- Brainstem and rhombencephalic structures remain
- Defect is covered by argyrosoma (strongly convex area cerebrovascularis)

CLINICAL ISSUES

Presentation
- Abnormal first trimester scan
- Can be reliably diagnosed by 10-14 weeks
- Elevated maternal serum alpha-fetoprotein (MSAAP)
- > 2.5 multiples of the median (MOM) considered abnormal
- Direct 90% of anencephaly
- Large-for-date secondary to polyhydramnios
- Obvious finding on routine mid trimester scan

Natural History & Prognosis
- Lethal malformation
- Maternal death rates in days
- < 10% live to one week
- 2-3% risk of recurrence of any ONTD

Treatment
- Termination offered
- Supportive care for family
- Genetic counseling
- Exencephaly: folic acid should be given for future pregnancies
  - 4 mg/day beginning at least 1 month prior and continuing through first trimester
  - Decrease risk of all ONTD by approximately 70%
  - 0.4 mg/day recommended for all women attempting pregnancy

DIAGNOSTIC CHECKLIST

Consider
- CHL: expected is not always incorrect
- May be early indicator of neural tube malformation
- Short term follow-up for any case where the head looks asymmetric or irregular

Image Interpretation Pearls
- Diagnosis may be made in 1st trimester with endovaginal ultrasound
- Exencephaly evokes isoencephaly

SELECTED REFERENCES

EXENCEPHALY, ANENCEPHALY

IMAGE GALLERY

Typical

[Images of ultrasound scans with annotations]

Typical

[Images of ultrasound scans with annotations]

Typical

[Images of ultrasound scans with annotations]
ACRANIA

**TERMINOLOGY**

**Abbreviations and Synonyms**
- Acrania
- Accephalia

**Definitions**
- Absent calvarium above orbits
- Considered part of exencephaly/anencephaly sequence

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue: Exposed brain with no cranium

**Ultrasoundographic Findings**
- Calvarium
  - Absent above orbits
  - Defect may be asymmetric with amniotic bands
  - Absent membranous flat bones
  - Skull base intact
- Brain
  - Brain seen “too well”
  - Distortion of parenchyma with loss of landmarks
  - May “wean away” during gestation
  - Can appear identical to anencephaly at delivery

- Measurements may be present
  - May provide protective barrier from erosion
- Face
  - Similar to anencephaly
  - Shallow orbits with protuberant eyes
  - Orofacial clefts if amniotic bands
  - Polyhydramnios common
  - Fluid often ectopic

**Imaging Recommendations**
- Look for amniotic bands as cause
- Asymmetric skull defects
- Look closely for bands associated with defect
- Other body parts frequently affected

**DIFFERENTIAL DIAGNOSIS**

**Exencephaly/anencephaly**
- Exposed, irregular neural tissue first trimester
- Little or no cerebral tissue above orbits by second trimester

**Encephalocele**
- Cranium present
- Neural tissue protrudes through defect
- Most commonly occipital

**DDx: Acrania**

![Diagrams of various cranial issues](image-url)
### ACRANIA

#### Terminology
- Absent calvarium above orbits

#### Imaging Findings
- Skull base intact
- Brain seen "too well"
- Shallow orbits with protuberant eyes

#### Top Differential Diagnoses
- Exencephaly/anencephaly

#### Key Facts
- Encephalocele
- Amniotic band syndrome
- Osteogenesis imperfecta (OI)

#### Clinical Issues
- Determination of cause imperative for genetic counseling
- If primary neural tube defect, recurrence risk 2-3%
- No recurrence risk with amniotic bands

#### Amniotic band syndrome
- Defects/metric
- "Slack" defects affecting other body parts
- Bands may be visible

#### Body stalk anomaly (limb-body-wall complex)
- Fetus adherent to placenta
- No free floating cord
- Scoliosis major feature

#### Osteogenesis imperfecta (OI)
- Poor skull ossification may mimic acrania
- Brain still looks "contained"
- Skull deformations under scapo pressure
- Underlying brain usually normal
- Entire skeleton involved, often with fractures

#### PATHOLOGY

#### General Features
- Etiology
  - Risk factors same as anencephaly
- Proposed mechanisms
  - Failure of anterior neuropore to close
  - Primary failure of membranous bone formation
- Epidemiology
  - 1:1,000 quoted incidence
  - Includes anencephaly so true incidence much less

#### CLINICAL ISSUES

#### Presentation
- Most common signs/symptoms
  - Elevated maternal serum alpha-fetoprotein
  - Found on routine tests
  - Polyhydramnios

#### Natural History & Prognosis
- Lethal malformation

#### Treatment
- Termination offered
- Determination of cause imperative for genetic counseling
- If primary neural tube defect, recurrence risk 2-3%
- No recurrence risk with amniotic bands

#### DIAGNOSTIC CHECKLIST

#### Image Interpretation Pearls
- Isolated acrania
- Primary neural tube defect
- Frontal bone/forehead defects
- Amniotic bands
- Body stalk anomaly

#### SELECTED REFERENCES

#### IMAGE GALLERY

(Left) General ultrasound shows obvious neural tube defect and surrounding calvarium tissue. The brain is adherent to the placenta (arrow). There was no evidence of other defects. In this case of amniotic band syndrome. (Right) General ultrasound shows normal placental development and normal fetus. There was no evidence of other defects.
**Terminology**

**Abbreviations and Synonyms**
- Encephalocele
- Cephalocele
- Cranial meningiocele
- Cranial bitemporal, craniocerebrosis, cranioresorbsis
- Encephalomeningiocele, encephalodermologysostecule, glionele.
- Chiari II

**Definitions**
- Herniation of intracranial structures through skull defect
  - Cephalocele
  - More generic term
  - Herniation of intracranial contents
  - Encephalocele
  - Meninges + brain
  - Most common
  - Cranial meningiocele
  - Meninges only
- Chiari II
  - Hindbrain malformation
  - Cerebellum herniated into cephalocele
  - Very rare

**Imaging Findings**

**General Features**
- Best diagnostic sign: Paracranial mass with honey defect
- Location
  - Associated with sutures
    - Occipital
    - Parietal
    - Vertex
    - Frontal
  - 80% are occipital in posterior hemisphere
- Size
  - Variable
  - May be atrial and mistaken for scalp mass

**Ultrasonographic Findings**
- First trimester
  - Head may look small or irregular
  - Must do endovaginal examination
  - Can see cranial defect in late first trimester
- Brain
  - Divert appearance of herniated tissue
  - Gyral pattern may be identified
  - Mixed cystic/solid mass
  - Purely cystic
  - "Cyst within a cyst" or "target" sign
  - Suggests prolapsed 4th ventricle

**DOx: Encephalocele**

- Encephalocele
- Meningocele
- Scalp Herniation
- Cysts

**Atrial ultrasound shows an obvious cranial defect (arrow).** The cephalocele is purely cystic (arrow) with only herniation of meninges. Contents of a cephalocele may vary in visibility, and progress.

**Clinical photograph shows a large occipital encephalocele.** Herniography shows the meningeal contents within the sac, through which a needle entered.
OCCIPITAL ENCEPHALOCELE

Key Facts
- Amniotic band syndrome
- Anencephaly/acrania
- Cystic hygroma

Pathology
- Associated with multiple syndromes
- Meckel-Gruber syndrome most common genetic disorder

Diagnostic Checklist
- If encephalocele is not associated with cranial sutures consider amniotic bands as cause
- Edge artifacts may simulate a cranial defect
- For isolated encephaloceles, prognosis most impacted by volume of herniated parenchyma, microcephaly, and ventriculomegaly

Terminology
- Herniation of intracranial structures through skull defect

Imaging Findings
- Diverse appearance of herniated tissue
- Gyril pattern may be identified
- "Cyst within a cyst" or "target" sign
- Ventriculomegaly in 70-80%
- Microcephaly in 25%
- Osseous defect should be demonstrated
- Both polyhydramnios and oligohydramnios described
- Oligohydramnios more likely to have concurrent defects

Top Differential Diagnoses
- Scalp masses
- Normal intracranial landmarks distorted
- Ventriculomegaly in 70-80%
- Impaired cerebral spinal fluid (CSF) flow
- Primary brain malformation
- Microcephaly in 25%
- Other central nervous system (CNS) anomalies common
- Agenesis of corpus callosum
- Dandy-Walker continuum
- Neuronal migrational anomalies
- Spina bifida

- Cranium
  - Osseous defect should be demonstrated
  - Usually midline: Occipital
  - Lateral: Parasagittal, inferior temporal
  - May be difficult to see with small defect
  - "Lemon sign" in 30%
  - Depression of frontal bones
- Both polyhydramnios and oligohydramnios described
- Oligohydramnios more likely to have concurrent defects
- Polyhydramnios
- Multiple other anomalies described

MR Findings
- Best modality for evaluating brain parenchyma
- Contents of cephalocele
- Major determining factor in prognosis
- Define relationship with dural sinuses
- Look for patency

CT Findings
- Not usually done in utero
- Best for evaluating bony defect postnatally

Imaging Recommendations
- Endovaginal scan in first trimester
- Follow-up scans
- Herniated contents may become more cystic over time
- Small cephaloceles may "disappear"
- Anterior connection found after delivery
- Mottled fetal skull
- Microcephaly poor prognostic sign
- Ventriculomegaly may be progressive
- Fetal MRI best for evaluation of herniated contents and associated parenchymal malformations

DIFFERENTIAL DIAGNOSIS
Scalp masses
- Hemangioma, epidermal cyst, cephalocele
- Cranium intact
  - Must scan from multiple angles for confirmation
  - Edge artifact may give erroneous appearance of cranial defect
  - May be located anywhere on scalp
  - Cephaloceles associated with sutures

Amniotic band syndrome
- May cause cranial defect and cephalocele
- Not associated with sutures
- Facial "slab" defects common
- Large, obliquely oriented facial clefts
- Bands may be visible
- Other body parts often affected

Anencephaly/acrania
- No cranium
- Variable amounts of brain tissue

Cystic hygroma
- Sequestered cystic neck mass
- Cranium intact
- No neural tissue
- Hydrops common

Body stalk anomaly (limb-body-wall complex)
- Severe disorganization with multiple body-wall defects
- Scoliosis
- Abnormal/short umbilical cord

Meningocele
- Encephalocele
**OCCIPITAL ENCEPHALOCELE**

- Rachischisis involving spine
- Absent cervical vertebrae
- Neck in hyperextension ("surgarsy" position)

**Metopic ridge**
- Closure of metopic suture
- Causes trigonocephaly
- Cranium intact

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**PATHOLOGY**

**General Features**

- Genetics
  - Multifactorial, many-sporadic
  - Genetic: Multiple syndromes
  - Many autosomal recessive
  - Chromosomal
    - Trisomy 13, 18
- Teratogens
  - Warfarin syndrome: Nasal hypoplasia, ocular defects, thymobucystoptia, multiple CNS anomalies including cephalocele
- Maternal obesity implicated as risk factor
- Etiology
  - Several proposed mechanisms
- Primary failure of cranial neuropore closure
- Secondary event with pressure erosion and herniation of neural tissue
- Failure of induction of membranous bone formation
- Epidemiology
  - 1-31/100,000 in United States
  - Majority occipital
  - Frontal encephaloceles more common in Southeast Asia
- Associated abnormalities
  - Body malformations common
  - Isolated or part of syndrome
- Associated with multiple syndromes
  - Meckel-Gruber syndrome most common genetic disorder
- Encephalocele, polydactyly, polycystic kidneys
- Autosomal recessive
- Walker-Warburg syndrome
- Li-Fraumeni, hydrencephalus, encephalocele, microcephaly, cataracts
- Autosomal recessive
- Knobloch syndrome
- Vitreoretinal degeneration and encephalocele
- Autosomal recessive

**Gross Pathologic & Surgical Features**

- Herniated brain dysplastic

**CLINICAL ISSUES**

Presentation

- Cephalad defect
- Meninges generally intact so maternal serum alpha-fetoprotein (MSAFP) usually not elevated

Natural History & Prognosis

- Varies with amount of brain tissue in defect and associated malformation
- 40% mortality in neonatal series
- Isolated cranial meningoecele better prognosis
- 79% mortality in fetal series
- Survivors: 80% neurologic impairment
  - Developmental delay, often significant
  - Seizures
- 2-3% recurrence risk, unless associated with syndrome
- 25% recurrence risk for autosomal recessive disorders

**Treatment**

- All fetuses should be karyotyped
- Termination offered
- Thorough family history and genetic counseling
- Referral to neurosurgery prior to delivery for surgical planning
- Delivery at tertiary care facility
- Cesarean section considered to reduce birth trauma

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**DIAGNOSTIC CHECKLIST**

**Consider**

- If encephalocele is not associated with cranial sutures consider amniotic bands in cause

**Image Interpretation Pearls**

- Edge artifacts may simulate a cranial defect
- For isolated encephaloceles, prognosis most impacted by volume of herniated parenchyma, microcephaly, and ventriculomegaly

**SELECTED REFERENCES**

**OCCIPITAL ENCEPHALOCELE**

**IMAGE GALLERY**

**Typical**

*Left:* Axial ultrasound shows a large encephalocele (curved arrow) protruding through a cranial defect (arrow). *Right:* Axial oblique ultrasound shows a "cyst within a cyst" or "target sign", which is created when the 4th ventricle (curved arrow) herniates into the cephalocele (arrow).

**Typical**

*Left:* Axial ultrasound shows a small cephalocele (curved arrow). Note there is also ventriculomegaly (arrow). Other US abnormalities are commonly present, even if the cephalocele is small. *Right:* Axial T2W MR through the posterior fossa shows a large cystic sac (white arrow) with herniation of a small amount of cerebellar tissue (black arrow). MRI can be very helpful in determining extent of brain involvement and associated parenchymal abnormalities.

**Typical**

*Left:* Sagittal translumbar ultrasound in the first trimester in which the head shape appears irregular and small. *Right:* Axial mid-sagittal ultrasound of the same fetus shows an obvious large encephalocele (curved arrow). Encephalocele may be identified in the first trimester and can be confirmed on a translumbar ultrasound scan should be further investigated with endoskeletal sonography.
FRONTAL ENCEPHALOCELE

**TERMINOLOGY**

**Definitions**
- Defect of the skull in the frontothmoidal region with herniation of intracranial structures

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue: Brain parenchyma herniating through an anterior skull defect
- Location: Frontothmoidal sulci

** Ultrasonicographic Findings**
- Many are likely missed on prenatal ultrasound due to small size
- Facial mass
- Look for associated midline anomalies
  - Hypertelorism
  - Dysgenesis/agenesis of the corpus callosum
  - Interhemispheric lipoma
  - Hypotelorism

**MR Findings**
- Consider in utero MRI
- Most useful tool to characterize cephalocele
  - Size

**DIFFERENTIAL DIAGNOSIS**

**Amniotic band syndrome**
- Should have other limb and body abnormalities
- Externalized portions of brain tissue due to amniotic bands

**Nasal glioma**
- Collection of dysplastic brain tissue
- Located in nasal cavity or subcutaneous tissue
- Infiltration of brain tissue into dural tract
- Subsequent resorption of intervening tissue

**Dermoid cyst**
- Persistent dural projection through foramen occipitale
  - Dermoid or epidermoid develops along tract
  - Can have connection with intracranial contents

**DDx: Facial Masses**

- Phaeochromocytoma
- Teratoma, Berin
- Nasal Turbinate
FRONTAL ENCEPHALOCELE

Terminology
- Defect of the skull in the frontoethmoidal region with herniation of intracranial structures

Imaging Findings
- Facial mass
- Hypertelorism

Top Differential Diagnoses
- Amniotic band syndrome

Key Facts
- Nasal glioma
- Dermoid cyst

Pathology
- More commonly seen in Southeast Asia

Diagnostic Checklist
- Consider when unexplained hypertelorism present, especially in Asian population

Other facial masses
- Nasal teratoma
- Facial neoplasms
- Vascular malformation
- Encephaloceles

PATHOLOGY

General Features
- Etiology
  - Late neurulation defect during fourth gestational week
  - Fertilization of intracranial parenchyma through persistent embryologic relationships
  - Failure of frontonasal ducts to close
  - Persistent dural projection through the frontal recess
- Epidemiology
  - Rare condition
  - More commonly seen in Southeast Asia
  - Incidence of about 1:5,000
  - Associated abnormalities
    - Microphthalmia
    - Hydrocephalus
    - Microphthalmos

Cross Pathologic & Surgical Features
- Extracranial location of brain parenchyma
  - Nasofrontal: Between frontal and nasal bones
  - Nasoethmoidal: Between nasal bones and nasal cartilage
  - Naso-orbital: Through medial orbital defect
  - bordered anteriorly by frontal process of maxilla
  - Posteriorly confluent by lacrimal bone and lamina papyracea

CLINICAL ISSUES

Presentation
- Prenatal
  - Incidental facial mass ± hypertelorism
- Postnatal
  - Skin-covered facial or nasal mass
  - Nasal congestion

Natural History & Prognosis
- Prognosis better for frontoethmoidal encephaloceles than occipital or parietal locations
  - Depends on the presence of other congenital brain anomalies

Treatment
- Surgical excision with closure of the dural defect and reconstruction of the skull defect
- Repair should be performed soon after delivery to minimize the risk of meningitis

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls
- Consider when unexplained hypertelorism present, especially in Asian population

SELECTED REFERENCES

IMAGE GALLERY
**TERMINOLOGY**

**Abbreviations and Synonyms**
- Chiari II
- Arnold Chiari II
- Spina bifida
- Open neural tube defect (NTD)

**Definitions**
- Symptomatic hindbrain herniation
  - Contents herniate through foramen magnum
  - Virtually 100% association with NTD

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue
  - Posterior fossa "banana sign"
  - Cervical "lemon sign"
  - Ventricleomegaly
  - Omphalocele
- Location
  - Spina bifida
  - 27% lumbar
  - 17% sacral
  - 9% thoracic
  - 1% cervical

**DDx: Hydrocephalus**

**Ultrasonographic Findings**
- First trimester findings
  - "Novak" shaped calvarium
  - Oval-shaped head (small biparietal diameter (BPD)
  - Narrow frontal bones
  - Flat occiput on sagittal view
  - Parallel cerebral peduncles on BPD view
  - Posterior fossa compression
  - Cisterna magna (CM) obliteration
  - Most common finding
  - CM is small or gone (<3 mm)
  - Seen on routine axial posterior fossa view
  - Cerebellar compression
  - Cerebellum curves around midbrain ("banana")
  - Absent cerebellum rare
  - Ventricleomegaly
    - Atrial width ≥ 10 mm
    - Seen on routine axial ventricle view
    - Ventricle measured at atrium
    - Usually borderline or mild
    - May develop during pregnancy
    - 55% at time of diagnosis
    - 33% progress during pregnancy
    - 90% at birth
Key Facts
- Pathology
  - 4th-aneuploidy rate with spina bifida

Clinical issues
- Maternal serum alpha-fetoprotein (AFP)
  - High morbidity and mortality
- Caudal regression syndrome
- Immediate postnatal ONTD surgery
  - 80% need ventriculoperitoneal shunt
- Chiari II can coexist with in utero surgery
  - Preventive treatment with folate acid

Diagnostic Checklist
- Genetic amniocentesis
- Compressed CM may be only finding
- Cranial findings often easier to see than ONTD

DIFFERENTIAL DIAGNOSIS

Sacrococcygeal teratoma (SC teratoma)
- Germ cell neoplasm
- Exophytic complex mass from sacrum
  - Rarely purely cystic
- Spine may be deformed
  - Rarely associated with ONTD

Aqueductal stenosis
- Obstruction of aqueduct of Sylvius
  - Noncommunicating hydrocephalus
  - Moderate and severe hydrocephalus most common
  - > 15 mm atria measurement
  - Dangling choroid plexus
  - Fetal head enlarged

Dandy-Walker continuum (DW continuum)
- Dysgenesis of cerebellar vermis
  - May be partial or complete
  - Fourth ventricle communicates with CM
- Cisterna magna is enlarged
  - > 10 mm on routine axial posterior fossa view
  - "Keyhole" CM with partial vermis absence
  - Hydrocephalus

Isolated frontal bone concavity
- Seen in 5% of normal fetuses
- Resolves in third trimester
- Normal cisterna magna

PATHOLOGY

General Features
- General path comments
  - Posterior fossa compression
  - Cerebellar vermis herniates via foramen magnum
CHIARI II MALFORMATION

- Fourth ventricle displaced inside neural canal
- Tentorium puffed downward
- Medulla displaced inferiorly and kinked
- Genetics
  - 4% aneuploidy rate with spina bifida
  - Trisomy 18 (T18)
  - Trisomy 13 (T13)
- Etiology
  - Prolonged prenatal cerebral spinal fluid (CSF) leak
  - Fluid escapes from cranial veins via ONTD
  - 4th ventricle blocked
  - Low cerebellum blocks reentry of fluid
- ONTD
  - Most sporadic and multifactorial
  - Folate deficiency
  - Teratogens: Anticonvulsants
  - Arthrogryposis theory of ONTD
  - Primary failure of neuroepithelial closure
  - Absent skin/muscle (from failed induction)
  - Hydrodynamic theory of ONTD
  - CSF imbalance
  - Excess CSF accumulates in closed neural tube
  - Secondary separation of dorsal wall
- Epidemiology
  - 0.4-1.0%
  - 3% all spontaneous abortions
  - 2% recurrence risk
  - Associated abnormalities
    - All Chiari II with spina bifida
    - 40% with other anomalies
- Gross Pathologic & Surgical Features
  - ONTD
    - Bony defect with exposed neural elements

Staging, Grading or Classification Criteria
- Chiari I
  - Cerebellar tonsill herniation
  - Usually asymptomatic
  - Not diagnosed prenatally
- Chiari III
  - Hindbrain herniation
  - Low occipital/supper cervical bony defect
- Spina bifida
  - Spina bifida aperta (85%)
  - Spina bifida occulta (15%)
  - No Chiari II with occulta

Clinical Issues

Presentation
- Most common signs/symptoms
  - 1 Maternal serum alpha-fetoprotein (AFP)
  - >2.5 multiples of median (MOM) detects 80% ONTD

Demographics
- Age
  - Advanced maternal age (AMA) slightly higher risk
  - >35 yrs at time of delivery
  - Secondary to association with T18 and T13
- Ethnicity
  - United States data
  - Hispanic > Caucasian, African-American, Asian

Natural History & Prognosis
- High morbidity and mortality
  - 35% live born die within first 5 yrs
  - Chiari I main cause of death < 2 yrs old
  - 60% with IQ < 80
  - In utero findings do not predict outcome
  - Obstructive hydrocephalus
  - From posterior fossa compression
  - Musculoskeletal dysfunction
  - 25% complete lower limb dysfunction
  - Gastrointestinal/genitourinary dysfunction
  - 17% with normal continence

Treatment
- Cesarean section delivery at term
  - I Injection rate
  - I Meperimidone sac rupture rate
  - Immediate postnatal ONTD surgery
  - Cover exposed spinal cord
  - 80% need ventriculoperitoneal shunt
  - In utero surgery in clinical trials
  - Chiari I can reverse with in utero surgery
  - I Shunt dependence
  - 54% vs. 38%
  - Paralysis and continence rates unchanged
  - I Preterm delivery risk
  - Preventative treatment with folic acid
  - Preconception therapy best
  - 4 mg/day reduces occurrence risk by 70%
  - 0.4 mg/day for all women

Diagnostic Checklist

Consider
- Genetic amniocentesis
- Search for ONTD when Chiari II seen

Image Interpretation Pearls
- Compressed CM may be only finding
- Cranial findings often easier to see than ONTD

Selected References
2. Tabilo BS et al. Treatment and management of the Chiari II malformation: an evidenced-based review of the literature. Childs Nerv Syst. 20(6-7):583, 2004
CHIARI II MALFORMATION

IMAGE GALLERY

Typical

(Left) Axial photograph shows Chiari II malformation. The cerebellar tonsil has herniated (arrow) within the foramen magnum.

(Right) Axial NECT scan with contrast shows Chiari II malformation. The cerebellar tonsil has herniated (arrow) within the foramen magnum.

Typical

(Left) Sagittal ultrasound shows significant obstruction to the cerebrospinal fluid flow with a myelomeningocele. The third and fourth ventricles are dilated. Note the dilated choroid plexus.

(Right) Sagittal ultrasound of the spine in the same fetus shows a small myelomeningocele (arrows). Cranial findings are also easier to see and more obvious than the spine findings.

Typical

(Left) Sagittal T2W MRI shows a Chiari II malformation and myelomeningocele. The cerebellar tonsil has herniated (arrow) within the foramen magnum. Open spinal defect (curved arrow) is also seen in the neck. (Right) Clinical photograph shows another myelomeningocele. The presence of a sac makes the diagnosis more difficult. However, Chiari II malformation findings are present and require a search for spina bifida.
AQUEDUCTAL STENOSIS

**TERMINOLOGY**

**Abbreviations and Synonyms**
- Aqueductal stenosis (AS)
- Isolated hydrocephalus

**Definitions**
- Narrowing or occlusion at aqueduct of Sylvius
- Important to differentiate hydrocephalus from ventriculomegaly
- Hydrocephalus
  - Increased intraventricular pressure
  - Increased ventricular size
  - Increased head size
  - Noncommunicating (obstructive)
  - Cerebral spinal fluid (CSF) flow blocked within ventricular system
  - Communicating
  - Failure of CSF resorption
  - Ventricularmegaly
  - Normal intraventricular pressure
  - Increased ventricular size
  - Head size normal or small
- True aqueductal stenosis blocks CSF flow causing obstructive hydrocephalus

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue: Hydrocephalus with normal posterior fossa
- Location
  - Aqueduct of Sylvius connects 3rd and 4th ventricles
  - More proximal stenoses cause greater hydrocephalus
- Size
  - Normal diameter of aqueduct at birth 0.5 mm² (range 0.2-1.8 mm²)
  - Narrowest portion of ventricular system

**Ultrasongraphic Findings**
- Moderate to severe ventricular dilatation (> 15 mm)
  - Often extreme
  - Cortical mantle thinned
  - May be severe mimicking hydrancephaly
- "Dangling" choroid
  - Choroid plexus does not fill lateral ventricle
  - Canoid from opposite side may fall through dilated foramen of Monro into dependent ventricle
  - "Double dangle"
- 3rd ventricle dilated
  - Dilatazon may be so extreme normal ventricular anatomy may not be discernible
  - Posterior fossa normal

**Dx: Fluid-Filled Cranium**

- Hydranencephaly
- Hydrocephaly
- Atrophy
- Echogray
Terminology
- Narrowing or occlusion at aqueduct of Sylvius
- True aqueductal stenosis blocks CSF flow causing obstructive hydrocephalus

Imaging Findings
- Best diagnostic clue: Hydrocephalus with normal posterior fossa
- Moderate to severe ventricular dilatation (> 15 mm)
- CORTical mantle thinned
- "Dangling" choroid
- 3rd ventricle dilated
- Dilatation may be so extreme normal ventricular anatomy may not be discernible
- Corpus callosum often thinned or not visible
- Cavum septi pellucidi (CSP) may be absent
- Head size often large

- Catena magna can be compressed with severe hydrocephalus
- Corpus callosum often thinned or not visible
- Cavum septi pellucidi (CSP) may be absent
- Severe hydrocephalus causes fenestrations within walls of CSP
- Head size often large
- May be severe
- Color Doppler
  - Look for flow in compressed cerebral mantle
  - Follow middle cerebral artery (MCA)
- Additional findings in X-linked hydrocephalus
  - Male fetus
  - Atlanto-axial deformity of thumbs
  - Present in 50% of cases

MR Findings
- Better for assessing presence of thinned cortical mantle
- More precise anatomic evaluation
- Midline sagittal view best for evaluating aqueduct of Sylvius
- May see aqueduct "funnel" to point of obstruction
- Posterior fossa, 4th ventricle are normal
- Third ventricle dilated with displacement of both roof and floor
- Corpus callosum thinned
- Periventricular interstitial edema may be present
- Evaluate for other brain anomalies
- Often see flow artifacts with very diverticulated ventricles
- CSF is turbulent within obstructed systems

Imaging Recommendations
- Use endovaginal probe if head is cephalic
- Rule out other causes of ventriculomegaly
- Normal in AS, although can be compressed if hydrocephalus is severe
- Often hydroplanar with other malformations
- Carefully assess remaining cortical mantle
- Differentiates AS from destructive lesions or other congenital malformations
- Doppler to look for flow in MCA and compressed parenchyma

Key Facts
- IGF history of prior child with AS, continue to follow even if initial scans are normal

Top Differential Diagnoses
- Hydranencephaly
- Holoprosencephaly
- Dandy-Walker continuum

Clinical Issues
- Developmental delay in up to 90%
- X-linked hydrocephalus severe mental retardation
- X-linked recurrence risk 50% for male fetuses
- 4% recurrence risk for all others
- Large head size may cause dystocia
- Genetic counseling for future pregnancies
- In utero shunting not proven effective

DIFFERENTIAL DIAGNOSIS

Hydranencephaly
- No cerebral tissue
- Use Doppler
- MRI may be necessary for confirmation
- Head size usually normal

Holoprosencephaly
- Absent falk
- Fused thalami
- Facial malformations often present

Dandy-Walker continuum
- Dysgenesis of cerebellar vermis
- May be partial or complete
- Posterior fossa cyst
- 4th ventricle appears "open" and contiguous with cyst
- Hydrocephalus may be present but more typically develops postpartum

Chiari II malformation
- Hindbrain herniation with posterior fossa compression
- Obliteration of cisterna magna
- Cerebellar tonsils around midline (T2 FLAIR signal)
- Focal bone concavity ("lemon" sign)
- Venous malformations
- Ventriculomegaly
- Usually biventricular or quad

- Be suspicious of X-linked form
- Document gender
- Carefully image hands
- Adducted thumbs have been reported in first trimester
- Complete genetic work-up and amniocentesis
- Follow-up scans every 2-3 weeks for progression
- If history of prior child with AS, continue to follow even if initial scans are normal
- Hydrocephalus may not develop until late in pregnancy or neonatal period
- Fetal MRI
• Head size not typically large

Encephalomádacia/porencephaly
• Destructive process of brain parenchyma
• Most commonly rhemized or infection
• Focal areas of destruction
• Progressive ventriculomegaly
• Head size not enlarged

**PATHOLOGY**

**General Features**
- Genetic path comments
  - Pathophysiology
  - Aqueductal hernia normally decreases throughout gestation
  - Narrowing secondary to growth of adjacent meningeal structures
  - A/S obstructs normal CSF flow
  - CSF production continues in lateral and 3rd ventricles
  - Ventricular fluid pressure increases compressing adjacent parenchyma, stretching corpus callosum
  - Pressure may disrupt ependymal cell junctions causing periventricular edema
  - Some pontine A/S may develop from communicating hydrocephalus
  - External compression of quadrigeminal plate by dilated cerebral hemispheres
- Genetics
  - Most sporadic
  - X-linked
  - X-linked hydrocephalus (Bicker-Adams syndrome)
  - Mutation of Xq28 which produces 11, a neural cell adhesion molecule
- c. 5% of A/S
- Males
- Adducted thumbs
- Mental retardation
- **Etiology**
  - Incidentally understood and likely multifactorial
  - Neuront may result from inflammation on infection in 50%
  - Disruption of epidural lining
  - White matter edema
  - Glialis and fibrosis (irreversible at this point)
  - Infections: Cytomegalovirus (CMV), toxoplasmosis, rubella, influenza, stumps, syphilis
  - Hemorrhage and tumors also implicated
- **Epidemiology**
  - 0-3:1,000 births
  - M:F = 2:1
  - Associated abnormalities
  - CRASH: Colpois, hypoplasia, mental Retardation, Adducted thumbs, Spastic paraplegia, X-Linked Hydrocephalus
  - MASA: Mental retardation, Aphasia, Shuffling gait, Adducted thumb
  - 50% may have extracranial abnormalities

**CLINICAL ISSUES**

**Presentation**
- Most common signs/symptoms: Hydrocephalus on routine scan
  - May have history of prior child with A/S
  - Hydrocephalus may not be seen until 3rd trimester or neonatal period

**Natural History & Prognosis**
- 10-30% neonatal mortality
- Developmental delay in up to 90%
  - X-linked hydrocephalus severe mental retardation
  - X-linked recurrence risk 50% for male fetuses
  - 4% recurrence risk for all others

**Treatment**
- Amnionceteses
  - Karyotype
  - Infection screen
  - Large head size may cause dystocia
  - Genetic counseling for future pregnancies
  - Ventricular shunting after delivery
  - Thickness of cortical mantle improves after shunting
  - In utero shunting: not proven effective
  - Endoscopic ventriculostomy

**DIAGNOSTIC CHECKLIST**

**Image Interpretation Pearls**
- Careful search for other anatomic causes before aqueductal stenosis is diagnosed

**SELECTED REFERENCES**

AQUEDUCTAL STENOSIS

IMAGE GALLERY

Typical

(left) Axial ultrasound shows severe hydrocephalus with a dangling choroid (arrow) in a baby with microcephaly. The curvature of Monro is so massively dilated that the choroid from the other ventricle has fallen through to the dependent side (curved arrow). (right) Axial midplane ultrasound through the posterior fossa shows a normal cerebellum and 4th ventricle (arrow) ruling out other causes of hydrocephalus such as Chiari I malformation.

Typical

(left) Sagittal T2W MR shows severe hydrocephalus. Note the markedly enlarged head (curved arrow) as compared to the face. The posterior fossa is normal. with the vermis and 4th ventricle (arrow) well seen. (right) Axial ultrasound confirms a normal cerebellum and 4th ventricle (arrow). The point of obstruction has to be above this level. These findings are typical of aqueductal stenosis.

Typical

(left) Axial ultrasound in a case of aqueductal stenosis shows severe hydrocephalus and a markedly dilated cortical mantle (arrow) (curved arrow - dangling choroid). Cerebral cortex in the near field could not be evaluated. (right) Axial T2W MR shows a structurally thinned parenchymal surface compressed against the calvarium. MRI can be very helpful in evaluating the remaining cortical mantle.
DANDY-WALKER CONTINUUM: CLASSIC

TERMINOLOGY

Abbreviations and Synonyms
- Dandy-Walker continuum (DWC)
- Dandy-Walker malformation (DWM), Dandy-Walker complex, Dandy-Walker spectrum

Definitions
- Group of cystic posterior fossa malformations (most severe): Dandy-Walker malformation, Dandy-Walker variant (DWO), persistent Blake pouch cyst (BPC), mega cisterna magna (MCM)
- Posterior fossa (PF) malformation characterized by
  - Dysgenesis of cerebellar vermis
  - Cystic dilatation of 4th ventricle (4V)

IMAGING FINDINGS

General Features
- Best diagnostic clue
  - Large PF with high cerebrospinal fluid (CSF) cyst
  - 4V appears "open" and contiguous with PF cyst
  - Location: Posterior fossa
  - Size: Varies widely
  - Morphology

DDx: Cystic Appearance Of Posterior Fossa

- Mega Cisterna Magna
- Dandy-Walker Variant
- Arachnoid Cyst
- Joachim Syndrome

Ultrasoundographic Findings
- Agenesis or severe hypoplasia of cerebellar vermis
- Communication of 4V with PF cyst/cisterna magna
- Hydrocephalus may be present but more typically develops postpartum
- Requires follow-up to evaluate for development or progression
- Associated findings
  - Central nervous system (CNS)
    - Ventriculomegaly
    - Dysgenesis of corpus callosum
    - Encephaloceles
    - Neostial tube defects
    - E-truncus
    - Cleft lip/palate
    - Cardiac defects
    - Polycystic kidneys

MR Findings
- Problem solving tool
- Better definition of PF abnormalities
- Identifies associated supratentorial anomalies
- Midline sagittal view best demonstrates vermis
- T2WI images most useful
### Terminology
- Dandy-Walker continuum (DWC)
- Neurosurgical terminology
- Refers developmental spectrum of findings
- Dysgenesis of cerebellar vermis

### Imaging Findings
- Large PF with big cerebrospinal fluid (CSF) cyst
- 4V appears "open" and contiguous with PF cyst
- Tectal plate derelinuated (mechanical hindrance of normal descent by PF cyst)
- Hydrocephalus may be present but more typically develops postpartum
- Diagnosis should not be made before 18 weeks gestation

### Key Facts
- **Top Differential Diagnoses**
  - Mega cisterna magna
  - Arachnoid cyst (AC)
  - Dandy-Walker continuum: Variant

### Pathology
- Approximately 70-90% have additional supratentorial or extracerebral anomalies
- Chromosomal abnormalities in approximately 50%

### Clinical Issues
- Extremely variable, ranging from normal psychomotor development to severe handicap or death
- 40% mortality in infancy and early childhood
- All fetuses should be karyotyped

### Differential Diagnosis

#### Mega cisterna magna
- Cisterna magna > 10 mm
- Vermis intact
- Thought to be mildest form of Dandy-Walker continuum
- Vast majority considered normal variant, although no long-term studies
- No associated anomalies

#### Arachnoid cyst (AC)
- Vermis intact
- Displacement of cerebellum and compressed 4th ventricle
- Not traversed by falx cerebri

#### Dandy-Walker continuum: Variant
- Milder vermian hypoplasia than DWM
- Small or no 4th cyst
- Posterior fossa not enlarged
- Normal location of tectal plate
- Keyhole appearance of 4th ventricle

#### Persistent Blake pouch cyst
- Most recently added diagnosis to DWC
- Lack of formation of floor of Magendie

### Pathology
#### General Features
- Genetics
  - Majority sporadic
  - Many syndromes with DWC

- Embryology
  - Not fully understood
  - 5th week: Neural tube develops sharp bend (genuine flexure), resulting in large 4th ventricle
  - 6th week: 2 areas in rhombencephalic roof form ependymal cells: Anterior area membranacea (AMA), posterior area membranacea (PMA)
  - AMA normally incorporated into vermis and/or tela choioidea
  - PMA eventually perforates and forms foramen of Magendie
  - Dandy-Walker continuum
  - Spectrum of diseases caused by abnormalities of 4th ventricular roof
  - Detection of_variant forms of AMA thought to cause classic and variant forms
Natural History & Prognosis

- Extremely variable, ranging from normal psychomotor development to severe handicap or death
- 40% mortality in infancy and early childhood
- Intellectual development dependent on ventricle abnormality, associated supratentorial anomalies and associated syndromes
  - Intelligence normal in 35-50% of cases
  - Large ventricular system with normal lobation and absence of supratentorial abnormalities = more favorable outcome
  - Absent or small ventricle with abnormal lobation, supratentorial abnormalities = poor outcome
- Recurrence risk 15%
  - Unless associated with syndrome

Treatment

- All fetuses should be karyotyped
- Hydrocephalus in 75% at 3 months postpartum
  - May require ventricular and/or cyst shunt

DIAGNOSTIC CHECKLIST

Consider

- Fetal MRI to detect associated anomalies

Image Interpretation Pearls

- Ensure appropriate scanning plane
  - "Too steep a scanning angle can simulate DWC"

SELECTED REFERENCES


DANDY-WALKER CONTINUUM: CLASSIC

IMAGE GALLERY

Typical

(A) Axial ultrasound of the brain shows two very hypogastic cerebellar hemispheres (arrows) with an enlarged posterior fossa.

(Right) Axial T1-weighted MR shows the open communication of the fourth ventricle (curved arrows) with the large posterior fossa cyst. This is a severe presentation of the Dandy-Walker continuum.

Typical

(A) Coronal ultrasound of the posterior fossa shows splitting of the cerebellar hemispheres (arrows) with a midline cyst (open arrows). Hydrocephalus (curved arrows) is also present in this case. (Right) Coronal MRI demonstrates the cyst (arrows) between the two cerebellar hemispheres confirming the periventricular diagnosis of a Dandy-Walker malformation.

Typical

(A) Axial ultrasound shows an absent cranium repleta pipheal operculum (arrows) as well as an absent ventricles (arrows). Hydrocephalus is present, which is seen in up to 30% of Dandy-Walker malformations. It typically progresses, being present in 90% of cases that persist postnatally. (Right) Axial ultrasound shows the hypogastic cerebellar hemispheres (arrows) displaced anteromedially (curved arrows).
**TERMINOLOGY**

**Abbreviations and Synonyms**
- Dandy-Walker variant (DWV)
- Part of the Dandy-Walker continuum (DWC), Dandy-Walker complex, Dandy-Walker spectrum
  - DWC in strict terminology
  - Group of cystic posterior fossa malformations (most-to-least severe): Dandy-Walker malformation, Dandy-Walker variant, Persistent Blake pouch cyst, mega cisterna magna (MCM)

**Definitions**
- Partial agenesis or hypoplasia of inferior vermis
- Cystic dilation of fourth ventricle

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue
  - Posterior fossa (PF) defect
  - Inferior vermis absent
  - 4th ventricle communicates with cisterna magna

**Ultrasoundographic Findings**
- Hypoplasia of echogenic vermis
  - Less extensive than classic form

**DIFFERENTIAL DIAGNOSIS**

**Dandy-Walker continuum: Classic**
- More severe vermis dysgenesis than DWV
- Large posterior fossa cyst
- Abnormal 4th ventricle communicates with PF cyst
- Enlarged PF with elevation of occipital Herophili

**Mega cisterna magna**
- Cisterna magna > 10 mm
- Vermis intact
- Vast majority considered normal variant

**Normal early development of vermis**
- Formation of vermis variable
  - Open vermis in 56% at 14 weeks gestation, in 6% at 17 weeks gestation
  - Incomplete vermis before 18 weeks may be normal

**DDx: Cystic Appearance Of Posterior Fossa**

- Sleep Cerebral Plane
- Arachnoid Cyst
- Mega Cisterna Magna
- DWC Classic
DANDY-WALKER CONTINUUM: VARIANT

Key Facts
- Normal early development of vermis
- Arachnoid cyst (AC)

Imaging Findings
- 4th ventricle communicates with cisterna magna
- "Keyhole" appearance of 4th ventricle

Top Differential Diagnoses
- Dandy-Walker continuum: Classic
- Mega cisterna magna

Arachnoid cyst (AC)
- Vermin intact
- Mass effect with displacement of cerebellum, compression of 4th ventricle
- Not traversed by falx cerebri

Persistent Blake pouch cyst
- No primary vermin hypoplasia or cerebellar dysplasia
- Mild pressure related vermin and/or cerebellar atrophy may be present

Congenital vermin hypoplasia
- Synonym: Molar tooth malformations
- Absent or hypoplastic vermin
- Abnormal superior cerebellar peduncles in conjunction with vermin dysgenesis resulting in molar tooth configuration
- No PF enlargement or PF cyst
- Prototype: Joubert syndrome

PATHOLOGY

General Features
- Genetics
  - Mostly sporadic
  - Abnormal karyotype in approximately 30%
- Etiology: Dandy-Walker continuum thought to arise from defect in area membranacea in rhombencephalic roof
- Associated abnormalities
  - Similar in frequency and type to classic form of DW
  - Brain: Ventriculomegaly, colloidal dysgenesis
  - Extracranial: Cardiac defects, genitourinary abnormalities, limb defects
  - Can be associated with syndromes

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - Prenatal diagnosis on routine screening
  - Postnatal presentation
  - Developmental delay
  - Signs and symptoms of hydrocephalus

Natural History & Prognosis
- Extremely variable prognosis

- Range from normal psychomotor development to severe handicap or death
- Strongly influenced by associated anomalies

Treatment
- All fetuses should be karyotyped

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls
- Avoid imaging posterior fossa in steep coronal plane
  - Can mimic DWV

SELECTED REFERENCES

IMAGE GALLERY

(Left) Axial oblique ultrasound is a late but important clue with a Dandy-Walker variant shows a characteristic "about face" vermian vermian, with the superior vermian area absent and there are also anomalies. (Right) Sagittal T1 MRI with arachno farmers shows communications of the fourth ventricle to the cisterna magna and a hypothyroid region seen posterior to the vermian herniation in not displaced normal cases.
**TERMINOLOGY**

*Abbreviations and Synonyms*
- Mega cisterna magna (MCM)

*Definitions*
- Cisterna magna measuring > 10 mm

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue: Enlarged posterior fossa cerebral spinal fluid (CSF) space
- Location: Posterior fossa

**Ultrasoundographic Findings**
- Measured in axial oblique plane at level of cerebellar hemispheres
  - Axial, angled semi-coronal plane
  - Minxics MCM or Dandy-Walker variant
- Cisterna magna measuring > 10 mm
- Fourth ventricle is normal
- Cerebellar hemispheres normally formed
- Cerebellar vermis is complete and normal
  - Can be difficult to differentiate from mild Dandy-Walker variant

**MR Findings**
- Enlarged cisterna magna
- Sagittal view shows vermis completely covering fourth ventricle
  - Rules out Dandy-Walker malformation/variant
- May show scalloping of inner table of skull
  - Due to CSF pulsations

**Imaging Recommendations**
- Evaluate carefully for associated abnormalities
  - Trisomy 18
  - Cardiac defects
  - Chromosomal cysts
  - Omphalocele
  - Clinodactyly
  - rocker-bottom feet

**DIFFERENTIAL DIAGNOSIS**

**Dandy-Walker malformation**
- Absent vermis
- Cystic dilation of fourth ventricle in direct communication with enlarged cisterna magna
- Hydrocephalus commonly present
- Associated with agenesis of the corpus callosum

**DDx: Cystic Lesions Of The Posterior Fossa**

- Dandy-Walker variant
- Aneurysmal Cist
- Too Small At Age
**Terminology**
- Cisterna magna measuring > 10 mm

**Imaging Findings**
- Measured in axial oblique plane at level of cerebellar hemispheres
- Evaluate carefully for associated abnormalities

**Top Differential Diagnoses**
- Dandy-Walker malformation

**Dandy-Walker variant**
- Partially absent inferior vermis
- Tectal Heterotopia not elevated
- Hydrocephalus typically absent

**Normal early cerebellar development**
- Inferior vermis may appear absent
- Vermis incompletely formed before 18 weeks

**Arachnoid cysts**
- Lateral infundibulum
- Extravasal CSF-containing lesion
- Mass effect on adjacent brain

**Vein of Galen malformation**
- Doppler flow identifiable in lesion
- Other associated abnormalities present
  - Cardiomegaly
  - Hydrocephalus
  - Dilated neck vessels
  - Hydrops

**PATHOLOGY**

**General Features**
- Thought to be in same spectrum as Dandy-Walker malformation and variant
- Tectal Heterotopia is in normal position
- Ectopic in Dandy-Walker malformation
- Completely formed vermis and cerebellar hemispheres

**CLINICAL ISSUES**

**Presentation**
- Usually an incidental finding
- Part of multiple findings seen with trisomy 18

**Demographics**
- Gender
  - Isolated MCM
  - No specific sex predilection
  - MCM associated with trisomy 18
  - More often seen in male fetuses

**Natural History & Prognosis**
- If isolated likely has no adverse clinical outcome

**Key Facts**
- Dandy-Walker variant
- Normal early cerebellar development

**Clinical Issues**
- If isolated likely has no adverse clinical outcome

**Diagnostic Checklist**
- Too steep a scanning angle may simulate a MCM
- Carefully document vermis to rule out Dandy-Walker variant

**DIAGNOSTIC CHECKLIST**

**Image Interpretation Pearls**
- Too steep a scanning angle may simulate a MCM
- Carefully document vermis to rule out Dandy-Walker variant

**SELECTED REFERENCES**

**IMAGE GALLERY**

*Left:* Ultrasound shows an enlarged cisterna magna. *Right:* The fetus had other anomalies including a cardiac defect. (Right) An ultrasound shows an enlarged cisterna magna in a third trimester fetus. The cerebellum is normally present. This case (military) is an example of normal brain growth.
Terminology

Definitions
- Congenital fusion of cerebellar lobes, dentate nuclei and superior cerebellar peduncles
- Agenesis of cerebellar vermis

Imaging Findings

General Features
- Best diagnostic clue: Single-lobed cerebellum

Ultrasonographic Findings
- Cerebellum looks small
  - Steep scanning angle can make cerebellum look abnormal
  - Real-time evaluation will confirm appropriate appearance on correct axial oblique plane
- May be other intracranial anomalies
  - Hydrocephalus
  - Holoprosencephaly
  - Callosal agenesis
  - Septo-optic dysplasia

MR Findings
- Fused cerebellar hemisphere
- Abnormal shape of 4th ventricle

Differentiation Diagnosis

Dandy-Walker continuum (DWC)
- Inferior vermis defect
- Posterior fossa cyst in DWC
- Cyst in continuity with 4th ventricle
- Cerebellar lobes not fused

Congenital vermis hypoplasia
- Jouhet syndrome prototype
- Abnormal vermis
- "Molar tooth" cerebellar peduncles
- Cerebellar lobes not fused

Cerebellar hypoplasia
- Transverse diameter small for gestational age
- Intact vermis, cerebellar lobes not fused

DDx: Abnormal Cerebellum

- DW Continuum
- Jouhet Syndrome
RHOMBENCEPHALOSYNAPSID

TERMINOLOGY
- Congenital fusion of cerebellar lobes, dentate nuclei and superior cerebellar peduncles
- Agenesis of cerebellar vermis

IMAGING FINDINGS
- Best diagnostic clue: Single-lobed cerebellum
- Cerebellum looks small
- May be other intracranial anomalies

PATHOLOGY

General Features
- Genetics: FGF8 and Lmx1a genes being considered
- Defective "thoracic organizer" vs. abnormal dorsal patterning
- Interstitial deletion 2q-
- Congenital anomaly: Possible autosomal recessive inheritance
- Etiology
  - Teratogen
  - Maternal diabetes mellitus
  - Maternal hypertensive
  - Phenylepididime
- Epidemiology
  - Extremely rare but becoming more recognized on postnatal MRI
  - Increasing postnatal recognition + prenatal identification
- Embryology
  - Very early defect, probably 33-34 days gestation
  - Failure induction/differentiation midline structures
  - Lateral structures relatively preserved
  - Cerebellar hemispheres form but fuse due to absent vermis

CLINICAL ISSUES

Presentation
- Most common signs/symptoms: Abnormal posterior fossa on routine antenatal US

Natural History & Prognosis
- Depends on associated anomalies
- Often short lifespan, occasional survivors to early adulthood
- Older survivors
  - Bipolar disorder
  - Self-injurious behavior
  - Hyperactivity
- Neurological defects
  - Ataxia
  - Cerebral palsy
  - Seizures
  - Developmental delay
  - Hydrocephalus may require shunt placement
  - Hypothalamic-pituitary axis dysfunction

Key Facts

Top Diﬀerential Diagnoses
- Dandy-Walker continuum (DWC)

Clinical Issues
- Often short lifespan, occasional survivors to early adulthood

Diagnostic Checklist
- Fetal MRI invaluable to clarify posterior fossa malformations

Treatment
- Offer Karnofsky
- Careful postnatal evaluation by pediatric neurologist and endocrinologist

SELECTED REFERENCES

IMAGE GALLERY

(left) Axial oblique ultrasound shows a small cerebellar vermis and lateral ventricles. Cerebellum has a beak-shaped appearance. Right panel shows the normal cerebellar vermis. The cerebellum can be compared with a Dandy-Walker malformation in the first and second trimesters. This is a case of rhombencephalosynapsis.
AGENESIS OF THE CORPUS CALLOSUM

TERMINOLOGY

Abbreviations and Synonyms
- Agenesis of the corpus callosum (ACC)
- Callosal dysgenesis

Definitions
- Failure of axons to cross midline and form corpus callosum (CC)
  - May be complete or partial

IMAGING FINDINGS

General Features
- "Best diagnostic clue"
  - Teardrop-shaped ventricles most consistent finding on routine axial views
  - Absent cavum septi pellucidi (CSP) and CC complex on coronal and midline sagittal views
- Location
  - Corpus callosum is midline structure composed of four parts (from front to back)
    - Rostrum
    - Genu
    - Body
    - Splenium

Ultrasoundographic Findings
- Mild ventriculomegaly
  - Look at shape of ventricles
- Cephalohyph
  - Teardrop-shaped ventricles
  - Lateral ventricles widely spaced anteriorly
  - Medial wall of ventricle is further from midline at frontal horn
  - Enlargement of ventricular atria and occipital horns
  - Prominent interhemispheric fissure
  - Elevation of 3rd ventricle
    - Contiguous with interhemispheric fissure
    - Best seen in coronal plane
  - Multiple descriptors for ventricular configuration
    - "Trident-shaped"
    - "Stret horn"
    - "Viking helmet"
    - "Mouse head"
  - Gyri
    - Cingulate gyri absent
  - Radial, "spoke-wheel", "sunray" appearance in sagittal plane
  - Radiate to 3rd ventricle
- Absent CSP
- Other CNS anomalies in 50%

DDx: Agenesis Of The Corpus Callosum
AGENESIS OF THE CORPUS CALLOSUM

Terminology
- Failure of axons to cross midline and form corpus callosum (CC)

Imaging Findings
- Teardrop-shaped ventricles most consistent finding on routine axial views
- Abnormal cavum septi pellucidi (CSP) and CC complex on coronal and midline sagittal views
- Elevation of 3rd ventricle
- Other CNS anomalies in 50%
- Lipomas
- Interhemispheric cyst
- fetal MRI recommended in routine work-up
- Detection of other abnormalities negatively impacts prognosis
- Absence of other abnormalities reassuring

Key Facts
- Lipomas
- Hyperechoic midline mass
- 50% of lipomas have ACC
- Interhemispheric cyst
- Cystic mass centered around falx
- Most are likely gliomegaly cysts
- Dandy-Walker continuum (DWC)
- Heterotopias and gyral abnormalities
- May manifest as asymmetry of cerebral hemispheres
- Microcephaly
- Encephalocoele
- Myelomeningocele
- Body anomalies
- Cardiac defects
- Genitourinary
- Renal abnormalities
- Undescended testes
- Congenital diaphragmatic hernia
- Color Doppler
- May have abnormal anterior cerebral artery
- Single unpaired vessel arising from confluence of left and right anterior cerebral arteries
- Abnormal course, running under frontal bones
- Abnormal course of penial artery

MR Findings
- Sagittal
  - Absent CC
  - Absent cingulate gyri
  - Abnormal radially oriented gyri
  - Converge toward 3rd ventricle
- Coronal
  - Absent CC
  - Widened interhemispheric fissure
  - "Rice-riding" 3rd ventricle
  - "Trident-shaped" ventricles
  - Lateral ventricles pointed superiority
- May see pulvinar
- Non-crossing commissural fibers that would have normally formed CC
- May form 4th ventricle instead of crossing midline
- Medial wall of lateral ventricle

Top Differential Diagnoses
- Mild ventriculomegaly
- Lobar holoprosencephaly
- Septo-optic dysplasia

Pathology
- Chromosomal anomalies in 10-20%
- Multiple syndromes described

Clinical Issues
- 3% of mild ventriculomegaly cases have ACC
- Karyotype recommended even if isolated finding

Diagnostic Checklist
- Diagnosis may be missed before 18-20 weeks
- Absent cavum, septi pellucidi should raise suspicion for ACC

Imaging Recommendations
- Best imaging tool
  - Fetal MRI recommended in routine work-up
  - Detection of other abnormalities negatively impacts prognosis
  - Absence of other abnormalities reassuring
  - Metabolic screening technique needed to make diagnosis
  - Often missed or misdiagnosed as hydrocephalus
- Look for CSP
  - Should be seen on routine views
  - Absence very concerning for multiple conditions including ACC
- If fetal presentation is cephalic, perform vaginal scan for better evaluation
- Midline sagittal and coronal planes often more helpful than routine transverse planes
- Look for associated anomalies

DIFFERENTIAL DIAGNOSIS

Mild ventriculomegaly
- Ventricles have normal configuration
- CSP present
- Normal gyral pattern

Lobar holoprosencephaly
- Falc may be absent or abnormal
- Fused frontal horns
- Fused fornices
- Fused thalami
- Absent CSP
- Facial anomalies may be present

Septo-optic dysplasia
- Fetal horns have "flat" or "squared-off" appearance
- Downward point of frontal horns
- Fused frontal horns
- Cushing sign may be trimmed
- Absent CSP
AGENESIS OF THE CORPUS CALLOSUM

PATHOLOGY

General Features
- Genetics
  - Most 1/2 to be sporadic
  - Autosomal dominant, recessive and X-linked described
- Chromosomal anomalies in 10-20%
  - Trisomy 18, 13, 8
  - Trisomy
- Epidemiology
  - Multiple case reports implicating a variety of etiologic agents
    - Traumatogen
    - Alcohol, cocaine, vaginostomy
    - Infections
    - Cytomegalovirus (CMV), rubella
    - Destructive etiologies
    - Ischemia, bleed
- Associated abnormalities
  - Fetal body anomalies seen in 60%
    - Cardiac
    - Genitourinary
    - Gastroschisis
    - Nuchal transluency
- Embryology
  - Complete formation of CC is late embryologic event
  - CC forms in midline lamina between 8-20 weeks
    - Develops from anterior to posterior except rostrum which is last
  - Genus = body = splenium = rostrum
    - Thinning continues until after birth
    - Partial agenesis, splenium and rostrum missing
    - Genus and body present to varying degrees
  - Multiple syndromes described
    - Lacatil syndrome
    - Dandy-Walker continuum, ACC, occulal abnormalities, choroid plexus cysts
    - Aper syndrome
    - Craniosynostosis, syndactyly
    - Fryns syndrome
    - Diaphragmatic hernia, scimngnathia, facial anomalies, distal limb hypoplasia
    - Meckel-Gruner syndrome
    - Exencephaly, polydactyly, polyphocomelic kidneys
    - Walker-Warburg syndrome
    - Microcephaly, encephalocele, occulal abnormalities

Natural History & Prognosis
- Isolated (pediatric data)
  - 75% normal or near-normal at 1 year
  - Subtle cognitive defects may develop later
- Large, longitudinal studies for fetal diagnosis lacking
- Poor prognosis if associated with other malformations, syndrome or chromosomal abnormalities

Treatment
- Karyotype recommended even if isolated finding
- Full work-up after delivery

DIAGNOSTIC CHECKLIST

Consider
- In setting of mild ventriculomegaly
- MRI very helpful in making diagnosis and evaluating for associated anomalies

Image Interpretation Pearls
- Diagnosis may be missed before 16-20 weeks
- Formations is not complete
- Absent cavum septum pellucidum should raise suspicion for ACC
- Other brain and systemic abnormalities common

SELECTED REFERENCES

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - MRI ventriculomegaly
  - Diagnosis easily missed
- 5% of mild ventriculomegaly cases have ACC
- Discovered with other more obvious findings
- Incidental finding
AGENESIS OF THE CORPUS CALLOSUM

[IMAGE GALLERY]

Typical

(Left) Axial ultrasound or echography of a case of ACC. Note that the occipital wall of the frontal horns is farther than the occipital horns (b). The 3rd ventricle is elevated (arrows). This was shown to better advantage in the coronal plane. (Right) Coronal ultrasound after delivery shows classic "butterfly-shaped" lateral ventricles (arrows) with an elevated 3rd ventricle.

Typical

(Left) Coronal ultrasound shows an echogenic, multicystic mass in the region of the interhemispheric fissure (arrows). This is characteristic of a lipoma raising a strong suspicion for ACC. (Right) Coronal gross pathology shows a lipoma (arrows) corresponding to the mass seen on ultrasound. Note the absence of the corpus callosum, which would normally connect the two hemispheres. 50% of lipomas have associated ACC. (Also shown in Radiographics, ref 1).

Typical

(Left) Sagittal T2W MR in a callosal hypogenesis showing a very acute portion of the corpus callosum anteriorly (arrows). The cingulate gyri is short, with the remaining gyrus arranged in a radial pattern. (Right) Axial T2W MR shows a complex, irregularly shaped, interhemispheric cyst (arrows), associated with ACC. The remaining brain has a classic "butterfly" shape, with joining of the frontal horns observed medially and widening of the atria and occipital horns.
MILD VENTRICULOMEGALY

TERMINOLOGY

Abbreviations and Synonyms
- Mild ventriculomegaly (MV)
- Borderline ventriculomegaly

Definitions
- Atrial of lateral ventricle measures 10-12 mm

IMAGING FINDINGS

General Features
- Best diagnostic clue: Enlarged atria of lateral ventricle on routine axial view
- Location: Bilateral > unilateral
- Size
  - Normal atria < 10 mm
  - Mean diameter of 7.6 mm (+/- 0.6)
  - 70% of hemispheric at 18 wks
  - 10% of hemispheric at 28 wks

Ultrasoundographic Findings
- Enlarged lateral ventricular atria
- Slight plane through lateral ventricle
- Internal wall-to-internal wall measurement
  - ≥ 10 mm and ≤ 12 mm considered MV
  - 30% relative in area

- Most are stable during pregnancy
- Some progress during pregnancy
- Rarely unilateral
- Isolated finding at time of ultrasound
- 4% with subsequent brain anomaly
- Progessive hydrocephalus
- Cystic brain lesion
- 9% with a malformation not diagnosed in utero

MR Findings
- Additional intracranial anomaly seen in 8%
- Best after 28 weeks

Imaging Recommendations
- Best imaging tool: Routine transverse atrial assessment
- Protocol advice
  - Measure atria of lateral ventricle in every case
  - < 10 mm in 20/23rd trimester
  - Serial ultrasound to follow mild ventriculomegaly
  - Fetal MRI
  - Look for markers of trisomy 21

DIFFERENTIAL DIAGNOSIS

Agenesis of corpus callosum (CC)
- Complete or partial absence of CC
- MV ± colpocephaly
- Teardrop-shaped ventricles

DDx: Obstructive Hydrocephalus
- Aqueductal Stenosis
- Aqueductal Stenosis
- C. Hidrotubefugae
- Opt. Colpocephaly
MILD VENTRICULOMEGALY

**Terminology**
- Borderline ventriculomegaly
- Atrium of lateral ventricle measures 10-12 mm

**Imaging Findings**
- Internal wall-to-internal wall measurement
- 30% resolve in utero
- Easily unilateral
- Serial ultrasounds to follow mild ventriculomegaly

**Key Facts**
- Absent carunc potency

**Obstructive hydrocephalus**
- Aqueductal stenosis
- Dandy-Walker continuum (DW continuum)
- Intracranial hemorrhage (IC hemorrhage)

**PATHOLOGY**

**General Features**
- Genetics
  - 4% with aneuploidy
  - Trisomy 21 most common
- Etiology
  - 90% idiopathic
  - Normal outcome
  - Maternal infection
  - Rare cause
  - Cytomegalovirus (CMV)
  - Chromosome anomaly
  - Intracranial hemorrhage
  - Other cerebral anomaly

**CLINICAL ISSUES**

**Presentation**
- Most common signs/symptoms: Abnormal second trimester routine ultrasound screen
- Other signs/symptoms: Abnormal maternal serum screen for trisomy 21

**Demographics**
- Age: Mean maternal age is 28
- Gender
  - M/F = 3:1
- Larger calvarial volume in males
- More likely idiopathic in males

**Natural History & Prognosis**
- 96% with abnormal outcome when isolated
- 4% aneuploidy
- Better prognosis when unilateral

**Treatment**
- Postnatal assessment
- Imaging surveillance
- Developmental follow-up at least until 6 yrs old

**Top Differential Diagnoses**
- Agenesis of corpus callosum (CC)
- Obstructive hydrocephalus

**Pathology**
- 4% with aneuploidy
- 90% idiopathic

**Clinical Issues**
- M/F = 3:1

**DIAGNOSTIC CHECKLIST**

**Consider**
- Idiopathic MV is a diagnosis of exclusion
- Genetic amniocentesis
- Maternal infection screen
- Fetal MRI

**Image Interpretation Pearls**
- More likely idiopathic in male fetuses, especially when presenting > 20 weeks

**SELECTED REFERENCES**


**IMAGE GALLERY**

**Note:**
- (Left) Axial ultrasound shows ventriculomegaly in a 19 week fetus. Calipers measure the depth of the lateral ventricle. The choroid plexus (arrows) is displaced peripherally. (Right) Axial ultrasound at the level of the thalami shows a moderately dilated ventricle with echogenic debris in the presence of two dilated, non-communicating lateral ventricles (arrows) and normal scalp vessels. (From: http://www.radiology.com)
TERMINOLOGY

Abbreviations and Synonyms
- Alobar holoprosencephaly
- Holoprosencephaly (HPE)

Definitions
- Severe brain malformation due to early arrest in brain cleavage and rotation
- Nonaencraniaceous for associated facial malformations
  - Cyclopia
  - Single midline eye
  - Arhinia (absent nose)
  - Proptosis may be present
- Ethrocephaly
- Severe hypotelorism
- Arhinia
- Proptosis
- Gelocephaly
- Hypotelorism
- Face with single nostril
- Face with median cleft lip
- Cleft lip and palate
- Hypotelorism
- Flattened nose
- Face with median philtrum premaxilla anlage and flat nose
- Bilateral cleft lip

IMAGING FINDINGS

General Features
- Best diagnostic clue
  - First trimester
    - Absent "butterfly" sign (see below); Abnormal appearance of choroid plexus
  - Second/third trimesters
    - Fused thalamus with monoventricle

Ultrasoundographic Findings
- Grayscale Ultrasound
  - "Butterfly" sign
    - Both choroid normally seen as "butterfly wings"
    - Used in the first trimester
  - If absent increases suspicion for HPE
- Single ventricle
  - Absent midline structures
    - Cavum septi pellucidi
    - Falc cerebri
    - 3rd ventricle
    - Corpus callosum
  - Fused thalami
  - Dorsal sac
    - Cystic extension of monoventricle
    - Herniation of tela choroidea

DDx: Alobar Holoprosencephaly

- Hydranencephaly
- Megencephalic Cyst
- Aqueduct Stenosis
- Aqueduct Stenosis
**Terminology**
- Severe brain malformation due to early arrest in brain cleavage and rotation

**Imaging Findings**
- Single ventricle
- Fused thalami
- Dorsal sac
- Remaining brain has 3 appearances: "Pancake", "cup" and "bull"
- Facial anomalies

**Top Differential Diagnoses**
- Hydranencephaly
- Aqueductal stenosis
- Polycystic
- Arachnoid/gliopendymal cyst

**Key Facts**
- Hydranencephaly/atonencephaly

**Pathology**
- Isolated HPE, often normal karyotype
- Trisomy 13 (T13) most common chromosomal association
- At least 13 different chromosomal regions contain genes involved in HPE pathogenesis
- Infants of diabetic mothers have 1% risk

**Clinical Issues**
- Karyotype abnormalities
- Termination offered

**Diagnostic Checklist**
- "The face predicts the brain"
- Facial malformations of any kind should trigger a very careful evaluation of the brain

- Facial clefts
- Nasal alveolar retrusion
- Apert syndrome
- Bitemporal hemiatrophy
- Aqueductal stenosis
- Head often large
- Dilated 3rd ventricle
- Thalami not fused
- Cavum septi pellucidi present
- May be thinned or obliterated in severe hydrocephalus

**Porencephaly**
- Usually asymmetric ventricular enlargement
- May see evidence of residual hematoma which evolves over time

**Atrachnoid/gliopendymal cyst**
- Can be confused with dorsal sac if large

**Aplasencephaly/atelencephaly**
- Rare severe malformation
- Absent brain above the tentorium
- Maldevelopment of face
- May have complete absence of orbits +/- none
- Facial skin tags cause confusion with facial clefting

**PATHOLOGY**

**General Features**
- Genetics
  - Most cases sporadic
  - Isolated HPE often normal karyotype
  - Chromosomal abnormalities
    - Trisomy 13 (T13) most common chromosomal association
    - Also trisomy 18, triploidy, monosomy 21
    - Autosomal recessive, dominant, and X-linked forms described
  - At least 12 different chromosomal regions contain genes involved in HPE pathogenesis
  - Sonic hedgehog (SHH) gene was the first gene identified in 1996
  - SHH mutations in 15% of familial HPE

**Differential Diagnosis**
- Hydranencephaly
  - No cerebral tissue
  - Tats present
  - Normal facial development
ALOBAR HOLOPROSENCEPHALY

- SHH mutation in < 5% of sporadic cases
- Other implicated genes
  - ZIC2
  - SIX3
  - TGIF
- Biology
  - Maternal diabetes
  - Infants of diabetic mothers have 1% risk
  - Teratogens
  - Retinoic acid
  - Alcohol
- Epidemiology
  - 1 in 16,000 births
  - More common in utero
  - 1.25% in terminated pregnancies
- Associated abnormalities
  - Part of multiple syndromes
  - Smith-Lemli-Opitz syndrome
  - Aicardi syndrome
  - Fryns syndrome
- Embryology
  - Primitive brain develops 3 vesicles at day 22-24
  - Prosencephalon
  - Mesencephalon
  - Rhombencephalon
- Cleavage of prosencephalon gives rise to telencephalon and diencephalon at 32 days
  - Telencephalon gives rise to
    - Cerebral hemispheres
    - Putamen
  - Diencephalon gives rise to
    - Thalamus
    - Hypothalamus
  - Globus pallidus
  - Optic vesicles
- Abnormal cleavage of prosencephalon results in spectrum of brain malformations
- Anatomists prefer term "abnormal cleavage" to "fusion"
- Abnormal budding of optic vesicles = eye and orbit malformations
- Associated general defect in midline cranial cartilage differentiation rostral to notochord
- Midface anomalies

Gross Pathologic & Surgical Features
- Malformations of midline structures anterior to sphenoid sinus
  - Compromised suture and cartilage development
  - Single central incisor
  - Single nasal bone
  - Absent cribsi galli

CLINICAL ISSUES

Presentation
- Other signs/symptoms:
  - May have an abnormal triple screen (T13)
  - May be diagnosed in 1st trimester

Natural History & Prognosis
- Stillbirth common
- Livestream infants have short lifespan
  - Seizure difficulties
  - Seizure disorder

Treatment
- Karyotype all fetuses
- Termination offered
- Fetal intervention not indicated
- Consider cephalocentesis to allow vaginal delivery if pregnancy carried
  - Avoids maternal morbidity of cesarean section for non-viable fetus

DIAGNOSTIC CHECKLIST

Consider
- Fetal MRI if findings equivocal
- Differentiates from other entities with better prognoses

Image Interpretation Pearls
- "The face predicts the brain"
  - Facial malformations of any kind should trigger a very careful evaluation of the brain

SELECTED REFERENCES

**TERMINOLOGY**

**Abbreviations and Synonyms**
- Semilobar holoprosencephaly
- Lobar holoprosencephaly
- Holoprosencephaly (HPE) developmental spectrum
  - Continuum with no sharp division among types

**Definitions**
- Less severe entities within holoprosencephaly spectrum
  - Semilobar HPE
    - Incomplete interhemispheric fissure
    - Rudimentary cerebral lobes
    - Fused anteriorly
    - Olfactory tracts and bulbs absent or hypoplastic
    - Abnormal corpus callosum
  - Lobar HPE
    - Interhemispheric fissure present
    - Well-formed lobes
    - May be normal size
    - Frontal lobes most likely to be hypoplastic
    - Often midline continuity of one or more gyri
    - Thalami normal or partly fused
    - Fornices fused
    - Argyos anterior cerebral artery (ACA)

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue
  - Semilobar HPE
  - Anterior hemispheric fusion
  - Lobar HPE
  - Fused brain, specific sign when present

**Ultrasoundographic Findings**
- Grayscale Ultrasound
  - Moosventricle anteriorly
  - Separate occipital horns
  - Absent cavity septi pellucidi (CSP)
  - Callosal dysgenesis
  - Deficient anterior
  - Abnormal course of ACA
  - Thalami
    - May be partly cleaved
    - Fornical fusion
    - Creates a round "mass" in third ventricle
  - Stachycephaly
    - Rounded head secondary to frontal lobe hypoplasia
  - Macroccephaly

**DDx: Holoprosencephaly**

- Aqueduct Stenosis
- Septo-Optic Dysplasia
- Septo-Cephalic Dysgenesis
- Schizencephaly
**TERMINOLOGY**
- Less severe entities within holoprosencephaly spectrum

**IMAGING FINDINGS**
- Monoventricle anteriorly
- Absent cavitum septi pellucidi (CSP)
- Callosal dysgenesis
- Facial anomalies

**TOP DIFFERENTIAL DIAGNOSES**
- Aqueductal stenosis
- Agenesis of the corpus callosum
- Schizencephaly
- Septo-optic dysplasia
- Syntelencephaly

**KEY FACTS**
- Pathology:
  - Infants of diabetic mothers have 1% risk
  - Overall HPE 1:16,000 births
- Clinical Issues:
  - Depends on type and severity
  - Semilobar HPE worse than lobar HPE
  - Karyotype all fetuses
- Diagnostic Checklist:
  - Fetal MRI if findings equivocal
  - Frontal lobe hypoplasia in all forms
  - Round appearance to head in multiple scan planes
  - Communication between frontal horns of lateral ventricles is never normal
  - Fused fornices is specific sign of lobar holoprosencephaly

**DIFFERENTIAL DIAGNOSIS**

**Aqueductal stenosis**
- Interhemispheric fissure present
- Dilated 3rd ventricle
  - Thalami not fused
  - Fornices not fused
- CSP present
- May be thinned or obliterated in severe hydrocephalus
- Normal face
- Abducted thumbs seen in X-linked recessive form

**Absent cavitum septi pellucidi**
- Agenesia of the corpus callosum
- Interhemispheric fissure present
- Lateral ventricles parallel
- Fetal hydrocephalus
- "Trident-shaped" appearance to anterior horns
- Abnormal course callosomarginal/pet/Callosal arteries
- Schizencephaly
- Interhemispheric fissure present
- Cerebral cortical cleft lined by gray matter
- Septo-optic dysplasia
- Downward point to anterior horns
- Flat top or squared-off appearance of frontal horns

**Syntelencephaly**
- Midline interhemispheric fusion
- Anterior and posterior horns separate
- Hemispheres fused centrally
- Associated with 13q deletion
- Hypoplastic thalami and syndactyly with 13q- deletion

**PATHOLOGY**

**GENERAL FEATURES**
- Genetics
  - Most cases sporadic
  - Autosomal dominant, recessive and X-linked forms described
SEMILOBAR, LOBAR HOLOPROSENCEPHALY

- At least 12 different chromosomal regions contain genes involved in HPE pathogenesis
- Known genes include:
  - Sonic Hedgehog (SHH)
  - ZIC2
  - SIX3
  - TGIF
- Also seen in trisomies 13, 18, & triploidy

- Etiology:
  - Maternal diabetes
  - Infants of diabetic mothers have 1% risk
  - Teratogens
  - Selective acidosis
  - Alcohol

- Epidemiology:
  - Overall HPE 1/16,000 births
  - Hard to separate semilobar/semilobar/lobar
  - Milder forms may not be recognized
  - All forms commoner in fetus than livebirths
  - HPE seen in 1250 terminated pregnancies

- Embryology:
  - Primitive brain develops 3 vesicles day 22-24
  - Prosencephalon
  - Rhombencephalon
  - Mesencephalon

- Clavages of prosencephalon gives rise to telencephalon and diencephalon at 32 days;
  - Telencephalon gives rise to:
    - Cerebral hemispheres
    - Putamen
    - Caudate nucleus
  - Diencephalon gives rise to:
    - Thalamus
    - Hypothalamus
    - Globus pallidus
    - Optic vesicles
  - Abnormal cleavage of prosencephalon results in spectrum of brain malformation

CLINICAL ISSUES

Presentation:
- Most common signs/symptoms: Abnormal communication between frontal horns of lateral ventricles

Natural History & Prognosis:
- Depends on type and severity
- Semilobar HPE worse than lobar HPE
- Mental retardation
- Developmental delay
- Seizure disorder
- Hypothalamic-pituitary malfunction
- Visual problems

Treatment:
- Fetal:
  - Karyotype all fetuses
  - Office teratoma
do
  - Cerebral evaluation by pediatric neuroradiology
- Postnatal:
  - Careful evaluation by pediatric neuroradiology
  - Postnatal imaging to define brain malformation

- Essential before embarking on extensive surgical repair of focal malformations

DIAGNOSTIC CHECKLIST

Consider:
- Fetal MRI if findings equivocal
- Characteristic degree brain malformation
- Assess with parental counseling

Image Interpretation Pearls:
- Fetal lobe hypoplasia in all fetuses
- Fetalcephaly
- Roepr appearance to head in multiple scan planes
- Communication between frontal horns of lateral ventricles is never normal
- Fixed fontes is specific sign of lobar holoprosencephaly

SELECTED REFERENCES

SEMILOBAR, LOBAR HOLOPROSENCEPHALY

IMAGE GALLERY

Typical

(Left) Axial ultrasonound ultrasound shows a single ventricle with communication anteriorly (open arrows) but with differentiation of the occipital horns (arrows). (Right) Coronal ultrasonound after delivery shows the monocephalic (arrows) but some change of thalass (curved arrows) in this case of semilobar holoprosencephaly.

Typical

(Left) Coronal ultrasonound shows ventricular communication and an apparent "mass" (arrows) within third ventricle. The "mass" is formed by fused thalami and is an important finding in lobar holoprosencephaly. (Right) Coronal T1 WI MR of fetal brain shows classic findings of lobar holoprosencephaly. There is an absent ependymal septal (arrow) with communication of ventricles. Fused thalami (arrows) are well demonstrated.

Typical

(Left) Coronal ultrasonound on day one at NICU shows separation of the thalami (curved arrows). Fused thalami are anterior to posterior in the third ventricle (arrows). (Right) Coronal T1 WI MR in the same infant shows well-developed cerebral hemispheres and interhemispheric fissure (arrows).Absent t1 and fused thalami (open arrows) are consistent with lobar holoprosencephaly.
SEPTO-OPTIC DYSPLASIA

**TERMINOLOGY**

**Abbreviations and Synonyms**
- Septo-optic dysplasia (SOD)
- De Morsier syndrome
- First described condition in 1956
- Kaplan-Glenn-Hoyt syndrome
- Suprasellar dysgenesis
- Septo-optic-pituitary dysgenesis
- SOD “pits”
- Term coined for cases with additional brain malformations
- Cortical dysplasias
- Schizencephaly

**Definitions**
- Heterogeneous group of disorders with anomalies including:
  - Hypoplasia optic nerves and tracts
  - Absence of cavum septi pellucidi
  - Hypothalamic pituitary dysfunction
  - Some consider SOD mildest form of holoprosencephaly

**IMAGING FINDINGS**

**General Features**
- First diagnostic clue: Absent cavum septi pellucidi

**Ultrasonographic Findings**
- CSP absent
- CSP normally seen as parallel echogenic lines in anterior midline of brain
- Seen on standard axial view for biparietal diameter and head circumference measurements
- Mild ventriculomegaly
- Look at ventricular wall for nodularity
- Nodules = heterotopia
- Anterior horns lateral ventricles have "flat" or "squared-off" appearance
- Anterior horns are connected across the midline
- Corpus callesum present but may be thinned

**MR Findings**
- Fetal MRI does not yet have sufficient resolution to evaluate optic chiasms and tracts
- Confirms absent cavum septi pellucidi (CSP)
- Excludes agenesis of corpus callosum as cause
- Demonstrates associated brain malformation
- Schizencephaly (seen in 50-70% postnatal cases)
- Heterotopia
- Axial

*Images of various medical conditions associated with Septo-Optic Dysplasia.*
SEPTO-OPTIC DYSPLASIA

Key Facts

Clinical Issues
- Isolated optic nerve hypoplasia = good developmental outcome
- Associated hemispheric anomalies = more guarded prognosis
- 75-90% have brain abnormalities
- 45% pituitary insufficiency
- Visual defects vary

Diagnostic Checklist
- Fetal MRI for complete evaluation in all cases
- CSP is a marker of normal fetal central nervous system development
- Lack of fused fonticuli helps differentiate from lobar holoprosencephaly

Differential Diagnosis

Agenesis of the corpus callosum
- Absent CSP
- Partial lateral ventricles
- Abnormal corona radiata/pericallosal arteries
- "Triad-shaped" appearance of anterior horns
- Gyral hypoplasia
- Teardrop-shaped ventricles
- Radial configuration of gyri
- May be associated with interhemispheric cyst

Lobar holoprosencephaly
- Forehead anomalies
- Anterior cerebral artery
- Single rather than paired anterior cerebral arteries
- Runs under frontal bone
- Facial anomalies
- If associated trisomy 13
- Omphalocele
- Congenital heart disease
- Polydactyly
- Cystic renal disease

Schizencephaly
- Absent CSP
- Cleft in cerebral parenchyma lined with grey matter
- Cleft extends from brain surface to ventricular space
- Ventricular wall may be "fused" toward defect
- Unilateral or bilateral defect
- Small unilateral defect may not be apparent on ultrasound
- May occur with SOD
- "SOD plus"

PATHOLOGY

General Features
- Genetics
  - Most cases are sporadic
  - Autosomal dominant and recessive types described
  - Mutation in homeobox gene Hex1/HESX1
  - Homozygous mutation = full syndrome
  - Heterozygous mutation = milder form
  - Inactivation Hex1 by an Arg53Cys substitution
  - Deficient anterior lobe of pituitary
  - IQg deletion
  - Retinal dysplasia
  - Valproate
  - Ethanol
  - Maternal diabetes mellitus
  - Cytomegalovirus (CMV) infection
  - Maternal drug abuse
  - Possible early vascular insult
  - Cerebellar
  - Hypothyroid

SEPTO-OPTIC DYSPLASIA

- Amphetamine
- Epidemiology
  - 1/50,000
  - M:F = 1
  - Younger mothers and first born infants

Gross Pathologic & Surgical Features
- Small optic chiasm and nerves
  - Sparse/absent myelinated fibers
  - Optic nerve hypoplasia unilateral in 20%
- Deficient or absent CSP
- Pituitary hypoplasia common

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - Absent CSP
  - Fused anterior horns of ventricles

Natural History & Prognosis
- Depends on degree of severity and associated abnormalities
  - Isolated optic nerve hypoplasia → good developmental outcome
  - Optic nerve hypoplasia occur on neuroimaging in 60% cases after birth
  - Clinical diagnosis by ophthalmologic examination
  - Fetal presentation probably implies more severe end of spectrum
  - Associated hemiparesis anomalies → more guarded prognosis
  - 75-90% have brain abnormalities
  - 45% pituitary insufficiency
  - Secondary to hypothalamic malformation
  - Short stature
  - Mental retardation
  - Anosmia
  - 50% bilateral optic nerve hypoplasia
  - Optic nerve hypoplasia can be unilateral
  - Visual defects vary
  - Color blindness to complete visual loss
  - Strabismus

Treatment
- Not indicated, for early delivery
- Careful assessment of infant by pediatric endocrinologist and ophthalmologist

DIAGNOSTIC CHECKLIST

Consider
- Fetal MRI for complete evaluation in all cases
- Identify associated malformations
- Not yet adequate to evaluate optic chiasm and tracts

Image Interpretation Pearls
- Do not assume an absent CSP is "technical"
- CSF is a matter of normal fetal vertical nervous system development
- If absent, significant neurological conditions to consider include
  - SOCD
  - Agenesis of the corpus callosum
  - Schizencephaly
  - Lack of fused foramina helps differentiate from lobar holoprosencephaly

SELECTED REFERENCES

Typical

(Left) Coronal ultrasound shows absence of the corpus callosum, septi pellucidi, and downward pointing of the frontal horns (arrows) which communicate across the midline and are "squared-off" (open arrow) superiorly. (Right) Coronal T200 MR confirms prenatal sonographic findings of downward pointing frontal horns (arrows) and communicating, "squared-off" ventricles (open arrow). Obstructive examination confirmed SDG.

Variant

(Left) Axial ultrasound shows continuity of the frontal horns across the midline (arrow) where the corpus callosum is absent. Additional images showed mildly ventriculomegaly. SDG confirmed at birth. (Right) Axial T200 MR shows an absent corpus callosum with ventricles in continuity across the midline. Note the "flat top" appearance (curved arrow) of the frontal horns and mild ventriculomegaly (arrows).

(Left) Axial ultrasound in a paced-controlled diabetic infant revealed a lacunar cavitary shows an absent CSP and squared frontal horns (arrow). (Right) Axial oblique ultrasound of the posterior fossa. A CSP should be seen on this scan plane in the region of the arrows. Septo-Optic Dysplasia diagnosed at birth. SDG can have further consequences for the neonate. Always look for the CSP.
ABSENT CAVUM SEPTI PELLUCIDII

TERMINOLOGY

Abbreviations and Synonyms
• Absent cavum septi pellucidi (CSP)

Definitions
• Absence of cerebrospinal fluid (CSF) filled space between frontal horns

IMAGING FINDINGS

General Features
• Best diagnostic clue: Nonvisualization of CSP
• Location: CSP normal fluid collection between frontal horns of lateral ventricles

Ultrasonographic Findings
• Continuity of frontal horns across midline
• Almost always associated with other anomalies
  • Holoprosencephaly spectrum
  • Agenesis of the corpus callosum
  • Schizencephaly

MR Findings
• Can often make more specific diagnosis than ultrasound
• Identify associated parenchymal abnormalities
  • Heterotopias

DIFFERENTIAL DIAGNOSIS

Septo-optic dysplasia (SOD)
• Some consider this mildest form of holoprosencephaly
• Absent CSP most important fetal finding
• Hypoplastic optic nerves
  • In utero imaging not adequate to evaluate
  • Requires postnatal MRI and ophthalmic examination
• May present in childhood with seizures

Holoprosencephaly
• Alobar
  • Monoventricle without midline structures (including absent CSP)
  • Absent thalami
  • Mantle of brain tissue surrounding monoventricle
  • May have dorsal sac
• Semilobar
  • Absent CSP
  • Some differentiation of occipital horns
• Lobar
  • Absent CSP
  • Further differentiation of ventricles, communication only between frontal horns
  • Fused foramina most specific finding
• All may have varying degrees of facial malformations

DDx: Conditions With An Absent CSP

- Agenesis CC
- Septo-Optic Dysplasia
- Schizencephaly
- Semilobar Holopros
ABSENT CAVUM SEPTI PELLUCIDI

Imaging Findings
- Continuity of frontal horns across midline
- Almost always associated with other anomalies

Top Differential Diagnoses
- Septo-optic dysplasia (SOD)
- Holoprosencephaly
- Agenesis of the corpus callosum
- Chiromicrocephaly
- Choroid plexus hypoplasia

Key Facts
- Chiari II malformation

Clinical Issues
- CSP should be documented on every scan
- Rarely an isolated finding

Diagnostic Checklist
- CSP is an important marker for normal fetal central nervous system development
- Possibly related to development pathology of the limbic system

DIAGNOSTIC CHECKLIST

Consider
- Fetalm MRI to clarify findings
- Postnatal MRI if isolated to look for optic tracts and other findings of SOD

Image Interpretation Pearls
- CSP is an important marker for normal fetal central nervous system development
- Never assume absent CSP is "technical", can be a marker of serious brain malformation

SELECTED REFERENCES

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
- Absence on routine views
- CSP should be noted on every scan

Natural History & Prognosis
- CSP usually seen in all fetuses
- Subsequently regresses with age
- May persist into adulthood as a normal variant
- Absent CSP is associated with schizophrenia
- Both absence of and persisten: CSP

Hydranencephaly
- Supratentorial space filled with CSP
- Absent normal brain parenchyma
- Fetal present
- Normal posterior fossa
- Absent middle and anterior cerebral artery flow

IMAGE GALLERY

(Left) Axial E20 MRI of fetal hydranencephaly shows extensive continuity of the lateral ventricles, no cavum septi pellucidi was identified. The arrow marks where the CSP should be seen at this level. (Right) Axial ultrasound shows polymicrogyria causes measure ventricle at 12 mm and absent CSP (same marks where it should be seen in this case with absence of the corpus callosum.)
**HYDRANENCEPHALY**

**TERMINOLOGY**

**Abbreviations and Synonyms**
- hydrencephaly

**Definitions**
- Complete destruction of cerebral hemispheres
- Normal cerebellum and brainstem

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue
  - Fluid-filled supratentorial space
- Falx present
- Normal posterior fossa

**Ultrasonographic Findings**
- Replacement of cerebral hemispheres by fluid
  - End stage of process
- May be seen at presentation
- Variable early intracranial findings
  - Focal hemorrhage
  - Echogenic mass
  - Diffuse parenchymal destruction
  - Diffusely abnormal intracranial echoes
- Head size usually normal

**MR Findings**
- Cerebral hemispheres/cortical mantle not present
- Occasional/ small, orbital surface of frontal lobes may remain
- Medial temporal or inner occipital lobes may be present
- Supplied by posterior circulation
- Anterior temporal lobes supplied by carotids
  - If present, hydrencephaly is unlikely
- Thalamus and basal ganglia usually present, although may be incomplete
- Separated thalamus
- Thalamus may herniate into supratentorial space
- Thalamic tissue may be nodular in appearance, mimicking fusion
- Normal cerebellum
- Normal/atrophic brainstem

**DDx: Hydrancephaly**

- Aqueductal Stenosis
- Bilateral Schizencephaly
- Holoprosencephaly
- Chiropocephalic Cyst
Terminology
- Complete destruction of cerebral hemispheres

Imaging Findings
- Fluid-filled supratentorial space
- Falsely present
- Normal posterior fossa
- Medial temporal or inner occipital lobes also may be present
- Head size usually normal
- Macroprosencephaly may occasionally be seen
- Best imaging tool: MRI to evaluate for presence of cortical mantle

Top Differential Diagnoses
- Hydrocephalus
- Holoprosencephaly

Imaging Recommendations
- Best imaging tool: MRI to evaluate for presence of cortical mantle
- Look for placental abruption as cause
- Look for signs of infection
- Complete anatomic survey

DIFFERENTIAL DIAGNOSIS

Hydrocephalus
- Cortical mantle present
- Posterior fossa often abnormal
  - Dandy-Walker continuum: Posterior fossa cyst
  - Chiari II malformation: Obliteration of cisterna magna
- Aqueductal stenosis
- Dilated third ventricle
- Head often large
- In severe cases, cortical mantle may be difficult to discern

Holoprosencephaly
- Cortical mantle
- Absent falx/monoventricle
- Fused thalamai
- Microgyria
- Frequently associated with abnormal face
  - Midline facial cleft
  - Cyclopia
  - Proptosis
  - Cleft lip

Schizencephaly
- Bilateral giant open lip may mimic hydranencephaly
- Frontal and parieto-occipital cortex present
- Large symmetric cortical defects lined by grey matter

Gliopendymal cyst
- Large cysts can displace/ compress normal brain
- Centered on midline

Key Facts
- Schizencephaly
- Gliopendymal cyst
- Aprosencephaly/atelencephaly

Pathology
- Likely encephaloclastic destruction of previously normal cerebrum
- Scattered case reports of hemi-hydranencephaly

Clinical Issues
- May be misdiagnosed as hydrocephalus
- Prognosis is dismal
- 50% Ebeborn infants die in first month
- 85% mortality by end of first year

Diagnostic Checklist
- Beware "bulging brainstem" may mimic fused thalamai
- And be confused with holoprosencephaly

Aprosencephaly/atelencephaly
- Primary malformation
  - No development of structures derived from prosencephalon
- Usually associated with abnormal face
  - Anopthalmia/microphthalmia
  - Abnormal nose
  - Limb positioning abnormal

Subdural hemorrhage
- Would have to be large/bilateral
- Cerebral hemispheres compressed

PATHOLOGY

General Features
- Genetics
  - Usually sporadic and isolated
  - Autosomal recessive
  - Consanguineous family with defect mapped to chromosome 16p13.3-12.1
  - X-linked type
- Etiology
  - Likely encephaloclastic destruction of previously normal cerebrum
  - Vascular occlusion
    - Hemorrhage
    - Fetal/maternal hypotension
    - Infection
  - Vascular occlusion
    - Absent internal carotid system
    - Carotid intraluminal webs
    - Bilateral supraclinoid carotid occlusion
- Hemorrhage
  - Coagulation disorders
  - Thrombocytopenia
- Fetal/maternal hypotension
  - Maternal trauma
  - Placental abruption
  - Monochorionic co-twin demise
  - Cocaine abuse
HYDRANENCEPHALY

- Intraventricular infection
- Herpes simplex/varicella
- Multiple other agents cited as causative in isolated case reports
- Miscellaneous reported causes
- Irradiation
- Aggressive tumor brain destruction
- Vascular malformation

- Epidemiology
  - 1:4,000 live births
  - 0.6% of CNS malformations in perinatal/neonatal autopsy series
  - Scattered case reports of hemi-hydranencephaly
  - Increased risk
  - Smoking
  - Decreased maternal age

Gross Pathologic & Surgical Features
- Cerebral hemispheres replaced by thin sacs containing CSF and necrotic debris
- Sacs lined by transparent double-layer membrane
  - Outer layer = leptomeningeal tissue
  - Inner layer = glial tissue wihout ependyma (cortical and white matter remnants)
- Postmortem pathologic examination of carotid arteries rarely shows abnormalities
  - Suggests that primary carotid pathology not common cause
  - More likely hypotension/destruction
  - Postnatal imaging has shown intralaminar carotid webs in liveborn cases
- Fowler type
  - Characteristic proliferative "glomus-like" vasculopathy
  - Impairs vascular invasion of cerebral mantle in first trimester
  - Possible mitochondrial dysfunction
  - Careful examination of membranes/placenta may reveal co-twin demise

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - Has been diagnosed by US as early as 11 weeks gestational age
  - Failure to identify normal lateral ventricles and choroid plexus
  - Usually detected in second trimester
  - May be misdiagnosed as hydrocephalus

Natural History & Prognosis
- Prognosis is dismal
  - 50% liveborn infants die in first month
  - 85% mortality by end of first year
  - Occasional long term survivors
    - No cognitive function, require institutional care
    - Management issues may include control of macrocephaly
    - May require shunt or choroid plexectomy
    - Longest living survivor 20 yrs
    - Hemihydranencephaly
    - Better prognosis

- Developmental delay "mild" in 4 of 6 reported cases
- No recurrence risk unless Fowler type (autosomal recessive)

Treatment
- Infection screen
- Coagulation screen
- Consider karyotype
- Offer termination
  - If pregnancy progresses
  - No monitoring in labor
  - No resuscitation attempts
- If macrocephaly
  - Offer cephalocentesis to allow vaginal delivery
  - No impact on fetal prognosis
  - Avoids maternal morbidity, especially for future deliveries

DIAGNOSTIC CHECKLIST

Consider
- fetal MRI for clarification of anatomy
- Hydranencephaly almost invariably lethal
- Hydrocephalic infants may do well with shunt placement

Image Interpretation Pearls
- Beware "bulging brainstem" mimics fused thalamus and be confused with holoprosencephaly

SELECTED REFERENCES
Typical

(Top Left) Coronal ultrasound in a 14 week fetus with hydranencephaly shows a flat (arrow) with complete absence of cerebral tissue. (Right) Sagittal T2WI MR in a different case shows a normal posterior fossa (arrow) but complete lack of cerebral tissue. In this case, there is macrocrania, which can occasionally be seen in hydranencephaly, and it is left to be secondary to decreased CSF resorption.

Typical

(Top Left) Axial ultrasound shows absence of cerebral hemispheres with the falx preserved (open arrow). The brainstem extends into the supratentorial space (curved arrow). (Right) Axial T2WI MRI shows a similar appearance of absent cerebral hemispheres (full arrow). The brainstem is bulging into the supratentorial space (open arrow). This appearance can be confused with lowed thalami seen in holoprosencephaly.

Typical

(Top Left) Axial ultrasound shows a small amount of remaining parenchyma in the occipital lobes (arrows) in an otherwise completely fluid-filled supratentorial space (full - open arrow). (Right) Coronal T2WI MRI in a neonate shows similar findings, with preservation of a portion of the occipital lobes (arrows) and the cerebellum. These structures are supplied by the posterior circulation and are preserved in hydranencephaly.
ENCEPHALOMALACIA

Terminology

Abbreviations and Synonyms
- Encephalomalacia
- Periventricular leukomalacia (PVL)
- Porencephaly
- Poremchepliac cyst

Definitions
- Destructive lesions of brain parenchyma with several manifestations
- Encephalomalacia
  - Regional brain parenchymal damage
  - Associated astrocyt proliferation, glial septations
  - May see multiple small parenchymal defects
  - Defects not in communication with cerebral spinal fluid (CSF) spaces
- Porencephaly
  - Cavitary lesion due to focal brain destruction
  - Minimal glial reaction
  - Usually communicates with CSF space
  - Some authors consider 2 types of porencephaly
    - Type 1: Parenchymal damage followed by liquefaction/resorption
    - Type 2: Defect from generation or migration of neurons (e.g. schizencephaly)
  - Type 2 best considered separately as a primary developmental abnormality

Imaging Findings

General Features
- Best diagnostic clue
  - Porencephalic cyst: Intraventricular, avascular, fluid-filled structure without mass effect
  - Encephalomalacia: Findings often subtle
  - Ventriculomegaly may be first clue

ULTRASONOGRAPHIC FINDINGS
- Encephalomalacia
  - Affected periventricular white matter tracts have variable echogenicity
  - May be normal, especially earliest
  - Often subtle increased echogenicity
  - May be decreased due to parenchymal edema
  - Periventricular lucencies
  - Equal areas of cystic degeneration
  - Occurs later
- Porencephalic cysts
  - Round or irregular shape
  - Ex-vacuo, no mass effect
  - No flow on Doppler
  - If secondary to bleed
  - Hyperechoic focus evolving into anechoic CSF-filled cyst
- Hydrocephalus
  - Two potential causes

DDx: Focal Cystic Brain Lesions

- Schizencephaly
- Parenchymal Cyst
- Anechoic Cyst
**Key Facts**
- Hydrocephalus
- **Clinical Issues**
  - Important potential complication of fetal intervention
  - Mucocoele or twins at risk if co-twin demise
  - Apparently mild maternal trauma may cause devastating fetal cerebral injury
  - Neurodevelopmental outcome poor
  - Emergency delivery at time of acute event does not alter outcome

**Diagnostic Checklist**
- Fetal MRI in all suspicious cases and at-risk patients
- US findings can be subtle despite severe damage
- Normal US at time of acute event does not exclude brain injury

**Terminology**
- Destructive lesions of brain parenchyma with several manifestations

**Imaging Findings**
- *Poencephalic cyst*: Intralacral, avascular, fluid-filled structure without mass effect
- Encephalomalacia: Findings often subtle
- Venous thrombosis may be first clue
- Abnormal high T2 signal in adjacent brain parenchyma = destruction
- Affected periventricular white matter tracts have variable echogenicity

**Top Differential Diagnoses**
- Schizencephaly
- Arachnoid cyst
- Parenchymal destruction
- Intracranial bleed = obstruction to CSF flow

**Differential Diagnosis**
- *Vascular 'steal' + venous hypertension = parenchymal destruction*
- *Vein of Galen malformation*
  - Located in quadrigeminal plate cistern, postero-septor to thalami
- *Dural arteriovenous fistula*
- *Extravasal*
- *Enlarged feeding and draining vessels*
- Careful survey for other defects
- Vascular compromise = ischemic lesions elsewhere
- *Ectopia*
- *Extremities*
- *Signs of infection*
- *Liver calcifications*
- *Intracranial calcifications*
- *Hydrops*
- *Monitor anamnestic fluid volume*
- *Renal ischemia = oligohydramnios*
- *CNS injury = impaired swallowing = polyhydramnios*

**Schizencephaly**
- Cortical cleft, lined with gray matter
- Wedge shaped rather than round or irregular

**Arachnoid cyst**
- Extraventricular
- Not associated with destructive process

**Hydrocephalus**
- Look for structural cause
- *Dandy-Walker continuum*
- *Chiari II malformation*
- *Aqueductal stenosis*

**Vascular malformation**
- Flow on Doppler interrogation

**MK Findings**
- *TIWI*
  - Increased signal in areas of ischemic injury = reactive astrocrosis
  - Focal areas of high signal may represent hemorrhage
  - Hemorrhage and ischemia often seen together
- *T2WI*
  - Encephalomalacia
  - Anomalously high T2 signal in adjacent brain parenchyma = destruction
  - Reactive astrocrosis
  - Glial septa better visualized on ultrasound
  - Foci of low T2 signal may represent areas of hemorrhage or calcification
- *Poencephaly*
  - Cyst fluid follows CSF signal
  - Space not lined with gray matter
  - Communication with ventricles
- *DWI*
  - Diffusion weighted imaging
  - Not routinely used in fetal MRI
  - Preliminary reports suggest increased sensitivity for ischemia

**Imaging Recommendations**
- Best imaging tool
  - Consider MRI in at-risk pregnancy
  - Better demonstration of blood products
  - Better demonstration parenchymal destruction
  - DWI may prove to be most sensitive method to detect acute ischemia
- Lesions develop over time
- Normal ultrasound scan at time of an acute "event" does not exclude brain injury
  - Re-imaging at 10 to 14 days
- Examine periventricular white matter carefully for abnormal echogenicity (encephalomalacia)
- Check for placental disruption
- Look for vascular malformations: Important cause of ischemic brain injury
PATHOLOGY

General Features
- General path comments
  - Fetal inflammatory response to infection or hypoxic/ischemic event
  - Cytokine release
  - Research focusing on control of inflammation to prevent oroging damage
- Epilepsy
- Seizure
  - Cerebral/Septal
  - Vascular: Hypoperfusion
- Intracranial hemorrhage
- Monochorionic twin demise/twin-twin transfusion syndrome
- Fetal intervention: Intraventricular transfusion, twin vessel laser coagulation
- Maternal drug use: Cocaine
- Maternal trauma/placental abruption
- Syndromic
  - Encephalocraniofacial dysmorphism
  - Familial otoacoustic syndrome type I
  - Urologic malformations
- Teratogen exposure
- Vitamin A
  - Fetal surgery
  - 21% incidence central nervous system (CNS) injury in 33 patients with fetal surgery
- Epidemiology: Rare

Gross Pathologic & Surgical Features
- Encephalocerebrospinal dysplasia
  - Focal destruction of normal parenchyma
  - Usually unilateral
  - Smooth-walled cavity
  - Surrounding brain structural normal
- Encephalomalacia
  - Marked diffuse brain insult = multicystic
  - Provokes astroglial response with gliotic reaction
  - Cysts may have shaggy walls
  - Can have calcifications

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - CSF-filled space at fetal skull
  - Ventriculomegaly without structural malformation
- Other signs/symptoms
  - Important potential complication of fetal intervention
  - Twin-twin transfusion
  - Twin reversed arterial perfusion
  - Fetal surgery
- Monochorionic twins at risk if co-twin demise
- Maternal trauma
  - Apparently mild maternal trauma may cause devastating fetal cerebral injury
- Placental abruption

Natural History & Prognosis
- Neurodevelopmental outcome poor
- Severe developmental delay
- Seizure disorder, often refractory to anticonvulsant therapy
- Precise deficit depends on size and location
  - Visual loss
  - Speech impairment
  - Sensory/motor deficit

Treatment
- Infection screen
- Evaluate for breeding diagnosis
- Offer termination
  - Encourage autopsy for definitive diagnosis
  - Intraventricular hemorrhage risk factors
  - Emergency delivery at time of acute event does not alter outcome
  - Add risks of prematurity to brain injury risk
  - Postnatal cyst uncapping/lavage may help
  - Hemiparesis improved in 30%
  - Intratable seizures
  - Resolved in 62%
  - Improved in 24%

DIAGNOSTIC CHECKLIST

Consider
- Fetal MRI in all suspicious cases and at-risk patients
- US findings can be subtle despite severe damage

Image Interpretation Pearls
- Normal US at time of acute event does not exclude brain injury
- Lesions develop over time
- Scan at 10-14 days from acute event
- Both encephalomalacia and ischemic changes commonly are present

SELECTED REFERENCES
(Left) Coronal 3DWI MR shows abnormal increased T2 signal surrounding the frontal horns (arrows).

(Right) Coronal gross pathology at autopsy shows confluent areas of white matter destruction correlating with the areas of abnormality on MRI. The walls of the cavities are jagged and irregular (arrows).

(Left) Coronal 3DWI MR shows periventricular and a parenchymal cyst (arrow) secondary to a thrombosed cerebral arteriovenous fistula (not visible on this image).

(Right) Sagittal ultrasound on the first day of life shows two periventricular cysts (arrows) communicating with the dilated ventricular system.

(Left) Coronal ultrasound of the brain on day one of life in a monozygotic twin with twin-twin transfusion syndrome. There is profound cystic encephalomalacia (arrows) secondary to intrauterine hypoxia. (Right) Gross pathology shows essentially complete destruction of the cerebral cortices with preservation of the cerebellum and midline. Areas of hemorrhage (arrows) can also be seen.
INTRACRANIAL HEMORRHAGE

TERMINOLOGY

Abbreviations and Synonyms
- Intracranial hemorrhage (ICH)

Definitions
- Bleeding within fetal cranium

IMAGING FINDINGS

General Features
- Best diagnostic clue: Non-perfused, echogenic, intracranial "mass"
- Location
  - Classified by anatomic location
  - Intraparenchymal
  - Most arc supratentorial
  - Posterior fossa uncommon
  - Subependymal (common)
  - Germinat matrix hemorrhage (GMH)
  - Intraventricular (common)
  - Subdural
  - Subarachnoid
  - Epidural (very rare)

Ultrasonographic Findings
- Hemorrhage usually extensive when diagnosed in utero
  - Normal intracranial landmarks often obscured
- Intraparenchymal
  - Hyperechoic mass within parenchyma
  - Parenchymal edema develops with time
- Subependymal
  - Same appearance/grading as neonatal GMH
- Intraventricular
  - Hyperechoic intraventricular clot
  - Irregular bulky choroid plexus
  - Echogenic, irregular ependyma
  - Hydrocephalus
- Subdural
  - Hyperechoic material outlining cortex
  - Separates Sylvian fissure from calvarium
  - Normal distance cortex to skull vault ≤ 4 mm

MR Findings
- Blood products
  - T1WI high signal (methemoglobin)
  - T1WI low signal
- Confirm location of clot on multiple planes
- Do not confuse with flow artifact
  - Turbulent cerebrospinal fluid (CSF) flow in a dilated system
  - Less defined signal

DDx: Hemorrhage

CP Papilloma
CP Papilloma
Neurinoma
Turbulence Artifact
Key Facts
- Trauma
- Maternal thrombocytopenia/coagulation disorders

Clinical Issues
- Maternal idiopathic thrombocytopenia (ITP) → Fetal ICH in < 1%
- Allimmune thrombocytopenia (ATIP) → Fetal ICH in 10-30%
- Outcome relates to severity and extent of bleed
- Maternal testing for coagulation disorder/platelet antibodies
- Consider delivery by cesarean section

Diagnostic Checklist
- Hemorrhage may be difficult to see on ultrasound
- Consider fetal MR in at-risk patients

Imaging Findings
- Best diagnostic clue: Non-perfused, echogenic, intracranial "mass"
- Classified by anatomic location
- Hemorrhage usually extensive when diagnosed in utero
- Porencephaly develops with time
- Hyperechogenic intraventricular clot
- Irregular bulky choroid plexus
- Look for vascular malformation as cause

Top Differential Diagnoses
- Intracranial tumor
- Infection

Pathology
- Alterations in maternal/fetal blood pressure

- "Swirl", not mass-like
- Location changes sequence-to-sequence
- Septations in CSF spaces/ventricles correlate with hemorrhage and infection
- Blood/CSF levels
- Large flow voids on T2WI = feeding/draining vessels from vascular malformation
- Look for periventricular leukomalacia / porencephaly

Imaging Recommendations
- Look for hydrops
  - Anemia secondary to hemorrhage increases risk for non-immune hydrops
  - Pericardial/pleural effusion
  - Ascites, skin edema
- Look for vascular malformation as cause
- Thrombosis of vascul ar malformation = venous hypertension = bleed
- Shape/location may suggest Vein of Galen malformation
- Tubular components suggest thrombosed feeding/draining vessels
- Use color Doppler

DIFFERENTIAL DIAGNOSIS

Intracranial tumor
- Large, heterogeneous, rapid growth
- Caution: Intracranial tumors may bleed
  - Look for blood flow in periphery of mass with color Doppler
- Clot is not perfused, tumor will show flow
- Macrocephaly common
- Choroid plexus (CP) papilloma is a potential mimic for intraventricular clot

Infection
- May cause destructive brain lesions
- Intracranial/liver calcifications, hydrops

Ischemia
- Periventricular leukomalacia

PATHOLOGY

General Features
- General path comments
  - Subependymal bleed
    - Related to fragile germinal matrix capillaries and poor autonomic control of fetal cerebral vascularity
    - Germainal matrix more susceptible < 32 weeks
    - Maternal hypotension/fetal hypoxia = cerebral blood vasodilatation followed by capillary rupture
      - Usually extends into ventricles
    - Intraparenchymal bleed
      - Usually due to trauma, more common in term infant
    - Subarachnoid/epidural bleeds
      - Usually due to trauma
- Genetics
  - Allimmune thrombocytopenia (ATIP): Autosomal dominant (AD)
- Coagulation disorders Some AD
- Hemophilia: X-linked recessive
- Etiology
  - Alterations in maternal/fetal blood pressure
    - Maternal seizure disorder/acute abdomen
  - Drug use: Cocaine, aspirin
  - Pre-eclamptic toxemia (PET)/Hemolysis-elevated liver enzymes-low platelets (HELLP) syndrome
  - Monochorionic twin demise can result in severe fetal hypotension and subsequent bleed in survivor
- Trauma
  - Motor vehicle accident/domestic violence
  - Polyhydramnios masage for external version of breech
  - Significant incidence of fetal subarachnoid hematoma
- Maternal thrombocytopenia/coagulation disorders
  - Factor V or V deficiency, coumarin therapy
INTRACRANIAL HEMORRHAGE

- Bacterial/viral infection
- Unbilical cord abnormalities
- Thrombosis, knot, hematoma
- Placental abnormalities
- Uteroplacental insufficiency
- Abruption/placenta previa
- Fetal arteriovenous malformation/fistula
- Amnionitis complication
- Should be avoidable with US guidance
- Hypoxemia
- Uncommonly diagnosed in utero
- 6% of autopsies for stillbirth have some type of hemorrhage
- Usually diagnosed between 26-33 weeks gestation

Staging, Grading or Classification Criteria
- Grade 1: Uninjured or subependymal area
- Grade 2: Intraventricular extension without hydrocephalus
- Grade 3: Intraventricular extension with hydrocephalus
- Grade 4: Intraparenchymal extension
- Generally indistinguishable from primary intraparenchymal hemorrhage

CLINICAL ISSUES

Presentation
- May be asymptomatic
- Decreased fetal movement
- Fetal death especially if polyhydramnios secondary to impaired fetal swallowing
- Non-reactive fetal heart rate tracing
- Sinusoidal fetal heart rate tracing secondary to fetal hypoxia
- Fetal anemia → impaired oxygen delivery

Natural History & Prognosis
- Maternal idiopathic thrombocytopenia (ITP) → Fetal ICH in < 1%
- Allotumors thrombocytopenia (AITP) → Fetal ICH in 10-30%
- Long term sequelae
  - Cerebral palsy/seizure disorder
  - Developmental delay, mentally subnormal
  - Hydrocephalus
  - Fetal or neonatal death
- Outcome relates to severity and extent of bleed
- Poor outcome = demise or severe neurological impairment
  - In 92% parenchymal bleeds
  - In 88% subarachnoid bleeds
  - In 45% intraventricular bleeds
- Good outcome = normal or mild neurological impairment
  - Germinial matrix need, good outcome
  - In 100% grade 1
  - In 60% grade 2
  - In 0% grade 3

Treatment
- Maternal testing for coagulation disorder/platelet antibodies
- Fetal transfusion may be required, platelets or whole blood
- AITP: Consider weekly infusion immune globulin / steroids
  - Good outcome in 8/11 infants
  - Prior to this therapy outcome was uniformly poor
- Consider delivery by cesarean section
  - Avoids mechanical stress at vaginal delivery and potential for repeat bleed
- May prefer to attempt vaginal delivery if severe parenchymal damage already present
  - Neurological outcome is often related to brain destruction, mode of delivery does not alter outcome
  - Avoids morbidity in future pregnancies

DIAGNOSTIC CHECKLIST

Consider
- Rebleeding may be difficult to see on ultrasound
  - Consider fetal MRI in at风险 patients

SELECTED REFERENCES
Typical

(Left) Axial ultrasound shows hydrocephalus and irregularity of the choroid plexus (arrow) concerning for hemorrhage. This is a monochorionic pregnancy with an intrauterine... (Right) Coronal T2W MRI with a large left-sided view shows the more global picture. The dead twin is small and has skin wrinkles (curved arrow). The living twin has hydrocephalus (open arrow) and a hypointense lesion (arrow) in the ventricle, confirming the suspicion of clot on ultrasound.

Typical

(Left) Coronal ultrasound shows an abnormal area of increased echogenicity in the region of the germinal matrix (arrow) with extension of the bleed into the ventricles. (Right) Sagittal T1W MRI of a fetus with a large thinned-out, curved anterior ventricle (open arrow). Hydrocephalus is present with a third-fluid level (arrow) from an associated intraventricular bleed.

Variant

(Left) Axial oblique ultrasound in a 3rd trimester fetus shows a "mass-like" area at the occipital lobes, possibly in the cerebellum (arrow). This finding was not present on previous scans. (Right) Axial nonenhanced CT scan on the 1st day of life shows a large cerebellar bleed (arrow). The posterior fossa is an uncommon location for focal hemorrhages. No underlying masses or vascular malformations were identified.
TERMINOLOGY

Abbreviations and Synonyms
- Choroid plexus cyst (CPC)

Definitions
- Cysts within substance of choroid plexus

IMAGING FINDINGS

General Features
- Best diagnostic clue
  ○ One or more anechoic cyst(s) in choroid plexus
  ○ First seen in second trimester
  ○ Disappears in third trimester
- Location
  ○ Usually in globs
  ○ Most seen in atria
- Size
  ○ Variable
  ○ Should be > 2 mm to be CPC
- Morphology
  ○ Discernable wall
  ○ Single or multiple
  ○ Surrounded by normal choroid plexus
  ○ Clustered small cysts mimic complex mass

Ultrasonographic Findings
- CPC easily seen on routine lateral ventricle view
  ○ Transverse image of lateral ventricle
  ○ Level of atria
  ○ Fluid-filled atria should not be confused with CPC
- Normal appearance of choroid plexus in lateral ventricle
- Echogenic
  ○ Giosis is focal thickening posteriorly
  ○ “Sponge-like” morphology
  ○ < 2 mm sonolucencies are normal
- CPC
  ○ Anechoic
  ○ Surrounded by choroid plexus
  ○ Oblique views confirm location
  ○ CPC only when diameter > 2 mm
  ○ < 2 mm considered normal
  ○ Discernable echogenic wall
  ○ No blood flow on color Doppler
  ○ 12% with other anomalies
- Large CPC
  ○ > 10 mm
  ○ ↑ Association with aneuploidy
  ○ Trisomy 13 (13T)
  ○ Resolve slower
  ○ May be mistaken for ventriculomegaly
- Multiple and bilateral CPC

DDx: Choroid Plexus Heterogeneity

- CP Papilloma
- CP Pilocytic A
- TC Hemangioma
- TC Hemangioma
**CHOROID PLEXUS CYST**

### Terminology
- Choroid plexus cyst (CPC)
- Cysts within substance of choroid plexus

### Imaging Findings
- One or more anechoic cyst(s) in choroid plexus
- Best seen in second trimester
- Disappear in third trimester
- Usually in glomus
- Should be > 2 mm to be CPC
- Dilute views confirm location
- 12% with other anomalies
- Almost all resolve by 32 weeks
- Seen in 1% of all second trimester exams
- 50% of T18 fetuses have CPC
- Almost all T18 have other detectable anomalies
- Document open hands

- Same risk for T18 as single
- Clusters common
- Transient
- Almost all resolve by 32 weeks
- Regardless of other anomalies
- Regardless of aneuploidy
- Not necessary to show resolution
- CPC and normal fetus
- Seen in 1% of all second trimester exams
- Benign and transient finding
- CPC and T18
- 50% of T18 fetuses have CPC
- > 10 mm more worrisome
- Almost all T18 have other detectable anomalies
- Common T18 anomalies
  - Intraventricular growth restriction (IVGR)
  - Cardiac defects
  - Clenched hands + overlapping fingers
  - rockerbottom foot
  - Dandy-Walker continuum
  - Bowel containing emaphalocele
  - strawberry shaped calvarium
  - Single umbilical artery
  - Isolated CPC and risk for T18
  - Correlate with maternal serum biochemistry
  - Like/hood ratio (LR) < 2 for T18
  - < 2x more likely to have T18 than abort risk
- CPC and trisomy 21 (T21)
  - No association when CPC isolated
  - Higher risk for T21 when other T21 markers present
  - Example: CPC + echogenic bowel (EB), greater risk than EB alone
  - Common T21 markers
  - Increased nuchal fold
  - Intracardiac echogenic foci
  - Short femur/tibiae
  - Echogenic bowel
  - Renal paplectasia
  - Fifth finger clinodactyly
  - CPC + any other anomaly
  - 2x increased risk for aneuploidy

### Imaging Recommendations
- Best imaging tool: second trimester genetic sonogram
- Protocol advice
  - Determine if CPC is isolated
  - No amniocentesis
  - Look for markers of aneuploidy
  - Document open hands
  - Document normal foot
  - Careful fetal heart evaluation
  - Consider amniocentesis if:
    - CPC not isolated
    - Abnormal serum screen
    - Advanced maternal age
    - NEEF for follow-up exam to show CPC resolution
    - Cysts themselves are of no consequence
    - Resolve in both normal and aneuploid fetuses
    - May consider follow-up for prenatal reassurance

### Differential Diagnosis
- Choroid plexus papilloma
  - Rare choroid plexus tumor
  - Lateral ventricle most common six
  - Same location as CPC
  - Tumor produces cerebrospinal fluid (CSF)
  - Rapid onset hydropspositis
  - Well-defined mass
  - Lobular
  - Hyperechoic
  - Color Doppler may show flow in mass
  - Mild ventriculomegaly
    - Arta of lateral ventricle measures 10.12 mm
    - Choroid displaced from medial wall
    - Usually idiopathic
    - Marked for T21
    - CPC may mimic distended lateral ventricle
    - > 10 mm CPC
  - Intraventricular hemorrhage
    - Rare
CHOROID PLEXUS CYST

PATHOLOGY

General Features
- Genetics: o <1:400 aneuploidy in low-risk group
  o T18 risk
- CPC + minor spongiform marker = 20% risk
- CPC + major spongiform marker = 50% risk
- T21 risk: o Only if other T21 markers seen

Etiology
- Entrained fluid
- 80-90% cerebral spinal fluid (CSF) produced by choroid plexus
- Epidemiology: o Pic normal 2nd trimester fetuses
  o 90% T18 fetuses
- Associated abnormalities
  o Anomalies seen with T18
  o Rarely, anomalies seen with T21
- Embryology
  - Choroid plexus
    - <13 wk: Fifths enter lateral ventricle
    - >13 wk: Reaches antrum
  - Glomus becomes most prominent
  - Fills body of lateral ventricle
  - No choroid in frontal or occipital horns

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - Isolated finding in low-risk patient
  - Not advanced maternal age (AMA)
  - Normal maternal biochemical screens
  - Major anomaly + CPC
  - Minor marker + CPC

Demographics
- Age
  - T18 associated with AMA
  - AMA ≥ 35 yrs at time of delivery

Natural History & Prognosis
- Transient benign finding
  - Resolves by 32 weeks in both T18 and normal fetuses
- Excellent prognosis for isolated CPC
- Guarded prognosis for CPC + other anomalies
  - Depends on karyotype result
  - Depends onverity of associated anomalies

Treatment
- None for CPC

DIAGNOSTIC CHECKLIST

Consider
- Careful evaluation of fetal heart
  - Normal four-chamber view
  - Normal outflow tract views
  - Consider fetal echocardiography
- Amniocentesis when CPC seen in high-risk patients
  - Abnormal maternal serum biochemistry
  - Advanced maternal age
  - Fetal tumor with aneuploidy
  - T18
  - T21
- Amniocentesis when CPC + other abnormalities
  - No amniocentesis when isolated finding in low-risk patient

Image Interpretation Pearls
- Careful fetal anatomic survey
- CPC and small for dates may indicate T18
- Symmetric IUGR may mimic poor maternal data

SELECTED REFERENCES
CHOROID PLEXUS CYST

IMAGE GALLERY

Typical

(Left) Axial ultrasound shows bilateral CPC (arrows) in a fetus with multiple anomalies and trisomy 18. (Right) Axial ultrasound of the heart in the same fetus shows a small left ventricle (arrow) and atrial septal defect. Other fetal anomalies were also present. The fetal heart and anomalies should be carefully evaluated when choroid plexus cysts (CPCs) are seen.

Typical

(Left) Coronal ultrasound of the fetal brain in the same fetus shows bilateral clefted hands and an overlapping index finger (arrow). The hand position is classic for trisomy 18. When CPCs are seen, the sonographer should try to obtain open hand views. (Right) Clinical photograph shows the classic hand position of trisomy 18. The fingers are tightly clefted with an overriding second finger.

Typical

(Left) Axial ultrasound shows a right-sided 10 mm CPC (arrow). Notice that the cyst is surrounded by echodense and is anechoic. No other anomalies were seen in this low-risk patient. Anamnestic data was not recommended. (Right) Axial ultrasound in the same fetus shows that the CPC resolved. Follow-up ultrasonography is not necessary but patients often want reassurance that the cyst is gone.
**ARACHNOID CYST**

**TERMINOLOGY**

**Abbreviations and Synonyms**
- Arachnoid Cyst (AC)

**Definitions**
- Cerebrospinal fluid (CSF) collection enclosed within layers of arachnoid

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue: Extra-axial cyst
- Location
  - Fetal series
  - Commonest over cerebral convexities
  - One-third of cases occur in posterior fossa
  - Between cisterns
  - Supracerebellar space
- Significant variation from postnatal series
  - Over convexities: only 5%
  - Middle cranial fossa: 50-65%
  - Quadrigeminal cistern: 5-10%
  - Suprasellar cistern: 5-10%
  - Posterior fossa: 5-10%
- Size
  - Variable

- May exhibit rapid growth and cause obstructive hydrocephalus

**Ultrasonographic Findings**
- Grayscale Ultrasound
  - Smoothly contoured, anechoic cyst
  - Remaining brain sonographically normal in majority of cases
  - Agenesia of corpus callosum reported in 5% with supratentorial AC
  - It is likely many of these are actually glioneuronal cysts
  - Mild ventriculomegaly/hydrocephalus
  - Mass effect on Aqueduct of Sylvius
  - Impaired CSF drainage
  - Color Doppler
    - Arachnoid lesion may not flow
    - Lateral cyst may displace major arterial vessels
  - Pulsed Doppler
    - No perfusion
    - Doppler signal only from adjacent vessels
  - 3D
    - May help to confirm extra-axial location
    - May show origin e.g. floor middle cranial fossa

**MR Findings**
- Simple AC: displaces normal parenchyma
- Buckles gray/white matter interface
- Follows CSF signal

**DDx: Arachnoid Cyst**

- DW Continuous
- DW Continuum
- Schiøtze (path)
- Coelocephalic Cyst
ARACHNOID CYST

Key Facts
• CSF-containing cyst with thin membranous wall
• Can be seen as part of syndromes

Pathology
• Prognosis good if isolated abnormality
• May require shunt or excision if significant mass effect
• Other anomalies determine prognosis when present
• Consider angiogenesis for karyotype, even if isolated
• Monitor for growth of cyst
• Head size may impact timing and mode of delivery

Clinical Issues

Diagnostic Checklist
• Always check Doppler of apparent cyst

TERMINOLOGY
• Cerebrospinal fluid (CSF) collection enclosed within layers of arachnoid

IMAGING FINDINGS
• Best diagnostic clue: Extra-axial cyst
• Commonest over cerebral convexities
• One third of cases occur in posterior fossa
• Remaining brain sonographically normal in majority of cases

TOP DIFFERENTIAL DIAGNOSES
• Glioneuromatous cyst
• Schwannoma
• Teratoma
• Dandy-Walker continuum (DWC)
• Porencephalic cyst

IMAGING RECOMMENDATIONS
• Protocol advice
  ○ Careful search for other anomalies
  ○ AC may be part of multiple malformation syndrome
  ○ Additional anomalies increase suspicion for
  • Aneuploidy
  • Autosomal recessive inheritance conditions
  ○ Consider fetal MRI for associated brain anomalies

DIFFERENTIAL DIAGNOSIS

Glioneuromatous cyst (GC)
• Greater association with agenesis of the corpus callosum
• Frontal, parietal, temporal
• Centered on midline
• Arachnoid cysts tend to extend to either side
• Protein content of cyst fluid higher than AC
• May alter MRI signal allowing differentiation
• Signal > CSF on T1WI
• Occasional fluid-fluid level
• Histology required to differentiate from AC
• Not generally clinically relevant
• Same treatment

Dandy-Walker continuum (DWC)
• Differential consideration for posterior fossa AC
• Tectal elevation is hallmark of DWC
• 4th ventricle in communication with cisterna magna
• Vermian agenesis/hypogenesis
• Vermis present ≥ 2 AC

Intracranial hemorrhage
• May appear cystic if subacute
• Associated with destruction of normal tissue
• Blood products
  ○ High signal on T1WI
  ○ Low signal on T2WI

Porencephalic cyst
• Replaces damaged brain
• Arachnoid cyst displaces normal brain
• Often associated with intracranial hemorrhage
• Look for encephaloclastic changes
• Abnormal high signal cerebral cortex on T2WI
• US findings can be subtle
• Loss of normal architecture
• Mild ventriculomegaly

Vein of Galen malformation
• Elongated midline structure
• Posterior
• Quadrigeminal plate cistern toward occiput
• Flow on color Doppler
• High velocity, low resistance flow on pulse Doppler
• Porencephaly may occur if significant “steal” phenomenon
• Intracranial hemorrhage may occur

SCHIZENCEPHALY
• Cleft in brain substance
• Wedge-shaped rather than round
• May be bilateral and symmetric
• Lined with gray matter on MRI

TERATOMA
• Can be predominantly cystic
• Soft tissue component, calcification, can usually be identified
• Rapid growth

• Macrocephaly

Dandy-Walker continuum (DWC)
• Differential consideration for posterior fossa AC
• Tectal elevation is hallmark of DWC
• 4th ventricle in communication with cisterna magna
• Vermian agenesis/hypogenesis
• Vermis present ≥ 2 AC

Intracranial hemorrhage
• May appear cystic if subacute
• Associated with destruction of normal tissue
• Blood products
  ○ High signal on T1WI
  ○ Low signal on T2WI

Porencephalic cyst
• Replaces damaged brain
• Arachnoid cyst displaces normal brain
• Often associated with intracranial hemorrhage
• Look for encephaloclastic changes
• Abnormal high signal cerebral cortex on T2WI
• US findings can be subtle
• Loss of normal architecture
• Mild ventriculomegaly

Vein of Galen malformation
• Elongated midline structure
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• Flow on color Doppler
• High velocity, low resistance flow on pulse Doppler
• Porencephaly may occur if significant “steal” phenomenon
• Intracranial hemorrhage may occur

Physiologic entities
• Diffferential
  ○ Enlarged cavum septi pellucidi
  ○ Cavum vergae
  ○ Cyst of cavum velum interpositum
• Do not increase in size
• May regress with advancing gestational age
  ○ Median size 10 mm (range 15-40 mm)
**ARACHNOID CYST**

- Pathologic cysts often larger and may grow as pregnancy progresses

**PATHOLOGY**

**General features**
- General path comments
  - CSF-containing cyst with thin meningeal wall
  - Embryology
    - Frontal, temporal embolamic meninges (ependyma) fail to merge as Sylvian fissure forms (middle cranial fossa)
    - Remain separate forming “duplicated” arachnoid
  - Older theory: Diverticulum of developing arachnoid
  - Middle cranial fossa AC → hypoplasia adjacent temporal lobe
  - Genetics
    - Mostly sporadic
    - Can be seen as part of syndromes
      - Neurofibromatosis type 1
      - Multiple congenital anomaly disorders with single gene mutation
      - Tretoyn 18
    - Usually multiple other anomalies
  - Etiology
    - Possible mechanisms
      - Active fluid secretion by cyst wall
      - Slow distension by CSF pulsations
    - CSF accumulates by one-way (ball-valve) flow
  - Epidemiology
    - Precipall incidence unknown
    - 1% space-occupying lesion at childhood
    - 0.5% autopsies
    - M > F
    - Left > right

**Microscopic features**
- Walls composed of thin vascular collagenous membrane (pale-stained arachnoid cells)
- Choroid plexus-like tissue may be present in walls
- Fluid secretion → progressive distention of cyst

**CLINICAL ISSUES**

**Presentation**
- Reported cases diagnosed in first trimester on endovaginal scans
- Most present at > 20 weeks gestational age
- Majority of postnatal cases present with macrocephaly

**Natural History & Prognosis**
- May cause hydrocephalus
- Hydrocephalus more likely if:
  - Early gestational age at diagnosis
  - Size > 15 mm
  - Progressive increase in size
  - Prognosis good if isolated abnormality
  - May require shunt or excision if significant mass effect
  - Excision/marsupialization favored
  - Avoids complications of shunt placement

- Infusion
- Blockage
- Recurrence
- Other anomalies determine prognosis when present
- Suspected cyst AC associated with hypothalamic hamartoma
  - Risk for precocious puberty
  - Gelastic seizures

**Treatment**
- Consider amniocentesis w/ karyotype, even if isolated
- No prenatal intervention
- Monitor for growth of cyst
  - Hydrocephalus
  - Macrocephaly
- Head size may impact timing and mode of delivery

**DIAGNOSTIC CHECKLIST**

**Consider**
- Fetal MRI
- Confirm cyst
- Evaluate associated structural abnormalities

**Image Interpretation Pearls**
- Always check Doppler of apparent cyst
- Atrventricular malformations immediately apparent
- Very different prognosis

**SELECTED REFERENCES**

Variant

(Left) Axial color Doppler ultrasound shows an associated cyst (curved arrow). The normal vessels are visible. MPR cine film shows displacement of the anterior cerebral arteries (arrows). (Right) Axial T2WI MR shows the large cyst (arrow) displacing normal brain. There had been significant enlargement in one month with developing hydrocephalus. Postnatal cyst decompression relieved hydrocephalus.

Typical

(Left) Sagittal T2WI MR shows a large simple extraaxial cyst over the convexity of the parietal lobe (arrow). The lateral ventricle (curved arrow) is displaced and there is mild ventriculomegaly. (Right) Axial ultrasound shows an anechoic choroid cyst (arrow) in a fetus with trisomy 18. Other findings include a "strawberry"-shaped calvarium (curved arrow), choroid plexus cyst (open arrow), and teratoma of Fallopian tube.

Typical

(Left) Sagittal T2WI MR shows a posterior fossa anechoic cyst (arrow) displacing the cerebellar hemisphere (curved arrow). The vermis was intact excluding Dandy-Walker continuum. (Right) Axial oblique ultrasound of the posterior fossa in a neonate with an anechoic cyst (arrow). The vermis is intact (curved arrow). One third of isolated arachnoid cysts occur in or near the posterior fossa.
GLIOEPENDYMAL CYST

TERMINOLOGY

Abbreviations and Synonyms

- Gliopendymal cyst (GC)
- Ependymal cyst
- Neuropiliform cyst
- Choroidal ependymal cyst

Definitions

- Intraaxial cyst with ependymal lining

IMAGING FINDINGS

Ultrasonographic Findings

- Grayscale Ultrasound
  - Smooth-walled, anechoic cyst in fetal cranium
  - Usually located on midline
  - Frontal
  - Panorhcephalic
  - Generally no communication with ventricular system
  - May be intraventricular
  - May be intra or extracranial
  - May be multiple
  - May cause hydrocephalus

- Compress Aqueduct of Sylvius or Foramen of Monro
- Obstruct cerebrospinal fluid (CSF) flow
- Associated with agenesis of corpus callosum (ACC)
- Many cysts previously called arachnoid cysts (AC) may actually have been GC
- Other features of ACC
  - Absent cavum septi pellucidii
  - Parallel lateral ventricles
  - Abnormal course pericallosal/callosomarginal arteries
  - "Tufted" lateral ventricles on coronal view
  - Cerebellum (deep floor of ventricles)
  - Gyri in radial "sunray" distribution in sagittal plane
- Not usually associated with extracranial anomalies
- Color Doppler
  - No internal flow
  - Vessels displaced by cyst
- 3D
  - May be helpful to evaluate location of cyst
- Shows relationship of large cyst to rest of brain

MR Findings

- Signal intensity usually follows CSF
  - Low signal T1WI
  - High signal T2WI
- May be hypointense on T1WI

DDs: Gliopendymal Cyst

- Arachnoid Cyst
- Schizencephaly
- Telencephalic
- Hydrocephalus
**GLIOEPENDYMAL CYST**

**Key Facts**
- Teratoma
- **Clinical Issues**
  - Follow for hydrocephalus/microcephaly
  - Hydrocephalus: Increased likelihood of postnatal intervention
  - Intellectual outcome dependent on associated structural abnormalities
  - Decompression preferable to surgery
- **Diagnostic Checklist**
  - Higher signal on T1WI supports diagnosis of GC
  - Differentiation of GC vs. AC often not possible or even necessary by imaging
  - Isolated cyst without mass effect has excellent prognosis

- **Imaging Recommendations**
  - Protocol advice
    - Careful search for other anomalies
    - Check size/date concordance
    - If anomalies or abnormal growth = increased suspicion for aneuploidy/syndrome

**DIFFERENTIAL DIAGNOSIS**

**Arachnoid cyst (AC)**
- May not be able to differentiate from GC
- AC more common over convexities
- AC more likely if cyst in posterior fossa
- AC more likely if multiple anomalies present
- Stronger association with aneuploidy

**Schizencephaly**
- Wedge-shaped defect
- Extends cortical surface to ventricular wall
- Lined with grey matter

**Alobar holoprosencephaly**
- Large GC may simulate a mononuclerice
- Mononuclerice is hallmark
- Abnormal brain tissue adjacent to mononuclerice
- Cerebellar tissue bulging
- GC displaces otherwise normal brain parenchyma
- Typically associated with abnormal facialites
  - Facial cleft
  - Cyclopia/hypotelorism
  - Cleft lip/palatine
  - Encephalopharyngeal cleft
  - If fetus has Trisomy 13
  - Omphalocele
  - Congenital heart disease
  - Polydactyly
  - Cystic renal disease

**Intracranial hemorrhage**
- Associated with tissue destruction

- Appearance evolves with time
  - Ectopic mass = hypoxic mass = cyst-like structure
- Look for fluid-fluid levels in ventricles
  - Blood-CSF
  - Fluid-fluid level in cyst reflects protein content

**Porencephalic cyst**
- Associated with brain destruction
- Intracranial hemorrhage
- Periventricular leukomalacia (PVL)
- Always intraparenchymal
- Cyst communicates with adjacent ventricle

**Teratoma**
- Can be predominantly cystic
- Soft tissue component, calcification, can usually be identified
- Intraparenchymal

**Physiologic entities**
- Differential
  - Enlarged cavum septi pellucidi
  - Enlarged cavum vergae
  - Cyst of cavum velum interpositum
- Do not increase in size
- Many regress with advancing gestational age
- Median size 10 cm (range 10-30 mm)
- Pathologic cysts like GC, larger, often grow

**PATHOLOGY**

**General Features**
- Genetics
  - Isolated GC not associated with aneuploidy
- No recurrence risk
- **Etiology**
  - Leptomeningeal neural crest heterotopia
- **Epidemiology**
  - Isolated GC extremely rare perinatal diagnosis
  - S145 postnatal intracranial cysts requiring surgery at tertiary institution
  - Associated abnormalities

- Proteinaceous fluid
- Occasional fluid-fluid level if high protein content
- If present aids differentiation from arachnoid cyst

- Protocol advice
  - Careful search for other anomalies
  - Check size/date concordance
  - If anomalies or abnormal growth = increased suspicion for aneuploidy/syndrome
GLIOEPIPENDYMAL CYST

- Agensis/dysgenesis corpus callosum
- Microgyria
- Heterotopia
- Cerebellar hypoplasia
- Elevated alpha fetoprotein levels reported

Gross Pathologic & Surgical Features
- May occur in spine as well as brain
- GC at posterior neuropore
- Case report of GC simulating sacrococcygeal teratoma

Microscopic Features
- Outer layer of wall
  - Basement membrane
  - Glial tissue
- Inner layer
  - Ependymal tissue + silla

CLINICAL ISSUES

Presentation
- Cystic intracranial mass detected on routine obstetric ultrasound

Natural History & Prognosis
- Depends on
  - Size
  - Associated abnormalities
  - Location
  - May obstruct CSF flow → hydrocephalus
  - Hydrocephalus → shunt placement
    - Shunts have associated morbidity
  - Infection
  - Obstruction
  - Recurrence
  - Mass effect on adjacent brain
  - Case reports of local hypoperfusion
  - Case report of undraining brain destruction secondary to ischemia
  - Seizure disorder attributed to local hypoxemia
  - Many GCs asymptomatic
  - Incidental detection described in postnatal series
  - Cyst decompression associated with good outcome
  - No known recurrence risk

Treatment
- No documented association of GC with aneuploidy
  - Aneuploidy may not be necessary if isolated anomaly
  - Often difficult to differentiate from AC, which is associated with aneuploidy
- Follow for hydrocephalus/macrocephaly
  - Either may influence timing and mode of delivery
- Hydrocephalus: Increased likelihood of postnatal intervention
- Infant should be assessed by pediatric neurologist
- Intellectual outcome dependent on associated structural abnormalities
- Progressive signs and symptoms require shunt placement
  - Raised intracranial pressure
  - Seizure disorder reported

- May improve with cyst decompression
- Decompression preferable to surgery

DIAGNOSTIC CHECKLIST

Consider
- Fetal MRI
  - Confirm diagnosis of 2018
  - Higher signal than CSF on T1WI supports diagnosis of GC
- Shows benign physiologic entities clearly
- Evaluate associated structural abnormalities

Image Interpretation Pearls
- Differentiation of GC vs. AC often not possible or even necessary by imaging
- Safe treatment
- Consider GC if cyst is midline and frontal
- Isolated cyst without mass effect has excellent prognosis

SELECTED REFERENCES

GLIOEPENDYMAL CYST

IMAGE GALLERY

Typical

(Bottom) Axial oblique ultrasound of a frontal CC (arrow) shows posterior displacement of the brain (curved arrows). The falx is normal. (Right) Axial T1WI MR shows the multiloculated cyst (white arrows) IOH. The midline is displaced posteriorly (black arrows) confirming the ultrasound findings. The occipital horns (curved arrows) are not dilated.

Variant

(Bottom) Coronal T1WI MR shows a large cyst bulging through the anterior fontanelle (curved arrows) in this fetus with associated agenesis of the corpus callosum. Hypoplasia (arrow) is secondary to mass effect. (Right) Coronal T1WI MR shows a CC cyst (arrow) displacing brain (curved arrows) in a different infant with hemimegalencephaly, unilateral hydrocephalus, ACC, heterotopias, and asymmetric brain growth.

Typical

(Bottom) Axial T1WI MR shows an interhemispheric cyst (curved arrow) in a twin with ACC. (Right) Axial T1WI MR of the same infant in the first week of life shows an interhemispheric cyst. The lateral ventricles (arrows) have a parallel indentation due to associated callosal agenesis. Histology would be needed to confirm, but the midline location and ACC suggest a CC.
**TERMINOLOGY**

**Definitions**
- Gray matter-lined cleft extending from brain surface to ventricle
  - Closed lip (type 1)
    - Gray matter "limbs" which are in contact with each other
  - Open lip (type 2)
    - Separated gray matter "limbs" with an intervening cleft of cerebrospinal fluid (CSF)
- CSF cleft extends to underlying ventricle

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue
  - Defect of brain parenchyma extending from inner table of skull to underlying ventricle
- Gray matter lines cleft
- Location
  - Cerebral hemispheres
  - Unilateral
  - Bilateral
- Uncommonly occipital
- Usually unilateral in this location
- Size: Any size possible

**DDx: Schizencephaly**

- Moderate Hydrocephalus
- Severe Hydrocephalus
- Choroid plexus cyst
- Hydrocephalus

**Ultrasoundographic Findings**
- Most often will detect only open lip type
- Small open-lip defects can be difficult to detect especially in near field
- Reverberation/ artifacts obscure cleft
- Closed lip type often missed
- CSF-filled cleft extending from surface of brain to ventricle
- Ventricular wall "tented" toward defect
- Ventriculomegaly
- Roofing membrane covering cerebral defect
- Uncommonly identified
- Cavernous septo-optic dysplasia (CSDP)
- Absent in 50%
- Almost always absent in bilateral schizencephaly
- Associated brain developmental abnormalities
- Heterotopia
- Polymicrogyria
- Pachygyria
- Septo-optic dysplasia
- Calvaria may be remodeled over open-lip defect
SCHIZENCEPHALY

Key Facts

- Forencephalic cyst
- Most likely primary malformation from abnormal neuronal migration
- Early prenatal injury has also been implicated

Clinical Issues
- Seizures
- Developmental delay
- Mental retardation
- Motor impairment

Diagnostic Checklist
- If diagnosis suspected, fetal MRI should be performed
- Confirms diagnosis with demonstration of gray matter lining cleft

Terminology
- Gray matter lined cleft extending from brain surface to ventricle
- Closed-lip (type 1)
- Open-lip (type 2)

Imaging Findings
- Defect of brain parenchyma extending from inner table of skull to underlying ventricle
- Gray matter lines cleft
- Closed-lip type often missed

Top Differential Diagnoses
- Acrachnoid cyst
- Alobar holoprosencephaly
- Agenesis of the corpus callosum with interhemispheric cyst

- Likely due to CSF pulsation originating from ventricle
- Face and profile are normal
- Differentiates schizencephaly from holoprosencephaly

MR Findings
- Higher resolution imaging of brain parenchyma than ultrasound
- Confirms gray matter lining cleft
- Detects other developmental anomalies
- Heterotopia
- Polymicrogyria
- "Mirror image" migrational abnormality in contralateral hemisphere
- Can be seen with unilateral schizencephaly defects

CT Findings
- No role in prenatal imaging
- Postnatal CT
  - Can usually see open or closed-lip defects
  - Grey matter lining confirms diagnosis
  - Not as sensitive as MRI

DIFFERENTIAL DIAGNOSIS

Acrachnoid cyst
- Extra-axial location
- Mass effect on adjacent brain
- Scalping of inner table of skull
- Most over convexities

Alobar holoprosencephaly
- Mesoventricle
- Absent cavum septum pellucidum
- Fused thalamus
- Abnormal facial features
  - Midline facial clefts
  - Cyclopia
  - Proboscis
  - Cleft lip/palate

Agenesis of the corpus callosum with interhemispheric cyst
- Absent CSE
- Polccephalhy
- Elevation of third ventricle
- Absent choroid plexus
- Associated interhemispheric cyst or lipoma
  - Displaces normal brain

Forencephalic cyst
- Round or irregular shape
- CSF-filled defect in brain parenchyma
- Not lined with gray matter
- May be associated with hydrocephalus

Hydrocephalus
- Severe obstructive
  - Head is enlarged
  - Cortical mantle may be so thin it is difficult to see
  - Doppler may show flow in compressed parenchyma
  - May require fetal MRI to identify cortical mantle
- Non-obstructive
  - Secondary to infection, ischemia or hemorrhage
  - Subsequent destruction of brain parenchyma
  - Increased ventricular size
  - Thinning cortical mantle

Hydranencephaly
- Complete destruction of cerebral hemispheres
  - Preserved cerebellum and brainstem
  - Replacement of supratentorial structures with CSF
- Falx present
- Absent Doppler flow
- Middle cerebral artery
- Anterior cerebral artery

PATHOLOGY

General features
- Genetics
SCHIZENCEPHALY

- Familial schizencephaly has been reported
- Has been associated with heterozygous mutations of the EMX2 gene
  - Normally expressed in germinal matrix
- **Etiology**
  - Neuronal migration anomaly
  - Final common pathway for several possible etiologies
  - Most likely primary malformation from abnormal neuronal migration
  - Early prenatal injury has also been implicated
  - Drug abuse
  - Maternal abdominal trauma
  - Infection (cytomegalovirus)

**Gross Pathologic & Surgical Features**
- Gray matter lined cleft extending from brain pial surface to ependymal lining of ventricle
- Cleft lining is dysplastic gray matter
- Abnormal cortical laminar
- Most often found near pre-central and post-central gyr
- Associated migration anomalies
- Polymericgia
- Pathyria

**CLINICAL ISSUES**

**Presentation**
- Prenatal: May be incidental finding on screening second trimester ultrasound
- Postnatal
  - Severity of seizures not related to size or extent of defect
  - Developmental delay
  - Seizures correlate with extent of defect
  - Mental retardation
  - Seizures correlate with extent of defect
  - Motor impairments
  - Seizures correlate with extent of defect
  - Symptoms usually minimal if motor cortex not involved
  - Blindness
  - Optic nerve hypoplasia
  - Up to 1/3 of patients with schizencephaly

**Natural History & Prognosis**
- Unilateral defect in 60%
  - If small, neurologic defect is milder
  - Late onset seizure disorder
  - Drug resistant epilepsy
  - Compliant with long life span
- Bilateral defect in 40%
  - Severe neurologic impairment
  - Often have intrinsic tendency for seizures
  - If epileptic, not drug resistant

**Treatment**
- Prevalence none
- Termination may be offered
- Postnatal treatment for seizures

**DIAGNOSTIC CHECKLIST**

- Image Interpretation Pears
  - If diagnosis suspected, fetal MRI should be performed
  - Confirm diagnosis with demonstration of gray matter lining cleft

- Ultrasound may miss a small defect
- Defect in other field may not be seen
- Bilateral defects have worse clinical outcome that unilateral

**SELECTED REFERENCES**

SCHIZENCEPHALY

IMAGE GALLERY

Typical

(LEFT) Axial ultrasound shows large bilateral open-lip schizencephalic clefts. The defects extend from the underlying ventricle to the inner table of the skull. The falx is present (arrow).

(RIGHT) Axial ultrasound of the same patient shows the thalami are not fused (arrow). This finding, along with the presence of a falx, helps distinguish schizencephaly from globe holoprosencephaly.

Typical

(LEFT) Axial T2W1 MR shows a small CSF-filled defect. Gray matter (arrow) can be identified lining the cleft, differentiating this from pachygyria. The corpus callosum is absent.

(RIGHT) Coronal T2W1 MR demonstrating “tenting” of the frontal horn of the ventricle (arrow) towards the schizencephaly defect, a diagnostic clue.

Typical

(LEFT) Axial ultrasound shows giant bilateral schizencephaly (clefts) extending from the ventricles to the undersurface of the skull. (RIGHT) Axial T2W1 MR confirms the diagnosis of giant open-lip schizencephaly. Note the gray matter (arrows) lining the very small amount of remnant brain parenchyma.
**Microcephaly**

**Terminology**

**Abbreviations and Synonyms**
- Microcephaly

**Definitions**
- Mild
  - Fetal head circumference (HC) 2-3 standard deviations (SD) below mean for gestational age (GA)
  - Severe: HC < 3 SD below mean for GA
- If GA unknown, HC compared to femur length (FL) and abdominal circumference (AC)
  - HC/AC < 3SD
  - FL/HC > 3SD

**Imaging Findings**

**General Features**
- Best diagnostic clue
  - Markedly small HC
  - Abnormal calvarial shape

**Ultrasoundsgraphic Findings**
- Severe microcephaly: HC 4-5 SD below mean GA
  - Sloping forehead
  - Preferential frontotemporal atrophy
  - Global cortical atrophy

**Differential Diagnosis**

**Craniosynostosis**
- Premature fusion of cranial sutures
- Small, abnormally shaped calvarium common
- Cloverleaf skull most severe example

- Ventriculomegaly
  - Large subarachnoid space
  - Brain may not be visible at all
- Mild microcephaly: HC 2-3 SD below mean GA
- Often normal outcome when isolated
- 67% with other brain anomalies
  - Holoprosencephaly
  - Agenesis of corpus callosum
  - Forehead
  - Non central nervous system anomalies common

**MR Findings**
- Cerebral convolution defects
  - Macroglossia, pachygyria
  - Diencephalic asymmetry
  - Large basal ganglia

**Imaging Recommendations**
- Protocol advice
  - Amniocentesis should be offered
- Fetal MRI

**DDx: Abnormal Calvarial Morphology**

- **Aneuploidy**
  - Trisomy 21
  - Trisomy 18

- **Cephalohematomas**
  - Perinatal trauma

- **Strabismus (T10)**

---

Image: Sagittal ultrasound shows severe microcephaly in an 18 week fetus. Head measurements are more than 4 SD smaller than expected. The frontal bone is sloped (arrow) as typically seen with ventriculomegaly.

Image: Lateral radiograph taken after birth in another baby with microcephaly. Once again shows a markedly sloped frontal bone (arrow) and small calvarial volume. The bony bones are normally sized.
**Microcephaly**

**Terminology**
- Severe: HC > 3 SD below mean for GA

**Imaging Findings**
- Splaying forehead
- Ventriculomegaly
- 67% with other brain anomalies

**Top Differential Diagnoses**
- Craniosynostosis

**Key Facts**
- **Anencephaly**
- **Clinical Issues**
  - Prognosis depends on severity of microcephaly
  - False positive diagnosis common

**Diagnostic Checklist**
- Fetal MR to see subtle associated brain anomalies
- Mild microcephaly is often a normal variant
- Aminocentesis warranted

**Anencephaly**
- Open neural tube defect involving cranium
- Calvarium is absent
- Dysraphic brain tissue often seen

**Atelencephaly/aprosencephaly**
- Rudimentary prosencephalon
  - Lack of supratentorial brain
- Dysraphmic facial features

**Pathology**

**General Features**
- Genetics
  - Chromosome abnormalities
  - Trisomies 13, 18, 22, 4p-, 5p-, 18q-
  - Single gene defect
  - Larcom, Roberts, Smitif-Leinii-Oplitz, etc.

- **Etiology**
  - Teratogen exposure
  - Alcohol, hydantoin, radionu
  - Prenatal infection
  - Cytomegalovirus (CMV), rubella, toxoplasmosis
  - Part of numerous syndromes
  - Cornelia de Lange, Neu-Laxova, etc.

- **Epidemiology**
  - Incidence: 1:6,100 births
  - Most not diagnosed until first year of age

**Microscopic Features**
- Decreased dendritic arborization

**Clinical Issues**

**Presentation**
- Most common signs/symptoms
  - Diagnosed in conjunction with other anomalies
- Isolated finding during routine exam
- Other signs/symptoms: May not develop until third trimester

**Natural History & Prognosis**
- Infants with microcephaly diagnosed in 1st year of life
  - HC < 3 SD below mean
  - 33% moderate or severely retarded
  - 62% moderate or severely retarded

**Diagnostic Checklist**
- Fetal MR to see subtle associated brain anomalies
- Sequential ultrasound for HC growth

**Image Interpretation Pearls**
- Mild microcephaly is often a normal variant
- Aminocentesis warranted

**Selected References**

**Image Gallery**

(Left) Sagittal ultrasound shows microcephaly; coronal and frontal bone following arcosyn arising. (Right) Clinical photograph of microcephaly; ultrasound normal in a newborn (left) with microcephaly.
ATELENCEPHALY, APROSENCEPHALY

Clinical photograph shows a stillborn infant with aprosencephaly. Note severe microcephaly, slipped (open) arrows, low set ears (curved arrow) and long angioptic, chin open arrow.

Axial oblique ultrasound shows a midline mass of a focus with aprosencephaly, showing a hypoplastic cerebral hem (arrow) and no other recognizable intracerebral structures.

TERMINOLOGY

Abbreviations and Synonyms
- Aprosencephaly/atelectencephaly spectrum
- Aprosencephaly
- Atelecephaly
- Apert's syndrome
- XK aprosencephaly
- Garcia-Saie syndrome

Definitions
- Rare lethal malformation sequence of the central nervous system (CNS)
- Developmental arrest of formation of telencephalon and/or prosencephalon
- Syndromal or XK aprosencephaly with associated limb, genital defect

IMAGING FINDINGS

General Features
- Best diagnostic clue
  - Appearance similar to anencephaly with intact scalp and calvarium
  - Craniofacial anomalies, often severe
  - Severe microcephaly with or without limb abnormalities

Ultrasoundographic Findings
- Brain
  - Severe microcephaly
  - Intact skull and scalp
  - No normal cerebral structures
  - Replaced with fluid
  - Anencephalic mass
  - Cerebellum often hypoplastic
- Face
  - Micrognathia
  - Midface–oculo-facial defects including cyclopia
  - May be severely dysmorphic without recognizable features
  - Absent eyes/nasal structures
  - Cleft palate
- Extremities
  - Hypoplastic thumbs and halluces
  - Radial ray anomalies including absent thumbs
  - Oligodactyly
  - Missing digits, especially thumb and great toe
  - Clitroductyly
  - Medial or lateral deviation of one or more digits
  - Campomelic
  - Persistent finger flexion
  - Clubfoot
  - Urogenital anomalies
  - Ambiguous genitalia

DDx. Calvarial Abnormalities

- Atelecephaly
- Aprosencephaly
- Microcephaly
- Spina Bifida

[Images of different anomalies]
ATELENCEPHALY, APROSENCEPHALY

### Terminology
- Rare lethal malformation sequence of the central nervous system (CNS)
- Developmental arrest of formation of telencephalon and/or prosencephalon
- Syndromal or X-linked aproencephaly with associated limb, genital defects

### Imaging Findings
- Craniofacial anomalies, often severe
- Severe microcephaly with or without limb abnormalities
- No normal cerebral structures
- Cerebellum often hypoplastic
- Best imaging tool: Endovaginal ultrasound in early gestation to confirm abnormal brain with intact skull

### Imaging Recommendations
- Best imaging tool: Endovaginal ultrasound in early gestation to confirm abnormal brain with intact skull
- Protocol advice: Consider MRI to evaluate CNS

### Differential Diagnosis

#### Severe microcephaly
- Splayed forehead
- Insect calvarium
- Brain may appear otherwise normal

#### Anencephaly
- No calvarium or soft tissue structures above orbits
- Associated spine abnormalities
  - Cervical myelomeningocele
  - Rachischisis
- Proptosis of eyes due to shallow orbits
- Irregular surface due to cerebrovascula
- Non-CNS anomalies uncommon

#### Holoprosencephaly (HPE)
- Monoventricle
- Prosencephalic structures (e.g., thalamus) present but malformed/fused
- Craniofacial anomalies common
  - Hypotelorism
  - Orofacial clefts
  - Cyclopia
  - Proptosis

#### Partial monosomy 13q
- Brain abnormalities in at least half of cases including
  - Aproencephaly

### Key Facts

#### Top Differential Diagnoses
- Severe microcephaly
- Anencephaly
- Holoprosencephaly (HPE)

#### Pathology
- Generalized spastic
- Autosomal recessive in some families
- Partial monosomy 13q
- Rudimentary prosencephalon present in atelencephaly
- Both prosencephalic and diencephalic structures fail to develop in aproencephaly

#### Clinical Issues
- Cranial contour may resemble that of anencephaly but with calvarium present
- Cerebellar hypoplasia

#### Hydranencephaly
- Fals present
- No visible cerebral tissue
- Midbrain, hindbrain structures preserved
- Craniofacial development normal
- Other anomalies rare

#### Acalvaria/acrania
- Absent calvarium above orbits
- Facial appearance similar to anencephaly
- Exposed, disorganized-appearing neural tissue
- Neural tissue "wears away" during gestation
  - Appearance may be indistinguishable from anencephaly at delivery
  - Anamnestic fluid often very echogenic
  - Other disruptions seen in cases of anamniotic bands
  - Orofacial clefts
  - Abdominal wall defects

#### Pseudoaprosencephaly
- Membranous remnant of prosencephalic structures apparent on histologic exam
- Vascular neonate
- May be link between abloar HPE and aprosencephaly

#### Demise with overlapping sutures
- "Spaulding's sign"
- Obvious absent heartbeat

### Pathology

#### General Features
- Genetics
  - Generally sporadic
  - Autosomal recessive in some families
  - Occurrence in siblings, twins support genetic contribution
- Partial monosomy 13q
- Deletion 13q
- Ring chromosome 13q
ATELENCEPHALY, APPOSENCEPHALY

- 13q32 region involved in malformations of brain, eyes, thymus
- Deletion of contiguous genes possible in cytogenetic cases
- Candidate gene(s) unknown
- DTX2 (homeodomain-containing gene expressed in prosencephalon) may have role
- Rare other chromosomal aneuploidies
- Triparidly
- Triomy 13
- Complex rearrangements
- Etiology
  - Unknown but developmental arrest more likely than encephaloclastic process
  - No confirmed viral or teratogenic cause
- Associated abnormalities
  - Dysorphic facial features
  - Extremity malformations
  - Especially digits
  - Urogenital anomalies
  - Cardiac anomalies

**Gross Pathologic & Surgical Features**
- Preliminary aposecephaly present in atelencephaly
- Both protercephalic and diencephalic structures fail to develop in aposencephaly
- Absence of telencephalon and pyridineal tracts, lateral and 3rd ventricles
- Cerebellum dysgenesis
- Normal or formed spinal cord
- Cranioyostosis common

**Microscopic Features**
- Clusters of premature neural cells in medulla
- Retinal dysplasia
- Periventricular meningeal proliferation in CNS

**CLINICAL ISSUES**

**Presentation**
- Monosomy common signs/symptoms
- Severe microcephaly on mid-trimester ultrasound
- Cranial contour may resemble that of anencephaly
- But with calvarium present
- Other signs/symptoms: Limb or genital defects

**Demographics**
- Age: Not known parental age effect
- Gender: Possibly more common in males

**Natural History & Prognosis**
- Prenatal or neonatal death
- One case with survival to 13 months

**Treatment**
- No known fetal or neonatal treatment
- Termination of pregnancy an option
- Antenatal monitoring in confirmed cases
- Caesarean section to be avoided

**DIAGNOSTIC CHECKLIST**

**Consider**
- MRI for confirmation of diagnosis, exclusion of hydranencephaly

**Image Interpretation Pearls**
- Severe microcephaly with apparent absence of normal infratentorial anatomy and limb defects
- Differentiation from anencephaly important given recurrence risk issues

**SELECTED REFERENCES**

ATELENCEPHALY, APPOSENCEPHALY

IMAGE GALLERY

**Typical**

(Left) Sagittal ultrasound shows severe microcephaly (open arrows). The face is dysmorphic with anophthalmia (open arrows) where the mouth, nose, and orbits should be seen. (Right) Coronal ultrasound shows the same fetus with non-fused falx (arrow) and hypoplastic cerebellum (curved arrows). No other malformations are apparent.

**Variant**

(Left) Gross pathology with the calvarium opened: faces completely absent of the cerebral and midbrain structures (curved arrows). The cerebellum is noted by the arrows. (Right) Axial ultrasound shows the brain of a mid-trimester fetus with MK aposencephaly. There is severe microcephaly (open arrows) with disorganized subcortical structures protruding through the orbit (curved). No normal cerebral structures could be identified.

**Typical**

(Left) Ultrasound of the hand shows an absent thumb (arrow) and digit 2 structure (curved arrow) in a face with MK aposencephaly. (Right) Clinical photograph shows the hand of the same infant at term. Note the absent thumb (arrow), ulnar deviation of the wrist (curved arrow), and digital contractures (open arrows).
CRANIOSYNOSTOSIS

TERMINOLOGY

Abbreviations and Synonyms
- Sagittal synostosis
- Oxycephaly
- Bilateral coronal synostosis
- Plagiocephaly
- Unilateral coronal synostosis
- Trigonocephaly
- Metopic synostosis

Definitions
- First described by Virchow in 1851
- Premature fusion of one or more cranial sutures
- Growth of brain deformities adjacent bones, resulting in abnormal calvarial shape
- Growth inhibited at right angles to fused suture
- Premature growth of cranium occurs at open sutures
- Affects all aspects of the craniofacial complex
- Both syndromal and non-syndromal forms of craniosynostosis exist

IMAGING FINDINGS

General Features
- Best diagnostic clue
  - Abnormal calvarial shape on mid-trimester ultrasound
  - Shape may be severely altered as in klebblattschädel ("cloverleaf") skull
  - Persistent asymmetry of calvarium
  - Proptosis, often severe
  - Associated limb defects
  - Hypothyroid
  - Polydactyly
  - Associated skeletal abnormalities
  - Short limbs
  - Sclerosis

Imaging Recommendations
- Best imaging tool
  - Prenatal ultrasound in mid-trimester
  - Prenatal radiograph
  - Postnatal CT scan
- Protocol advice
  - 3D ultrasound may help distinguish between normal molding and craniosynostosis
  - Delineation of soft tissue abnormalities
  - Fetal MRI best for assessment of brain

DDx: Abnormal Calvarial Shape

- Trigonocephaly
- Chiari II
- Spina Bifida
- Meckel Syndrome
CRANIOSYNOSTOSIS

Terminology
• Premature fusion of one or more cranial sutures
• Growth of brain deform adjacent bones, resulting in abnormal calvarial shape
• Both syndromal and non-syndromal forms of craniosynostosis exist

Imaging Findings
• Abnormal calvarial shape on mid-trimester ultrasound
• Peepotism, often severe
• Associated limb defects

Top Differential Diagnoses
• Isolated craniosynostosis
• Apert syndrome (FGFR2)
• Crouzon syndrome (FGFR2)

Key Facts
• Pfeiffer syndrome (FGFR1,2)
• Thanatophoric dysplasia (TD) (FGFR3)

Pathology
• Craniosynostosis in ~150 genetic disorders
• Prenatal diagnosis possible in some disorders

Clinical Issues
• Age: Syndromal forms often associated with increased paternal age (new dominant mutations)
• Prognosis dependent upon underlying diagnosis
• Severe craniosynostosis associated with neonatal death

Diagnostic Checklist
• Abnormal calvarial shape/asymmetry with other skeletal findings in syndromal craniosynostosis

Differential Diagnosis

Isolated craniosynostosis
• Non-syndromal
• Affects single or multiple sutures
• Ultimate calvarial shape determined by which suture(s) fused
• Causative mutations rarely identified in isolated cases

Fibroblast growth factor receptor (FGFR1,2,3) associated craniosynostosis
• Apert syndrome (FGFR2)
  • Acraniocephaly/syndactyly
  • Mental retardation common
  • "Mitten" syndactyly of hands, feet with broad distal phalanges of thumb, great toe
  • Midface hypoplasia with malocclusion
• Crouzon syndrome (FGFR2)
  • Autosomal dominant - most new cases sporadic
• Crouzon syndrome (FGFR2)
  • Autosomal dominant with variable expressivity
• Protoposis +/- divergent strabismus
• Degree of malocclusion highly variable
• Coronal, lambdoid, sagittal synostosis with bridging
• Intellectual function variable
• Pfeiffer syndrome (FGFR1,2)
  • Bilateral coronal craniosynostosis
• Midface hypoplasia
• Baked bunsal tip
• Broad and medially deviated thumbs, great toes
• 3 clinical subtypes
  • Type 1: Classic with normal - near normal intelligence, autosomal dominant or sporadic
  • Type 2: Klebbersdalsdail skull with extreme proptosis, usually early lethal, sporadic
  • Type 3: Severe proptosis without cloverleaf skull, neurologic compromise, early death, sporadic
• Thanatophoric dysplasia (TD) (FGFR3)
  • Lethal skeletal dysplasia
• Type II TD with klebbersdalsdail ("cloverleaf" skull)
• Micrognathia
  • Small chest with pulmonary hypoplasia
  • Jackson-Weiss syndrome (FGFR2)

TWIST mutation associated craniosynostosis
• Saethre-Chotzen syndrome
  • Most common heritable disorder involving coronal suture synostosis
  • Shallow orbits
  • Dysplastic ears
  • Partial cutaneous syndactyly of fingers, toes
  • Ptosis of eyelids
  • Most with normal intelligence
• Saethre-Chotzen phenotype with mental retardation
  • Large deletions of 7p encompassing TWIST locus

Abnormal steroidogenesis
• Antley-Bixler syndrome
  • Chronic atresia
  • Radial ray syndrome
• Curved femora
• High postnatal mortality
• Autosomal recessive

Unknown molecular basis
• Carpenter syndrome
  • Autosomal recessive
  • Klebbersdalsdail skull common
  • Premature polyandricity (fingers)
  • Cardiac defects in ~30-50%
• Umbilical hernia/omphalocoele
• Variable cranial capacity
• Noonan craniosynostosis
  • Present with mid-face hypoplasia, hypertelorism
• Signs of increased intracranial pressure

Deformational plagiocephaly
• Skull asymmetry
• Usually not associated with fusion of sutures
• Cranial molding helmet, behavioral modification

Molding of the head
• Self-limited
• Associated with vaginal birth process
CRANIOSYNOSTOSIS

Neural tube defect
- "Lemon" shaped head associated with Chiari II
  malformation

Trisomy 18
- "Strawberry" shaped head

Dolichoccephaly
- Associated with intracranial constraint
  • Front, occipital flattening
- Some due to sagittal suture synostosis

Metopic ridge without synostosis
- Prominent ridge without fusion

Fetal demise
- Overlapping sutures "Spaulding sign"

PATHOLOGY

General Features
- Genetics
  • Craniosynostosis in ~150 genetic disorders
  • Premal diagnosis possible in some disorders
- Molecular diagnosis possible if mutation known
- Mutations in FGFR, TWIST, MSX2 involved in
  syndromic craniosynostosis
- Most autosomal dominant or sporadic

Gross Pathologic & Surgical Features
- Gross obliteration of the suture
- Natural ailing, especially with sagittal and metopic

Microscopic Features
- Zone of osseous obliteration in central position of
  fusion
- Nonlamellar bone across the suture
- Zone of partial osseous union involving nonlamellar
  bone and connective tissue

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - Abnormal cranial shape
  - Cranial asymmetry
- Other signs/symptoms
  - Proptosis
  - Limb, other skeletal abnormalities

Demographics
- Age: Syndromic forms often associated with increased
  paternal age (few dominant mutations)

Natural History & Prognosis
- Prognosis dependent upon underlying diagnosis
- Severe craniosynostosis associated with neonatal death
  • Airway obstruction in 40% with severe abnormality
  • Midface hypoplasia
  • Choanal atresia
  • Lower airway obstruction
  • Tracheostomy may be required
- Developmental delay including mental retardation in
  50%
- Severe proptosis with corneal scarring, visual loss
- Hydrocephalus
- Hearing loss
- Orthopedic issues: Scorifosis, limb defects
- Non-syndromal cases with milder abnormalities, little or
  no clinical sequelae

Treatment
- No prenatal treatment available
- Non-surgical correction
- Early correction may prevent sequelae of cerebral
  exposure, increased intracranial pressure
- Cranial molding helmet therapy in milder cases
- Syndromal cases
  • Extensive craniofacial surgery
  • Other orthopedic or plastic surgical procedures

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls
- Abnormal calvarial step/ asymmetry with other
  skeletal findings in syndromal craniosynostosis

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Typical Clinical photograph shows prominent fontanel with Carpenter syndrome. Note the severe protusion (curved arrow), the patent forhead (curved arrow) and low set ear (open arrow) due to craniosynostosis. (Right) Coronal ultrasound shows the same features with Carpenter syndrome in the midsclerosis. Note the craniosynostosis of the coronal sutures associated with ridging of the calvarium (arrows).

Typical Axial ultrasound shows trigonocephaly (arrow) due to metopic suture synostosis in a 23-week fetus with trephine. (Right) Profile of a different infant with trigonocephaly shows a very prominent metopic ridge (arrow).

Typical Axial ultrasound shows a typical bifrontal/bridged skull (arrows) in a mid-trimester fetus with type II thanatophoric dysplasia (TD). Note the patent forhead due to synostosis of multiple sutures. (Right) Clinical photograph shows a stillborn protein infant with a bifrontal/bridged skull due to type II TD. Note the occipital "shovel" canthus and frontal bossing (curved arrows).
VEIN OF GALEN MALFORMATION

**TERMINOLOGY**

**Abbreviations and Synonyms**
- Vein of Galen malformation (VGM)
- Vein of Galen aneurysm
- Misiurak: Actually involves median prosencephalic vein (MPV) of Markowski

**Definitions**
- Arteriovenous fistula
  - Aneurysmal dilatation of median prosencephalic vein of Markowski

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue: Enlarged midline vascular structure
- Location: Cistern of veinam interpositum and quadrigeminal plate cistern
- Size
  - Variable
  - Depends on volume of shunt

**Ultrasonographic Findings**
- Grayscale Ultrasound
  - Elongated midline cystic structure

**MR Findings**
- T2WI
  - Flow void in arterial feeders
- May be difficult to differentiate from small foci of hemorrhage
- Hemorrhage high signal on T2WI
- Flow void or mixed signal in MPV due to turbulent flow

**DDx: Vein Of Galen Malformation**

- Arachnoid Cyst
- Dural AVF
- Porencephaly
- Venous Cerebellum
### Termination
- Most common prenatally diagnosed cerebral vascular malformation

### Clinical Issues
- Most common signs/symptoms: Cardiac failure
- Most cases detected in third trimester
- Prognosis depends on volume of shunt
- If survives to birth will need treatment
- At birth vascular shunt usually increases
- Postnatal cognitive impairment may be present

### Diagnostic Checklist
- Color Doppler should always be performed on any cystic brain lesion

### CT Findings
- No role prenatally
  - Postnatal imaging findings
  - Venous malformation may be slightly hyperdense
  - Hydrocephalus
  - Parenchymal atrophy
  - Wall calcification in older children

### Imaging Recommendations
- Fetal MRI recommended
  - Valuable for postnatal planning
  - Better assessment of vascular anatomy
  - Evaluate for complications
  - Hemorrhage
  - Ischemic changes

### DIFFERENTIAL DIAGNOSIS

#### Arachnoid cyst
- Extraaxial cerebrospinal fluid (CSF) filled lesion
- Displaces adjacent brain
- No Doppler flow

#### Congenital dural arteriovenous fistula (AVF)
- Lutroparenchymal cerebrospinal vessels normal in size
- Enlarged meningeal arteries
- Most involve transverse-sigmoid sinuses or torcular

#### Porencephaly
- CSF-filled intraparenchymal lesion
- Irregular or round shape
- No Doppler flow
- No mass effect
- Hydrocephalus

#### Venous sinus engorgement
- Can be seen in high volume states
  - Arteriovenous fistulas
  - Intercranial
  - Elsewhere in body
  - Hydrodrops

### Choroid plexus cysts
- Located within choroid plexus
- No Doppler flow
- Resolves in third trimester
- Present in 50% of fetuses with trisomy 18 (T18)
  - Careful search for other signs of T18 warranted

### PATHOLOGY

#### General Features
- Genetics: Sporadic
- Etiology
  - Arteriovenous fistula of MPV
  - Normally choroid plexus drains via temporary midline vein (MPV)
  - MPV normally regresses in fetal development
  - Usually after formation of paired internal cerebral veins
  - High flow through VGM
  - Inhibits involution of normal fetal venous drainage
  - MPV persists
  - Joins internal cerebral veins to form VGM

#### Epidemiology
- Rare
- < 1% of all cerebral vascular malformations
- Most common prenatally diagnosed cerebral vascular malformation

#### Gross Pathologic & Surgical Features
- Dilated arterial vessels
- Midline engorged MPV
- Venous drainage
  - Straight sinus
  - Embryonic falx sinus
  - If embryonic falx sinus present, straight sinus usually absent
- Hydrocephalus
  - Various theories on etiology
  - Compression of the aqueduct
  - Venous hypertension impairing resorption of CSF
VEIN OF GALLEN MALFORMATION

- Ex-vacuo from cerebral atrophy
- Cerebral atrophy
- Secondary to occlusive vascular steal phenomenon
- Could also be from chronic venous hypertension

Microscopic Features
- Direct arterial → venous connections
  - No intervening capillaries
  - Allows rapid, high volume flow

CLINICAL ISSUES

Presentation
- Most common signs/symptoms: Cardiac failure
  - Most cases detected in third trimester
  - Usually > 44 weeks
  - Spontaneous rupture detection as early as 22 weeks
  - Presenting with cardiomegaly
- Cardiomegaly
  - May be asymptomatic if shunt small
- Hydrocephalus
- Hydrops from high-output heart failure
  - Skin edema
  - Necrosis
  - Pleural effusions
  - Pericardial effusion
  - Intracranial hemorrhage
  - Rarely, fetal death
  - Calcifications may be seen in thrombus
  - Spontaneous vaginal delivery possible
  - High perinatal mortality and mortality
  - Often due to congestive heart failure (CHF)

Demographics
- Gender: M:F = 2:1

Natural History & Prognosis
- Prognosis depends on volume of shunt
  - Worse neonatal prognosis if CHF present at birth
  - In utero high-output state
  - High output heart failure
  - Hydrops
  - If survives to birth will need treatment
  - At birth vascular shunt usually increases
  - Cessation of flow to low resistance placenta
  - Can cause hemodynamic decompensation
  - Potentially requires maternal circulatory support
  - Wide range of manifestations
  - Delayed milestones
  - Mental retardation
  - Secondary to chronic hypoxia

Treatment
- No known in utero treatment
- May lead to neonatal death if untreated
  - Major risk factors include:
    - Cardiac failure if shunt is large
    - Requires aggressive management
  - Medical therapy for CHF
    - Usually until 3-6 months of age
    - Intervention easier and safer than neonatal period
  - Eventual requires transcatheter embolization
  - Arterial embolization
  - Reduce shunt flow
  - Improve high-output CHF
  - Prevent consequences of chronic cerebral venous hypertension
  - Color Doppler can be used for follow-up
  - Access flow after embolic or surgical treatment
  - Emergency embolization may be necessary
  - Neonates with refractory CHF

DIAGNOSTIC CHECKLIST

Consider
- Fetal MRI to assess vascular anatomy

Image Interpretation Pearls
- Color Doppler should always be performed on any cystic brain lesion
- Evaluate for presence of vascular malformation
- Early prenatal detection imperative for aggressive management
- Requires close sonographic follow-up
- Delivery planning essential

SELECTED REFERENCES
 VEIN OF GALEN MALFORMATION

IMAGE GALLERY

Typical

(Bottom) Axial color Doppler ultrasound through the fetal chest confirms hypoplasia with a small patent ductus arteriosus (curved arrow).

(Bottom) Color Doppler flow within this cystic structure, including an aneurysmal cyst and polycystic dysplasia. It is essential to perform color Doppler ultrasound to evaluate for a vascular malformation. (Right) Pulsed Doppler ultrasound shows turbulent arterial flow within a feeding vessel, consistent with an arteriovenous fistula.

Typical

(Bottom) Axial T2WI MRI shows an elongated, heterogeneous mass with flow voids (arrow).

There are areas of low signal in the surrounding white matter (curved arrow). It is difficult to differentiate increased edema from areas of hemorrhage without T1WI.

(Bottom) Coronal gross pathology shows the collapsed, dilated vein (arrow). There are diffuse neurologic changes (B.S.), with areas of hemorrhage (arrow) and aneurysm (arrow), consistent with the case.

Typical
ARTERIOVENOUS FISTULA

TERMINOLOGY

Abbreviations and Synonyms
- Arteriovenous fistula (AVF)
- Arteriovenous malformation (AVM)

Definitions
- Abnormal connection of intracranial vessels
  - Arterial to venous connection
  - No intervening capillary network

IMAGING FINDINGS

General Features
- Best diagnostic clue: Enlarged vessels with alternating direction of flow on color Doppler

Ultrasoundographic Findings
- Grayscale Ultrasound
  - Macroadenoma
  - Volume of shunt vessels
  - Hydrocephalus
  - Microadrenoma
  - Impaired cortical atrophy
  - May occur secondary to premature closure cranial arteries
  - Ischemic changes

Color Doppler
- Alternating red and blue within vessel cross section
- Forward and backward shunt flow
- Pseudo Doppler
- High velocity, low resistance arterial flow
- Arterialized venous structures
- Features of hydrops
- Pulsatile umbilical vein flow

DX: Extra-Axial Cystic Mass

Arachnoid Cyst

Arachnoid Cyst

Vessels Of Cerebro

Vessels Of Cerebro
**Imaging Findings**
- Best diagnostic clue: Enlarged vessels with alternating direction of flow on color Doppler
- Cortical atrophy
- Juxtalesional hemorrhage
- Periventricular leukomalacia
- "Tangle" of dilated vessels
- Enlarged neck vessels
- Hydrocephalus may develop if sufficient shunt volume
- Polyhydramnios

**Top Differential Diagnoses**
- Vein of Galen malformation (VGM)
- Vascular tumor
- Intracranial cyst

**Key Facts**
- **Pathology**
  - Ischemic brain injury
  - High-output cardiac failure
  - Majority of fetal vascular malformations are VGM
  - Dural sinus malformations commnosed after VGM

**Clinical Issues**
- No intrauterine intervention
- Early delivery does not prevent ischemic damage

**Diagnostic Checklist**
- Fetal MRI
- DWI may be more sensitive to ischemia than T2WI
- Careful search for AVM in fetuses with apparent isolated cardiomegaly
- Always check Doppler of apparent intracranial cyst

**DIFFERENTIAL DIAGNOSIS**

**Vein of Galen malformation (VGM)**
- Specific type of arteriovenous fistula
- Vein of Galen malformation actually a pseudo aneurysm
- Aneurysmal dilatation of median prosencephalic vein of Markowski
- Elongated midline cystic structure extends from quadrigeminal plate cistern toward occiput
- Drains via straight sinus or embryonic falx sinus

**Vascular tumor**
- Solid mass component even if necrotic
- Dilated draining veins unlikely
- Enlarged neck vessels unlikely

**Intracranial cyst**
- Extra-axial fluid-filled lesion
- No Doppler flow
- Rarely associated with ischemic lesions

**Fetal anemia**
- High velocity flow in middle cerebral artery
- No associated draining veins
- No enlarged neck vessels

**Venous dilatation**
- Rare cases with diffuse vertebral venous dilatation
- No arterial shunt or venous thrombosis identified
ARTERIOVENOUS FISTULA

PATHOLOGY

General Features
- Genetics: Not associated with sutured plasty
- Etiology
  - Ischemic brain injury
  - Vascular steal phenomenon
  - Hydrops = hypoperfusion, hypoxia
  - Direct compression of AVM in limit brain perfusion = atrophy
  - Venous hypertension = hemorrhage
  - Venous thrombosis
  - High-output cardiac failure
  - Decreased coronary blood flow
  - Myocardial ischemia +/- infarction
- Epidemiology
  - Majority of fetal vascular malformations are VGM
  - 92% of reported cases
  - Dual sinus malformations commonest after VGM

Microscopic Features
- Periventricular leptomeninges
- Diffuse meningothelial

CLINICAL ISSUES

Presentation
- Hydrops
- Ventriculomegaly
- Polyhydramnios
- Most aVPM present late
  - Typically in third trimester
  - May have had a normal early scan

Natural History & Prognosis
- No recurrent risk
- Prognosis depends on associated findings
- Hydrops
- Brain injury
- Additional anomalies
- High perinatal mortality rate when fetus is "asymptomatic"
- New published outcome data available on non-VGM cases
  - Authors personal experience of two cases
  - One neonatal death
  - One severe encephaloclastic changes with cerebral palsy

Treatment
- No intra-uterine intervention
- Perinatal consultation with pediatric neurology
- Discuss potential treatment options
- Discuss risk of neurological impairments
- Perinatal consultation with pediatric cardiology
- Discuss potential additional congenital heart disease
- Discuss management of high output cardiac failure
- Deph on tertiary center
- No consensus on mode of delivery
- May wish to avoid caesarean section if confirmed ischemic brain damage
- Not shown to be advantageous in VGM
- No benefit to fetus
- Additional morbidity for mother
- Early delivery does not prevent ischemic damage
- Prematurity adds to risks for tenant
- For survivors consider
  - Embolization
  - Surgery

DIAGNOSTIC CHECKLIST

Consider
- Fetal MRI
  - Full extent of lesion
  - Hemorrhage
  - Ischemic damage
- DWI may be more sensitive to ischemia than T2WI

Image Interpretation Pearls
- Careful search for AVM in fetuses with apparent isolated cardiopathy
- Always check Doppler of agenesis intracranial cyst
- AVM immediately apparent on color Doppler
- Prognosis very different from lesions such as anechoic cyst

SELECTED REFERENCES
ARTERIOVENOUS FISTULA

IMAGE GALLERY

Typical

(Top) Axial ultrasound in a fetus referred for possible holoprosencephaly shows a cystic area (arrow) mistaken for a massa intermedia. The "cyst" was extra-axial and two hemispheres were seen on other scan planes. (Right) Sagittal color Doppler ultrasound of the same fetus shows swirling red and blue color secondary to turbulent flow in the clear arteriovenous malformation. Always check for flow in apparent cysts.

Typical

(Top) Axial T2W MRI in the same case shows a large flow void (open arrow) correlating with the abnormal color Doppler findings and the gray-scale "cyst." Note ventriculomegaly and cortical atrophy (curved arrows) due to vascular "steal." (Right) Axial T2W MRI through the markedly dilated superior sagittal sinus (arrow) also shows a tangle of abnormal vessels on the cerebral surface (curved arrows).

Variant

(Top) Sagittal T2W MRI of the fetal brain shows a large mixed-signal, extra-axial mass (arrow). Areas of hemorrhage and parenchymal edema were also present. A thrombosed ductal vessel was noted at birth. (Right) Sagittal T2W MRI in a Down syndrome fetus shows a hyperintense neck and dural arteriovenous shunt (arrow) secondary to an extra-axial shunt. Flow was arterialized venous flow on Doppler but no AV shunt was present.
CNS TUMORS

TERMINOLOGY

Definitions
- Benign or malignant intracranial neoplasm

IMAGING FINDINGS

General Features
- Best diagnostic clue: Solid intracranial mass with Doppler flow
- Location
  - Most are supratentorial
  - Contra/associated with pediatric tumors which are more commonly infratentorial
  - Most common sites of origin
    - Pineal gland
    - Supratentorial
    - Cerebral hemispheres
  - Precise point of origin can often not be determined
  - May extend through skull base into oral cavity
- Size
  - Often massive
  - May exhibit rapid growth over short period of time
- Morphology
  - Gross distortion of cerebral architecture
  - Intratumoral hemorrhage may cause further distortion

DDx: Intracranial “Mass”
- Hemorrhage
- Intramedullary Hemorrhage
- Arachnoid Cyst
- Cerebrospinal Cyst

- Hydrocephalus
- Most often obstructive from mass
- May be from overproduction with choroid plexus papillomas
- Polymicrodysplasia
- Decreased swallowing from hypothalamic dysfunction
- Hypertrophy or polyhydramnios may present before tumor, sonographically detectable
- Intratumoral hemorrhage not uncommon

Ultrasoundographic Findings
- Considerable overlap in appearance of tumor types
- Differentiation often not possible or even necessary
- Teratoma
  - Most common tumor
  - Complex masses with cystic and solid components
  - Calcifications
    - Typically midline
  - May fill entire cranial vault
  - May extend through skull base into mouth
- Astrocytoma
  - Solid tumor
  - Arises in cerebral hemispheres
  - Marked contrast distinction to pediatric astrocytomas, which are most common in the cerebellum
- Craniopharyngioma
CNS TUMORS

**Imaging Findings**
- Best diagnostic clue: Solid intracranial mass with Doppler flow
- Most are supratentorial
- Contrasts with pediatric tumors which are more commonly infratentorial
- Precise point of origin can often not be determined
- May exhibit rapid growth over short period of time
- Hydrocephalus or polyhydramnios may present before tumor is sonographically detectable

**Top Differential Diagnoses**
- Intracranial hemorrhage
- Astrocytoma
- Ependymoma
- Rhabdoid tumor

**Pathology**
- Malignant
- Metastatic

- **Suprasellar mass**
- Heterogeneous complex mass
- Frequently calcify
- Indistinguishable from teratoma

- **Choroid plexus papilloma**
  - May occur anywhere in ventricular system
  - Lateral ventricle most common
  - Well-defined, lobular, hyperechoic mass
  - Hydrocephalus from over production of cerebral spinal fluid (CSF)
  - Cystic masses
  - Mass may also obstruct ventricle causing asymmetric enlargement

- **Lipoma**
  - Well-defined, echogenic mass
  - Midline or lateral ventricles
  - Up to 50% of midline lipomas associated with agenesis of the corpus callosum
  - Absent cavum septi pellucidi
  - Colpocephaly (tear-drop-shaped ventricles)
  - Elevation of 3rd ventricle creating "trident" shape in coronal plane

**MR Findings**
- Better for delineating anatomy
- Can confirm fat in lipoma
- Can better evaluate for associated agenesis of the corpus callosum
- Sensitive modality for detecting hemorrhage

**Imaging Recommendations**
- Best imaging tool: Fetal MRI
- Protocol advice:
  - Select Doppler essential to look for flow
  - Variable degrees of vascularity
  - Important to distinguish from intracranial hemorrhage
- Intracranial tumors have propensity to bleed
- Cautiously evaluate periphery of mass
- Close surveillance if pregnancy continued
- Often very rapid growth
- Warceous hydrocephalus
- Macrocystic

**Key Facts**
- Astrocytoma
- Lipoma
- Choroid plexus papilloma
- Cranioopharyngioma
- Primitive neuroectodermal tumor

**Clinical Issues**
- Macrocephaly from hydrocephalus, tumor, or both
- Large size portends grave prognosis regardless of histology
- Lipomas and choroid plexus papillomas have better prognosis

**Diagnostic Checklist**
- Underlying neoplasm should always be considered in setting of spontaneous intracranial hemorrhage

**Differential Diagnosis**

- **Intracranial hemorrhage**
  - May be intraparenchymal, intraventricular or subdural/subarachnoid
  - Variable echogenicity
  - Dose-organized appearance of brain
  - No flow with Doppler
  - Evolves over time
  - Fetal MRI to evaluate anatomic extent

- **Arachnoid cyst**
  - Purely cystic
  - Extra-axial mass
  - No solid component
  - More common over cerebellar convexities and posterior fossa

- **Gliopependymal cyst**
  - Purely cystic
  - No solid component
  - More common in midline
  - Associated with agenesis of the corpus callosum
  - Protonencephalic fluid
  - High signal on T1WI

- **Choroid plexus cysts**
  - May be confused with choroid plexus papilloma
  - Cystic, not solid
  - Resolve on follow-up examination
  - No hydrocephalus
  - Associated with trisomy 18
  - Multiple major aneuploids
  - Uneructed hands
  - Cardiac defects
  - Early, severe intracranial growth restriction (IUGR)
PATHOLOGY

General Features
- Genetics
  - Sporadic
  - No recurrence risk
- Epidemiology
  - Rare
  - 10% of all neoplasms
  - In children, CNS tumors are the most common solid tumor
- Astrocytic tumors, neurinomas, and choroid plexus tumors are all more common in the brain
- Association with other tumors
  - 50% of lipomas have a genetic link to carotid sinus tumors
  - 10% of other tumors have specific genetic abnormalties
- Microscopic Features
  - Heterogeneity in order of occurrence
  - Teatoma
    - Contains all three germ cell layers
  - Lithroblasts, mesenchymal, neuronal, melanoma
  - Approximately 50% of fetal CNS tumors
  - Astrocytes
  - Neuroepithelial tumors
  - Vary from well-differentiated to poorly differentiated
  - Lipoma
    - Benign fatty tumor
    - Located in subarachnoid space
    - Presence underestimated in pathologic series
  - Choroid plexus papilloma
  - Arise anywhere where choroid plexus present
  - Produce CSF
  - Generally benign
  - Choroid plexus carcinomas have been reported
  - 3-9% of fetal tumors
  - Glioblastoma multiforme
    - Arise from Rathke pouch, an ectodermal diverticulum from roof of mouth
  - Gliomatosis cerebri tumor
    - Highly malignant small-cell tumor
  - Arise from neural crest
- Clinical Issues
  - Presentation
    - Most common signs/symptoms
  - Macrogolopy: from hydrocephalus, tumor, or both
    - Most commonly present in 3rd trimester
    - May have had normal scan as recently as 2 weeks prior
  - Natural History & Prognosis
    - Fetal prognosis
      - In utero demise common
      - 97% mortality if diagnosed before 30 weeks
    - Far worse than pediatric brain tumors
    - Large size portends grave prognosis regardless of histology
    - Benign tumors equally as lethal as malignant ones
    - Two important exceptions
      - Lipomas and choroid plexus papillomas have better prognosis
    - Choroid plexus papilloma
      - Surgical resection often possible
      - Survival rate 78%
      - Significant neurologic deficits reported
      - Psychomotor retardation
      - Seizures
      - Spastic quadriaparesis
    - Lipoma
      - Best prognosis of all intracranial tumors
      - Often asymptomatic
- Treatment
  - Embryonics offered
  - Supportive care
    - Symptomatic care
    - At onset of labor for vaginal delivery
    - Has been used therapeutically to reduce hydrocephalus
    - Improvement in survival reported
    - Cesarean section may be required to prevent dystocia
    - Postnatal
      - Surgical resection often not possible
      - Radiation contraindicated
      - Severe adverse effect on normal brain growth and development
    - Chemotherapy
      - Survivors left with significant psychomotor deficits

DIAGNOSTIC CHECKLIST

Image Interpretation Pears
- Underlying neoplasms should always be considered in setting of spontaneous intracranial hemorrhage

SELECTED REFERENCES

CNS TUMORS

IMAGE GALLERY

Typical

(Right) Coronal ultrasound shows a cystic, irregular mass. This could be confused with an arachnoid cyst but note that there is extension of the mass through the skull base (arrow). An echogenic solid component (curved arrow) is also seen, making arachnoid cyst unlikely.

(Right) Axial ultrasound shows a soft tissue component with loci of calcification (arrow). Autopsy confirmed a cystic teratoma.

Typical

(Right) Axial ultrasound shows a complex, midline mass with both cystic and solid components (arrows) with associated obstructive hydrocephalus (curved arrow). (Right) Axial T1W MR shows marked gadolinium enhancement of the solid component of this tumor (arrow). There has been worsening of the hydrocephalus since the previous study. Histology confirmed a teratoma.

Typical

(Right) Sagittal ultrasound of a child with papilledema shows a well-defined lobular, hyperechoic mass within the atrium of the lateral ventricle (arrow). Hydrocephalus is the result of over production of CSF.

(Right) Coronal ultrasound of a baby with the arteriovenous malformation shows the arteriovenous malformation. 50% of cases have associated agenesis of the corpus callosum, and thorough evaluation of midline structures is essential. Where the Radiographers rely on
SECTION 3: Spine

Introduction and Overview
Spine Development & Imaging 3-2

Spine
Spina Bifida 3-6
Intercolumnal 3-10
Cauda Regression Sequence 3-14
Kyphosis, Scoliosis 3-18
Sacroccygeal Teratoma 3-22
**Imaging Anatomy**

**Ultrasound**
- Sagittal view
  - Cervical lordosis
  - Lumbar lordosis
- Posterior elements seen just under skin
- Vertebral body ossification center deep to amniotic spinal canal
- Late in gestation echogenic spinal cord may be visualized in spinal canal
- Axial view
  - 3 ossification centers seen in second trimester
  - Vertebral body and 2 lateral masses
  - Lateral mass-transverse process-spinoous process-articular process
  - Ossification visible sonographically by 16 weeks
  - Lower lumbar ossification may not be seen until 19 weeks
- Third trimester distinct bony anatomy can be identified
  - Vertebrae
  - Pedicles
  - Laminae
  - Transverse processes
  - Spinous processes
  - "Humper" appearance of posterior vertebral body
  - Inward angulation of posterior arch elements
- Coronal view
  - May be useful if vertebral anomalies detected
  - Characterize extent of involvement
  - Posterior elements appear as paired echogenic lines
- Flared at cervical spine
- Slight widening at lumbar spine
- Tapered at sacrum
- Echogenic linear signals covering the fetal spine should be documented
  - Exclude subtle neural tube defects (NTD)

**MRI**
- Ultrasound typically used for characterization of fetal osseous abnormalities
- Useful for identifying anatomy in difficult to image patients
- May reveal other causes of anencephaly
- Suggests absence of posterior fossa structures
- Chiari II brain findings by ultrasound
- Look for subdural effusion
- Can aid in identification of exact level of defect
- Level of NTD may have significant impact on prognosis
- Can help document extent and origin of spinal masses
- Characterization of sacrococcygeal teratomas
- May use to visualize spinal cord
- Normal T2WI appearance
- Hypointense vertebral bodies
- Hyperintense disk spaces

**Anatomy-Based Imaging Issues**

**Imaging Protocols**
- American Institute of Ultrasound in Medicine (AIUM) spine examination
  - Axial and longitudinal views
  - Cervical
  - Thoracic
  - Lumbar
  - Sacral
- Real-time evaluation important for spinal defects
  - Carefully scan entire spine in axial plane
  - Clearing lumbar spinal canal very important as most common site for spinal bCX
  - Consider performing endovaginal ultrasound exam if fetus is breech

**Imaging Pitfalls**
- Bilateral spine ossification not visible until 36 weeks gestation
- May falsely suggest NTD prior to ossification
- Neonatal scoliosis of fetal spine may be seen
SPINE DEVELOPMENT & IMAGING

Key Facts
• Avoid incorrect diagnosis of small NTD

Serum Screening for NTD
• MSAFP screening performed at 16-18 weeks
• ONTD allows AFP to escape fetal circulation and enter amniotic fluid
• Subsequent PE in MSAFP
• Larger lesions cause greatest deviation
• Skin covered defects will not be detected
• Role of sonography
• Establish dates
• Incorrect dates common cause of ↑ MSAFP
• Rule out multiple gestations or demise
• If MSAFP is elevated and dates correct, careful search for ONTD and other anomalies warranted

Imaging Issues
• Scan entire spine in longitudinal and axial planes
• Visualization of fetal spine tip and skin covering crucial
• Can otherwise miss small NTD
• Lumbosacral anlage common location NTD
• Posterior arch elements should angulate inward
• If cannot adequately visualize entire spine, normal posterior fossa with normal MSAFP is reassuring
• 99% of spinal NTD have Chiari II findings
• Consider performing endovaginal ultrasound exam if fetus is breech

Imaging Pitfalls
• Lower lumbar spine may not be visibly ossified until 12 weeks

May simulate NTD
• Axial views should clear any confusion
• Always look at posterior fossa
• 99% of spina bifida have Chiari II findings
• Cervical compression
• Cisterna magna obliteration

Normal Measurements
• Routine measurements not required by AUM
• Spine length measurements
• Correlate with fetal growth parameters at 11-14 weeks gestation

Embryology

Embryologic Events
• 3rd-4th week
  • Neural cord development
  • Neural plate converted to hollow neural tube (neuralization)
  • Neural folds meet dorsally to form neural canal
  • Subsequently invaginates into posterior body wall
  • Closure of neural tube occurs bidirectionally
  • Caudal neuropore becomes spinal cord
  • Caudal neuropore closes day 26
  • Occurs in cranio-caudal direction
  • Finishes at level of superior sacrum
  • Inferior sacrum and coccyx formed by secondary neurulation from caudal eminence
• 4th week
  • Vertebrae column formation
  • Sclerotome cells migrate and surround neural tube and notochord
  • Vertical portion → rudimentary vertebral body
  • Lateral portion → rudimentary vertebral arch
  • Sclerotomes split into cranial and caudal segments
  • Spinal nerves grow out between split segments
  • Caudal segment of sclerotome recombines with caudal segment of sclerotome above
  • Forms early vertebral body
• 5th week
• 6th week
• Neural tube defects (NTDs)
• Abnormal induction of vertebral arch rudiments
• Failure of closure in 3rd week of development
• Milder defect results in meningocele or myelomeningocele
• In more severe defects neural folds fail to fuse, differentiate, invaginate, and separate from surface ectoderm
• Cranial NTD → anencephaly
• Caudal NTD → rachischisis or myeloschisis
• Occipital/lower spinal NTD → meniscus
• Entire neural tube does not close → camorachischisis totals
• Scoliosis
• Defective induction of vertebral bodies on one side of body
• Can also be secondary to bony vertebra
• Diastematomyelia
• Longitudinal division of vertebral canal by bony, fibrous, or cartilaginous septum
• Variable length of involvement
• May be associated with other vertebral body anomalies
• Multiple theories of pathogenesis
• Serum Screening
  • Maternal serum alpha-fetoprotein (MSAFP)
  • Alpha-fetoprotein (AFP) is a glycoprotein produced first by yolk sac and later by fetal liver and gastrointestinal tract
  • Major serum protein in embryo
  • Fetal plasma levels peak 16-18 weeks
  • Clinical Implications
• Abnormal induction of sclerotomes causes spinal defects

Practical Implications
• Abnormal induction of sclerotomes causes spinal defects
• Costal processes elongate in thoracic region to become ribs

Clinical Importance
• Neural tube defects (NTDs)
  • Abnormal induction of vertebral arch rudiments
  • Failure of closure in 3rd week of development
  • Milder defect results in meningocele or myelomeningocele
  • In more severe defects neural folds fail to fuse, differentiate, invaginate, and separate from surface ectoderm
  • Cranial NTD → anencephaly
  • Caudal NTD → rachischisis or myeloschisis
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  • Entire neural tube does not close → camorachischisis totals
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  • Defective induction of vertebral bodies on one side of body
  • Can also be secondary to bony vertebra
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  • Longitudinal division of vertebral canal by bony, fibrous, or cartilaginous septum
  • Variable length of involvement
  • May be associated with other vertebral body anomalies
  • Multiple theories of pathogenesis
• Serum Screening
  • Maternal serum alpha-fetoprotein (MSAFP)
  • Alpha-fetoprotein ( AFP) is a glycoprotein produced first by yolk sac and later by fetal liver and gastrointestinal tract
  • Major serum protein in embryo
  • Fetal plasma levels peak 16-18 weeks
A small amount accumulates in amniotic fluid
Early: Diffusion through skin
Later: Expelled by kidneys ⇒ fetal urine ⇒ amniotic fluid
Peak amniotic fluid AFP (AFAFP) 12-15 weeks
Placental permeability to fetal plasma proteins causes increase in MSAFP
Maternal serum levels are a small fraction of fetal and amniotic fluid levels
MSAFP continues to increase to 32 weeks despite decreasing fetal plasma AFP (likely reflects increasing placental permeability)
Screening for neural tube defects
Open neural tube defects (ONTD) allow AFP to escape fetal circulation and enter amniotic fluid
Subsequent rise in MSAFP
Larger lesions cause greatest elevation
Greater surface area for plasma protein to "weep" into amniotic fluid
Largest elevations with anencephaly
Virtually all cases of amnecphaly and open spina bifida detectable by MSAFP
Skin covered defects will not be detected
20% of spina bifida
80-90% of encephalocele
Screening usually performed at 16-18 weeks
Results expressed as multiples of the median (MoM)
2.0 MoM, 85-90% detection rate of ONTD, 4-6% false-positives
2.5 MoM, 75-80% detection rate of ONTD, 2-3% false-positives
Given accuracy and non-invasive nature of ultrasound, consider using lower value to prompt evaluation.
Median value for anencephaly 6.5 MoM
Median value for open spina bifida 3.8 MoM
Appropriate dating is critical
Variation of 2 weeks may cause erroneous results
Epidemiologic variations
MSAFP higher in obese women and African-Americans
MSAFP lower in insulin-dependent diabetics
Role of sonography
First establish dates
Inaccurate dates common cause of 1 MSAFP
Rule out multiple gestations or demise
Look for cause of 1 MSAFP
ONTD
Abdominal wall defects: Gastrochisis, omphalocele, body stalk anomaly
Prior Peter's anomaly
Role of amniocentesis
Consider when ultrasound results are negative
Measure amniotic fluid AFP
Acetylccholinesterase (AChE), neural tissue specific

Related References
**Left:** Coronal ultrasound of the upper cervical spine and skull base shows the typical, gentle fan of the posterior fossa. (Arrow) An axial ultrasound of the cervical spine shows the posterior elements converging to form a "teeped" arrow. There is marked posterior shadowing from the vertebral body. (Curved arrow).

**Left:** Coronal ultrasound shows the typical tapered appearance of the distal spine and sacrum in the second trimester. Shadowing from the fetal wing can simulate an inferiort NTD (arrow). **Right:** Sagittal ultrasound shows a thin, echogenic line of skin overlying the tip of the spine (arrow). Documentation of this skin covering is essential to exclude an open neural tube defect.

**Left:** Coronal 3D ultrasound of a 10-week fetus shows the length of spine from the upper thoracic area through the sacrum. **Right:** Sagittal T2W FS performed prior to delivery on a 3rd trimester fetus shows the normal hypointense disk spaces (arrow) and hyperintense vertebral bodies (open arrow). The spinous processes are also identified (curved arrow).
SPINA BIFIDA

Graphic of spina bifida classification. Meninengocytes (arrow) contain only fluid while myelomeningocytes also contain neural elements (curved arrow). The defect is covered in myeloschisis (open arrow).

3D ultrasound multiplanar capability allows simultaneous views of a meningocele (arrow) in sagittal (top) and axial (bottom) projections. The sac extends from the canal (open arrow) and contains only fluid.

TERMINOLOGY

Abbreviations and Synonyms
- Open neural tube defect
- Meningoceles
- Spinal dysraphism
- Spina bifida aperta

Definitions
- Bony vertebral defect + natal content exposure
  - Dorsal arch defect most common

IMAGING FINDINGS

General Features
- Best diagnostic clue
  - Chiari II malformation
  - Splayed dorsal ossification centers
  - Myelomeningocele sac
- Location
  - 73% lumbar
  - 17% sacral
  - 9% thoracic
  - 1% cervical
- Size: Variable
- Morphology: Dependent on location and type of defect

Ultrasoundographic Findings
- Vertebral findings
  - Splayed dorsal ossification centers
  - Normally lateral masses are parallel or convergent
  - Transverse view best for seeing bony defect
  - "T" shaped vertebra on axial view
  - Coronal view best for evaluating extent of defect
  - Multiple levels usually involved
  - Use ribs to identify 12th thoracic level
  - Sagittal view best for seeing soft tissue sac
  - 80% with overlying sac
  - Meningocele
  - Anechoic cystic mass
  - Sac contains meninges only
  - Rarely covered by intact skin
  - Myelomeningocele
  - Complex cystic mass
  - Sac contains meninges + neural elements
  - 20% with no overlying sac
  - Myeloschisis
  - Open spinal cord is part of defect
  - Calvarial findings: 99% have Chiari II malformation
  - CineMRI magna obliteration
  - Most commonfinding
  - Usually fluid-filled subarachnoid space is gone or small
  - (c. 3 mm)
  - Cerebellar compression

DDx: Dystrophic Spine

- SC Tetralogy
- SC Tetralogy
- Holophrase
- Acrania
- Acrania
SPINA BIFIDA

Key Facts
- Almost 100% of cases are detectable
- Top Differential Diagnoses
  - Sacrococcygeal teratoma (SC teratoma)
  - Amniotic bands
- Clinical Issues
  - Maternal serum alpha-fetoprotein (AFP)
  - Preventive treatment with folic acid
- Diagnostic Checklist
  - Genetic amniocentesis
  - Presence of normal cisterna magna nearly eliminates diagnosis
  - Cerebral malformations (to see if spine defect)
  - Attempt to identify level of defect

Imaging Recommendations
- Best imaging tool
  - Second trimester screening ultrasound
- Examinations
  - Ventral spine bifida
  - Normal fetal body
  - Vertebral anomaly
  - Sacrococcygeal teratoma
- Differential Diagnosis
  - Sacrococcygeal teratoma (SC teratoma)
  - Germ cell neoplasm
  - Exophytic mass extending from sacrum
  - Rarely purely cystic
  - May be internal or external
  - No associated Chiari II malformation
- Isolated scoliosis/kyphosis
  - Abnormal curvature of spine
  - Usually from anterior vertebral body anomaly
  - Hemivertebrae
  - Fused vertebrae
- Amniotic bands
  - Entrapment of fetal parts by disrupted amnion
  - Asymmetric distribution
  - Spine involvement asymmetric and bizarre
  - Associated scoliosis common
  - Spine finding rarely isolated

MR Findings
- Not for primary diagnosis

Terminology
- Open neural tube defect
- Myelomeningocele
- Bony vertebral defect + neural content exposure

Imaging Findings
- Spinal canal enlargement
- Myelomeningocele sac
- 73% lumbar
- Transverse view best for seeing bony defect
- Use ribs to identify 12th thoracic level
- 80% with overlying sac
- Calvarial findings: 99% have Chiari II malformation
- Usually fluid-filled cisterna magna is gone or small (< 3 mm)
- 24% clubfoot
- 40% with additional anomalies

- “Banana sign” = cerebellum curved around midbrain
- Absent cerebellum rare
- Ventriculomegaly
  - Arterial width > 10 mm
  - Borderline or mild most common
  - 50% at time of diagnosis
  - 75% progress during pregnancy
  - 90% at birth
  - Frontal bone scalloping
  - Lesion-shaped calvarium
  - Found in 1% of normal fetuses
  - Usually resolves by third trimester
  - Lipomeningocele
  - Spine defect + sacral lipoma
  - Thyroid mass
  - Chiari II sign may be absent
  - Associated tethered cord common
  - Spinal bifida occulta
  - Small bony defect covered by skin
  - Rarely diagnosed in utero
  - Overlying soft tissue abnormalities
  - Subcutaneous lipoma
  - Soft of hair
  - Skin dimple
  - Usually asymptomatic
  - Ventral spinal bifida
  - Extremely rare
  - Splitting of vertebral body
  - Lower cervical or upper thoracic
  - Associated neurogenic cyst
- Common associated anomalies
  - Syndactyly and hypoplasia
  - Seen at level of defect
  - Lower extremity anomalies
  - 24% clubfoot
  - Rockerbottom foot
  - Hip dislocation
  - 40% with additional anomalies
  - 67% arachnoid cysts have other anomalies
- Helpful if ultrasound visualization poor
- Requested before fetal surgery
PATHOLOGY

General Features
- Genetics
  - 1% aneuploidy rate
  - Trisomy 18 (T18)
  - Trisomy 13 (T13)
  - Triploidy
  - Translocation
- 4% aneuploidy rate when isolated
- Embryology
  - Mostly sporadic and multifactorial
  - Folate deficiency
  - Folate metabolic pathway gene defect
  - Teratogens
  - Anticonvulsants: Carbamazepine, valproic acid
  - 1% risk
- Amnion theory
  - Primary: failure of neural closure
  - Absent skin/muscle from failed induction
- Hydrotic theory
- Cerebrospinal fluid (CSF) imbalance
  - Excess CSF accumulates in closed neural tube
  - Secondary separation of dural wall
- Lower extremity abnormalities
- From unopposed muscle group action
- Epidemiology
  - 0.4-1,000
  - 3% of all spontaneous abortions
  - 1%-2% recurrence risk
- Associated abnormalities: 40%

Gross Pathologic & Surgical Features
- Dural arch defect with exposed neural elements

Staging, Grading or Classification Criteria
- Ventral defects
- Extremely rare
- Dorsal defects
  - Spina bifida aperta (85%)
  - Spina bifida occulta (15%)

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - 1 Maternal serum alpha-fetoprotein (AFP)
- > 2.5 multiples of median (MOM) detects 80%

Demographics
- Age
  - Advanced maternal age (AMA) at slightly higher risk
- AMA ≥ 35 yrs at time of delivery
- Secondary to association with T18 and T13
- Ethnicity
  - United States data
  - Hispanic > Caucasian, African-American, Asian
- Difference persists after immigration
- Highest rates in United Kingdom
- Lowest rates in Japan

Natural History & Prognosis
- Depends on level and severity of defect
- 35% live born die within first 5 yrs
- 50% with IQ > 80
- In utero findings do not predict outcome
- Obstructive hydrocephalus
- From posterior fossa compression
- Musculoskeletal dysfunction
  - 25% complete (lower) limb dysfunction
- Gastrointestinal/ genitourinary dysfunction
  - 17% with normal continence

Treatment
- Cesarean section delivery at term
  - I Infection rate
  - Meningomyelocele sac rupture rate
- Immediate postnatal surgery
  - Cover exposed spinal cord
  - Treat hydrocephalus
  - 80% need ventriculoperitoneal shunt
- In utero surgery in clinical trials
  - Shunt dependence
  - 54% vs. 80%
  - Paralysis and incontinence rates unchanged
- Premature delivery risk
- Preventive treatment with folate acid
  - Preconception therapy best
  - 4 mg/day reduces risk of recurrent neural tube defect by 70%
  - 0.4 mg/day for all women

DIAGNOSTIC CHECKLIST

Consider
- Genetic amniocentesis

Image Interpretation Pearls
- Presence of normal criteria magna nearly eliminates diagnosis
- Cranial markers easier to see than spine defect
- Attempt to identify level of defect

SELECTED REFERENCES

SPINA BIFIDA

IMAGE GALLERY

Typical

(Left) Axial ultrasound of myeloschisis. The vertebra is "V" shaped as posterior elements (arrows) are divergent. There is no overlying skin (open arrows point to intact skin) and no overlying sac. (Right) Sagittal T2W MR in another myeloschisis case shows a large spinal defect without a sac (curved arrows). Also, there is vermianurial tornal herniation (open arrows) indicating Chiari II malformation.

Typical

(Left) Sagittal ultrasound shows a cervical spine myelomeningocele. The sac (arrows) contains neural elements (curved arrows). Communication with the spinal canal through the skin and brain defect are well seen (open arrows). The head is to the left and the chest is to the right. (Right) Clinical photograph in the same case shows the large cervical myelomeningocele. The sac is covered by muscle.

Typical

(Left) Axial ultrasound of the cranium shows Chiari II malformation. The cerebellum is banana-shaped (arrows) as it wraps around the medulla. The cisterna magna is obliterated. The cerebrum is lemon-shaped (open arrows) and the ventricles are dilated. (Right) Coronal ultrasound in another fetus shows occipital club feet (arrows). These secondary anomalies are commonly seen with spina bifida.
INIENCEPHALY

Graph shows features of encephalophy including a well defined (arrow), encephalophy and spinal dysraphin spina bifida leading to an exaggerated cervical lordosis.

Ultrasonogram of a 12 week gestation shows marked hypoplasin of the head (arrow). The body appears small secondary to the shortened neck. These are last trimester features of encephalophy.

TERMINOLOGY

Abbreviations and Synonyms
- "Stargazer" malformation

Definitions
- Extensive open neural tube defect (ONTD) characterized by
  - Defect in occipital bone andinion
  - Occipital encephalophy
  - Spinal dysraphin
  - Fixed hypoplasin of head

IMAGING FINDINGS

General Features
- Best diagnostic clue
  - Combination of findings is diagnostic
  - Cephalophy
  - Spina bifida
  - Location
    - Metopic and cervical spine always involved
    - Dysraphin often extends into thoracic and even lumbar area

Ultrasonographic Findings
- First trimester
  - Hyperextension of head
  - Crown-rump length (CRL) less than expected
  - Head appears large in relation to body
    - Body shortened from absent vertebral bodies
  - Cervical spine
    - Fixed exaggerated lordosis
    - Spina bifida
  - Face turned upward creating "stargazer" appearance
  - Lower neural tube defect which may extend to involve thoracic and lumbar spine (rachischisis)
  - Short neck
  - Vertebral missing or fused
  - Causes angulation
  - Face
    - Orbits directed upward ("stargazer")
    - "Fatted appearance"
      - Mandibular skin contiguous with chest
      - Cleft lip/palate in some cases
  - Other brain anomalies frequently present
    - Anencephaly
    - Microcephaly
    - Hydrocephaly
    - Dandy-Walker continuum
    - Isolated encephaphy

DX: Encephalophy

Cervical MMC
Encephaphy
Cervical Tetraomy
Hydrocephaly
INIENCEPHALY

Imaging Findings
- Crown-rump length (CRL) less than expected
- Head appears large in relation to body
- Body shortened from absent vertebral bodies
- Fixed exaggerated lordosis
- Face turned upward creating 'stargazer' appearance
- Large neural tube defect which may extend to involve thoracic and lumbar spine (sacrococcyx)
- Short neck
- Vertebral are missing or fused
- Mandibular skin contiguous with chest
- Polydactylymosis common
- Routine views in midtrimester should detect all cases

Top Differential Diagnoses
- Cervical hyperextension
- Klippel-Feil syndrome

Key Facts
- Cervical myelomeningocele (MMC)
- Encephaloid

Pathology
- M.F = 1:9
- Microcephaly and encephaloid most common associations

Clinical Issues
- Lethal malformation
- Hypereextension may cause dystocia
- Consider early induction

Diagnostic Checklist
- CRL < expected is not always incorrect dates
- May be diagnosed in late first trimester
- Hypereextension may be transient finding

MR Findings
- Not necessary for diagnosis
- Consider if ultrasound evaluation is limited
- Sagittal view can give complete picture
- Skull base defect
- Encephalocele
- Spinal defect
- Vertebral anomalies better seen

Imaging Recommendations
- Best imaging tool.
- Endovaginal ultrasound in first trimester
- Routine views in midtrimester should detect all cases
- First trimester
- Look at proportion of head to body
- Persistent hyperextension of head throughout exam
- Midline sagittal plane best
- Head position
- Relative size of head to body
- Thorough evaluation of spine
- Scan in multiple planes
- Attempt to count cervical vertebrae
- Follow-up examination
- Isolated hyperextension without ONTD may resolve

DIFFERENTIAL DIAGNOSIS

Cervical hyperextension.
- Head held in extension throughout exam
- No structural abnormalities detected
- Resolves on follow-up exam = normal outcome
- Persistent finding
- 73% normal
- 27% unsuspected anomalies at delivery

Klippel-Feil syndrome
- Cervical vertebral fusion
- Short, webbed neck
- Neck hyperextended
- No ONTD
- Some consider mildest form of encephaloid

Cervical myelomeningocele (MMC)
- Defect involves cervical spine only
- Cranium intact

Encephalocele
- Defect involves cranium only
- Cervical spine intact

Jarcho-Levin syndrome
- Vertebral anomalies
- Rib anomalies
- Small thorax

Masses causing hyperextension of head
- Cervical teratoma
- Quincke
- Lipomyelomeningocele
- Nuchal cord
- Uterine leiomyomas
- Uterine malformations
- Multiple gestations
- Cranium and cervical spine intact in all of above
INIENCEPHALY

PATHOLOGY

General Features
- Genetics
  - Sporadic inheritance pattern
  - Not associated with syndromes
  - Has been reported with trisomy 13
- Etiology
  - Unknown
  - Shares common risk factors with other ONTD
- Epidemiology
  - 0.6-10,000 births
  - Higher incidence in United Kingdom
  - M:F = 1:9
- Associated abnormalities
  - In up to 86%
- Marked disorganization of central nervous system
  - Microcephaly and anencephaly most common associations
  - Migrational abnormalities
  - Polymicrogyria
  - Virtually every organ system may be involved
- Embryology
  - Two proposed mechanisms
  - Primary failure of anterior neuropore to close
  - Occurs slightly later than in anencephaly
  - Persistent embryonic cortical lysis
  - Developmental arrest in 3rd week
- Cerebral spine is normally retroflexed at this time
  - Persistent retroflexion results in failure of neural tube closure

Gross Pathologic & Surgical Features
- Defect always involves forebrain magnus
- Cervical dysraphism
  - May extend to thoracic and lumbosacral spine
- Two types described
  - Intencephaly clausus
  - No associated encephalocele
  - May rarely be skin covered
  - Intencephaly quintus
  - Encephalocele present
  - Most common type

Microscopic Features
- Significant disorganization of many neural tissues

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - First trimester
    - CRL expected
  - Second trimester
    - Obvious neural tube defect
  - Other signs/symptoms
    - Elevated maternal serum alpha-fetoprotein (MSAFP)
    - Polyhydramnios

Natural History & Prognosis
- Lethal malformation
  - Case reports of long-term survivors with mild clausus form
  - Most stillborn
  - Recurrence risk 1-4%

Treatment
- No treatment
- Termination offered
- Supportive care for family
- Hypoextension may cause dystocia
- Consider early induction
  - Cesarian section to be avoided
- Preconceptional follicle acid should be given for future pregnancies
  - 4 mg/day beginning at least 1 month prior and continuing through first trimester
  - Decreases risk of all ONTD by approximately 70%
  - 0.4 mg/day recommended for all women attempting pregnancy

DIAGNOSTIC CHECKLIST

Consider
- CRL expected is not always incorrect dates
  - May be early indicator of neural tube malformation
  - Transvaginal ultrasound must be performed to evaluate embryo
  - May be diagnosed in late first trimester

Image Interpretation Pearls
- Hypoextension may be transient finding
  - Should alert for careful evaluation for structural abnormalities
  - Follow-up to document resolution

SELECTED REFERENCES
INENCEPHALY

IMAGE GALLERY

Typical

[Left] Sagittal ultrasound shows hypoechonemia at the fetal head with discontinuity of the occipital bone (arrow) and an interhemispheric cyst (curved arrow). There was associated spinal dysraphism. [Right] Gross pathology in the same case shows the typical head positioning, with the eyes directed upward (“staghead”). Note the shortened neck with the clavicles contiguous with the chest. A portion of the large open neural tube defect is seen (arrow).

Typical

[Left] Axial ultrasound of the lumbar spine in the same case shows splaying of the posterior elements (arrow). There is no ossification with exposed neural tissue (curved arrow). [Right] Axial ultrasound shows inferior continuation of the spinal defect (curved arrow) to the level of the sacrum (arrow).

Typical

[Left] Gross pathology from the case above confirms the large Chiari II malformation from the skull base to the sacrum. [Right] Sagittal postcontrast T2WI MR in a different case showing typical features of iiencephaly. The spine is markedly abnormal with missing and fused vertebral arches and a large craniocaudal and gaspsive defect (open arrow). There is marked remodeling of the occiput and the eyes are held in the “staghead” position (curved arrow).
CAUDAL REGRESSION SEQUENCE

Graphic illustrates several features of caudal regression sequence including abnormal lower extremity position with muscle wasting, shortened spine (arrows), and medial positioning of the iliac wings (arrow).

Ultrasound shows characteristic appearance of the lower extremities in the "crossed-legged turtle" position. There was no lower extremity movement during prolonged scanning.

TERMINOLOGY

Abbreviations and Synonyms
- Caudal regression sequence (CRS)
- Caudal dysplasia
- Caudal aplasia
- Sacral agenesis
- Axial mesodermal dysplasia spectrum
  - Additional midface craniofacial anomalies

Definitions
- Varying degrees of distal neural tube disruption
  - Spectrum includes agenesis of distal neural tube
  - Severe cases may involve thoracic spine
  - May have lumbar agenesis with preserved sacral and coccygeal vertebrae

IMAGING FINDINGS

General Features
- Best diagnostic clue: Absent sacrum with hypoplastic lower extremities is diagnostic

Ultrasonographic Findings
- First trimester findings
  - Short crown-rump length
  - "Protuberance" of lower spine
  - Increased nuchal translucency
  - Abnormal nuchal translucency
  - Second and third trimester findings
  - Abrupt termination of spine
  - Seen best on sagittal section
  - Looks as if spine has been "shaved out"
  - No spine visible on axial views of abdomen
  - Iliac wings approximated or fused
  - "Shield" appearance
  - Decreased interspace between femoral heads
  - Short trunk
  - Clubfoot
  - Lower extremity contractures: "Crossed-legged gait" or "buddha" pose
  - Normal to increased amniotic fluid
  - Associated gastrointestinal (GI) anomalies
    - Anorectal atresia
    - Duodenal atresia
  - Associated central nervous system (CNS) anomalies
    - Chiari II malformation
    - Associated genitourinary (GU) anomalies
    - Cystic renal dysplasia
    - Dilated bladder, hydrourephrosis
    - Penoscrotal inversion
    - Penis agenesis
    - Cryptorchidism
    - Congenital heart disease (CHD)

UED: Spine + Limb Anomaly

Spina Bifida
Spina Bifida
VACTERL
Arthrogryposis
CAUDAL REGRESSION SEQUENCE

Key Facts
- Sirenomelia
- Arthrogryposis-akinesia sequence

Pathology
- 1% of infants born to diabetic mothers have caudal regression sequence (CRS)
- 12-16% infants with CRS have diabetic mothers
- Poor glycemic control thought to be etiologic factor

Clinical Issues
- Described as early as 11 weeks gestation
- High mortality due to associated anomalies

Diagnostic Checklist
- Fetal MRI may be helpful, especially in the obese patient
- Always check for spine ossification centers in an axial scan plane at level of iliac wings

MR Findings
- Potential benefit for associated anomalies especially with maternal obesity
  - Confirms absent or disorganized distal ossification centers
  - Shows cord termination
  - Wedge-shaped or tapered termination of cord is classic feature
  - Dorsal edge of taper longer than ventral
  - Anterior and posterior roots separated at level of cauda equina
  - May demonstrate additional defects
  - Myelocystocele
  - Syringomyelia
  - Intraspinal arachnoid cyst
  - Tethered cord

Imaging Recommendations
- Protocol advice
  - First trimester endovaginal scan in diabetes
  - Particularly important if poor perigestational glycemic control
  - Verify dates
  - Look for abnormal contour of lower spine area
  - Beware "tapering" distal spine in fetus at risk for CRS
  - May taper where it terminates even if not at sacrum
  - Normal sagittal spine tapers to a point at level of fetal buttock
  - Coronal section shows ribs, count down lumbar segments to show five present
  - Axial view at level iliac crests best to show sacrum
  - Sacrum not well ossified until mid second trimester
  - Cannot confidently rule out < 18 weeks
  - Mild cases easily missed
  - Fetal echocardiography
  - Should be routine with maternal insulin-dependent diabetes
  - Strong association with cardiovascular anomalies

Differential Diagnosis

Myelomeningocele
- Ostialization centers present
- Posterior elements splayed
- Look for meningocele sac
- Associated with Chiari II malformation
  - Obliteration of cisterna magna
  - "Banana" cerebellum
  - "Lemon" sign: bitemporal concavity

VACTERL association
- Combination of abnormalities, including some or all of
  - Vertebral
  - Anal atresia
  - Cardiac
  - Tracheoesophageal fistula
  - Renal
  - Limbs
  - Not associated with maternal diabetes

Sirenomelia
- Renal agenesis
- Single fused lower extremity

Arthrogryposis-akinesia sequence
- Spine normal
- May involve lower extremities only
- Not associated with maternal diabetes

Segmental spinal dysgenesis
- Probably part of same spectrum as CRS
- Thin or indiscernible cord at dysgenetic level
- Bulky cord-segment caudal to abnormality

Pathology
- General Features
  - General path comments
    - Embryology
      - Defective blastogenesis

General Features
- General path comments
  - Embryology
    - Defective blastogenesis
CAUDAL REGRESSION SEQUENCE

- Originates in primary developmental field
- Internal organ derangement
- Distal renal tube fails to form
- Genetics: Occasional familial cases
- Epidemiology
  - M/F = 1:1
  - 1-5/100,000
  - 1% of infants born to diabetic mothers have caudal regression sequence (CRS)
  - 12-16% infants with CRS have diabetic mother
  - Poor glycemic control thought to be etiologic factor
- Dreg use in pregnancy
- Reported cases with minoxidil, trimethoprim-sulfamethoxazole

Gross Pathologic & Surgical Features

- Spectrum
  - Abnormal skull with normal lower extremities
  - Absent sacrum
  - Abnormal, low lumbar spine, occasional thoracic spine involvement
  - Clubfeet
  - Flexion deformities hips/knees
  - "Crossed-legged tailor" or "Buddha" pose
  - Deceased or absent lower extremity movement
  - Splanchnoma no longer considered part of this sequence
  - Fixed lower extremities
  - Renal agenesis
  - Anus at stenosis
  - Vascular defect as cause
  - Lethal

CLINICAL ISSUES

Presentation
- Described as early as 11 weeks gestation
- May affect only one of twin pair

Natural History & Prognosis
- Similar to high/mid lumbar myelomenigocele
- Neurogenic bladder
- Motor deficit > sensory
- High mortality due to associated anomalies
- Survivor, have normal intellectual function

Treatment
- Prenatal
  - Maternal diabetes testing
  - No fetal intervention
- Postnatal
  - Urologic consultation
  - Sacral anomaly determines bladder dysfunction
  - Neurogenic bladder
  - Reflux nephropathy
  - Aim to prevent progressive renal dysplasia
  - Orthopedic surgery
  - Clubfeet
  - Contractures
  - Spine instability
  - Hip dislocation

- Aim for proper sitting and standing without amputation, if possible

DIAGNOSTIC CHECKLIST

Consider
- Fetal MRI may be helpful, especially in the obese patient
- Allows more accurate parental counseling

Image Interpretation Pearls
- Always check for spine ossification centers in an axial scan plane at level of iliac wings
- In diabetics with poor percutaneous glycemic control, perform dopplor ultrasound for accurate dating and atonic assessment
- Skeletogram of fetus suggestive of CRS

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CAUDAL REGRESSION SEQUENCE

IMAGE GALLERY

Typical

[Left] Coronal ultrasound shows apparent normal tapering of the spine (arrow). Material already limited visualization. However, it was clear that the tapering occurred a very short distance from the lowest ribs. [Right] Sagittal ultrasound in the same view (top) shows "rubber band" appearance of the lumbar spine (open arrow) at the level of the sacrococcygeal curve (bottom - curved arrow).

Typical

[Left] Sagittal T2W1 MR shows abrupt termination of the spinal cord with characteristic "wedger" shape (curved arrow). Dilated spinal canal (arrow) thought to represent an associated terminal myelocystocele. Instilled within hours of birth. [Right] Axial endoanal ultrasound (EUS) shows the "shelled" appearance caused by fusion of the sacrococcygeal (arrows). EUS is particularly useful in obese patients if the fetus is in breech position.

Typical

[Left] Clinical photograph of newborn infant with caudal regression sequence. Note the small pelvis with the typical "Buddha" or "cross-legged toddler" position of the lower extremities. There is muscle atrophy (arrows) from abnormal innervation. [Right] Frontal radiograph of a severe caudal regression case with no spine formed distal to T7. Note fusion of the sacrococcygeal (arrows). This gives rise to the "shelled" sign on ultrasound.
**TERMINOLOGY**

**Abbreviations and Synonyms**
- Congenital scoliosis (C3)
- Hemivertebra

**Definitions**
- Scoliosis
  - Abnormal lateral spine angulation
  - Kyphosis
  - Abnormal anterior spine angulation
- Kyphoscoliosis
  - Kyphosis + scoliosis

**IMAGING FINDINGS**

**General Features**
- Location: Anywhere in spine
- Sae: Single or multiple levels
- Morphology
  - Acute angle
  - Long, abnormal curve
- May be more difficult to detect

**Ultrasoundographic Findings**
- Abnormal spine angulation
  - Longitudinal views b/c

**DDx: Dysmorphic Spine**

- Caudal Regression
- Microdeletion
- Isomerophalus
- SC syndrome

- C6omral for scoliosis
- Sagittal for kyphosis
- Identify level of defect
- Use ribs to identify 12th thoracic level
- Isolated vertebral body anomaly (5%)
  - Hemivertebra
  - Only half of vertebral body develops
  - Triangular bone acts as wedge
  - Butterfly vertebrae
  - Two hemivertebra side by side
  - Central resorption
- Block vertebra
- Vertebral fusion
- Body or dorsal elements or both
- Hemivertebra may fuse
- Rectangular large vertebra
- Symmetric or asymmetric appearance
- CS more often with asymmetric fusion
- Diastematomyelia
  - Posteriorly directed spur from vertebral body
  - 3 dorsal bones on transverse view (2 is normal)
  - Spinal cord splits around spur
  - Difficult diagnosis in utero
- Vertebral anomaly without CS
- Scoliosis may develop with time
- Multiple levels
- Multiple dysmorphic vertebrae
- "Jumbled spine"
KYPHOSIS, SCOLIOSIS

Terminology
- Congenital scoliosis (CS)

Imaging Findings
- Longitudinal views best
- Hemivertebrae
- Butterfly vertebrae
- Block vertebra
- "Jumbled spine"
- Associated anomalies (95%)
- Sxima bifida
- VACTERL association
- Agenesis bone syndrome
- Beware of positional curvature
- Consider MR in difficult cases

Key Facts

Top Differential Diagnoses
- Caudal regression sequence
- Iniencephaly
- Sacrococcygeal teratoma (SC teratoma)
- Arthrogryposis

Clinical Issues
- M.F = 1:3
- Thoracic insufficiency syndrome
- Prophylactic surgery
- Corrective surgery
- Expansion thoracoplasty

Diagnostic Checklist
- Anomalous fluid M.F in spina bifida suspected but not seen
- Look at limbs

Imaging Recommendations
- Best imaging tool: Detailed orthogonal views of spine
- Protocol advice
  - Consider 3D ultrasound
  - Multiplanar capacity may help identify levels
  - May better show vertebral dysmorphology
  - Consider MR in difficult cases

DIFFERENTIAL DIAGNOSIS

Caudal regression sequence
- Absent sacrum
- Variable absence of lumbar spine
- Lower vertebral bodies may be dysmorphic
- Associated anomalies
  - Lower limb contractures
  - "Buddha" pose
  - Gastrointestinal
  - Genitourinary

Iniencephaly
- Extensive open neural tube defect
- From skull base to tip of sacrum
- Shortened spine
- Exaggerated lordosis
- Extended head
- "Stargazer"

Sacrococcygeal teratoma (SC teratoma)
- Germ cell tumor
  - Most often solid + cystic
  - Variable size
- Internal + external components
- Associated hydronephrosis
  - High output cardiac failure

Arthrogryposis
- Multiple congenital joint contractures
- Extremities more involved than spine
- Usually without lower limb abnormality
- Polyhydramnios common
  - Abnormal swallowing
KYPHOSIS, SCOLIOSIS

PATHOLOGY

General Features
- Genetics
  - Isolated
    - No increased risk for aneuploidy
    - Associated spina bifida
  - 4% with aneuploidy
  - VACTERL association
  - No increased risk for aneuploidy
- Etiology
  - Anomalous development of vertebrae
  - Failure of formation
  - Failure of segmentation
  - Abnormal fusion
- Epidemiology
  - Hemivertebra
    - 5-10
    - Spina bifida
    - 0.4
    - VACTERL
    - 1
  - Associated abnormalities
    - Spinal cord
    - Heart
    - Renal

CLINICAL ISSUES

Presentation
- Most common symptoms
  - Isolated CS seen during routine exam
  - Isolated vertebral anomaly
  - CS + multiple other anomalies
  - VACTERL
  - Syndromic features
  - Chromosome abnormality
  - M+1 maternal serum alpha-fetoprotein (AFP) results
    - > 2.5 multiples of median (MOM)
  - Spina bifida
  - Amniotic band syndrome

Demographics
- Gender
  - Isolated, hemivertebra
  - M:F = 1:3.
- Multiple vertebral defects
  - M:F = 2:3

Natural History & Prognosis
- Isolated CS
  - Curve progression (> 10 degrees)
    - 25% no further curve progression
    - 50% slow curve progression
    - 25% rapid curve progression
  - 20-30% with additional intraspinal anomaly
  - Often diagnosed early on posterior MR
  - Thoracic insufficiency syndrome
  - Rib anomalies + concave hemivertex
  - Prognosis depends on presence of other anomalies

Treatment
- Prophylactic surgery
  - Avoid further curve progression
  - Bone grafting
  - In situ fusion
- Corrective surgery
  - Spinal fusion
  - +/- vertebral body resection
- Expansion thoracoplasty
  - For thoracic insufficiency
  - Wedge thoracotomy
  - Chest wall distraction

DIAGNOSTIC CHECKLIST

Consider
- Anomalies
  - Amniotic fluid AFP if spina bifida suspected but not seen

Image Interpretation Pearls
- CS = no Chiari II
  - Probable isolated vertebral anomaly
  - CS + Chiari II
  - Look for spina bifida
  - Defect at apex of curve
  - Longitudinal views best for visualization of bony deformity
  - Look at limbs
  - VACTERL
  - Radial ray anomalies
  - Amniotic band syndrome
  - Ampullations
  - Spina bifida
  - Club feet

SELECTED REFERENCES
(Left) Sagittal ultrasound shows acute kyphosis involving the upper lumbar spine (arrows). Careful interrogation of this area revealed spina bifida at the same level as the abnormal angulation. (Right) Axial ultrasound in the same fetus shows divergent posterior elements (arrows) and a meningo(myel)ocoele sac (open arrow). Most abnormal spine curves are associated with open neural tube defects.

(Left) 3D ultrasound shows black vertebrae of the upper lumbar spine (arrows). Fusion vertebrae are large and rectangular. M-mode ultrasonography drew the sonographer’s attention to this area. (Right) Coronal postmortem MRI and photograph of a fetus with VACTERL association show a butterfly vertebra (curved arrows). The open arrows point to the empty renal fossae with renal agenesis. Steel rod follows scoliosis.

(Left) Coronal ultrasound shows a normal fetus with typical positioning. No bony defects were seen. Fissures are quite flexible and abdominal spine curvature congenital scoliosis. (Right) Coronal ultrasound in the same fetus at the end of the examination shows normal cervical spine positioning.
**SACROCOCGYGEAL TERATOMA**

**TERMINOLOGY**

**Abbreviations and Synonyms**
- Sacrococcygeal Teratoma (SCT)

**Definitions**
- Neoplasms derived from all three germ cell layers
- Endoderm, mesoderm, ectoderm
- 70-80% of all teratomas located in sacrococcygeal area

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue: Exophytic mixed cystic/solid mass extending from sacrum
- Size
  - Variable but often large
  - Size alone is not an independent factor for prognosis
  - Amount of solid component far more important
  - Large purely cystic mass has better prognosis than smaller solid one
  - Has potential for extremely rapid growth

**Ultrasoundographic Findings**
- Greyscale Ultrasound
  - Heterogeneous, mixed solid/cystic mass
  - Purely cystic in 15%

- May contain calcifications
- May extend into pelvis or abdomen
- Important in staging and surgical planning
- Hydrops
- Grave finding
- Placentomegaly
- Associated with hydrops
- Polyhydramnios
  - Commonly present
- Oldehydranmios
  - Secondary to intrapelvic portion of mass
  - Obstructing urinary tract
  - Infrequent association
  - May exhibit rapid growth in short period of time
  - Intratrumcal hemorrhage
  - Common in large solid tumors
  - Very poor prognostic sign
  - Associated malformations in 11-38%
  - Mostly local effects secondary to tumor growth
  - Hydronephrosis
  - Renal dysplasia
  - Urethral atresia
  - Urinary ascites
  - Hydrocolpos
  - Undescended testes
  - Imperforate anus
  - Hip dislocation
  - Clubbed feet

**DDx: Cystic Spinal Masses**

- Myelomeningocoele
- Myelomeningocoele
- Menigocele
- Meningocele
**Terminology**
- 70-80% of all teratomas located in sacrococcygeal area

**Imaging Findings**
- Best diagnostic clue: Exophytic mixed cystic/solid mass extending from sacrum
- Has potential for extremely rapid growth
- May extend into pelvis or abdomen
- Hydrops
- Placentomegaly
- Polyhydramnios
- Intratumoral hemorrhage
- Associated malformations in 11-38%
- Color Doppler essential to evaluate vascularity
- Solid tumors may have significant arteriovenous shunting

**MR Findings**
- Better delineation of anatomy
- Presence and extent of internal component
- Possible involvement of spinal canal
- More accurate classification and postnatal planning
- More accurate diagnosis of intratutumal hemorrage
- Differential diagnosis solid tumor from microcystic one
- Both appear echogenic on ultrasound
- Solid tumors worse prognosis

**Imaging Recommendations**
- Protocol advice
  - MRI extremely useful for evaluating intrapelvic extent and evaluating spine
  - Shadowing from iliac wings and sacrum decreases sensitivity of ultrasound
  - Large solid tumors at risk for developing hydrops
  - Scan every 1-3 weeks depending on size, vascularity, etc.
  - Evaluate for sign of impending cardiovascular compromise
  - Tamor volume
  - Intraventricular fluid index
  - Placental thickness
  - Inferior vena cava diameeer
  - Caudal thoracic artery
  - Doppler evaluation of umbilical cord and ductus venous

**SACROCOCCYGEAL TERATOMA**

**Key Facts**
- MRI extremely useful for evaluating intrapelvic extent and evaluating spine

**Top Differential Diagnoses**
- Myelomenigocele
- Meningocele

**Clinical Issues**
- Described as early as 13.5 weeks
- Significant obstetric complications in 81%
- Prognosis significantly worse for fetus than neonate
- Fetal diagnosis: 50% mortality
- Hydrops almost universally fatal

**Diagnostic Checklist**
- In utero aeration for impending high-output failure potential option

- Sac extends posteriorly in most cases
- Anterior myelomenigocele may be more difficult to differentiate from SCGT
- Always look at brain
- 99% of spinal defects have associated brain findings
- Meningocele
  - Anechoic cystic mass
  - Sac contains meninges only
- Brain findings
  - Posterior fossa compression
  - Obilation of cisterna magna
  - Cerebellum wraps around brainstem ("banana" sign)
  - Ventriculomegaly
  - Frontal bone concavity ("lemon" sign)
  - Caution: Myelomenigocele and SCGT may occur together
- Always look at brain

**Other Solid Tumors**
- Malignant isolated case reports
- Generally intrapelvic with no exophytic component
- All extremely rare

**Differential Diagnosis**
- Myelomenigocele
  - Complex cystic mass
  - Sac contains meninges + neural elements
  - Sylviad auditory ossification centers

**PATHOLOGY**

**General Features**
- Embryology
  - Primitive germ cells migrate from yolk sac to germinat ridge (weeks 4-6)
  - They are then incorporated into primitive sex cords to form gonad
  - Unincorporated cells normally involute
  - Continued division of unincorporated sex cords gives rise to teratoma
- Epidemiology
  - 1:40,000
  - Likely higher given large number of in utero deaths and terminations, which may be underestimated
SACROCCOCCYGEAL TERATOMA

- Commonest neonatal tumor
- MF = 1/5
- Malignant change M > F

Staging, Grading or Classification Criteria
- American academy of pediatrics: surgery section (AAPSS)
  - Type 1
    - Completely external or minimal presacral component
  - Type 2
    - External and internal component extending into presacral space
  - Type 3
    - External and internal component extending into abdomen
  - Type 4
    - Completely internal, no external component
    - Must go to undergo malignant degeneration (postnatal)
    - Malignancy more likely in solid than cystic or mixed tumors
  - Staging system less important prognostically in fetuses
  - Amount of solid component and degree of arteriovenous shunting far more important for survival

CLINICAL ISSUES

Presentation
- Most common sign/symptoms
  - Described as early as 13.5 weeks
  - Most diagnosed in 2nd trimester
  - Often presents as size > dates
  - Secondary to large mass
  - Polyhydramnios
  - Presentation at delivery
  - Dystocia 6-13%
  - Tumor avulsion
  - Fetal exanguination

Natural History & Prognosis
- Failure to diagnose has potentially catastrophic consequences for fetus and mother
- Significant obstetric complications in 81%
- Prolonged gestation
  - Fetal diagnosis: 50% mortality
    - Hydrops from high-output state
    - Intrathoracic hemorrhage
    - Newborn diagnosis: 5% mortality generally related to malignancy
- Poor prognostic factors
  - Hydrops almost universally fatal
  - Material indication for scan (e.g., large for dates)
  - Diagnosis < 30 weeks
  - Large solid component
  - Better outcome if cystic
  - Less vascular = decreased risk hemorrhage, hydrops
  - Maternal complications
    - Hyperemesis
    - Pre-eclampsia
    - "Miles" syndrome
    - Maternal fluid retention and hemodilution
  - Prognostic maternal edema "mirroring" sick fetus
  - Necessitates immediate delivery
  - Preferr labor
  - HELLP (hepato-, elevated liver enzymes, low platelets) syndrome

Treatment
- Therapeutic amnioreduction for symptomatic polyhydramnios
- Deliver in tertiary care center at lung maturity
- Cesarean section preferred if tumor > 5 cm
- Larger masses may require classical incision
- Aspiration of cystic lesions may allow vaginal delivery
- Fetal surgery
  - Consider when fetus has signs of impending hydrops
  - Must have normal tarsotype

DIAGNOSTIC CHECKLIST

Consider
- Fetal MRI for intrauterine extension
- In utero sacrectomy for impending high-output failure potential option

Image Interpretation Pearls
- Most compelling issues for fetal/neonatal survival
  - Composition
  - Solids much worse prognosis than cystic
  - Diagnosis < 30 weeks
  - Vascularity
    - Vascular masses have significant arteriovenous shunting = high-output failure = hydrops
  - Associated chromosomal anomalies
  - Complicating factors
    - Hydrops
    - Polyhydramnios
    - Intrathoracic hemorrhage

SELECTED REFERENCES
Typical

(left) Coronal ultrasound shows an enigmatic cystic mass (arrows). This appeared to be a teratoma with an anechoic cystic area (arrow). The mass was incompletely evaluated.

(right) Sagittal ultrasound shows the extension of the solid component (curved arrow) to the level of the fetal insertion (arrow). This is extremely valuable in evaluating the area adjacent to the fetal insertion of the mass.

Typical

(left) Sagittal ultrasound in the third trimester shows a large, predominantly solid enigmatic mass (arrows). This mass may have rapid growth and is at risk for developing LVH and pregnancy-induced hypertension with possible referral for intervention is warranted.

(right) Sagittal ultrasound in the same fetus as above shows extension of the mass (cortical). Compare with the aorta (curved arrow). This is one sign of impending cardiovascular compromise.

(right) Cerebralopathology in the fetus shows obvious intracranial hemorrhage. This may have significant morbidity and mortality, putting these at risk for hemorrhage and hypoxia. (also shown in sagittal section of the fetal head.)
### SECTION 4: Face and Neck

**Introduction and Overview**

Facial Development & Imaging  

Face & Neck

- Cleft Lip, Palate  
- Absent Nasal Bone  
- Micrognathia  
- Macroglossia  
- Epignathus  
- Ear Anomalies  
- Midface Anomalies  
- Hypotelorism  
- Hypertelorism  
- Orbital Tumors  
- Scalp Masses  
- Cystic Hygroma  
- Cyst  
- Cervical Teratoma

Page numbers:
- Cleft Lip, Palate: 4-6
- Absent Nasal Bone: 4-10
- Micrognathia: 4-14
- Macroglossia: 4-18
- Epignathus: 4-22
- Ear Anomalies: 4-26
- Midface Anomalies: 4-30
- Hypotelorism: 4-34
- Hypertelorism: 4-38
- Orbital Tumors: 4-42
- Scalp Masses: 4-44
- Cystic Hygroma: 4-48
- Cyst: 4-52
- Cervical Teratoma: 4-56
**Terminology**

**Abbreviations**
- Nasal bones (NB)
- maxillary transillumination (NT)
- Cleft lip (CL)
- Cleft palate (CP)
- Cystic hygroma (CH)
- Nuchal fold (NF)
- Fetal medicine foundation (FMF)

**Imaging Anatomy**

**Critical Anatomic Structures**
- Orbit
- Nasal bones
- Upper lip and palate
- Chin
- Neck
- Calvarial shape

**Anatomy-Based Imaging Issues**

**Key Concepts or Questions**
- Is face surrounded by fluid and seen well?
- Are there any facial clefts?
- Is nasal septum normal?
- Is NB appropriately ossified?
- Are orbit's appropriately spaced?
- Is calvarial shape normal?
- Are tongue, ears and anterior neck normal?

**Imaging Approaches**
- First trimester genetic screening
  - NF, NB
- Second trimester screening
  - Orthogonal views through face
  - Genetic ultrasound
  - NF, NB
  - 3D ultrasound
  - Problem solving tool

- Increasingly used as primary screening tool
- MRI
- Problem solving tool
- Associated brain anomalies
- Posterior soft palate assessment
- Intracranial extension of facial mass
- Helpful when ultrasound is limited
- Maternal body habitus
- Oligohydramnios

**Imaging Protocols**
- 1st trimester 10K and NT assessment
- 11.6-14 wk scan to assess aneuploidy risk
- High detection rates for trisomy
- Trisomy 21 most common
- Fetal medicine certification recommended
- Didactic course
- Hands-on training
- Cases submitted for review
- Continuous audit
- Mid-sagittal view of head and neck
- Must be appropriately magnified
- Amniotic separate from NT
- NB assessment
  - Present or absent NB
- NT measurement
  - Maternal serum testing
  - Compared with NT/NB finding
- 2nd trimester views of facial face
  - Mid-sagittal profile
  - Can measure NB (> 2.5 mm)
  - Assess chin
  - Angled coronal nose-mouth view ("snout" view)
  - Show intact upper lip
  - Normal mandible
  - Posterior axial view
  - Measure NT
  - Rule out CL
  - Axial face views
  - Orbital binometry
  - Maxilla
  - Coronal view
  - Eyes
Obtain Orthogonal Images Of Fetal Face
- Midsagittal profile view
  - Level of nasal bone
  - Rule out micrognathia
- Angled coronal nose-mouth view
  - Normal found rare
  - Intact upper lip
- Axial views as necessary
  - Orbital biometry
  - Intact palate
- 3D ultrasound best tool
  - Orthogonal images with 1 acquisition
  - Surface rendered images
  - Bone rendered images
  - Recognizable features for parents

Assess Nasal Bone Ossification
- Present or absent in 1st trimester
  - Normal or small in 2nd trimester

Evaluate Nuchal Region
- Nuchal translucency in 1st trimester
- Nuchal fold in 2nd trimester

Facial Anomalies
- Cleft lip/palate
- Micrognathia
- Hypotelorism
- Hypertelorism
- Cystic hygroma
- Ear anomalies
- Goltz
- Facial mass

Normal Measurements
- NF in 2nd trimester
  - < 5 mm considered normal
- NB length in 2nd trimester
  - Nomogram in literature
- Orbital biometry
  - Orbital diameter (OD)
  - Interorbital distance (IOD)
  - Bioorbital diameter (BOD)
- Normal IOD = OD
  - Nomogram in literature

Pathology-Based Imaging Issues

Key Facts

- Show 2 nasal bones
- Overall calvarial shape assessment
- Orthogonal "whole head" views
- 3D ultrasound
- Multisplanar advantages
- Orthogonal planes with one acquisition
- Surface rendered images
- Recognizable facial features
- Bone rendered views
- Skeleton-like image
- Better visualization of palate
- Snow 2 NB better than midsagittal views
- Canthal suture assessment
- 4D (color time 3D ultrasound) shows facial expression and movement
- Shows to enhance parent-child bonding
- Additional observations
  - Color Doppler of nasal breathing
  - Help confirm intact palate
  - Tongue size
  - Ear assessment
  - Location and morphology
  - Fetal opens and closes eyes in 3rd trimester
  - Finger/hand fisting

Imaging Pitfalls
- NB
  - Skin can mimic NB in 1st trimester
  - 90º angle of rotation
  - Measure/show both NBs
  - Unilateral hypoplasia possible
- Gap between NBs can mimic absent NB
- Posterior neck (NT, NE, CH)
  - Anion can mimic NT
  - Image both NT and amniotic fluid
  - Overly coronal posterior fossa view
  - Can mimic 1 NF
- Large CH can mimic amniotic fluid
- Nose/mouth assessment
  - Lip folds or full lips can mimic CI
  - Isolated CP often missed
- Soft tissue defect
- Extent of CP difficult to assess

Key Concepts or Questions
- 1 NF, 1 NT and CH strongly associated with aneuploidy
- 1 NF in 1st trimester
  - Trisomy 21 most common
  - Trisomy 18, Trisomy 13
  - Cystic hygroma in 2nd trimester
  - Turner syndrome > trisomies
  - Often with hydroptics
- Type of CL/CP important for prognosis and treatment
  - 80% of CL with CP
  - Extent of CP difficult to assess
  - Unilateral CL + CP most common (type 2)
  - > 20% aneuploidy rate
  - Median CL/CP (types 3 and 4)
  - 50% aneuploidy rate
  - Trisomy 13 and 18 most common
- Delayed NB ossification is marker for aneuploidy
  - Absent NB in 1st trimester
  - Small NB in 2nd trimester
  - Most often trisomy 21
- Hypotelorism associated with holoprosencephaly
  - Other severe facial anomalies common
  - Cyclopia with proboscis
  - Ethmocephaly
  - Cerbrocephaly
  - Median CL/CP
The angled coronal nose/mouth view ("nose" view) is routinely obtained to rule out cleft lip and palate. The normal nose, are rounded (open arrows) and the upper lip (arrow) is intact.

 Sagittal ultrasound shows a normal nasal bone (arrow), intact bony maxilla (curved arrow) and normal chin. The profile face view is desirable for parents and contains diagnostic information.

**Practical Implications**
- CL/CP type 1-3
  - Failure of lip/palate fusion
- CL/CP type 4
  - Median maxillary agenesis
- Facial anomalies in Holoprosencephaly
  - Absence of divergence of frontonasal process
  - Brain + orbit/rhino anomalies
  - "Face panniculus the brain"

**Clinical Implications**

**Clinical Importance**
- Fetal facial anomalies are especially difficult for families to cope with.
- Isolated findings with much better prognosis
- Genetic testing often indicated
- Prenatal visit to plastic surgeon for CL/CP
- Brain anomalies associated with facial anomalies

**Related References**

**Embryology**

**Embryologic Events**
- Facial development
  - Five facial prominences
  - Unpaired frontonasal process
  - Paired maxillary swellings
  - Paired mandible swellings
  - Fusion and chondrification complete by 12 wks
- Normal lip/palate embryology
  - 3 primary segments
  - 2 lateral + 1 medial
  - Complete lip fusion by 8 wks
  - Complete palate fusion by 12 wks

**Ultrasound Classification Of CL/CP**
- Type 1: Unilateral CL only
- Type 2: Unilateral CL + CP (most common)
- Type 3: Bilateral CL/CP
- Type 4: Midline CL/CP
(Left) Axial ultrasound shows orbital hyperechogenicity (arrows). The R1 calipers measure the BOC. The R2 calipers measure the IOD and the IOD lies between the R1 and R2 calipers. The eye lens can also be seen (open arrows).

(Right) 3D US (upper) and 3D US (lower) show the fetal eye open (open arrow) and close (arrow) during the 3rd trimester as blinking is a normal fetal activity. The lens can be seen on the open eye views.

(Left) Sagittal ultrasound shows a normal first trimester nasal bone (arrows). The OB is the echogenic line separate from the skin (curved arrow) and the tip of the nose (open arrow).

(Right) Coronal 3D ultrasound of an 18 wk fetus shows bilateral nasal bone ossification (arrows) as well as normal sutures. Unilateral nasal bone hypoplasia may be easily missed with 2D ultrasound.

(Left) Sagittal power Doppler ultrasound shows nasal breathing. The inner margin of the floor (arrow) outlines the palate. Absence of flow into the oral cavity suggests an intact palate.

(Right) 3D ultrasound shows normal nasal cav as well as left line (arrow) in a third trimester fetus. Ear anomalies are not often associated with nasal bone anomalies and are seen best with 3D.
CLEFT LIP, PALATE

TERMINOLOGY

Abbreviations and Synonyms
- Cleft lip (CL)
- Cleft palate (CP)
- Facial cleft

Definitions
- Failure of lip and/or palate closure

IMAGING FINDINGS

General Features
- Best diagnostic clue:
  - Upper lip linear defect on nose-mouth view
  - Parsmaxillary protuberance with bilateral CL/CP
  - Profile view
  - Location: L > R when unilateral
  - Size: Highly variable, from thin line to large gap
  - Morphology
  - CL +/- CP
  - 80% with cleft lip also have cleft palate
  - Isolated CP rare

Ultrasoundographic Findings
- Imaging of fetal nose and lip

DDx: Cleft Lip/Cleft Palate

Normal Photograph Normal Photograph Unicleft Palate Unilateral Cleft
Terminology
• Failure of lip and/or palate closure

Imaging Findings
• Upper lip linear defect on nose-mouth view
• Premaxillary protuberance with bilateral CL/CP
• 90% with cleft lip also have cleft palate
• Unilateral CL without CP (type 1)
• Unilateral CL with CP (type 2)
• Bilateral CL/CP (type 3)
• Median CL/CP (type 4)
• CP without CL (rare)
• Type 3-4 CL/CP often associated with aneuropolydactyly
• 3D ultrasound for more precise diagnosis of CL/CP

Key Facts

Top Differential Diagnoses
• Normal philtrum
• Amniotic bands
• Facial mass

Pathology
• Aneuploidy rate related to type of CL/CP
• Most often trisomy 13 and trisomy 18

Clinical Issues
• CL often repaired at 2-3 months
• CP often repaired at 9-18 months

Diagnostic Checklist
• Referral to CL/CP clinic during pregnancy
• CL/CP difficult to diagnose before 20 wks

o Premaxillary protuberance on profile view
  • Mass-like area just below nose
  • "Island" of bone separate from rest of palate
  • Dysplastic medial anterior palate
  • Bilateral lip/palate defects on axial view
  • Finding not subtle, but may be confusing
  • Severe nose deformity
  • Median CL/CP (type 4)
  • Anterior mid palate defect
  • Large gap often seen
  • Medial maxillary agenesis
  • Associated with midface hypoplasia
  • Flat midface on profile view
  • Flattened dysplastic nose
  • Small, posteriorly displaced maxilla
  • CP without CL (rare)
  • Isolated cleft palate
  • Often involves posterior soft palate only
  • Rarely diagnosed in utero
  • Color Doppler of nasal breathing
  • Flow from nasal fossae = mouth
  • Fetal MR may show soft palate
  • Associated
  • Type 3-4 CL/CP often associated with aneuropolydactyly/syndromes
  • Holoprosencephaly
  • Trisomy 13
  • Trisomy 18
  • Many syndromes
  • Other structural anomalies
  • All organ system anomalies described

Imaging Recommendations
• Best imaging tool
  • 3D ultrasound for more precise diagnosis of CL/CP
  • Orthogonal views with one acquisition
  • Recognizable face with surface rendered images
  • Bone rendered views shows palate best
  • Psychologically prepares parents
  • Best images at 26-12 wks
• Protocol advice
  • Obtain orthogonal plates of fetal face
  • Coronal anf lateral nose-mouth view

DIFFERENTIAL DIAGNOSIS

Normal philtrum
• Normal folds may mimic cleft
  • Folds more exophytic than clefts
  • Most often in late gestation
  • Big baby or full lips
  • Additional views helpful
  • Show intact skin/palate

Amniotic bands
• Disruption of amnion with fetal entrapment
  • Slit-like facial defects
  • Asymmetric, random clefts
  • No embryologic pattern
  • Fetus may swallow disrupted bands
• Other body wall/extremity defects
  • Bizarre abdominal wall defects
  • Amputations

Facial mass
• Tumors tend to be large and aggressive
  • Teratoma (epignathus)
  • Nasal/oral origin
  • Can mimic premaxillary protuberance
  • Frontal encephalocele
  • Bone defect + herniated brain/meninges
  • Hemangioma
  • Superficial and asymmetric
  • Intact palates
  • Thyroid Nevus/sarcoma
CLEFT LIP, PALATE

PATHOLOGY

General Features
- Genetics
  - Aneuploidy rate related to type of CL/CP
  - Rare for type 1
  - Type 2: 20%
  - Type 3: 30%
  - Type 4: 50%
  - Most often trisomy 13 and trisomy 18
  - CL/CP rarely isolated finding in these conditions
- Etiology
  - Normal lip/palate embryology
  - 1st primary lip/palate segments
  - 2 lateral and 1 medial
  - Complete lip fusion by 8 wks
  - Complete palate fusion by 12 wks
- CL/CP embryology
  - Type 1-3: Failure of fusion
  - Type 4: Medial segment fails to form
- Infectious-etiologic
  - Rubella
  - Teratogen associations
  - Retinoic acid
  - Valproic acid
  - Hyaluronan
  - Alcohol
  - Cigarette smoking
- Epidemiology
  - 80% with CL have CP
  - 0.15% of liveborn
  - 12% of first trimester loss

Staging, Grading or Classification Criteria
- Ultrasound classification system
  - Type 1: CL
  - Type 2: Unilateral CL/CP (most common)
  - Type 3: Bilateral CL/CP
  - Type 4: Multiple CL/CP
  - Type 5: Slant-type defect

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - Incidentally noted at routine scan
  - CL/CP + associated anomalies
- Other signs/symptoms
  - Polyhydramnios from swallowing difficulties

Demographics
- Age
  - Trimesters associated with advanced maternal age
  - ≥ 35 yr at time of delivery
- Gender
  - M > F for CL/CP
  - M < F for cleft palate
- Ethnicity
  - 1,000 Asian
  - 1,100 Caucasian
  - 1,200 African-American

Natural History & Prognosis
- Excellent prognosis with surgical repair
- Associated craniofacial problems
  - Feeding difficulties
  - Hearing impairment
  - Speech impairment
- CL/CP + other anomalies with poor prognosis

Treatment
- Treatment by CL/CP team
  - Plastic surgeon
  - Ear/nose/throat surgeon
  - Dentist
  - Speech and language specialist
  - Social worker/psychiatrist
  - Genetic counselor
- Surgical treatment
  - CL often repaired at 2-3 months
  - CP often repaired at 9-18 months
  - Severe clefts may need immediate repair
  - Second procedures often necessary
- Possible fetal surgery in future
  - Experimental fetoscopic surgery with good results
  - Fetal skin heals without scar
  - Fetal bone heals without callus

DIAGNOSTIC CHECKLIST

Consider
- Referral to CL/CP clinic during pregnancy

Image interpretation Pearls
- CL/CP difficult to diagnose before 20 wks
- Most CL have associated CP
- Repeat scan if CP not initially seen
- Variable accuracy for predicting CP extension
- 3D ultrasound and MRI often helpful

SELECTED REFERENCES
Typical

(left) 3D ultrasound with soft tissue (left) and bone (right) rendered views shows cleft lip and palate. The CL (arrows; flat plane (curved arrows) and palate defect (open arrow) are easily recognized. These images were obtained from a single volume acquisition. (right) Clinical photograph of the same baby shows the right-sided CUP before and after repair.

Typical

(left) Coronal angled (top) and axial (bottom) views through the nose and maxilla show a large cleft lip (arrows) and cleft palate (open arrows). The palate defect is seen better on axial views through the sphenoid ridge. (right) Clinical photograph of the same baby after birth shows the palate defect and repaired nose. Post-op repair results are excellent.

Typical

(left) Sagittal oblique shows premaxillary process (open arrow) from bilateral CUP. Anterior nasal spur is seen extending from the oral cavity into the nasal cavity (open arrow) via the palate defect. (right) Coronal 3D ultrasound shows the premaxillary max. (arrow) and the bilateral cleft palate defect (open arrows). The island of mid mandibular tissue is hypertrophic and more than when CUP is bilateral.
**ABSENT NASAL BONE**

**TERMINOLOGY**

**Abbreviations and Synonyms**
- Hypoplastic or absent nasal bone (ANB)

**Definitions**
- **Absent nasal bone**
  - No NB ossification at 11-14 wks
  - New criteria recently established
  - Part of normal transverse (NT) screen
  - Absent NB also may be noted in 2nd trimester
- **Hypoplastic nasal bone**
  - Small NB at 2nd trimester screen
  - NB length is measured
- **1 NB is important marker for aneuploidy**

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue
  - No NB in 1st trimester
  - Short or absent NB in 2nd trimester
  - Location: 2 nasal bones on either side of septum
  - Size
    - > 2.5 mm at 13-20 wks considered normal
    - NB length nomograms in literature
  - NB thickness
    - 10-20 wk percentiles

**Ultrasoundographic Findings**
- **1st trimester NB evaluation technique**
  - Fetal face mid sagittal view
  - 90° angle to nose
  - Transducer parallel to NB long axis
  - Soft magnification
  - Image only head and upper chest
  - Normal 1st trimester NB
    - NB first seen at 42 mm crown rump length (CRL)
    - NB echogenic > skin
    - Correct view of NB shows 3 distinct lines
    - Skin over NB
    - Echogenic NB parallel to skin
    - Tip of nose
      - NB cartilage
      - Echogenic focus near tip of nose
    - Not as echogenic as NB
  - 1st trimester absent NB
    - NB not seen
    - Only one nasal line (skin line)
    - Poorly echogenic NB
    - NB echogenicity < skin
    - Considered "absent NB"
  - 1st trimester absent NB significance
    - Independent of other markers for aneuploidy
    - Absent NB associated with T14 + translocation risk

**DDx: Abnormal NB**

- Normal
- Hypertelorism
- Anterior Chamber
- Ectopia

**Images:**
- Sagittal ultrasound in a normal first trimester fetus shows normal nasal bone (arrow). The tip of the nose (open arrow) and maxillary teeth (arrow) are seen separate from the NB.
- Sagittal ultrasound in a first trimester fetus with trisomy 21 shows an absent nasal bone (arrow). Increased NB was also present (open arrow). The curved arrow points to the amnion.
**Terminology**
- Hypoplastic or absent nasal bone (\( \sim NB \))
- \( \sim NB \) is important marker for aneuploidy

**Imaging Findings**
- No NB in 1st trimester
- Short or absent NB in 2nd trimester
- \( \geq 2.5 \, \text{mm} \) at 15-20 wks considered normal
- NB first seen at 42 mm crown rump length (CRL)
- NB echogenicity > skin
- Correct view of NB shows 3 distinct lines
- **CRL 45-64 mm** + absent NB = 17x \( \sim T21 \) risk
- **CRL 65-84 mm** + absent NB = 44-48x \( \sim T21 \) risk
- \( \triangleleft \) NB at 15-20 wks: 83x \( \sim T21 \) risk
- 3D ultrasound helpful
- Look for both NBs in 2nd trimester

**Key Facts**
- **Top Differential Diagnoses**
  - Normal NB (poor technique)
  - Thanatophoric dysplasia (TD)
  - Warfarin (coumadin) embryopathy

**Pathology**
- 2.8% of normal fetuses have an absent NB
- 67% of T21 have an absent NB
- 1.2% of normal fetuses have a hypoplastic NB
- 62% of T21 have a hypoplastic NB

**Diagnostic Checklist**
- Certified first trimester screening program
- Amniocentesis when NB seen in high-risk patients
- Do not mistake skin for NB in 1st trimester
- Finding less clinically significant in Asian and Afro-Caribbean parents

**Differential Diagnosis**
- **Normal NB (poor technique)**
  - First trimester
    - Inadequate magnification
    - NB mistaken for skin (or vice versa)
  - Second trimester
    - \( \geq 90^\circ \) angle of insolation
    - Minimizes NB length
  - Off-axis scanning
  - Scan through cartilage
  - Mimics absent NB

- **Thanatophoric dysplasia (TD)**
  - Lethal skeletal dysplasia
  - Extremely short limbs
  - Type II with severe calvarial findings
  - Kleeblattschädel (cleft/oversize skull)
  - Abnormal profile
  - Depressed nasal bridge + short NB
  - Upturned nasal tip
  - Hypoplastic maxilla
  - Frontal bossing

**Warfarin (coumadin) embryopathy**
- Fetal effects of early exposure to coumadin
- Facial anomalies
  - Hypoplastic maxilla
  - Severely deformed nasal bridge
  - \( \sim \) NB length
Deep nasal grooves
- Between alae nasi and nasal tip
- Stippled rhinophyces
- Punctate rhopylese calcification

PATHOLOGY

General Features
- Genetics
  - 14% associated with aneuploidy
  - Trisomy 21 (T21) most common
  - Trisomy 18 (T18)
  - Trisomy 13 (T13)
  - Turner syndrome
- Etiology
  - Delayed bone maturation
  - Associated with aneuploidy
- Epidemiology
  - First trimester
    - 2.8% of normal fetuses have an absent NB
  - 45% of T21 have an absent NB
  - 57% of T18 have an absent NB
  - 32% of T13 have an absent NB
  - 7% of Turner syndrome have an absent NB
  - Second trimester
    - 1.2% of normal fetuses have a hypoplastic NB
  - 62% of T21 have a hypoplastic NB
  - 7% of T18 have a hypoplastic NB
- Associated abnormalities
  - Other markers for T21
    - 1 NT in first trimester
    - 1 Nuchal fold in 2nd trimester
  - Echogenic bowel
  - Renal pelvis/tufts
  - Short humerus/forearm
  - 5th finger clinodactyly
  - Echogenic intrinsic cardiac focus
  - Major anomalies of T21
    - Atrialventricular canal
    - Duodenal atresia
  - Major anomalies of T18 and T13

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - Incidentally noted
  - First trimester screen
  - Second trimester screen
  - Seen in association with other markers/anomalies
  - Higher risk for aneuploidy

Demographics
- Age
  - Trisomies associated with advanced maternal age (AMA)
  - AMA: > 35 yrs at time of delivery
  - Turner syndrome not associated with AMA

Natural History & Prognosis
- Depends on karyotype
- Fetuses with normal karyotype have an excellent prognosis
- Postnatal hypoplastic nose
  - Often not clinically significant

Treatment
- Genetic counseling with risk calculation
- Consider amniocentesis based on risk assessment
- No prenatal treatment necessary

DIAGNOSTIC CHECKLIST

Consider
- Certified first trimester screening program
- Risk calculation software
  - Compares NBE, CR, maternal age and blood test results
  - Assigns individual risk for aneuploidy
  - Amniocentesis when 1 NBE seen in high-risk patients

Image Interpretation Pearls
- Do not mistake skin for NB in 1st trimester
  - 1st trimester "a" sign is skin + NB
  - Skin alone resembles "a" sign
- Finding less clinically significant in Asian and Meso-American patients

SELECTED REFERENCES
ABSENT NASAL BONE

IMAGE GALLERY

Typical

(Left) Sagittal ultrasound in a second trimester fetus with trisomy 21 shows hypoplastic NB (arrow). The angle of insertion is 90° to the nose yet only a tiny echogenic focus in NB (< 3.5 mm). (Right) Axial color Doppler ultrasound through the nasal bone in the sameetus shows a small anterior vestibular canal defect (arrow).

Typical

(Left) Sagittal ultrasound of the face in a third trimester fetus with trisomy 21 shows a barely ossified hypoplastic nasal bone (arrow) and micrognathia (open arrow points to tongue between upper and lower lips). (Right) Clinical photograph of a child with trisomy 21 shows the small nasal bridge associated with hypoplastic nasal bone.

Other

(Left) 3D ultrasound of the NB shows the advantages of multiplanar imaging. With one volume acquisition, the NB is seen in sagittal (cursors), coronal (open arrow) and axial (curved arrows) views. (Right) 3D ultrasound with maximal mode-rendering shows the triangular NB (arrow) and coronal "skull" view of both NB (open arrows). Unilateral NB hypoplasia is identifiable with 3D ultrasound.
**TERMINOLOGY**

**Definitions**
- Micrognathia: Small mandible
- Retrognathia: Abnormal position of mandible → receding chin
- Often coexists with micrognathia
- Glabellum: Abnormal posterior position of tongue

**IMAGING FINDINGS**

**General Features**
- Receding chin on true sagittal image of face

**Ultrasonographic Findings**
- 3D US may be best method to evaluate facial structures
  - Volumetric acquisition
  - Ensures accurate sagittal section
- Jaw index
  - Anteroposterior (AP) diameter mandible/biparietal diameter x 100
  - AP diameter taken from symphysis mentis to a line drawn between bases of mandibular rami
  - Normative data available
  - Provides objective assessment of mandibular size
- Jaw index < 23 → 100% sensitivity, 98.7% specificity for micrognathia

**MR Findings**
- Used to evaluate associated central nervous system anomalies
- May be helpful in evaluation of cleft palate, especially with oblique facial habits
- Hard palate is low signal intensity on T2WI
- Forms intact line between nasopharynx and oropharynx

**Imaging Recommendations**
- Use 3D if available
- Beware pitfalls in diagnosis of micrognathia
  - Image profile in true sagittal plane, if off axis may “create” receding jaw
  - Oligohydramnios: Obscures detail
  - Agnathia
  - Extremely rare, lethal malformation
  - Profile abnormal but absence of mandible may not be appreciated prenatally
- Look for associated cleft lip/palate
- Obtain axial section through toothbuds in maxilla
  - Look at nose in coronal plane
  - Nasal septum deviated with cleft lip
- Tongue may be unusually well seen with cleft palate
- Evaluate fetal ears

**DDx: Pitfalls In Diagnosis Of Micrognathia**

- Off-Axis
- Correct Plane
- Cleft lip/palate
- Agnathia
MICROGNATHIA

Key Facts
- Sleep-related airway obstruction
- 66% have abnomal chromosomes
- Consider detailed clinical genetic assessment of family if chromosones are normal
- Consider use of EXIT (ex utero intra partum treatment) procedure
- Postnatal treatment requires multidisciplinary team

Diagnostic Checklist
- In at-risk fetus, normal 20 week scan does not exclude micrognathia
- Significant mandibular growth occurs in third trimester
- True sagittal scan plane vital for assessment of micrognathia
- 3D ultrasound very helpful

Terminology
- Micrognathia: Small mandible
- Retrognathia: Abnormal position of mandible → receding chin

Imaging Findings
- Jaw index < 21 – 100% positive predictive value
- Polyhydramnios seen in up to 70% of cases

Top Differential Diagnoses
- Pseudo-micrognathia

Clinical Issues
- Outcome depends on final diagnosis
- 54% with airway difficulties at birth requiring intervention
- 31% with feeding problems

- Treacher COLLINS syndrome
  - Associated with small ears, ears may not be visible sonographically
  - Nager syndrome
  - Malformed ears, poorly ossified upper extremity bones
  - Goldenhar syndrome
  - Malformed ears, hemifacial microsomia
  - Otocephaly; Hypoplasia or absence of mandible associated with
    - Syndactyly: Ventromedial displacement external ears
    - to midline neck
    - Microstomia, aglossia, nose-mouth fusion
    - Can be very difficult diagnosis to make prenatally
  - Evaluate fetal eyes
  - Neu-Laxova syndrome: Hypotelorism, protruding eyes, absent eyelids
  - Goldenhar syndrome: Microphthalmia, hypophthalmal,
    - hypotelorism
  - Hypotelorism, cyclops suspicious for trisomy 13
  - Look at extremities
    - Clefted fingers suspicious for trisomy 18
  - Club or rockerbottom foot suspicious for trisomy 18
  - Polydactyly 1 suspicion for trisomy 13
  - “Flipper” like upper extremities with ulnar defect → Cornelia de Lange syndrome
  - Look for signs of skeletal dysplasias
  - Campomelic dysplasia
  - Femorotibial syndrome
  - Other associated abnormalities
  - Congenital heart disease in 20%
  - Intrauterine growth restriction

Thanatophoric dysplasia
Achondroplasia

Ammniotic band sequence
- Destructive “slash” defects, often multiple
- Look for band from fetus to uterine wall or placenta

PATHOLOGY

General Features
- Genetics
  - Autosomal dominant → recurrence risk 50%
  - Treacher Collins syndrome: Mutation mapped to TCOF1 gene
  - Stickler syndrome: Mutation of COL2A1 gene on chromosome 12q13
  - Autosomal recessive → recurrence risk 25%
  - Smith-Lemli-Opitz syndrome
  - Neu-Laxova syndrome
  - Syndromes associated with Pierre Robin sequence
  - Stickler syndrome
  - 22q11 deletion
  - Epidemiology
    - Actual incidence of micrognathia unknown
    - Micrognathia seen in heterogeneous group of conditions
  - Trisomy 18 1:3,000 live births
  - Goldenhar syndrome 1:4-25,000 births
  - Pierre Robin sequence: 5-10,000 births
  - Treacher Collins syndrome 1:10-25,000 births
  - Incidence of Treacher Collins syndrome is increasing as more affected infants survive to adulthood
  - Associated abnormalities
    - Micrognathia often associated with limb abnormalities
    - Oral-facial-digital syndromes
    - Oral-mandibular-limb hypogenesis syndromes

DIFFERENTIAL DIAGNOSIS

Pseudo-micrognathia
- Incorrect imaging plane
  - Need true midline sagittal image
  - Look at nose, especially nasal bone
  - Chin may look small if head shape is abnormal,
    - especially frontal bossing

5
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MICROGNATHIA

- Embryology
  - Defect in first and second branchial arches
  - Abnormal migration or proliferation of neural crest cells
  - Mandibular hypoplasia → superior displacement of tongue → failure of palate fusion
  -家族 history (3 cases were due to defect on prenatall US
  - Lip formation not affected, this is a mechanical effect on hard palate

CLINICAL ISSUES

Presentation
- Abnormal findings on routine sonography
- First trimester detection of Pierre Robin sequence reported with use of endovaginal sonography

Natural History & Prognosis
- Prenatal diagnosis
  - 50% intrauterine or early neonatal demise
  - In a series of 19 chromosomally normal fetuses, only one survived
  - 66% have aneuploidy
- Outcome depends on fetal diagnosis
  - Series of sonographically “isolated” micrognathia
    - 54% with airway difficulties at birth requiring intervention
    - 31% with feeding problems
    - Sleep-related airway obstruction
    - 38% developmental delay, mild to severe
  - Intellectual outcome
    - Goldenhar syndrome: 5-15% mentally subnormal
    - Treacher Collins syndrome: 5% developmental delay, may relate to undetected hearing problems
  - Pierre Robin sequence: Speech and hearing compromise but < 5% of survivors classified as educationally subnormal
  - Recurrence risk
    - Aneuploidy: 1% in maternal-age-related cases
    - Syndromes often sporadic, rare mutations but several have autosomal dominant or recessive inheritance

Treatment
- Genetic counseling
  - Detailed family history
  - Teratogen exposure
  - Offer karyotype
    - 66% have abnormal chromosomes
  - Consider detailed clinical genetic assessment of family if chromosomes are normal
  - Relatives may have minor features in Goldenhar syndrome
  - Prenatal consultation with neonatologist
  - Plan delivery at tertiary center
    - Consider use of EXIT (ex utero intrapartum treatment) procedure
    - Successful use reported in dysgnathia complex:
      - Severe micrognathia, cleft/cleft/micrognathia, ear anomalies
    - Postnatal treatment requires multidisciplinary team
      - Plastic surgery
      - Maxillofacial surgery

- Pierre Robin sequence outcome improved with early mandibular distraction surgery
- Ear, nose, throat surgery
- Orthodontics
- Speech therapy

DIAGNOSTIC CHECKLIST

Consider
- Irrelevant, fetal normal 20 week scan does not exclude micrognathia
- No significant mandibular growth occurs in third trimester

Image Interpretation Pearls
- True sagittal scan plane vital for assessment of micrognathia
- 3D ultrason examination very helpful
- Micrognathia rarely isolated finding in fetus
- Associated with three major disease categories
  - Aneuploidy
  - Skeletal dysplasia
  - Primary mandibular disorders

SELECTED REFERENCES

**MICROGNATHIA**

**IMAGE GALLERY**

**Typical**

(Below) Sagittal T2W MR shows micrognathia (curved arrows), glossopitrus (arrow) and cleft palate (open arrow) in a fetus with Pierre Robin sequence. (Right) Sagittal T2W MR shows the normal appearance of the clav (black arrow), doges (curved arrow) and palate of 24 weeks gestation. The palate (white arrow) forms the low signal band separating the oropharynx from the nasopharynx.

**Typical**

(Below) Sagittal ultrasound shows severe micrognathia and macroglossia (curved arrow) in a fetus with Treacher Collins syndrome. The mandible is small and posteriorly positioned in relation to the nose (arrow) and frontal bone (open arrow).

(Right) 3D ultrasound of the same case clearly shows the hypomagnesia in the fetus with mandible hypoplasia (arrow). The downward slope of the orbits is hard to appreciate in the fetus, even with 3D imaging.

**Typical**

(Below) Axial ultrasound shows the normal bony/fat appearance of the fetal maxilla. The AP diameter (double-headed arrow) is measured from the symphysis to the symphysis to a line joining the bases of the canines. (Right) Clinical photograph shows the typical appearance of an infant with 2/21 syndrome. There is micrognathia (curved arrow), a broad nasal root and long, dished fingers (arrow).
MACROGLOSSIA

TERMINOLOGY

Definitions
• Enlarged tongue
  ○ True: Tongue exceeds 95th percentile for gestational age
  ○ Relative: Tongue appears large secondary to small oral cavity

IMAGING FINDINGS

General Features
• Persistent protrusion of tongue through lips
  ○ Best seen on sagittal or coronal images
• Trisomy 21 fetuses also exhibit “tongue thrusting”
  ○ Repetitive “in and out” motion of tongue tip
• Polyhydramnios
  ○ Large tongue obstructs swallowing

Imaging Recommendations
• Best imaging tool
  ○ 3D ultrasound very helpful for global view of fetal face
• Also helpful counseling tool
  ○ Parents may understand anatomy better with 3D images

DDx: Pitfalls In Diagnosis Of MacroGLOSSia

- MR imaging may be useful if quality of ultrasound compromised (e.g. maternal obesity)
- Protocol advice
  ○ In at-risk pregnancy, measure tongue circumference
    • Normative data available
  ○ Careful anatomic survey
  • Macroglossia is rarely an isolated abnormality
  ○ Look for signs of trisomy 21
  • Akrosyndactyly
  • Midfacial hypoplasia
  • Rhizomelic limb shortening (numerous more specific than femur)
  • Clinical exam
  • Pelvic crisis
  • Look for signs of triploidy
  • Multiple anomalies
  • Dysmorphic face: Micrognathia, macroglossia, broad root of nose, low-set ears
  • Growth restriction
  • Thick cystic placenta
  ○ Look for signs of Beckwith-Wiedemann syndrome
    • Macroglossia
    • Omphalocele
    • Hepatomegaly
    • Enlarged kidneys
    • Adrenal cyst
MACROGLOSSIA

Key Facts

- Macrognathia strongly associated with aneuploidy

Clinical Issues

- Genetic counseling for detailed family history
- Offer karyotype
- In one series, 77% of fetuses with macrognathia had an abnormal karyotype, mostly trisomy 21
- Plan delivery in tertiary care facility
- Long term treatment requires multidisciplinary team
- Goal of tongue resection is to reduce size to near normal while preserving function

Diagnostic Checklist

- Macrognathia is rarely an isolated finding
- Micrognathia may give false impression of macrognathia

Imaging Findings

- Persistent protrusion of tongue through lips
- Best seen on sagittal or coronal images
- Trisomy 21 fetuses also exhibit "tongue thrusting"
- 3D ultrasound very helpful for global view of fetal face
- In at-risk pregnancy, measure tongue circumference
- Look for signs of trisomy 21
- Look for signs of triploidy
- Look for signs of Beckwith-Wiedemann syndrome

Top Differential Diagnoses

- Lymphangiomat
- Tongue cysts
- Epignathus

- Look for signs of hypothyroidism
- Goltz
- Beware pitfalls in diagnosis of macrognathia
- Normal fetal tongue activity
- Circumference is normal
- Tongue "fits" inside mouth
- Micrognathia
- Tongue may look large in relation to small mandible
- Facial cleft
- Tongue may be unusually well seen, appears large
- Circumference is normal
- Coreal views of face show cleft

Differential Diagnosis

Lymphangiomat

- Typically focal superficial mass, but may be infiltrative
- Enlargement of tongue
- Multilocular mass
- Usually isolated finding
  - Macrognathia strongly associated with aneuploidy, therefore seldom isolated

Tongue cysts

- Enteric duplication cyst
- Macroche of anterior lingual salivary glands
- Rare: Obstructed sublingual salivary glands

Epignathus

- Specific form of teratoma which protrudes through oral cavity
- Complex, amorphous solid mass
- Often hypervascular
- No spontaneous movement

Pathology

- Macrognathia strongly associated with aneuploidy

- Trisomy 21
- Triploidy
- Beckwith-Wiedemann syndrome
- Major facial anomalies
- Autosomal dominant in 10-15% of cases
- Harter syndrome
- Autosomal recessive
- Cronzon syndrome
- Autosomal dominant craniofacial dysostosis

- Etiology
  - Macrognathia strongly associated with aneuploidy
  - Majority trisomy 21
  - Epidemiology
  - Incidence depends on underlying condition
  - Beckwith-Wiedemann syndrome 1:3,000 live births
  - Harter syndrome 1:150,000 births
  - Associated abnormalities
  - May be seen with anencephaly
  - CHARGE association (coloboma, heart defects, choanal atresia, growth restriction, genitourinary anomalies, ear anomalies)

Gross Pathologic & Surgical Features

- Beckwith-Wiedemann syndrome: muscular enlargement of tongue
- Micrognathia: glycogen deposition in tongue

CLINICAL ISSUES

Natural History & Prognosis

- Normal tongue growth is considerable after birth
  - Tongue length, width, thickness double from birth to adolescence
- Mechanical problems with macrognathia
  - Airway obstruction
  - Feeding difficulties
  - Speech impediment
- Constant drooling
- Offer major concern for parents
- Trisomy 21
MACROGLOSSIA

- Down syndrome infants have relative macroGLOSSIA
  - Small oral cavity
  - Muscular hypotonia of tongue → exacerborder poor "F" to oral cavity
- Risk congenital heart disease, especially atrioventricular septal defect
- Developmental delay variable, mildest to severe
  - Average IQ 50-60
- Average life expectancy in 20 years, many older survivors
- 20-fold risk acute leukemia
- Beckwith-Wiedemann
  - Infant mortality 20%
  - Risk of neonatal hypoglycemia
  - Risk of hypothroid tumors
- Turner syndrome
  - Progressive disease with mental retardation, heart disease, joint disease
  - Death by early teens in majority of cases

TREATMENT
- Genetic counseling for detailed family history
- Offer karyotype
  - In one series, 77% of fetuses with macrosomia had an abnormal karyotype, mostly trisomy 21
  - Conversely only 18% of fetuses with trisomy 21 had facial abnormality
- Turner syndrome can be diagnosed prenatally by testing cultured amniocytes
- Termination may be offered for aneuploidy, mucopolysaccharidoses
- Plan delivery in tertiary care facility
  - Counsel parents regarding risk of airway compromise
- Risk for mental hypoglycemia in Beckwith-Wiedemann syndrome
- Monitor for development of polyhydramnios
  - Increases risk of severe congenital anomalies
  - Advise may be premature to airway compromise from large tongue
- Monitor mother for signs of preeclampsia
  - Increase risk with Beckwith-Wiedemann syndrome
- Long term treatment requires multidisciplinary team
  - Orthodontics
  - Orofacial regulation therapy
  - Palatal plate stimulation improves muscle tone, decreases tongue protrusion
  - Speech therapy
  - Maxillofacial surgery
- Beckwith-Wiedemann syndrome may be particularly difficult to manage with some children, requiring tracheostomy
- Goal of tongue resection is to reduce size to near normal while preserving function
- Surgery generally improves tongue and airway function
- Swallowing may not be helped
- Speech impediment relates to neurological condition
  - Children with significant intellectual impairment may not show improved speech patterns
- Lymphangiomas are most likely to recur and does least well with surgery
  - Laser coagulation useful for superficial malformations
  - Usually requires multiple treatments

DIAGNOSTIC CHECKLIST

Consider
- Most likely diagnoses in a fetus with macroGLOSSIA
  - Turner Syndrome
  - Beckwith-Wiedemann syndrome

Image Interpretation Pearls
- Macroglossia is rarely an isolated finding
- Look for additional abnormalities to assist with specific diagnosis
- Micrognathia may give false impression of macroGLOSSIA

SELECTED REFERENCES

(Left) Sagittal ultrasound shows an extremely large tongue (curved arrows) in a third trimester fetus. This was an isolated finding in this case. Note the normal nasal bone (arrow). (Right) Sagittal ultrasound shows the tongue (arrow) protruding from the mouth in a fetus with Beckwith-Wiedemann syndrome. The tongue is too large to fit inside the oral cavity.

(Left) Sagittal ultrasound shows an abnormal profile in a fetus with Down syndrome. The tongue (curved arrows) is large and "tongue-thrashing" was observed in real time. Note degenerated nasal bridge (arrow). (Right) Clinical photograph shows the typical facial appearance of an infant with Down syndrome. The mouth is often held open secondary to the large tongue, resulting in perpetual drooling. Also note the flattened nasal bridge (arrow).

(Left) 3D ultrasound of a fetus with Beckwith-Wiedemann syndrome shows macroglossia, with the tip of the tongue (curved arrow) protruding through the lips (arrow). (Right) Coronal ultrasound shows the tip of the nose (open arrow), the lips (curves) and the pendulous tongue (curved arrow) of a fetus with Down syndrome.
EPIGNATHUS

TERMINOLOGY

Abbreviations and Synonyms
- Epignathus
- Nasopharyngeal teratoma
- Oral-teratoma
- Facial-teratoma

Definitions
- Teratoma arising in oral/nasal cavity or pharynx

IMAGING FINDINGS

General Features
- Best diagnostic clue
  - Large, fungating oral mass
  - Calcifications are virtually pathognomonic of teratoma but are present in only half of cases and may not be visible with ultrasound
- Location
  - Most commonly arise from hard or soft palate
  - Fills oral cavity and encases from mouth and/or nose
  - Transspinoideal intracranial extension can occur
  - Produces an extra-axial mass
  - Can cause marked distortion of intracranial structures

Ultrasonographic Findings
- Predominantly solid or mixed cystic/solid
- Commonly distorts surrounding anatomy
  - Jaw is held in a fixed open position
  - Splinted mandible
  - Hypoechoic
  - Exophthalmos
  - Cervical hyperextension
  - Polyhydramnios secondary to pharyngeal obestation
  - Often severe
  - Color Doppler
  - Solid portions of mass often very vascular
  - Arteriovenous shunting may be present
  - Hydrops may develop with large masses

MR Findings
- Helpful in determining anatomic extent
  - Important for intracranial involvement
  - Can identify fat within lesion

CT Findings
- In utero CT with 3D reforman has been done
  - Better evaluation of calcifications and bone anatomy

DDx: Oral/Facial Masses

Macroglossia
Macroglossia
Bilateral CUP
Bilateral macroglossia
EPIGNATUS

Terminology
- Teratoma arising in oral/nasal cavity or pharynx

Imaging Findings
- Large, fungating oral mass
- Most commonly arise from hard or soft palate
- Tumors involving intracranial extension may occur
- Predominantly solid or mixed cystic/solid
- Jaw is held in a fixed open position
- Polytubular anomalies secondary to pharyngeal obstruction
- Hydromedullary development with large masses
- MRI recommended to better delineate anatomy
- Evaluate brain carefully for intracranial extension

Top Differential Diagnoses
- Cervical teratoma
- Aminotic band syndrome

Imaging Recommendations
- Routine head and face views should detect virtually all cases
- Color Doppler to evaluate vascularity
- MRI recommended to better delineate anatomy
  - Presence of intracranial extension negatively impacts prognosis
  - Close interval scanning
    - May grow rapidly to massive size
    - Often larger than fetal head
    - Evaluate brain carefully for intracranial extension
    - Compares and displaces normal brain parenchyma
    - Head enlargement
    - Hydrocephalus
    - Worsening polyhydramnios
  - Mass may cause high-output cardiac failure and hydrops
  - Cardiomegaly
  - Anomalies
  - Pleural effusion
  - Skin thickening

DIFFERENTIAL DIAGNOSIS

Cervical teratoma
- Point of origin of large masses may be difficult to discern
- Look carefully at mouth and brain
  - No intracranial extension
- Neck often held in hyperextension
- May extend into mediastinum

Aminotic band syndrome
- May cause facial mass from "slash" defects
  - Large, obliquely oriented facial clefts
  - Bands may be visible
  - Other body parts often affected

Frontal cephalocele
- Frontoethmoidal skull defect with herniation of brain

Key Facts
- Frontal cephalocele
- Other rare tumors

Clinical Issues
- May show rapid in utero growth
- Substantial improvement in survival achieved with ex utero intrapartum treatment (EXIT) procedure
- Fetus is partially delivered by cesarean section while placenta and umbilical cord remain intact
- Uteroplacental gas exchange maintained
- Fetus remains hemodynamically stable while airway is established

Diagnostic Checklist
- Very large, fungating oral mass is virtually diagnostic of a teratoma
- Usually small and may be missed prenatally
- Higher than typical epignathus
- Hypertelorism
- MRI confirms diagnosis

Other rare tumors
- Myoblastoma
  - Reported in oral cavity
  - Found exclusively in females
- Nasal glioma
  - Collection of dysplastic brain tissue
  - Located in oral cavity or subcutaneous tissue
- Dermoid cyst
  - Persistent dural projection through foramen cecum
  - Dermoid or epidermoid envelops along tract
  - Can have connection with intracranial contents
- Soft tissue tumors (both benign and malignant) may cause a facial mass
  - Hemangioma
  - Fibromatosis, myofibromatosis
  - Fibrosarcoma, rhabdomyosarcoma

Bilateral clef I lip/palate (CL/CP)
- Premaxillary protrusion in axial plane may appear as like soft tissue mass
- Coronal/axial views show bilateral clefts
  - Clefts extend posteriorly through alveolar ridge

Macroglossia
- Mouth open, with persistent protrusion of fetal tongue
- Seen with multiple syndromes

PATHOLOGY

General Features
- Genetics
  - Sporadic
  - No recurrence risk
- Etiology
  - Embryology
    - Primordial germ cells migrate from yolk sac to genital ridges (weeks 4-6)
EPIGNATUS

- Germ cells are then incorporated into primitive sex cords to form gonad
- Unincorporated cells normally involute
- Continued division of unincorporated pluripotential cells gives rise to teratoma
- Epidemiology
  - Rare
  - Head and neck second most common site for teratomas after sacrococcygeal
  - More common in females
- Associated abnormalities: Increased incidence of cardiac anomalies reported

Gross Pathologic & Surgical Features
- Complex, mixed cystic and solid components
- Teeth and hair not at common in as in teratomas later in life

Microscopic Features
- Unique histologic feature: compared to teratomas presenting later in life
- Composed of all three germ cell layers
-ECTodermal tissues main histologic component of fetal teratomas
  - Often contain neural tissue ("brain-like") as a dominant component
- Mesoderm
  - Fat
  - Cartilage
  - Smooth muscle
  - Bone
  - Endoderm
  - Lecithocystic component
  - Respiratory epithelium
  - Coelomic/retinal tissues

Staging, Grading or Classification Criteria
- Teratoma classified as mature or immature
  - Immature teratoma do not have same poor prognosis as those presenting later in life
  - Immaturity of tumor may reflect immaturity of fetus rather than biologic behavior of tumor
- Size and vascularity are much more important than histology in a fetus

CLINICAL ISSUES

Presentation
- Most common signs/symptoms: Obvious fungating oral mass
- Other signs/symptoms
  - Polyhydramnios
  - Reported as early as 15 weeks

Natural History & Prognosis
- May show rapid in utero growth
- Polyhydramnios may cause preterm labor
- Routine obstetric techniques
  - Lethal if unable to establish airway
- Event with maximal emergency procedures, hypovia, acidosis and massive brain injuries occur
- Mortality 80-100%

- Substantial improvement in survival achieved with ex utero intrapartum treatment (EXIT) procedure
  - In large series airway established in 79%, with overall survival of 69% for head and neck masses

Treatment
- Termination offered
- If pregnancy continued, deliver at tertiary care facility with capability for ex utero intrapartum treatment (EXIT) procedure
- EXIT procedure provides controlled environment to establish airway (either intubation or tracheostomy)
  - Fetus is partially delivered by cesarean section while placenta and umbilical cord remain intact
  - Uteroplacental gas exchange maintained
  - Fetus remains hemodynamically stable while airway is established
  - Avoid "crash" attempt at achieving airway at birth

DIAGNOSTIC CHECKLIST

Consider
- MRI to better delineate anatomy and evaluate for intracranial extension
- If pregnancy is continued refer patient to tertiary care facility with capability of performing EXIT procedure

Image Interpretation Pearls
- Any large, fungating oral mass a virtual diagnostic of a teratoma

SELECTED REFERENCES
Typical

(Left) Intraoperative photograph of the ENT procedure. The keys is partially delivered via otoscopic canal and placed on the maternal abdomen. The placenta and amniotic fluid remain intact and uteroplacental gas exchange maintained. The mass is controlled while the intubation is performed.

(Right) The tongue is intubated, showing the successful intubation. (Also shown in radiographs, ref. 15)

Typical

(Left) Coronal (left) and sagittal (right) views of the fetal head show a complex cystic mass centered at the skull base, with intracranial growth (arrow) and extension out the mouth (curved arrows). (Right) Postmortem T1WI (left) and photograph (right) show the oral component of the mass (white arrow) with swelling of the mandible and deviation of the tongue (open arrow). The Beck arcus shows intracranial extension.

Typical

(Left) Sagittal T1WI MRI of a nasopharyngeal exostoma shows a predominantly solid mass (arrows) involving the midface. There was no unusual extension, and the brain was normal. (Right) Sagittal gadolinium enhanced scan after delivery shows areas of enhancement within the large solid mass, which involved both the maxillary and nasal cavities. The inset shows the injected mass.
EAR ANOMALIES

TERMINOLOGY

Abbreviations and Synonyms
- Congenital auricular anomalies

Definitions
- Abnormal external ear formation
  - Heterogeneous group of disorders
  - Malformation anomalies
  - Embryologic maldevelopment
- Deformation anomalies
  - 2° to in utero physical forces

IMAGING FINDINGS

General Features
- Best diagnostic clue
  - Abnormal ears seen best with 3D ultrasound
  - Isolated or with other anomalies
- Often with other craniofacial defects
- Location: Unilateral or bilateral
- Size: Unusually small or large ears
- Morphology: Highly variable

Ultrasoundographic Findings
- Fetal ear evaluation
  - Determine ear position
- Identify eyes
- Inner canthi line (join 2 inner canthi)
- Top of helix should be at level of inner canthi line
- Identify top and bottom of ears
- Measure ear length
- Evaluate ear morphology
- Enlarge ear view
- 3D Ultrasound
- Multifaceted capability
- Soft tissue rendering
- Look for other fetal face anomalies
- Normal ear size
  - Normal length
  - Ear growth is linear through gestation
  - Ear length + 1/3 biparietal diameter (BPD)
  - May use neonates for percentiles
  - Ear width more difficult to assess
  - Neonates for 38-42 weeks most accurate
  - Measurement unreliable with 1 fetal age
- Normal auricular topography
  - Helix
  - Most external curve of helix
  - Antihelix
  - Y-shaped internal auricle
  - Tragus
  - Inferior to root of helix, over external acoustic meatus
  - Antitragus

DDx Craniofacial Anomalies (3D Ultrasound)

- Cleft Lip
- Cleft Palate
- Micrognathia
- Anomalously
Terminology
- Abnormal external ear formation
- Heterogeneous group of disorders

Imaging Findings
- Abnormal ears seen best with 3D ultrasound
- Determine ear position
- Evaluate ear morphology
- Ear length = 1/3 biparietal diameter (BPD)
- Anotia
- Microtia
- Absent auricular components
- Low-set ears: Top of helix lower than inner canthal line
- Protuding ears often isolated idiopathic finding
- Auricular tags
- Look at ears when other facial anomalies seen
  - Superior to lobe and faces tragus
  - Lobule (ear lobe)
  - Non-cartilaginous (fibrofatty tissue)
  - Concha fossa
  - Tumor fossa near root of helix
  - Contiguous with external auditory canal
  - Different ear
  - Anotia
  - Absent ear
  - Microtia
  - Small ear
  - Cephalo-caudal ear length < 1/3 of BPD
  - < 10th percentile for gestational age
  - Absent auricular components
  - Partial or complete helix absent
  - Antihelix absent
  - Absent lobule (lobule)
  - Malpositioned ears
  - Low-set ears: Top of helix lower than inner canthal line
  - Malrotated ears
  - Often also dysplastic, may be large or small
  - Protuding ears often isolated idiopathic finding
  - > 2 cm from mastoid skin (at birth)
  - Supernumerary parts
    - Duplication of embryologic components
    - Auricular tags
    - Found at embryologic junction
    - Pre-auricular tag most common
    - Mirror image auricular duplication
    - Polyotia
    - Partial or complete duplication
    - Mirror image orientation to 1st ear
    - Appears as long dysplastic ear
  - Deformation of ear cartilage
    - Loop ear
      - Top of ear is curved downward
      - Conical ear
      - Crinkled helix
    - Ear anomaly associations
      - Trisomy 21 (T21)
      - 60% of T21 fetuses have short ears

Key Facts
- Offer genetic counseling

Top Differential Diagnoses
- Normal ear
- Facial clefts
- Severe facial anomalies

Pathology
- T21, T18, T13, Turner syndrome
- Often with other craniofacial anomalies

Clinical Issues
- Surgical treatment for malformations
- Non-surgical treatment for deformations
- Auricular cartilage suitable first 3 months of life

Diagnostic Checklist
- Ear anomalies often missed prenatally
  - Susceptible 80%
  - Positive predictive value 73%
  - Rarely an isolated finding
  - Trisomy 18 (T18)
  - Short malformed ear
  - Multiple other anomalies
  - Trisomy 13 (T13)
  - Microtia/anotia
  - Holoprosencephaly is hallmark finding
  - Turner syndrome
  - Short ear length
  - Cystic hygroma is hallmark finding
  - Treacher Collins syndrome
  - Microtia/anotia common
  - Microgastria
  - Abnormal eyes with ocular tissues
  - Anomalous
  - Low-set/lop ear
  - Open neural tube defect
  - Abnormal calvarium superior to face
  - Potter syndrome
  - Deformation from severe oligohydramnios
  - Low-set ears
  - Microgastria from any cause
  - Heterogeneous disorders
  - Low-set dysplastic ear common

Imaging Recommendations
- Best imaging tool
  - 3D ultrasound
- Asses ear location, size, morphology
- Protocol advice
  - Look in ears when other facial anomalies seen
  - Often associated with microgastria
  - Offer genetic counseling

DIFFERENTIAL DIAGNOSIS

Normal ear
- Full diagnosis of low-set ears
- Difficult to judge without 3D ultrasound
- Not part of routine exam
EAR ANOMALIES

- May be difficult to see
  - Complex morphology

Facial clefts
  - Cleft lip +/− palate
  - Amniotic band syndrome
  - Disruption of aorta with fetal entrapment
  - Bizarre facial clefts

Severe facial anomalies
  - Ears may or may not be normal
  - Holoprosencephaly
  - Hypothermia
  - Polyneurones
  - Midline/bilateral cleft lip & palate
  - Mandibular hypoplasia

PATHOLOGY

General Features
  - Genetics
    - Anomaly
      - T21, T18, T13, Turner syndrome
    - Hereditary
      - Single gene mutation
    - Sex-linked traits
    - Many syndromes
    - Often with other craniofacial anomalies
  - Embryology
    - Embryology of normal ear
      - Ears arise from 1st and 2nd branchial arches
    - Ears migrate dorsal and lateral
    - Migration as mandible/maxilla develop
    - Folding of auricular cartilage
    - Fully developed auricle by 9th wk
  - Abnormal ear
    - Abnormal genetic information
    - Ischemia (stapedial artery hemorrhage)
    - Chondrogenesis/interference
  - Toxic exposure
  - Thalidomide
  - Retinoic acid
  - Epilepsy
    - Microtia/anotia
    - 0.8 to 2.4 in 10,000 live births
      - 8.3 in 10,000 live births in Nava
      - 75% of children with microtia due to maternal smoking
  - Associated abnormalities
    - Craniofacial sequence
  - Cardio, renal, eye anomalies
  - Same embryologic streamline

Staging, Grading or Classification Criteria
  - Failure of formation
  - Failure of differentiation
    - Duplication
    - Overgrowth
  - Undergrowth
  - Part of craniofacial sequence

CLINICAL ISSUES

Presentation
  - Most common signs/symptoms
    - Isolated ear anomaly incidentally noted
  - Low detection rates (e.g., not routinely scanned)
    - In association with other severe anomalies
  - Other signs/symptoms: Often seen with microtia

Demographics
  - Age
    - Trisomies associated with advanced maternal age
      - 9.5 years of age
  - Sex

Natural History & Prognosis
  - Depends on severity of anomaly
  - Presence of other anomalies

Treatment
  - Surgical treatment for malformations
    - Multiple procedures over time
  - Non-surgical treatment for deformations
    - All ear components present
    - Auricular cartilage malleable after 3 months of life
  - Age to maternal estrogen effect
  - Mold and splitting
  - Surgery: molding often necessary

DIAGNOSTIC CHECKLIST

Consider
  - Ear anomalies often missed prenatally
  - Perinatal ultrasound to detect anomalies suspected

Image Interpretation Pearls
  - Early referral to plastic surgeon
  - Nonsurgical treatment works best in first 3 months
  - Prenatal consultation possible (CT images helpful)
  - Look carefully at ears when mandible anomalies are

SELECTED REFERENCES

EAR ANOMALIES

IMAGE GALLERY

Typical

(Left) Coronal oblique ultrasound shows a low-set dysplastic ear (arrows) in a fetus with multiple other anomalies, including micrognathia. (Right) Clinical photograph of another fetus with aplastic (absent mandible) shows cheilorrhinism, low-set ears, with some lower jaw duplication. Mandible and ear anomalies are often seen together.

Typical

(Left) Sagittal oblique 3D ultrasound shows a deformed ear (arrows) in a fetus with anencephaly. The mass effect of the herniated brain (open arrows) may be the cause of the top ear. (Right) Clinical photograph of anencephaly shows a low-set, deformed ear. Ear anomalies often occur in conjunction with craniofacial defects, including anencephaly.

Typical

(Left) 3D ultrasound of a fetus with Pierre Robin syndrome shows micrognathia (curved arrow) and low-set ears (shorter arrows). The arrow points to the expected location of the top of the helix, based on the inner canthus line. (Right) 3D ultrasound of normal 2nd trimester fetus and 3rd trimester fetus shows exquisite morphologic detail.
**MIDFACE ANOMALIES**

**TERMINOLOGY**

**Definitions**
- Abnormalities of fetal midface
- 2 major categories
  - Midface hypoplasia
  - Depressed nasal bridge
- Maxillary hypoplasia
- Holoprosencephaly spectrum

**IMAGING FINDINGS**

**General features**
- Best diagnostic clue
  - Abnormal fetal profile
  - Hypoplastic flat midface
  - Dysplastic midface
  - Location: Maxilla + nose + orbit involvement
  - Morphology
    - Highly variable
    - Midface hypoplasia
    - Findings may be subtle
  - Holoprosencephaly
  - Nose, mouth, eyes may be unrecognizable

**Ultrasoundographic Findings**
- Midface hypoplasia

**DDx: Midface Anomalies**

- Trisomy 21
- Cleft palate
- Cleft lip
- Hydrocephalus
- Ventriculomegaly

- Profile view shows flat face
- Abnormal lower-mid facial bone angle
  - Flat nasal bridge
  - Short nose
- Hypoplastic maxilla
  - Maxilla displaced posteriorly
  - Reverse overbite, if severe
  - Mandible anterior to maxilla
  - Cleft lip (CL) +/- cleft palate(CP) may be seen
  - Isolated CL, often with only flattened noses
- Midface hypoplasia associated with skeletal dysplasia
  - Thalassemic dysplasia
  - Most common lethal skeletal dysplasia
  - Severe limb shortening
  - Small chest
- Acraniofacial
  - Autosomal-dominant
  - Homozygous form is fatal
  - Rhizomelic limb shortening
  - Heterozygous: Mild midface hypoplasia
  - Craniosynostosis syndromes
  - Apert syndrome
  - Carpenter syndrome
  - 1q4 deletion (Jacobsen syndrome)
- Midface hypoplasia associated with aneuploidy
  - Trisomy 21 (T21)
  - Frontal bossing
  - Midface findings often subtle
MIDFACE ANOMALIES

Terminology
- 2 major categories
  - Midface hypoplasia
  - Holoprosencephaly spectrum

Imaging Findings
- Flat nasal bridge
- Hypoplastic maxilla
- Inverse orbitome, if severe
- Midface hypoplasia associated with skeletal dysplasia
- Spectrum of holoprosencephaly face anomalies
- Cyclopia with proboscis
- Ethrocephaly
- Cephalocele
- Spectrum of median cleft lip/palate
- 3D helps delineate midface anomalies
- MRI helpful for brain anomalies
- Most obvious later in gestation

- Trisomy 13 (T13)
- Median CP/CP = midface hypoplasia
- More often with holoprosencephaly

Holoprosencephaly
- Midline brain anomalies +/- face anomalies
- Complete or partial fused thalamus
- Monoventricle or fused ventricles
- Abnormal brain mantle
- Spectrum of brain findings
- Holoprosencephaly
- Moebius (most severe)
- Semilobar
- Lobar
- Septo-optic dysplasia (most mild)
- Face predicts the brain
- Brain is abnormal if face is abnormal
- Brain does not always predict the face
- 20% with normal face
- Spectrum of holoprosencephaly face anomalies

- Normal face
- Holoprosencephaly brain
- Cyclopia with proboscis
- Single eye globe +/- some doubling
- Blind-ending tube instead of nose
- Proboscis located superior to orbit
- Ethrocephaly
- Severe hypotelorism
- Arhinia (no nose) or proboscis
- Proboscis often at orbit level
- Cebocephaly
- Hypotelorism
- Nose with single nostril

- Spectrum of midface cleft lip/palate
- Midline CL/CP
- Bilateral CL/CP
- Maxillary maxillary agenesis
- Isolated midline CP

3D helps delineate midface anomalies
- Multiplanar advantages
- Sagittal, coronal, axial images with single volume acquisition
- Soft tissue rendering

Key Facts
- Top Differential Diagnoses
  - Normal face
  - Unilateral cleft lip and palate
  - Midface mass
- Pathology
  - Holoprosencephaly (50-60% with aneuploidy)
  - Holoprosencephaly associated with diabetes
- Clinical Issues
  - T18, T13, T21 association
  - Alcohol (fetal alcohol effects)
- Diagnostic Checklist
  - Look at fronto-nasal bone angle on profile views
  - Recommend genetic counseling
- Recognizable fetal face
- Bone rendering
- Visualization of sutures, bone detail
- MRI helpful for brain anomalies
- Holoprosencephaly spectrum
- Can detect subtle anomalies missed with ultrasound

Imaging Recommendations
- Best imaging tool
  - We routinely look at face for "take home" pictures
  - Look carefully at nasal bone
  - Orb/face/maxilla/mandible relationships
- Protocol advice
  - Look for other anomalies
  - Markers for aneuploidy/syndromes
  - Consider fetal DK
  - Anytime midline facial defects seen
  - Mild holoprosencephaly can be missed

DIFFERENTIAL DIAGNOSIS

Normal face
- Mid-sagittal plane
  - Assess fronto-nasal bone angle
  - Nasal bone can be measured
  - Maxilla in front of mandible
- Coronal plane-smart view
  - 2 nasal maxes + intact upper lip
- Axial views
  - 2 orbits normally spaced
  - Can measure orbital biometry
  - Intact alveolar ridge of palate

Unilateral cleft lip and palate
- Cleft is lateral to philtrum
- Most common is CL + CP
- Palate often dysplastic, if large CP
- Abnormal profile
- Premaxillary protrusion
  - Similar to unilateral CL/CP profile
- Depressed maxilla with CL
- More likely than depressed nasal bridge
**MIDFACE ANOMALIES**

- Associated midface hypoplasia common

### Midface mass
- Rare
- Aggressive large tumors
- Teratoma, rhabdomyosarcoma, 
  ▪ Neural origin
  ▪ Can grow through nose (tracheal obstruction)
- Frontal encephalocele
- Bone defect with herniated brain
- Rhabdomyosarcoma
  ▪ VR helpful to slow extension of tumor

### PATHOLOGY

#### General Features
- Genetics
  ▪ Midface hypoplasia
  ▪ T21, T13, Iq deletion
- Many syndromes
  ▪ Holoprosencephaly (50-60% with aneuploidy)
  ▪ T13 (2/3)
  ▪ Trisomy 18 (Patau), triploidy, monosomy 21
  ▪ 3p-, 11p-, 18q-
  ▪ 12 different chromosome loci identified
  ▪ Sonic hedgehog gene (SHH)
  ▪ SHH mutation in 33% of facial cases
- Etiology
  ▪ Normal facial embryology
  ▪ Five facial prominences fuse by 10 wks
  ▪ Unpaired frontonasal process contains orbits
  ▪ Paired maxillary swellings
  ▪ Paired mandibular swellings
  ▪ Midface hypoplasia
  ▪ Inнерmaularity process hypoplasia
  ▪ Affects nasal maxilla and nose
- Holoprosencephaly
  ▪ Precerebral mesenchyme fails to induce cleavage
  ▪ Failure of prosencephalic cleavage
  ▪ Failure of frontonasal process cleavage
  ▪ Abnormal mid face migration and cleavage
- Epidemiology
  ▪ 1:16,000 births with holoprosencephaly
  ▪ 1250 terminated pregnancies
- Associated abnormalities
  ▪ Holoprosencephaly associated with diabetes
  ▪ 13% risk for fetuses of diabetic mothers

### CLINICAL ISSUES

#### Presentation
- Most common sign/symptom
  ▪ Abnormal maternal screen result
- T21, T13, T21 association
- Incidentally identified at time of routine scan
- Other signs/symptoms
  ▪ Teratogens associated with midface hypoplasia
  ▪ Alcohol and alcohol effects
  ▪ Carbamazepine (Tegretol)
  ▪ Coumadin
  ▪ Thyroxine (Dilantin)
  ▪ Vitamin acid
  ▪ Teratogens associated with hypoprosencephaly
  ▪ Alcohol
  ▪ Betaine acid

### Demographics
- Age: Teratologies associated with advanced maternal age

#### Natural History & Prognosis
- Midface hypoplasia
  ▪ Depends on associated findings
  ▪ Mild isolated cases with good prognosis
  ▪ Holoprosencephaly
  ▪ Splitter common
  ▪ Lowbirth infants with short lifespan
  ▪ Severe feeding, occlusions
  ▪ Seizure disorder

### Treatment
- Maxillary advancement surgery
- Gradual lengthening of bone
- Soft tissue maxillary expansion
- Significant relapse rates

### DIAGNOSTIC CHECKLIST

#### Consider
- fetal MRI for equivocal/difficult cases
- fetal face often semi- well
- Subtle brain anomalies detectable

#### Image Interpretation Pearls
- Look at fronto-nasal bone angle on profile view
- Maxilla/mandible relationship
- Use 3D ultrasound if face looks atypical
- Recomended genetic counseling
- Identify familial syndromes
- Antenatal

### SELECTED REFERENCES
**Typical**

*Left* Sagittal ultrasound shows midline malformations of the nasofrontal or nasal bone, midline hypoplasia (arrowed areas) are characteristic features. *Right* Clinical photograph of a fetus with midline hypoplasia and a hypoplastic maxilla. The nose is relatively hypoplastic and the midline is small. The hypoplasia is a blind-ending tube.

*Left* Sagittal ultrasound shows severe midline malformations associated with trisomy 13. Associated depressed nose and small maxilla are common features of midline hypoplasia.

**Typical**

*Left* Sagittal ultrasound shows a markedly abnormal fetal profile secondary to the presence of a proboscis (arrowed areas). Instead of a nose, this fetus has a proboscis. *Right* Clinical photograph of another fetus with trisomy 13 shows a proboscis and a hypertelorism (arrows), which is abnormally elongated and the smooth is small. The proboscis is a blind-ending tube.

*Left* Sagittal ultrasound shows midline malformations and hypoplasia (arrowed areas) in another fetus with trisomy 13. Associated depressed nose and small maxilla are common features of midline hypoplasia.
TERMENOLGY

Definitions
- Eyes too close together

IMAGING FINDINGS

General Features
- Best diagnostic clue: Decrved interocular distance
- Morphology: Variable from mild to cyclopia

Ultrasoundographic Findings
- Orbital bionetry
  - Ocular diameter
  - Orbital width
  - Measurement of bony orbit
  - Interocular diameter (IOD)
  - Measurement between orbits
  - From inner-to-inner bony margin
  - Binocular diameter (IOD)
  - Measurement of both orbits
  - From outer-to-outer bony margin
  - Axial image of orbits for bionetry
    - At Thalamus/bicavernous diameter (BPD) level
    - Cortical face view helpful
    - Hypotelorism often more recognizable
    - Normal ocular distances

DDx: Hypotelorism

- Normal Eyes
- Proptosis
- Proptosis
- Hypoposphate
HYPOTELORISM

Terminology
- Eyes too close together

Imaging Findings
- IOF is diagnostic
- Holoprosencephaly is major association
- Face predicts the brain
- Cyclopia most extreme type
- Proptosis (tube-like nose) superior to orbit
- Ethmocephaly: Severe hypotelorism with nose or proboscis
- Cephalocele: Severe hypotelorism, nose with single nostril
- Often with median cleft palate
- Microcephaly
- Trigonocephaly (craniosynostosis)

○ Cyclopia most extreme type
  - Single bony orbit
  - Variable amounts of globe doubling
  - Orbit often covered by dysplastic tissue
  - Proptosis (tube-like nose) superior to orbit
  - Most often with aboral holoprosencephaly
  - Ethmocephaly: Severe hypotelorism with nose or proboscis
  - Orbits may touch
  - Cephalocele: Severe hypotelorism, nose with single nostril
  - Mild hypotelorism
  - Less severe nasal anomalies
  - Often with median cleft palate
  - Normal orbits
  - Brain does not always predict face
  - 28% of holoprosencephaly have normal face
  - Other detectable associations with hypotelorism
  - Microphthalmal
    - Very small head/circumference (HC)
    - HC < 2 standard deviations/gestational age
  - Occipital bossing often symmetric but 4
  - Associated (facial) anomalies common
  - Multifactorial etiology
  - Trigonocephaly (craniosynostosis)
  - Metopic suture fusion
  - Forehead is pointed
  - Triangle appearance from top of head
  - Meckel-Gruber syndrome
  - Posterior encephalocele
  - Cystic kidneys
  - Polydactyly
  - Autosomal recessive inheritance
  - Myotonic dystrophy
  - Absent or reduced fetal movement
  - Extremity contractures
  - Polyhydramnios
  - Trisomy 13
  - Holoprosencephaly
  - Median cleft lip/palate
  - Polydactyly
  - Cystic kidneys

Key Facts

Top Differential Diagnoses
- Anophthalmia

Pathology
- Trisomy 13 (T13), trisomy 18 (T18)
- Chromosome deletions
- Meckel-Gruber syndrome

Clinical Issues
- Maternal alcohol
- Maternal phenytoin (ATD)

Diagnostic Checklist
- Fetal MR for all cases
- Hypotelorism rarely seen in isolation
- Use 3D ultrasound if face looks atypical

○ Cardiac anomalies
○ Intrauterine growth restriction
○ Trisomy 18
○ Choroid plexus cysts
○ Clenched hands
○ Cardiac anomalies
○ Omphalocele
○ Intrauterine growth restriction
○ 3D helps define facial features
○ Cleft lip/palate
○ Craniosynostoses
○ Abnormal head shape
○ Can see sutures best with 3D
○ MR helps show brain morphology
○ Holoprosencephaly is a spectrum

Imaging Recommendations
- Best imaging tool
- Axial orbit view
- Measure IOF and BOF
- Compare with nomograms
- Coronaal face views
- Facial clefts
- Identify 2 bony orbits
- Profile view
- Probes
- Protocol advice
- Careful evaluation of brain
- Holoprosencephaly can be subtle
- Consider fetal MR
- Genetic counseling
- Many associated syndromes
- Anexaglyidy

DIFFERENTIAL DIAGNOSIS

Anophthalmia
- Almost globe
  - Optic vesicle fails to form
- May mimic cyclopia
- Normal globe is not midline
- Orbit in normal paraorbital position
HYPOTELORISM

- Unilateral or bilateral

Hyperelorism
- Eyes too far apart
- T IOI is best diagnostic clue
- ROD may be normal
- Often associated with other anomalies
  - Congenital heart disease
  - Anomalies of the mandible
  - Midline facial clefts
  - Facial clefts

Proposis
- Persistent eyes
- Forward displacement of globe
- Associated with many syndromes
  - Microphthalmia syndrome
  - Apert syndrome
  - Treacher-Collins syndrome
  - Zare prenatal diagnosis

Dacrocystocele
- Dilatation of lacrimal drainage system
- Cyst medial to orbit
- Can be large and mimic 2nd orbit
- Unilateral or bilateral
- Most resolve spontaneously in utero

PATHOLOGY

General Features
- Genetics
  - Trisomy 13 (T13), trisomy 18 (T18)
- Chromosome deletion
  - Moesik-Grunder syndrome
  - Autosomal recessive
  - Autosomal dominant
  - Coffin-Siris syndrome
  - Williams syndrome
- Sporadic inheritance
- Embryology
  - Five facial prominences fuse by 13 wks
  - Unpaired frontonasal process coalesces orbits
  - Fused maxillary swellings
  - Fused maxillary swellings
  - Holoprosencephaly
  - Pronecephaly, microcephaly
  - Failure of prosencephalon cleavage
  - Failure of frontonasal process cleavage
  - Abnormal midface migration
- Epidemiology
  - 1:16,000 births with holoprosencephaly
  - 1:250 terminated pregnancies

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - Brain anomaly + hypotelorism
  - Most often holoprosencephaly
  - Abnormal nuchal cord screen result
  - T13, T18
- Other signs/symptoms
  - Malformations
  - Holoprosencephaly in % fetuses
  - Malformations of the brain (PKU)
  - Poor control associated with anomalies
  - Microcephaly
  - Hypotelorism
  - Congenital heart disease
  - Intracranial growth restriction

Demographics
- Age
  - Trisomies associated with advanced maternal age
  - ≥ 35 yo at time of delivery

Natural History & Prognosis
- Depends on associated anomalies
- Severe hypotelorism with severe prognosis
- Holoprosencephaly
  - Stillbirth common
  - Liveborn infants with short lifespan
  - Severe feeding difficulties
  - Seizure disorders

DIAGNOSTIC CHECKLIST

Consider
- Fetal MRI for all cases
- Subtle brain anomalies detectable

Image Interpretation Pearls
- Hypotelorism rarely seen in isolation
- Recommend genetic counseling
- Use 3D ultrasound if face looks atypical

SELECTED REFERENCES
HYPOTELORISM

IMAGE GALLERY

Typical

(Left) Coronal ultrasound of the face shows midline cheek palate (open arrows) and small hypotelorism (arrow). Mild fusion of eye and palate is associated with both midface hypoplasia and hypotelorism. (Right) Clinical photograph shows median cleft palate (perinasal agenesis), a flattened dysmorphic nose and mild hypotelorism. The interocular distance (arrows) is less than the orbital diameter (open arrows).

Typical

(Left) Sagittal ultrasound shows characteristic separation (curved arrows) and diffuse anasarca (open arrow) in a 16 wk fetus with trisomy 18. A coronal view of the face inset shows severe hypotelorism (arrows). Hypotelorism can be diagnosed early in pregnancy with transvagal ultrasound. (Right) Clinical photograph of a neonate with syndactyly, hand renal creases and mild hypotelorism. Note the open mouth and mandible anomalies.

Typical

(Left) Coronal ultrasound shows cleft lip (arrow) in a partially duplicated globe in a single orbit and proptosis is noticed (arrow) in this with trisomy 18 and holoprosencephaly. Open arrow points to a 2 cm umbilical cord. (Right) Clinical photograph of cleft lip shows the lateral finding proptosis shared in the right orbit. A small amount of choroidal tissue covers the globe.
HYPERTelorism

Terminology

Definitions
- Eyes too far apart

Imaging Findings

General Features
- Best diagnostic clue: increased interocular distance

Ultrasoundographic Findings
- Normal orbit biometry
  - Orbital width
  - Measurement of bony orbit
  - Interocular diameter (IOD): Measurement between orbits
  - Biocular diameter (BOD): Measurement from outer-to-outer orbit
- Measurement technique
  - Often first noticed on coronal face view
  - Measurement best performed in axial plane at biparietal diameter (BPD) level
- Normal ocular distances
  - "Rule of thirds"
  - BOD can be divided into thirds
  - Lateral thirds are orbits

DDX: Abnormal Orbits

- Hypotelorism
- Hypertelorism
- Proptosis

- Middle third is IOD
  - Normal IOD = single orbital width
  - Orbital nomograms in literature
  - I1 wk to term percentiles available
- Hypertelorism diagnosis
  - IOD more prominent feature than BOD
  - IOD > 95th percentile
  - BOD often just < 95th percentile
- IOD > 0.45 or diameter easier to make diagnosis
- Isolated primary hypertelorism rare
- Many associations
- Craniosynostosis
  - Premature fusion of skull sutures
  - Deformed skull and face
  - +/- Other skeletal dysplasia
- Craniofrontonasal dysplasia
- Narrow face, snout (acnasphalyh)
- Conotruncal heart anomaly
- Hypertelorism + midline facial clefting
- Apert syndrome
- Acrosyndactyly type 1
- Flat palate with hypertelorism
- Conotruncal heart anomaly
- Acnasphaly, high forehead
- Brachycephaly (flat occipital)
- Synostosis is key feature
- Autosomal dominant
- Carpenter syndrome
HYPERTelorISM

**Imaging Findings**
- Intercocular diameter (IOD): Measurement between orbits
- Binocular diameter (BOD): Measurement from outer-to-outer orbit
- "State of thirds"
- BOD can be divided into thirds
- Lateral thirds are orbits
- Middle third is IOD
- Normal IOD > single orbital width
- IOD more prominent feature than 1 BOD
- Isolated primary hypertelorism rare
- Many associations
- Craniosynostosis
- Anterior encephalocele
- Midline facial mass (displaces orbit laterally)

**Key Facts**
- Agniesz of corpus callosum
- Median cleft syndrome
- Chromosome abnormalities
- 3D US helpful to show associated face anomalies

**Top Differential Diagnoses**
- Pynotosis

**Clinical Issues**
- Antiepileptic drugs can cause hypertelorism
- Prognosis grim if other severe anomalies present

**Diagnostic Checklist**
- Orbital biometry when facial defects seen
- 1/2 of all isolated facial defects are missed
- 1 BOD is not best determinant of hypertelorism
- IOD > 95th percentile is best definition
- Often genetic counseling and amniocentesis

**Imaging Recommendations**
- Best imaging tool
- Axial view through fetal orbits
- Most accurate measurements
- Coronal face view
- Can still compare IOD with BOD
- 3D ultrasound
- Recognizable facial features
- Protocol advice
- Careful evaluation of fetal brain when facial anomalies seen
  - "The face predicts the brain"
- Compare orbital measurements with nonograms
- Can detect subtle hypertelorism
- 3D helpful
- Craniosynostosis
- Other facial anomalies
- Consider fetal MR to rule out subtle frontal encephalocele, if no other obvious cause
- Measure long bones
- Associated skeletal dysplasia
- Genetic counseling
- Amniocentesis
- Chorionic villus sampling

- Acrocephalosynostaly type 2
- Similar to Apert
- Polydactyly
- Cardiac defects
- Duophalaloele
- Autosomal recessive
- Crouzon syndrome
- Craniofacial dysostosis type 1
- Coronal suture synostosis
- Midface hypoplasia
- Occular proptosis
- Hypertelorism > hypertelorism
- Thanatophoric dysplasia
- Severe skeletal dysplasia with craniosynostosis
- Cloverleaf skull
- Displaced eyes
- Anterior encephalocele
- Herniation of intracranial contents via bony defect
- May contain brain or fluid/meninges
- MRI helpful to show involved tissue
- Bony defect best seen on axial views
- Frontal, ethmoid, sphenoid
- Variable size
- Small encephaloceles can be subtle and missed
- Midline facial mass (displaces orbit laterally)
- Extremely rare
- Often aggressive and grow very large
- Rhabdomyosarcoma
- Retinoblastoma
- Epignathus
- Oral teratoma
- Agents of corpus callosum
- Venticle findings
- Colpocephaly with splaved frontal horns
- Hypertelorism often mild finding
- Variable prognoses
- Associated with other syndromes
- Median cleft syndrome
- Median facial clefts
- Eyes displaced laterally
- Chromosome abnormalities
- Turner syndrome
- Cystic hygroma is hallmark finding
- Trisomy 13
- Holoprosencephaly is hallmark finding
- Hypertelorism > hypertelorism
- Midline cleft palate associated with hypertelorism
- MRI
  - Helpful in delineating other cranial anomalies
  - Agniesz of corpus callosum
  - Brain involvement with frontal encephalocele
  - Facial features often seen well
  - 3D US helpful to show associated face anomalies
  - Cleft lip/palate
  - Mandibular anomalies
**DIFFERENTIAL DIAGNOSIS**

- Exophytic orbits
- Often associated with hypertelorism
- Associations
  - Treacher-Collins syndrome
  - Craniosynostosis
  - Orbital cyst or mass

**Azopthalminia**
- Absent globe
- Optic vesicle fails to form
- Unilateral or bilateral
- Associations
  - Goldenhar-Soto syndrome
  - Alobar microsomia
  - Trisomy 13
  - Microphthalmia more common
  - Lens syndrome
  - X-linked microphthalmia

**Hypotelorism**
- Eyes too close together
  - > 1 ODD
  - > 1 ODD
  - Associations
    - Holoprosencephaly
    - Tretoxy 13
    - Microphthalmia
    - Mecel-Guchler syndrome

**PATHOLOGY**

**General Features**

- Genetics
  - Turner syndrome
  - Trisomies
  - Translocations
  - Gene deletions
- Etiology
  - Normal eye embryology
  - Divergica of forehead
  - Optic cup migrates to surface
  - Ectoderm thickens to form lens
  - Eyes initially laterally displaced
  - Normal face embryology
  - Five facial prominences fuse by 10 weeks
  - Unpaired frontonasal process (contains orbit)
  - Paired maxillary swellings
  - Paired maxillary swellings
  - Hypotelorism
  - Disrupted eye migration
  - Abnormal fusing of facial prominences
- Epidemiology
  - Children born with cranofacial anomalies
  - Hypotelorism in 33%
  - Craniosynostosis in 7%
  - 50% with identifiable syndrome
  - Associated anomalies
    - Facial clefting
    - Craniosynostosis
  - Skeletal dysplasia
  - Hydrocephalus
  - Aneuploidy

**CLINICAL ISSUES**

**Presentation**

- Most common signs/symptoms
  - Rarely seen in isolation
  - Isolated cases often missed
  - Orbits are not part of routine exam
  - In association with other anomalies
  - Often severe craniofacial anomalies
- Other signs/symptoms
  - Antiepileptic drugs can cause hypertelorism
  - Fasudilin (Dilantin)
  - Caesarean section (Tegretol)
  - Valproic acid
  - Phenoxibin

**Natural History & Prognosis**
- Prognosis grimm if other severe anomalies present

**Treatment**
- Laxellia osteotomy + rigid fixation
- Orbital rim and wall reconstruction
- Intracranial osteotomy may be necessary

**DIAGNOSTIC CHECKLIST**

**Consider**

- Orbotic biopsy when facial defects seen
- Routine evaluation of eyes at 2nd trimester screen
- 1/2 of all isolated facial defects are missed

**Image Interpretation Pearls**

- Distance between orbits approximates orbit diameter
  - Only enough room for a "red eye between eyes"
- > 1 ODD is not best determinant of hypertelorism
- > 1 ODD > 95th percentile is best definition
- Use transvaginal ultrasound (TVUS) for early diagnosis
- Nomograms for 1-6 weeks per TVUS available
- Other genetic counseling and amniocentesis

**SELECTED REFERENCES**

1. Ma X et al: Surgical correction of orbital and periocular dystrophiae using lateral and inferior osteotomies in both orbital rim and wall. J Craniofac Surg. 16:11;144-9, 2005
HYPERTelorISM

IMAGE GALLERY

Typical

(Left) Coronal ultrasound shows hypertelorism (shared broadsided orbits) and unusual frontal skull shape (arrows) secondary to craniosynostosis in case of Apert syndrome.

Hypertelorism is often associated with craniosynostosis, regardless of cause. (Right) Clinical photograph of a child with Carpenter syndrome shows hypertelorism (arrow) as well as a flat face, astigmatism, high forehead, and brachycephaly.

Typical

(Left) Coronal ultrasound shows hypertelorism secondary to frontal encephalocoele. The distance between the orbits (arrows) is greater than the orbital diameter (open arrows).

(Right) Coronal T2WI MR shows asymmetric hypertelorism as one globe (arrow) point to both eyes is displaced by a large fronto-ethmoid mass (open arrows). Typical of most facial tumors. This chalazion orcoma was large and aggressive.

Typical

(Left) Coronal T2WI MR of a 29 week fetus with agenesis of the corpus callosum, shows hypertelorism (arrows). The distance between the eyes is greater than the orbital diameter.

(Right) T1WI MR of the brain in the same fetus shows callopathy (arrows), splintered frontal horns (open arrows) secondary to a high riding 3rd ventricle (curved arrows) and complete absence of the corpus callosum.
**ORBITAL TUMORS**

**TERMINOLOGY**

**Definitions**
- Group of rare tumors, which may involve the orbit
  - Retinoblastoma
  - Teratoma
  - Soft tissue sarcomas

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue: Unilateral proptosis

**Ultrasoundographic Findings**
- Cystic or solid lesion may not be visible
- Soft tissue anatomy may be distorted or destroyed
- Predominantly solid masses
- Calcifications virtually pathognomonic of teratoma
- Most masses vascular by Doppler
- Polyhydramnios may be present

**Imaging Recommendations**
- MRI recommended to better evaluate intracranial contents
- Rule out brain abnormality causing orbital mass
- Evaluate for extension of orbital tumor into brain

**DIFFERENTIAL DIAGNOSIS**

**Dacryocystocele**
- Obliteration of nasolacrimal duct resulting in cystic dilatation of proximal duct
- Located inferomedial to orbit, may be bilateral
- Does not displace globe
- Average size 7-13 mm
- Atelectasis or with low-level echoes
- No flow seen with Doppler
- Generally presents after 30 weeks
- Benign self-limited entity, which usually resolve in first 6 months of life

**Facial hemangioma**
- May occur around orbit
- Globe not displaced, honey orbit normal
- Homogeneous echogenicity
- Flow often seen with color Doppler

**Nasopharyngeal (NP) teratoma**
- Fascinating masses involving mouth and nose

**Amniotic band syndrome**
- "Slash defects" of face
- Multiple body parts often involved

**Frontal encephalocele**
- Midline, between orbits

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**DDx: Orbital Mass**

- NP Teratoma
- Frontal Encephalocele
- Disciform osteoma
- Midline

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**Sagittal color Doppler ultrasound of the left face shows a vascular soft tissue mass. No globe could be seen on the involved side. An MRI was performed to better evaluate anatomy.**

**Axial T2W MRI through the level of the orbit shows a fusiform soft tissue mass (arrow) emanating from the left orbit. The right eye (curved arrow) is normal. A retinoblastoma was diagnosed at autopsy.**
**ORBITAL TUMORS**

**Terminology**
- Group of rare tumors, which may involve the orbit

**Imaging Findings**
- Best diagnostic clue: Unilateral proptosis
- Globe of involved orbit may not be visible

**Top Differential Diagnoses**
- Barrettes uveitis
- Facial hemangiomata

**Proboscis**
- May be confused with odontal mass
- Flexy midline mass above orbit
  - Usually single orbit (cyclopia) or severe hypotelorism
  - Occurs with alobar holoprosencephaly

**PATHOLOGY**

**General Features**
- Retinoblastoma:
  - Malignant growth of neuroepithelial cells of retina
  - Deletion or mutation of chromosome 13q14
  - Prenatal testing available
  - May be bilateral
  - Leukokoria (white pupillary reflex) seen on physical exam
- Teratoma
  - Complex cystic/solid mass
  - Calcification diagnostic but not always visible
  - Other tumors
  - Rhabdomyosarcoma
  - Rhabdoid tumor
  - Neuroblastoma

**CLINICAL ISSUES**

**Presentation**
- Most common signs/symptoms: Prenatally diagnosed cases have all been large masses

**Natural History & Prognosis**
- Depends largely on size and extent of tumor
- Retinoblastoma
  - Optic nerve involvement and extraorbital spread have poor prognosis
- Bilateral neonatal tumors usually lethal
- Teratoma benign but may cause extensive damage from large size
- Sarcomas usually lethal

**Diagnosis**
- Nasopharyngeal (NP) teratoma

**Pathology**
- Retinoblastoma
- Teratoma

**Diagnostic Checklist**
- Unilateral proptosis should prompt search for retrobulbar mass
- Always evaluate brain carefully

**DIAGNOSTIC CHECKLIST**

**Consider**
- Prenatal testing if a parent has a history of retinoblastoma

**Image Interpretation Pearls**
- Unilateral proptosis should prompt search for retrobulbar mass
- Always evaluate brain carefully

**SELECTED REFERENCES**

**IMAGE GALLERY**

![Image](image_url)
TERMINOLOGY

Definitions
- Mass arising from fetal scalp

IMAGING FINDINGS

General Features
- Asymmetric soft tissue mass over fetal scalp
- Hemangioma
  - Heterogeneous echogenicity
  - Solid or mixed cystic/solid
  - Color Doppler shows diffuse network of vessels
- MRI Findings
  - T1WI: Heterogeneous low to intermediate signal
  - T2WI: Heterogeneous high signal
- Flow voids seen due to vascular nature of tumor
- Lymphangioma
  - Multilocular cystic mass
  - No internal flow
- Epidermoid cyst
  - Well-circumscribed cyst
  - Between skull bone and scalp surface
  - No bony defect
  - Acute cephalohematoma
  - Midline
  - Intraparietal or occipital

○ May appear cystic or solid
○ May decrease in size over duration of pregnancy

Imaging Recommendations
- Beware pitfalls in diagnosis of scalp mass
  - Scalp edema
    - Uniform thickening of scalp skin
    - Usually a manifestation of hydrops
    - Look for fluid elsewhere: pericardial, pleural, ascites
  - Fetal hair
    - Fetal hair may be long, thick in third trimester
    - No internal flow
  - Strands will float in amniotic fluid
  - Cystic hygroma
    - Septated cystic mass arising from posterior fetal neck, rather than scalp
    - Often associated with hydrops
    - Strong association with Turner syndrome and Down syndrome
    - Look for other findings to confirm diagnosis
  - Umbilical cord
    - Coils of cord may be seen beside scalp or wrapped around fetal neck
    - Color Doppler shows umbilical vessels, clarifies true etiology of apparent mass
  - If mass continued, careful anatomic survey

DDx: Pitfalls In Diagnosis Of Scalp Mass

- Cystic Hygroma
- Scalp Ectasia
- Nuchal Cord
SCALP MASSES

Key Facts
- Clinical Issues
  - Some masses involute over course of pregnancy
  - Outcome depends on associated malformations more than on lesion itself
  - X-ray not indicated if isolated finding
  - Large mass may be an indication for cesarean section

- Diagnostic Checklist
  - Always check brain anatomy carefully when a scalp mass is identified
  - Abnormal venous sinus anatomy strongly suggests arteriovenous malformation
  - Scanning angle may give false impression of an underlying calvarial defect
  - Scalp edema and fetal hair are common pitfalls in diagnosis

Top Differential Diagnoses
- Encephalocoele

Pathology
- Causes of fetal scalp masses are many and varied
- Hemangioma
- Lymphangioma
- Epidermoid cyst
- Dermoid
- Fibroepidermatoic, myofibroepidermatoic
- Arteriovenous malformation

- Reported association with hydrocephalus, duplex renal system, hand and genital anomalies
- Consider MRI for further anatomic delineation
- Look for venous malformations associated with arteriovenous malformations
- Sagittal sinus duplication
- Falx sinus in addition to, or replacing, straight sinus
- Falx sinus has ascending course toward skin lesion
- Most important role of MRI is to exclude encephalocoele

DIFFERENTIAL DIAGNOSIS

Encephalocoele
- Neonate tube defect
- Brain or meninges protrude through calvarial defect

Bone tumor of skull vault
- May be hard to differentiate from scalp lesion in fetus
- Look for intra + extracranial extension
- Report case of cavernous angiomata of temporal bone with successful resection

Meningeal tumor
- Intracranial, extra-axial location
- Reported case of meningeal hemangiopericytoma with successful resection

PATHOLOGY

General Features
- Genetics
  - Lymphangioma may be associated with Turner syndrome
  - Usually cystic hygroma of neck, but may involve scalp
- Etiology
  - Causes of fetal scalp masses are many and varied
- Hemangioma
- Lymphangioma
- Epidermoid cyst
- Dermoid
- Mesenchymal neoplasms
- Fibroepidermatoic, myofibroepidermatoic
- Lipomatous hamartoma
- Arteriovenous malformation
- Sequestrated meningocele
- Heterotopic neural tissue
- Metastasis
- Epidemiology
- Rare: True incidence unknown
- Most series of scalp masses in literature are postnatal
- Only case reports of prenatal diagnosis
- Associated abnormalities
  - Arteriovenous malformations associated with:
    - Local scalp alopecia
    - Intracranial venous anomaly, if cephalocoele above temporal herpetic
    - Brain malformations which may be clinically occult in neonate (e.g. Walker-Warburg syndrome)
    - One series: 13% hydrocephalus, 7% midventricularholoprosencephaly
    - Another series 25% brain "malformation" (anomalous venous sinuses were included, as malformations)
- Encephalocoele-cystic intracranial lipomatosis
- Epidermatoic linitis plastica scalp, eyelids and globe
- Unilateral porencephalic cysts
- Central nervous system lipomas
- Etiology
  - Arteriovenous malformations are a form of posterior dysraphism
  - Arteriovenous malformations during 3rd-5th weeks of gestation
  - Scalp masses can arise from any layer of embryonic tissue
  - Mesenchyme
    - Hemangioma, lymphangioma, lipoma, ectoderm
SCALP MASSES

- Epidermoid cyst, dermoid
  - Neuroectoderm
  - With bone defect. Atretic cephalocoele, leptomeningeal cyst
  - Without bone defect. Exotic meningioma, heterotopic brain tissue

Gross Pathologic & Surgical Features
- Dermoid cyst
  - Keratinizing squamous epithelium
  - Hair and glandular tissue
- Atretic cephalocoele
  - May contain cerebrospinal fluid, finous tissue or atretic brain tissue
- Squeezed meningescles
  - Meningothelial cells
  - Stain with vimentin, epithelial membrane antigen

CLINICAL ISSUES

Presentation
- Scalp mass detected on antenatal sonography

Natural History & Prognosis
- Depends on lesion
  - Some masses involute over course of pregnancy
  - Hemangioma
    - If significant flow → high output cardiac failure → hydrops
    - Tend to enlarge at birth
    - Enlargement may precipitate natalar heart failure
  - Emergency intervention required to obliterate systemic shunt
  - Atretic cephalocoele
    - May become infected → meningitis or abscess
  - Outcome depends on associated malformations more than on lesion itself
  - Venous sinus anomalies of little significance
  - Walker-Warburg syndrome → most infants die within first year of life, 25% recurrence risk
  - Encephalocele/craniofacial lipoatromatosis
  - Meneninx
  - Developmental delay
  - Metastasis
    - All reported cases of metastatic maternal adenocarcinoma to fetal scalp did well with wide local resection
    - Some instances of local recurrence requiring re-excision
  - Scalp reconstruction required skin grafts/soft tissue flaps
  - Maternal prognosis poor

Treatment
- Karyotype not indicated & isolated finding
  - Consider for scalp lymphomas, which has been described with Turner syndrome
  - Large mass may be an indication for cesarean section
  - Risk of dystocia
  - Risk of injury to mass, with potential extravasation if vascular
    - Hemangioma
  - Premature surgical resection
  - Atretic cephalocoele
    - Often covered by sloped scalp
    - Must be excised due to risk of infection
  - Neurosurgical evaluation, not simple plastic surgery
  - 75% cases in one series had associated brain malformation
  - Dermoid/epidermoid
  - Elective resection
  - Excellent prognosis

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls
- Always check brain anatomy carefully when a scalp mass is identified
- Abnormal venous sinus anatomy strongly suggests atretic cephalocoele
- Biopsy of pitfalls in diagnosing scalp mass
- Scanning angle may give false impression of an underlying calvarial defect
- Scan in multiple planes with and color Doppler for confirmation
- Scalp edema and fetal hair are common pitfalls in diagnosis

SELECTED REFERENCES
SCALP MASSES

IMAGE GALLERY

Typical

- Axial color Doppler ultrasound shows no vessel flow in a soft tissue mass (curved arrow) overlying the skull. Note the apparent defect (open arrow) in the skull vault echo (arrows) at the level of the mass. (Right) Sagittal ultrasound shows the skull vault (arrows) is intact deep to the mass (curved arrow) including meninges and encephalohemat. The apparent bone defect on the axial view was due to beam refraction.

Variant

- Sagittal T2WI MR from the case above shows a subtle signal change in the paramedian occipital skin (arrow) where the scalp mass had been identified. The brain was normal and no residual scalp mass was found at birth. Small scalp masses may resolve in utero. (Right) Head ultrasonography in a fetus with complex intracranial malformations shows an apparent scalp or skull mass (arrows). MRI showed this to be focal calcified dermal remnant secondary to encephalohemat.

Typical

- Axial NCCT on day one of life shows a hematoma arising from the scalp (curved arrows). The calvarium (white arrows) is intact but remodelled by the large mass. Note the calcifications (black arrows) in the intercranial of the mass. (Right) Cross pathology of the removed hematoma shows multiple vesicle spaces (arrows). Flow is well demonstrated by color Doppler and flow voids may be present on MRI.
**CYSTIC HYGROMA**

**TERMINOLOGY**

**Abbreviations and Synonyms**
- Cystic hygroma (CH)
- Nuchal cystic hygroma
- Cavernous lymphangioma

**Definitions**
- Dorsal and lateral nuchal cyst
  - 2° to jugular vascular-lymphatic anomaly

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue: Multiseptated nuchal fluid
- Location
  - Posterior neck
  - Lateral neck
  - Often with diffuse body wall edema
- Size: Extremely variable
- Morphology
  - Mass-like
  - Many have thin septations

**Ultrasoundographic Findings**
- Posterior/lateral nuchal cyst
- Skin and subcutaneous fluid
- Best seen on axial posterior fossa view
- Sagittal views show extent of edema
- Internal septations
  - Multiple fine linear septations
  - Thick midline septation is nuchal ligament
- Size can be massive
  - Larger than fetal head
  - Can mimic amniotic fluid
- May be only fluid source for amniocentesis
  - Small CH can evolve into thick nuchal fold (7 NF)
  - 1 Nuchal skin thickness without cysts
  - Often precursor to webbed neck
  - Large CH almost never resolves spontaneously
  - Non-institute hydrops common with large hygromas
  - Excess fetal fluid accumulation
  - Fluid in 2 separate areas
  - CH counts as 1 area
  - Anasarca
  - Most often seen with CH
  - Pleural effusion
  - Pericardial effusion
  - Ascites
  - Cardiovascular anomalies often present
  - Aortic arch defects most frequent
  - Aneuploidy in 2/3 fetuses with 2nd trimester CH
  - Turner syndrome
  - Most common
  - Trisomy 21 (T21)

**DDx: Complex Exophytic Neck And Chest Masses**

- Cervical teratoma
- Cervical neurofibroma
- Cystic hygroma
- Lymphangioma
- Encephalocele
Cystic Hygroma

Terminology
- Bursal and lateral nasal cyst

Imaging Findings
- Best diagnostic clue: Multiseptated nuchal fluid
- Multiple fine linear septations
- Thick midline septation is nuchal ligament
- Site can be multiseptated
- Small CH can evolve into thick nuchal fold († NF)
- Non-invasive hydrops common with large lymphomas
- Cardiovascular anomalies often present
- AneuEplody in 2/3 fetuses with 2nd trimester CH
- Turner syndrome
- Trisomy 13 (13T)
- Largest 1st trimester nuchal translucencies seen in Turner syndrome.

Key Facts

Top Differential Diagnoses
- Increased nuchal fold
- Cervical teratoma
- Body/trunk lymphangioma
- Occipital encephalocele

Clinical Issues
- Fetal demise
- Only 9% survive without major morbidity
- Webbed neck from smaller retrosternal lymphomas

Diagnostic Checklist
- Genetic testing when CH seen
- T21 > Turner with 1st trimester CH
- Turner > T21 with 2nd trimester CH
- CH + hydrops with grim prognosis

Imaging Recommendations
- Best imaging tool
  - Second trimester
  - Angled posterior fossa inset
  - Routine NF measurement
  - First trimester NT evaluation
  - Protocol advice
    - First trimester CH
    - Accurately obtain NT
    - Look carefully for septations
    - Offer chorion villus sampling
    - Second trimester
      - Careful exam for additional anomalies
      - Formal fetal echocardiography
      - Rule out hydrops
      - Offer amnioceesis
      - follow-up ultrasound
      - High rates of in utero demise
      - May see other anomalies as fetus grows

DIFFERENTIAL DIAGNOSIS

Increased nuchal fold
- Posterior fetal neck skin thickening
  - Not fluid
- May be byproduct of CH but should not be called CH
- T21 more likely than Turner syndrome
- More likely to be idiopathic
- Better prognosis

Cervical teratoma
- Germ cell tumor
  - Aggressive growth common
  - May be malignant
  - Most often anterior neck
CYSTIC HYGROMA

- Fetal neck often hyperextended
- Associated with airway obstruction
- Solid or mixed solid-cystic mass
  - +/- Calcification

Body/Trunk lymphangioma
- Non-nuchal cystic mass
  - Morphology identical to CH
  - Z to lymphatic channel disruption
- Axillary most common site
- + Upper extremity lymphedema
- Not associated with aneudeficy
- Better prognosis than nuchal CH

Occipital encephalocoele
- Open neural tube defect
- Posterior fossa contents herniate via cranial defect
- Must see calvarial bony defect
- Variable amounts of brain/meninges involved
- Abnormal intracranial anatomy

PATHOLOGY

General Features
- Genetics
  - Normal chromosomes in 26-49%
  - Aneuploidy
    - Turner syndrome
    - T21
    - T18
    - T13
  - Non-aneuploid syndromes
    - Noonan syndrome
    - Multiple pterygium syndrome
    - Apert Syndrome
    - Cornelia & Large syndrome
- Etiology
  - Normal embryology
  - Lymphatics form outgrowth of venous system
  - Paired jugular venous buds – lymphatic sacs
  - Communication established by 40 days
  - CH
  - Failed/delayed venous – lymphatic connection
- Hydrops
  - Fluid overload from lymphatic failure
- Epidemiology
  - 1:200 spontaneous abortions
  - 1:600 low-risk pregnancies
  - 1:1,750 live births
  - Associated abnormalities
    - Cardiovascular anomalies
    - Large variety of other anomalies
    - Mostly associated with aneuploidy/syndromes

Gross Pathologic & Surgical Features
- Cavernous lymphatic spaces with flattened endothelial lining

CLINICAL ISSUES

Presentation
- Incidental finding or 1st or 2nd trimester ultrasound
- Non-immune hydrops
- Fetal demise
- Abnormal maternal serum-quadruple test screen
  - 53% detection rate for Turner syndrome
  - 80% detection rate for Trisomy 21
- Matrue CH can mimic amniotic fluid
- Can tap CH for amniocentesis if necessary

Demographics
- Age
  - T21 associated with advanced maternal age (AMA)
  - AMA = 35 at time of delivery
  - Turner syndrome not associated with AMA
- Gender: F > M

Natural History & Prognosis
- Spontaneous pregnancy failure rate
  - 12% in 2-T21 and 2nd trimester CH
  - Only 9% survive without major morbidity
- Webbed neck from smaller resolved hygroma
- Hydrops associated with grim prognosis
  - 80-90% demise
  - 10-20% resolve in uterus
  - More likely if small CH
  - Often in expulsive fetuses

Treatment
- Complete surgical resection
  - Often difficult 2° to infiltrative nature of CH
  - Post surgical recurrence (15%)
  - Screening agents
    - Injected directly into cysts
    - Most often for recurrence
    - Bleomycin / interferon
- OK-433
- Instructed streptococcal organism

DIAGNOSTIC CHECKLIST

Consider
- Genetic testing when CH seen

Image Interpretation Pearls
- T21 > Turner with 1st trimester CH
- Turner > T21 with 2nd trimester CH
- CH + hydrops with grim prognosis

SELECTED REFERENCES
(Left) Axial ultrasound through the back of the neck in a second trimester fetus shows a multiseptated cystic mass (arrow) just behind the placenta (4). The open view pain is the cervical spine. (Right) Gross pathology of a cystic hygroma shows multiple septations inside the hygroma (arrows). CH are smooth cystic masses, which are often multi-knobbed and are lined by a single layer of flattened endothelium.

(Typical) Two axial images obtained at 16 wks shows a small, septated cystic hygroma (calipers) and abnormal in a fetus with trisomy 21. No other anomalies were seen and amniocentesis was recommended based on this finding alone. (Right) Sagittal ultrasound of the same fetus at 24 weeks shows increased nuchal fold (arrows). The CH that resolved and residual skin thickening is seen.

(Variant) (Left) Ultrasound shows marked axilla-4 (arrows) and CH (open arrows) in a 35w GD with T21. The extent of tachypnea in this case is unusually severe. CH, however, is often associated with hydrocephalus. (Right) Ultrasound shows a small septated CH (arrow) and cleft palate (open arrows point to the cleft) at 16 wks with trisomy 13. CH is now sized with T21, 21, and T22 and many syndromes.
GOITER

Septal T2WI MR shows fetal goiter (curved arrow) secondary to stimulation by maternal antibodies. The esophagus (spotted) is distorted due to esophageal compression, which impaired swallowing.

Clinical photograph of a neonate who was successfully treated with intramuscular injections of Synthroid for hypothyroidism and goiter. Rebound skin and solid goiter remains but the iodine was euthyroid.

TERMINOLOGY

Definitions
- Enlargement of fetal thyroid
- Fetal goiter may be due hyper- or hypothyroidism
- Fetal hypothyroid state due to maternal thyroid stimulating antibodies
- Fetal hypothyroid state most commonly due to maternal anti-thyroid medication or endemic iodine deficiency

IMAGING FINDINGS

General Features
- Best diagnostic clue: Anterior neck mass of homogeneous echogenicity

Ultrasoundographic Findings

- Neck mass
  - Maintains thyroid contour
  - Normative data available for thyroid size at various gestational ages
- Mass effect
  - May obstruct swallowing → polyhydramnios
  - May prevent normal fetal "chin tuck" → extended neck → obstructed labor

- May compress trachea → airway compromise at birth
- Hydrops
- Vascular shunts in enlarged gland → high output state
- Shunting occurs in hypothyroidism
- Growth disturbance:
  - Intrauterine growth restriction (IUGR) is common
  - Skeletal maturation is delayed in hypothyroidism, accelerated in hyperthyroidism
- Fetal hypothyroidism
  - Tachycardia
  - Craniosynostosis
- Color Doppler
  - May see spaying of neck vessels by soft tissue mass
  - If hypervascular carotid and jugular vessels are increased in size
  - Diffuse increased flow in gland → hyperthyroid
- Color at periphery of gland → hypothyroid

MR Findings

- T1WI
  - Uniform high signal due to iodine content
  - Helps differentiate from other neck masses, which are less homogeneous
- T2WI
  - Intermediate signal
  - Straps/paraspinal muscles are low signal

DDx: Fetal Neck Mass

- Nuchal Cord: Coronal
- Nuchal Cord: Cervical
- Nuchal Cord: Axial
- Cervical Koszoroo
GOITER

Terminology
- Hyperplasia of thyroid gland
- Congenital goiter

Key Facts
- Skeletal maturation is delayed in hyperthyroidism, accelerated in hypothyroidism
- Diffuse increased flow in gland \( \rightarrow \) hyperthyroid
- Cold at periphery of gland \( \rightarrow \) hypothyroid
- Consider serial measurements of fetal thyroid in at-risk pregnancy

Imaging Findings
- Best diagnostic clue: Anterior neck mass of homogeneous echogenicity
- May obstruct swallowing \( \rightarrow \) polyhydramnios
- May prevent normal fetal “chin tuck” \( \rightarrow \) extended neck \( \rightarrow \) obstructed labor
- May compress trachea \( \rightarrow \) airway compromise at birth
- Intrauterine growth restriction (IUGR) is common

Imaging Recommendations
- Monitor
  - Fetal growth
  - Heart rate and rhythm
  - Amniotic fluid volume
  - Watch for signs of hydrops
- Consider serial measurements of fetal thyroid in at-risk pregnancy
  - Axial section mid thyroid level
  - Measure maximum transverse diameter and circumference
  - Monthly, starting at 22 weeks
- Consider establishing normative data for local population
- Regional variations in iodine availability influence “normal” for a given population
- Use color Doppler to assess thyroid vascularity

DIFFERENTIAL DIAGNOSIS

Cervical teratoma
- Often very large, irregular shape
- Mixed echogenicity \( \pm \) large irregular calcifications
- May extend into mediastinum
- Most teratomas exhibit rapid growth

Cervical neuroblastoma
- Heterogeneous solid mass
- Microcalcifications

Cystic neck masses
- Lymphangioma
- Cystic hygroma
- Congenital laryngeal cyst
- Thyroglossal duct cyst
- Branchial cyst

PATHOLOGY

General Features
- Genetics
  - No association with aneuploidy
  - Peedeed syndrome
  - Sensoneural deafness \( \oplus \) goiter
  - Autosomal recessive condition with deficient thyroid hormone synthesis
- Etiology
  - Hyperthyroid
  - Transplacental passage of maternal thyroid-stimulating antibodies
  - Hypothyroid
  - Transplacental passage of maternal anti-thyroid drugs
  - Both iodine insufficiency and intoxication
  - Infant: exogenous thyroid metabolism
  - Maternal lithium use
- Epidemiology
  - Hyperthyroidism
    - 2:1,000 pregnant women
    - 1:4,000,000 fetuses/neonates
  - Hypothyroidism
    - 1:4,000 neonates as indicated by neonatal screening
  - Pregnancy stresses maternal thyroid \( \rightarrow \) increased risk of fetal hyperthyroidism in iodine-deficient areas
  - Mothers with Graves disease (autoimmune hyperthyroidism)
    - 2-12% incidence of abnormal fetal thyroid function
    - 1.4% with Graves disease have a fetus with a goiter

Neural cord: Diagnosis easily confirmed with color Doppler
GOITER

CLINICAL ISSUES

Presentation
- Anterior neck mass
  - May be overlooked, unless directed search
- Maintain high index of suspicion with maternal history of Graves disease
- Fetus may have goiter despite maternal euthyroid state

Natural History & Prognosis
- Graves disease patients with persistent hyperthyroidism are more likely to have: hyperthyroidism in pregnancy
  - Incidence of spontaneous abortion 9.6% intrauterine fetal demise (IUFD) or stillbirth
- Series of 72 pregnant women with history of Graves disease
  - 57% mother antibody positive or on antithyroid medication
  - 22% (11 fetuses) had goiter by 32 weeks gestation
  - One IUFD due to hyperthyroidism/heart failure
  - Ten treated successfully
  - 4% antibody negative, no medication
- No fetal goiter, even infant mildly hypothyroid at birth
- Maternal hyperthyroidism associated with impaired fertility, higher incidence of spontaneous abortion
- Fetal goiter
  - Polyhydramnios
  - Dyspnea from abnormal head position
  - Airway compromise at birth
- Associated findings with fetal hyperthyroidism
  - Tachycardia → hydrops
  - IUGR
  - Cardiovascular
- IUFD, increased perinatal mortality
- Fetal hyperthyroidism
  - Studies suggest deficient thyroprotein synthesis difficulties
  - Unlikely to result in cretinism as neonatal treatment alone is effective in prevention
- Fetuses generally respond rapidly to treatment
  - Reduction in size of goiter, resolution of polyhydramnios

Treatment
- Check maternal thyroid antibody status if not known
- If thyroid stimulating hormone (TSH) receptor antibody levels are high, monitor pregnancy carefully
- Repeat titers in third trimester
  - If detectable at 36 weeks, risk for neonatal hyperthyroidism is increased
- Monitor maternal thyroid status with free T3, free T4
  - Increased thyroxine-binding globulin in pregnancy causes spurious elevation of total T3, T4 in euthyroid patients
- In pregnancy at risk for goiter due to maternal hyperthyroidism treatment, monitor fetal thyroid size
  - If thyroid is large, assume fetal hypothyroid due to maternal drugs crossing placenta
  - Decrease maternal antithyroid drugs and monitor fetal thyroid size

- If thyroid size returns to normal, no fetal intervention required
- May need beta blocker for maternal symptomaticology when antithyroid drugs are reduced
- If no response, or progressive increase in size, fetus likely hyperthyroid
- Consider cordocentesis for direct measurement of fetal thyroid hormones
- Measure fetal free T3, free T4, and TSH levels in cord blood
  - Normal ranges established
  - Fetal serum levels more reliable than amniotic fluid levels
- If fetal hyperthyroidism confirmed
  - Increase maternal medication until fetal response
  - Propranolol protected
  - Thyroid replacement is needed to keep mother euthyroid
  - If fetal hyperthyroidism: Weekly intra-amniotic injection of thyroxine
  - Refer to tertiary center for delivery
  - May require cesarean section for persistent head extension
  - If persistent goiter, consider EXIT procedure (extreme uterine transposition for delivery)
  - Infant maintained on placental support while airway is established
  - Serial cord blood for antibody titers
  - Better predictor of neonatal thyrotoxicosis than cord thyroid function tests, which reflect the fetal situation

DIAGNOSTIC CHECKLIST

Consider
- Fetal MRI is useful to evaluate airway compromise and plan for surgical delivery
- Fetal goiter can occur even if maternal euthyroid state

Image Interpretation Pearls
- Use color Doppler
  - Diffuse flow = hyperthyroid
  - Peripheral flow = hypothyroid

SELECTED REFERENCES
Typical

(Left) Axial ultrasound shows an enlarged thyroid gland (arrows) displacing the jugular and carotid vessels (curved arrows) posteriorly. A goiter displaces the vessels, whereas tumors encase them. (Right) Coronal ultrasound in the same view shows enlarged lobes (arrows) on either side of the fluid-filled trachea (curved arrow). Ankylosing spondylitis is a major concern with a large goiter, and the EDD procedure may be required for delivery.

Typical

(Left) Axial ultrasound shows the normal appearance of the thyroid (arrows) in the mid-sagittal (curved arrows) and transverse (open arrows). (Right) Axial ultrasound shows a large goiter (bracket) displacing the trachea. Laryngeal muscles (arrows) and the paralaryngeal muscles (open arrows) are also well seen in this view.

Typical

(Left) Axial T2W MR shows an intermediate signal, large neck mass (arrow). The spinal cord can be seen surrounded by high signal concentric fluid (curved arrow). (Right) Axial T1W MR shows a normal high signal intensity throughout the mass (arrows), confirming that it is nonmalignant. Although variation is poorly seen on this sequence, it is important diagnostically, as the high signal contact (closed arrow) increased signal is worrisome.

GOITER
CERVICAL TERATOMA

CONTRAST T2W MRI of a cervical teratoma shows a large, mixed-signal-intensity mass (arrow) arising within the soft tissues of the fetal neck. The head (curved arrow) is displaced to the side.

Clinical photograph after delivery shows the mass involving the anterior neck, with hypoplasia of the hand. The neck is supported by rolled towels (arrows). (Also shown in Radiographics, ref 1.)

TERMINOLOGY

Definitions
- Teratoma: Neoplasm derived from all three germ cell layers (ectoderm, mesoderm, endoderm)

IMAGING FINDINGS

General Features
- Best diagnostic clue: Mixed cystic and solid mass involving anterior aspect of neck
- Location
  - Anterior neck mass
  - Frequently extends to involve surrounding structures
  - May involve trapezius
  - May be nearly circumferential but bulk of mass is anterior
  - Superior extension
  - Frequently up to mastoid
  - May displace ear and distort jaw
  - Inferiorly
  - To clavicle or even into mediastinum
- Size
  - Variable
  - Often large and can be massive

Ultrasoundographic Findings
- Predominately solid or mixed cystic/solid
- Calcifications are virtually pathognomonic of teratoma
  - Present in only half of cases
  - May not be visible by ultrasound
  - Head is often held in hyperextension
  - May be dramatic
  - Head may be deviated to one side
  - Polyhydramnios from upper esophageal obstruction
  - Often severe
  - Worsens as pregnancy progresses
  - Color Doppler
    - Solid portions of mass often very vascular
    - Arteriovenous shunting may be present
  - Hydrops may develop with large masses

MR Findings
- Helpful in determining anatomic extent
- Masses usually mixed signal intensity
  - Cystic component
  - Low signal T1WI, high signal T2WI
  - Soft tissue component
  - Intermediate signal on both T1WI, T2WI
  - Fat component
    - High signal T1WI, high signal T2WI
    - Signal supresses with fat-saturation sequence

DDx: Neck/Facial Masses

- Cyst
- Encephalocele
- Neuroblastoma
- Cystic Hygroma
### Imaging Findings
- Anterior neck mass
- Frequently extends to involve surrounding structures
- May displace or distort jaw
- Often large and can be massive
- Predominantly solid or mixed cystic/solid
- Calcifications are virtually pathognomonic of teratomas
- Head and neck held in hyperextension
- Polyhydramnios from upper esophageal obstruction
- Risks grow with large masses
- MU recommended to better delineate anatomy and extent of tumor

### Top Differential Diagnoses
- Epignathus
- Cystic hygroma

- Could potentially confirm diagnosis of teratoma if fat components are large enough for detection

### Imaging Recommendations
- Routine views of chest, head, and face should detect virtually all cases
- Color Doppler to evaluate vascularity
- MRI recommended to better delineate anatomy and extent of tumor
- Close interval follow-up
  - May grow rapidly to massive size
  - Worsening polyhydramnios
- Mass may cause high-output cardiac failure and hydrops
  - Cardiomegaly
  - Oliguria
  - Pleural effusion
  - Skin thickening
  - Pericardial effusion

### DIFFERENTIAL DIAGNOSIS

<table>
<thead>
<tr>
<th>Epignathus</th>
<th>Cystic hygroma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasopharyngeal teratoma</td>
<td>Fluid collection in posterior and lateral neck</td>
</tr>
<tr>
<td>Point of origin of large teratomas may be obscure</td>
<td>Internal septations</td>
</tr>
<tr>
<td>Mouth is usually held open</td>
<td>Multiple thin septations common</td>
</tr>
<tr>
<td>May have intracranial extension</td>
<td>Thickened thick septation is nuchal ligament</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Goiter</th>
<th>Pathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Homogeneously echogenic neck mass</td>
<td>Head and neck second most common site for teratomas after sacrococygeal area</td>
</tr>
<tr>
<td>Maintains normal thyroid contour</td>
<td>Exodermal tissues main histologic component of fetal teratomas</td>
</tr>
<tr>
<td>Distinct lobes seen in coronal plane</td>
<td>Often contain neural (&quot;brain-like&quot;) tissue as dominant component</td>
</tr>
<tr>
<td>Prominent isthmus connects lobes in axial plane</td>
<td>Hypereosinophilic or neural tissue results in malpresentation and dystocia, precluding vaginal delivery</td>
</tr>
</tbody>
</table>

### Clinical Issues
- Hypereosinophilic in female results in malpresentation and dystocia, precluding vaginal delivery
- May occur with either increased or decreased fetal thyroid function
- Soft tissue tumors (both benign and malignant) may cause neck mass
  - Hemangioma
  - Fibromatosis
  - Myofibromatosis
  - Fibrosarcoma
  - Rhabdomyosarcoma

### DIAGNOSTIC CHECKLIST
- Refer to tertiary care facility with capability of performing EXIT procedure

### PATHOLOGY

<table>
<thead>
<tr>
<th>General Features</th>
<th>Histopathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genetics</td>
<td>Primordial germ cells migrate from yolk sac to genital ridges (weeks 4-6)</td>
</tr>
<tr>
<td></td>
<td>Germ cells are then incorporated into primitive sex cord to form gonads</td>
</tr>
<tr>
<td></td>
<td>Unincorporated cells normally involute</td>
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<tr>
<td></td>
<td>Continued development of unincorporated germ cells gives rise to teratomas</td>
</tr>
<tr>
<td></td>
<td>Embryology</td>
</tr>
<tr>
<td></td>
<td>Rare</td>
</tr>
<tr>
<td></td>
<td>Head and neck second most common site for teratomas after sacrococygeal area</td>
</tr>
<tr>
<td></td>
<td>Equal distribution between males and females</td>
</tr>
<tr>
<td></td>
<td>Different from most teratomas which are more common in females</td>
</tr>
</tbody>
</table>

### Gross Pathologic & Surgical Features
- Complex, mixed cystic and solid components
- May see cartilage and bone
  - Teeth and hair not as common as in teratomas later in life
CERVICAL TERATOMA

Microscopic Features
- Frequently involves thyroid gland
- Not thought to directly arise from thyroid tissue
- Unique histologic features compared to teratomas presenting later in life
- Composed of all three germ cell layers
  - Endodermal tissue
  - Mesodermal tissue
  - Ectodermal tissue
- Often, contain neural ("brain-like") tissue as dominant component
- Mesothelium
- Fat
- Cartilage
- Smooth muscle
- Bone
- Endoderm
- Least common component
- Respiratory epithelium
- Gastrointestinal tissue

Staging, Grading or Classification Criteria:
- Teratomas classified as mature or immature
  - Immaturity of tumor may reflect immaturity of fetus rather than biologic behavior of tumor
  - Size and vascularity are much more important than histology in a fetus

Clinical Issues

Presentation
- Most common signs/symptoms: Obvious soft tissue mass involving neck
- Other signs/symptoms
  - Head often held in hyperextension or deviated to side
  - Nystagmus
  - Natural History & Prognosis
- Polyhydramnios may cause protein loss
- Hyperextension of neck results in malpresentation and gynoid, precluding vaginal delivery
- May show rapid in utero growth
- Routine resuscitation techniques
  - Lethal if unable to establish airway
  - Even with maximal emergency procedures, hypoxia, acidosis, and anoxic brain injury may occur
- Mortality for head and neck teratomas 80-100%
- Substantial improvement in survival achieved with ex utero intrapartum treatment (EXIT) procedure
  - In large series, airway established in 79%, with overall survival of 69% for head and neck masses

Treatment
- Termination may be effected
- Delivery continued, deliver at tertiary care facility with capability of performing EXIT procedure
- EXIT procedure provides controlled environment to establish airway
- Fetus is partially delivered by cesarean section
- While placenta and umbilical cord remain intact
- Uteroplacental gas exchange maintained
- Fosses remains hemodynamically stable while airway is established
- Avoid "crash" attempt at achieving airway at birth

Diagnostic Checklist

Consider
- MRI to better delineate anatomy
- Delivery planning crucial, especially for large masses
- Referral to tertiary care facility with capability of performing EXIT procedure

Image Interpretation Pearls
- Calculations within a neck mass are diagnostic of a teratoma

Selected References
CERVICAL TERATOMA

IMAGE GALLERY

Typical

(Below) Coronal (upper) and sagittal (lower) images of a moderate-sized cervical teratoma (rupture). It has both cystic (arrows) and solid components. (Right) Sagittal T1W MR of a massive cervical teratoma (arrows) shows dramatic hypointensities of the head (curved arrows).

Typical

(Below) Sagittal T2W MR shows a mixed signal neck mass (arrows) extending up to the level of the skull base. (Right) axial T1W MR through the mass shows extensive involvement of the anterior and lateral neck. Thin cystic areas are seen (arrows), as well as a large soft tissue component (spinal canal - open arrow).

Typical

(Below) Continuing from the case above, the mass was debulked via the COT procedure and a tracheostomy placed. Posterior sagittal T2W image shows posterior extension of the mass (arrows) with an admixture of layered soft tissue structures. (Right) Clinical photograph shows the mass extending from the ear to chest (marked area). Histology showed an immature teratoma.
SECTION 5: Chest

Introduction and Overview
Chest Development & Imaging 5-2

Chest
Pulmonary Hypoplasia 5-6
Congenital Diaphragmatic Hernia 5-10
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Bronchopulmonary Sequestration 5-18
Pleural Effusion 5-22
Teratoma, Chest 5-26
Tracheal Atresia 5-28
Lymphangioma 5-30
Imaging Anatomy

Ultrasound

- Heart most obvious finding in chest
  - Should occupy 1/4 to 1/3 of thoracic cavity
  - Apex directed to R:
  - Cardiac axis approximately 45°
  - Normal axis excludes significant chest mass
- Lungs
  - Homogeneous intermediate echogenicity
  - Echogenicity increases with gestational age
  - Can be used to predict hypoplasia
  - Right lung volume slightly greater than left
  - Left lung 3 lobes, left lung 2 lobes
- Liver anatomy can usually be identified
- Diaphragm
  - Continuous hypoechocic band between pleural and peritoneal cavities
- Thyroid
  - Anterior mediastinum
- Visualization reported in 74%
- < 27 weeks hypoechoic
- > 27 weeks hypoechocic

MRI:

- Excellent soft tissue contrast
- Ideal for evaluation of chest masses, especially congenital diaphragmatic hernia (CDH)
- Lungs
  - Intermediate-signal intensity T1WI
  - High-signal intensity T2WI
- Liver
  - High signal intensity T1WI
  - Low signal intensity T2WI
- Good for volumetric lung measurements

Anatomy-Based Imaging Issues

Imaging Protocols

- American Institute of Ultrasound in Medicine (AIUM) chest evaluation

Imaging Pitfalls

- Oblique axis can give false appearance of CDH
- If multiple ribs are seen, image is oblique
- One continuous rib in true axial plane
- Be sure to image entire diaphragm
- Diaphragm may be intakt amniotically in Bochmick CDH
- Sagittal plane best for posterior defect

Normal Measurements

- Routine measurements not necessary
- Ratio of thoracic circumference to abdominal circumference (TC/AC) remains stable throughout pregnancy
- Normal > 0.80

Embryology

Embryologic Events

- Embryonic stage
  - 26 days to 6 weeks
  - Lung bud arises as ventral outpouching of foregut
  - Penetrate surrounding mesenchyme
  - Branches to form lungs and bronchopulmonary segments
- Pseudoglandular stage
  - 6-16 weeks
  - Continued branching to form terminal bronchioles
- Canaliculur stage
  - 16-28 weeks
  - Terminal bronchioles divide into respiratory bronchioles
- Respiratory vasculature develops
- Progressive flattening of epithelial cells
- Necessary for gas exchange
- Saccular stage
  - 28-36 weeks
  - Respiratory bronchioles divide to produce terminal sacs
CHEST DEVELOPMENT & IMAGING

Key Facts
- Normal amniotic fluid
- Fetal breathing
- Lung development: single most important factor determining survival for many conditions
- Oligohydramnios is an important etiologic factor for pulmonary hypoplasia
- CDH most common chest mass to cause pulmonary hypoplasia

Imaging Issues
- Lung homogeneity, intermediate echogenicity
- Most ideally suited for evaluation of chest masses
- Oblique axis can give false appearance of a congenital diaphragmatic hernia (CDH)

Clinical Issues
- Multiple factors needed for lung development
- Normal thoracic cavity

- Occurs in a caudocephalad progression
- Process continues until 8 years of age
- 20-70 million terminal sacs at birth
- 300-400 million at maturation
- Absorptive stage
- 36 weeks to term
- Alveolar maturation
- Diaphragm development
- Composite of four embryologic structures
  - Septum transversum
  - Pleuroperitoneal membranes
  - Paraxial mesoderm
  - Esophageal mesenchyme

Requirements for Normal Development
- Normal thoracic cavity
- Absence of skeletal dysplasia restrict lung growth
- Normal amniotic fluid
- Fetal breathing
- Hydrostatics of fetal lung fluid
  - Fluid is both secreted and absorbed
  - Complex interchange of lung fluid production and absorption
- Fluid exchange during breathing
- Net efflux of fluid with breathing
- Fetal lung fluid functions as stent keeping developing air spaces distended
  - Decreased fetal lung fluid = hypoplasia
  - Increased fetal lung fluid (i.e., tracheal atresia = blocking efflux) = overgrowth and advanced maturation

Clinical Implications

Clinical Importance
- Pulmonary hypoplasia single most important factor determining survival for many conditions
- Oligohydramnios important etiologic component of pulmonary hypoplasia
  - Fetal compression causes decreased space for lung growth
  - Restriction of breathing movements
  - Efflux of lung fluid into amniotic space
  - Oligohydramnios as short as 6 days may cause pulmonary hypoplasia
  - Oligohydramnios > 14 days at 25 wks gestational age has 90% mortality
- Not all chest masses have same effect on developing lungs
  - CDH has more severe hypoplasia than other masses of comparable size

Related References

Image Gallery

(Left) Axial oblique ultrasound of the chest gives the erroneous appearance of a congenital diaphragmatic hernia. The stomach appears to be adjacent to the heart. Note that multiple ribs are seen (arrow) indicating that this is not a true thoracic plane. (Right) Sagittal ultrasound of the diaphragm shows a continuous hypodense band between the thoracic and abdominal compartments. It is further confirmed by the stomach (open arrow) and heart (curved arrow) in the correct cavities.
PULMONARY HYPOPLASIA

TERMINOLOGY

Definition:
- Decreased number of cells, alveoli and alveoli resulting in decreased size and weight of lungs
- Often result of an in utero thoracic mass or small chest circumference

IMAGING FINDINGS

General Features
- No universally accepted diagnostic criteria for predicting hypoplasia
- A plethora of measurements and ratios exist
- Pending issue which continues to be area of ongoing research
- Lung volumes become more variable with advancing gestational age (GA)
  - Greater correlation with fetal size than GA

Ultrasoundographic Findings
- Lung echogenicity increases with GA
  - Does not predict lung maturity
- Fetal breathing movements
  - Important for lung development
  - Absence over extended period poor prognosis sign
  - No quantifiable predictive measurement

DDx: Conditions Resulting In Pulmonary Hypoplasia

- ARPKD
- PH
- SGA
- CDH

- Direct lung measurements:
  - Area, length and diameter have been used
  - Often difficult
  - Poor soft tissue contrast
  - Oligohydramnios
  - Unfavorable fetal position
- Thoracic circumference (TC):
  - Performed at level of four-chamber view
  - Exclude soft tissues
  - Compare to expected value for GA or area ratio with abdominal circumference (AC), femur length (FL), or head circumference (HC)
  - TC/AC ratio stable throughout pregnancy
  - Normal > 86
  - Useful when chest size is small
  - Skeletal dysplasia
  - Oligohydramnios
  - Not useful for chest masses
- Lung-to-head ratio (LHR):
  - Used predominately with congenital diaphragmatic hernia (CDH)
  - Lung area contralateral to CDH is calculated by multiplying 2 orthogonal cross-section lung measurements
  - Measurements taken at level of four-chamber view
  - Epigastrial lung usually obscured by hernia
  - Calculated area of contralateral lung divided by head circumference to give LHR
PULMONARY HYPOPLASIA

Key Facts

- No universally accepted diagnostic criteria for predicting hypoplasia
- A plethora of measurements and ratios exist
- Perplexing issue which continues to be area of ongoing research
- Lung volumes become more variable with advancing gestational age (GA)
- Not all malformations affect developing lungs to same degree

Top Differential Diagnoses
- Chest masses
- Conditions causing oligohydramnios
- Abnormal thoracic cavity

Pathology
- Oligohydramnios > 14 days at 25 weeks GA has 90% mortality

Clinical Issues
- Respiratory distress at birth
- Pneumothorax
- Bell-shaped chest

Diagnostic Checklist
- Single most important factor determining survival for many conditions
- Lung volumes alone do not always correlate with outcome
- Persistent severe oligohydramnios poor prognostic sign

- Slice volumes are summed for total volume
- Lung volumes are compared with multiple biometric indices
- Lung signal intensity may also correlate with hypoplasia

Disadvantages
- Labor intensive to perform calculations
- As yet, no simple standard approach

Imaging Recommendations
- Protocol advice
  - Through evaluation of chest anomalies
  - Not all malformations affect developing lungs to same degree
  - Consider fetal echo
  - Heart often difficult to evaluate when mass is present
  - Ability to detect cardiac defects more difficult
  - Cardiac anomaly with chest malformation worsens prognosis
- Commonly used techniques to evaluate lungs
  - TC/AC ratio
  - LHR
  - Doppler: AT/ET ratio
  - MRI

Differential Diagnosis

Chest masses
- Congenital diaphragmatic hernia (CDH)
- Most common mass to cause pulmonary hypoplasia
- Hypoplasia more severe than for other chest masses of similar size
- Congenital cystic adenomatoid malformation (CCAM)
- Sequestration
- Teratoma
- Large pleural effusions

Conditions causing oligohydramnios
- Bilateral renal agenesis
- Bilateral multicystic dysplastic kidney
- Bladder outlet obstruction
PULMONARY HYPOPLASIA

- Posterior urethral valves (PUV)
- Urethral atresia
- Obstructing mass
  - Anencephaly
    - Polycystic kidney disease (ARPKD)
    - Prematurity
      - Nipple retraction of membranes (PROM)
      - Especially before 26 weeks

Abnormal thoracic cavity
- Thymic hypoplasia
- Asphyxiating thoracic dystrophy (Jeune syndrome)
- Achondrogenesis
- Osteogenesis imperfecta
- Carpotrochlear dysplasia
- Short rib-polydactyly syndrome

Cardiac malformations
- Right-sided obstructive lesions decrease pulmonary blood flow and lung growth
- Pulmonary atresia/stenosis
- Hypoplastic right heart
- Ebstein anomaly

Neuromuscular anomalies
- May cause decreased fetal breathing and subsequent poor lung development
  - Anencephaly
  - Ischemic brain injury
  - Intracranial masses
  - Fetal hypokinetic/spinal sequence

PATHOLOGY

General Features
- Epidemiology
  - 9,411,000 live births
  - 8-22% of autopsies series
- Oligohydramnios important etiologic component
- Fetal compression causes decreased space for lung growth
- Restriction of breathing movements
  - Efflux of lung fluid into amniotic space
  - Oligohydramnios as short as 6 days may cause pulmonary hypoplasia
- Factors affecting prognosis with PROM
  - GA of rupture
  - Duration
  - Degree of oligohydramnios
  - Oligohydramnios > 14 days at 25 weeks GA has 90% mortality

Gross Pathologic & Surgical Features
- Decreased ratio of lung weight to body weight
- Decreased alveolar count
- Number of alveolar septa at center of respiratory bronchiole
- Decreased lung DNA relative to body weight

CLINICAL ISSUES

Presentation
- Respiratory distress at birth
- Chest X-ray

- Pneumothorax
- Pneumomediastinum
- Bell-shaped chest

Natural History & Prognosis
- Pulmonary hypoplasia critical determining factor in survival
  - Major cause of death in premature infants
  - Severity dependent on timing and degree of insult
  - Neonatal death in severe cases

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls
- Single most important factor determining survival for many conditions
- Lung volumes alone do not always correlate with outcomes
- Complex problem of multiple varying etiologies
- Persistent severe oligohydramnios poor prognostic sign

SELECTED REFERENCES
PULMONARY HYPOPLASIA

IMAGE GALLERY

Typical

(Left) Axial ultrasound of the fetal chest shows a CDH with the stomach (arrow) in the thorax and displacement of the heart to the right (curved arrow). (Right) Gross pathology at autopsy shows a small, hypoplastic lung being retracted, the stomach (arrow) and a portion of the left lobe at the liver (curved arrows) are in the thoracic cavity. The heart (top arrow) is displaced to the right. Pulmonary hypoplasia is worse for CDH than other chest masses of comparable size.

Typical

(Left) Sagittal ultrasound shows a very small chest cavity (curved arrow) in the case of thoracic duct hypoplasia. Compare to the normal diaphragm (arrow). (Right) Clinical photograph confirms the very small chest size (arrows) as well as markedly shortened limbs. Pulmonary hypoplasia was secondary to a small thoracic cavity restricting lung growth.

Typical

(Left) Frontal radiograph shows classic features of pulmonary hypoplasia in a case of unexplained fetal agenesis. The chest is bell-shaped, there are bilateral pneumothoraces with chest tubes in place, and ascites is present (arrow). (Right) Gross pathology from a different case of fetal agenesis shows very small hypoplastic lungs (arrows) in comparison to the normal sized (curved arrow).
CONGENITAL DIAPHRAGMATIC HERNIA

TERMINOLOGY

Abbreviations and Synonyms
- Congenital diaphragmatic hernia (CDH)

Definitions
- Herniation of abdominal contents into chest cavity
  - Foramen of Bochdalek
  - Posterolateral defect in diaphragm
  - Foramen of Morgagni
  - Anterior
  - Right-sided
  - Uncommonly herniation through esophageal hiatus

Imaging Findings

General Features
- Best diagnostic clue
  - Cystic chest mass and absent stomach bubble
  - Peristalsis within cystic chest mass is pathognomonic
- Location
  - Left-sided 80-90%
  - Right-sided 10%
  - Bilateral < 5%

DDx: Cystic Lung Mass

- Bronchogenic Cyst
- Macrocystic CCAM
- Microcystic CCAM

Ultrasoundographic Findings
- Cystic mass in left side of chest
- Absence of fluid-filled stomach
- Deviation of heart toward right
- Polyhydramnios
- Up to 85% contain herniated liver ("liver up")
- Often difficult to diagnose
- Typically left lobe herniates adjacent to heart
- Stomach is displaced posteriorly
- Always use Doppler to follow portal veins
- Umbilical segment of portal vein begins to left
- Right-sided more difficult
- May be confused for chest mass
- Contains liver and bowel
- Doppler will show portal veins
- Stomach is below diaphragm

Abdominal circumference will measure less than expected
- Most prenatally diagnosed CDHs are large
- Hydrops uncommon unless associated malformations present
  - Poor prognostic indicator
- Small CDH may be missed, especially if stomach is not herniated
  - Abnormal cardiac axis may be only clue
CONGENITAL DIAPHRAGMATIC HERNIA

Key Facts

- Herniation of abdominal contents into chest cavity

Imaging Findings

- Cystic chest mass and absent stomach bubble
- Peristalsis within cystic chest mass is pathognomonic
- Small CDH may be missed, especially if stomach is not herniated
- Up to 85% contain herniatis liver ("liver up")
- Calculate lung-to-head ratio (LHR)
- LHR < 1.0 poor prognosis
- LHR > 1.4 favorable prognosis
- MRI best test to evaluate anatomy and contents

Top Differential Diagnoses

- Congenital cystic adenomatoid malformation (CCAM)

Pathology

- Pulmonary hypoplasia worse than from other chest masses of comparable size
- Up to 50% have an associated abnormality
- Chromosomal abnormalities are common
- All fetuses should be karyotyped

Clinical Issues

- Factors which worsen prognosis:
  - Presence of other abnormalities
  - Liver in chest
  - Diagnosis before 24 weeks gestational age

Diagnostic Checklist

- Incorrect scan plane may result in erroneous diagnosis

- May be more midline in location
  - Gallbladder often herniates
- Bilateral
  - Be suspicious when stomach is in chest but little mediastinal shift
  - Use color Doppler to look for liver on right

MR Findings

- Excellent for identifying contents of hernia
- Bowel appears as tubular serpiginous structure with variable signal intensity
  - Fluid-filled small bowel
  - Low signal T1WI, high signal T2WI
  - Mucinous
  - High signal T1WI, low signal T2WI
- Accurately diagnoses presence of liver in CDH
  - High signal T1WI, low signal T2WI
- Can perform volumetric lung measurements

CT Findings

- Used rarely in cases of maternal obesity
- Fetus will swallow contrast injected into amniotic fluid
  - Confirms stomach in chest
- May be an alternative if patient can not undergo MRI

Imaging Recommendations

- Best imaging tool: Higher frequency transducers
  - Helpful for differentiating herniated bowel vs. liver
- Confirm that CDH findings are real
  - Oblique axial image my simulate a "pseudo CDH"
  - Check ribs
  - If multiple ribs seen, axis is incorrect
  - Cardia axis is normal
- Calculate lung-to-head ratio (LHR)
- Area of contralateral lung divided by head circumference
- Ill-defined lung usually obscured by hernia
- Lung area is calculated by multiplying 2 orthogonal cross-sectional lung measurements taken at level of four-chamber view
  - Example: All calculations done in millimeters
  - Lung measurements 22 mm and 18 mm
- Lung area 396 mm² (22 mm x 18 mm)
  - Head circumference 256 mm
- LHR = 1.5 (396 divided by 256)
  - LHR < 1.0 poor prognosis
  - LHR > 1.4 favorable prognosis
- All fetuses with CDH need dedicated fetal echo
  - CDH and cardiac defect is considered lethal
  - MRI best test to evaluate anatomy and contents

DIFFERENTIAL DIAGNOSIS

Congenital cystic adenomatoid malformation (CCAM)

- Macroscopic type
  - Stomach below diaphragm
  - Diaphragm intact
  - Abdominal circumference normal
  - No peristalsis
  - Doppler shows pulmonary artery supplying mass

Hybrid lesion

- Combination of CCAM + sequestration
- Consider when a cystic mass is fed by a systemic vessel

Other cystic masses

- Bronchogenic cyst
  - Esophageal duplication cyst
- Neuroenteric cyst
  - Thoracic boney abnormality usually present
  - All rare
  - More often associated with mediastinum than lung

Teratoma

- Solid and cystic components
- Calcifications most specific finding

RARE

PATHOLOGY

General Features

- General path comments

- Lung area 396 mm² (22 mm x 18 mm)
- Head circumference 256 mm
  - LHR = 1.5 (396 divided by 256)
  - LHR < 1.0 poor prognosis
  - LHR > 1.4 favorable prognosis
- All fetuses with CDH need dedicated fetal echo
  - CDH and cardiac defect is considered lethal
  - MRI best test to evaluate anatomy and contents
CONGENITAL DIAPHRAGMATIC HERNIA

- Pulmonary hypoplasia worse than from other chest masses of comparable size
- Hypoplasia always present to varying degrees
- Lungs are small and histologically immature
- Abnormal pulmonary arteries
- Muscular hypoplasia of arterial walls
- Results in pulmonary hypertension and persistent fetal circulation
- Up to 50% have an associated abnormality
- 30% central nervous system (CNS) malformations
- 20% cardiac anomalies
- Renal
- Spinal
- Chromosomal abnormalities are common
- Reported in 16-37% of cases
- Triploies 18, 13, 21, 9
- All fetuses should be karyotyped
- Associated syndromes
- Fanys syndrome: COH, facial abnormalities, distal limb hypoplasia, CNS malformations
- Genetics: Generally sporadic inheritance
- Epidemiology: 1:2,000-5,000 births
- Embryology
- Failure of fusion of posterior pleuroperitoneal membranes

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - May be an incidental finding
  - Stomach in chest
  - Patient may be large-for-dates secondary to polyhydramnios
  - Respiratory distress in newborn

Natural History & Prognosis
- 65% survival if isolated
- Factors which worsen prognosis:
  - Presence of other abnormalities
  - Liver in chest
  - Mortality "live-up" 57%
  - Mortality "live-down" 7%
  - Diagnosis before 24 weeks gestational age
  - Large size
  - Right-sided or bilateral
  - Polyhydramnios

Treatment
- In utero repair not shown to be useful
- Thoracocentesis
  - PLUG: Plug lung until it grows
  - FETO: Fetoscopic thoracocentesis
  - Causes retention of fetal lung fluid which accelerates lung growth
  - Perform before 26 weeks gestational age on fetuses with poor prognosis
  - "Live-up"
    - LHR < 1.0
  - "Live-down"
    - LHR > 1.0

Necessitates delivery by cesarean section using ex utero intrapartum treatment (EXIT) procedure
- Uteroplacental circulation is maintained while thoracic occlusion is removed and fetus inhabited
- Clinical trials ongoing
- Mixed results
- May not improve outcome over conventional treatment in most cases
- May be limited to select group of severely affected fetuses
- Planned delivery at tertiary care facility essential
- Antenatal steroids
- Surfactant, high-frequency oscillatory ventilation, inhaled nitric oxide, parenteral hypercortisolemia
- Extracorporeal membrane oxygenation (ECMO) needed if severe
- EXIT to ECMO may be best strategy
- Uteroplacental circulation maintained while arterial and venous lines are placed
- Avoid barotrauma
- Oxygenation and nutrition maintained
- Aggressive treatment of pulmonary hypertension

DIAGNOSTIC CHECKLIST

Consider
- MRI to better evaluate anatomy and contents

Image Interpretation Pearls
- Always use Doppler to evaluate for liver
- Incorrect scan plane may result in erroneous diagnosis

SELECTED REFERENCES

CONGENITAL DIAPHRAGMATIC HERNIA

IMAGE GALLERY

Typical

(Left) Axial ultrasound image of the fetal chest shows an abnormal axis of the heart with displacement to the right (open arrows). The fetal stomach is seen within the chest (curved arrow). The abdominal circumference measured less than expected. (Right) At birth, the infant was noted to have a saphenous abdomen and significant respiratory distress. Surgical repair of the diaphragmatic hernia was undertaken at 2 days of age.

Typical

(Left) Axial ultrasound through the chest of a 16 week fetus shows the stomach (S) within the thorax with the heart shifted to the left (curved arrow). Anterior to the stomach is a retrosternal area comprised of multiple small bags representing small bowel (arrow) and a portal venous system (open arrow). (Right) Gross pathology at autopsy shows both small bowel (curved arrow) and liver (open arrow) in the chest.

Variant

(Left) Axial color Doppler ultrasound of a right-sided CDH shows shift of the heart to the left (curved arrow). The left portal vein is easily identified (arrow). Color Doppler should be performed in every case of CDH to evaluate for volvulus (arrow). (Right) Sagittal 3DW MR in another case of right-sided CDH shows liver (arrow) lying the right hemithorax. MRI is an excellent modality for determining the contents of a CDH.
CYSTIC ADENOMATOID MALFORMATION

TERMNOLOGY
Abbreviations and Synonyms
• Congenital cystic adenomatoid malformation (CCAM)

Definitions
• Lang hamartoma with proliferation of terminal bronchioles and lack of normal alveoli
• Communicates with tracheobronchial tree

IMAGING FINDINGS

General Features
• Best diagnostic clue: Solid or cystic lung mass with arterial supply from pulmonary artery
• Size
  o Variable
  o Usually contained within a single lobe
  o Can be massive
• Morphology: Variable from solid appearing (microcystic) to complex cystic mass (macrocystic)
  o 95% are unilateral and affect only 1 lobe
• No side predilection
• May spontaneously regress
  o "Disappearing CCAM"

Ultrasoundographic Findings
• Gray scale Ultrasound
  o Macrocytic
    o 1 or more cysts > 5 mm
    o Often multiple cysts of varying sizes
    o May have single large cyst
    o Borders poorly defined
  o Microcystic
    o Cysts < 5 mm
    o Uniformly echogenic
    o Well-defined masses
  o Heart is displaced
  o Stomach in normal location
• Hydrops
  o Most important predictor of outcome
  o Occurs in < 10%
• Doppler
  o Polyhydramnios
  o Compression of esophagus
  o Associated with hydrops
• Color Doppler
  o Vascular supply from pulmonary artery
  o Venous drainage to pulmonary vein
• More difficult to see

MR Findings
• T2WI
  o Microcystic

DDx: CCAM Mimics

CDH
Sequestration
Sequestration
Tracheal Aneurysm
**Terminology**
- Lung hamartoma with proliferation of terminal bronchioles and lack of normal alveoli

**Imaging Findings**
- Morphology: Variable from solid appearing (microcystic) to complex cystic mass (macrocystic)
- No visible pleura
- May have single large cyst
- Vascular supply from pulmonary artery
- Greatest growth 20-26 weeks

**Top Differential Diagnoses**
- Bronchopulmonary sequestration (BPS)
- Hybrid lesion (CCAM + BPS)
- Congenital diaphragmatic hernia (CDH)

- High signal intensity mass
  - Macrocystic
  - Discrete cysts discernible
  - Vascular supply better seen with Doppler
- MR usually not necessary

**Imaging Recommendations**
- Use color Doppler to identify feeding vessel
- Monitor closely
  - Every 1-2 weeks after initial diagnosis
  - Check size
  - Development of hydrodrops
  - Polyhydramnios
  - Greatest growth 20-26 weeks
  - If regression or no change, can increase time interval between scans
  - Calculate CCAM volume ratio (CVR)
    - CCAM volume/total lung volume > 1.6 increased risk of developing hydrodrops

**Differential Diagnosis**

**Bronchopulmonary sequestration (BPS)**
- Similar appearance to microscopic CCAM
- Feeding vessel from aorta
- Uniformly echogenic
- 90% left-sided
- Pseudotumoral pleural effusion highly suggestive

**Hybrid lesion (CCAM + BPS)**
- Consider when a systemic vessel supplies a cystic lung mass
- Histology shows both lesions

**Congenital diaphragmatic hernia (CDH)**
- Absent normal fluid-filled stomach
- Abdominal circumference small
- Penstahis is pathognomonic
- Other anomalies common

**Congenital lobar emphysema**
- Uniformly echogenic

**Pathology**
- Most common fetal lung mass

**Clinical Issues**
- Majority remain stable or regress in utero
- Excellent prognosis without hydrodrops even if large at diagnosis
- Near 100% mortality with hydrodrops if untreated
- Postnatal workup of all lesions even if regressed in utero
- Most feel risk of infection and malignancy warrants resection in all cases

**Diagnostic Checklist**
- Large size early does not predict poor outcome
- Development of hydrodrops is single most important predictor of outcome

- More commonly upper lobe
- Rare to diagnose in utero

**Tracheal atresia**
- May be confused for bilateral CCAM
- Symmetric, bilateral lung enlargement
- Inversion of diaphragm
- Fluid-filled trachea and bronchi

**Other cystic masses**
- Bronchogenic cyst
- Esophageal duplication cyst
- Neurenteric cyst
  - Thoracic bony abnormality usually present
  - More often associated with medullary thymus gland

**Teratoma**
- Solid and cystic components
- Calcifications most specific finding
- Medial or pericardial

**PATHOLOGY**

**General Features**
- Genetics
  - Sporadic inheritance
  - No recurrence risk
- Epidemiology
  - Most common fetal lung mass
  - 75% of all lesions
  - Associated abnormality: Seen in 3-12%

**Staging, Grading or Classification Criteria**
- Pathologic staging system based on aerulon series
  - Type I
    - Cyst > 2 cm
  - Cysts lined by pseudostatified epithelium
  - Normal alveoli between cysts
- Good prognosis
  - Type II
  - Cyst < 2 cm
  - Cysts resemble terminal bronchioles
  - Associated abnormalities
Cystic Adenomatoid Malformation

Clinical Issues

Presentation
- Usually a incidental finding
- Cystic or echogenic lung mass
- Patient may be large-for-date if polyhydramnios is present

Natural History & Prognosis
- Prenatal
  - Majority remain stable or regress in utero
  - Excellent prognosis without hydrops even if large at diagnosis
  - Hydrops significantly impacts prognosis
  - Near 100% mortality with hydrops if untreated
  - Faster increasing risk of hydrops
  - CVR > 1.6
  - Dominant large cyst
  - Postnatal
    - Risk for infection
    - Small risk for developing malignancy
    - Infants and young children: Pleuropulmonary blastoma, rhabdomyosarcoma, myxosarcoma
    - Older children and adults: Bronchial adenocarcinoma

Treatment
- None unless hydropic
- Hydrops > 32 weeks
- Maternal betamethasone administration and early delivery
- Immediate resection
- May be resected during delivery using ex utero intrapartum treatment (EXIT) procedure
- Uteroplacental circulation maintained while lesion is resected
- Hydrops < 32 weeks: In utero therapy
  - Macroscopic CCAM
  - Cyst drainage: Temporizing measure only, fluid will recur
  - Thoracoamniotic shunt
  - Microscopic CCAM
  - In utero resection
- Delivery at a tertiary care facility
  - At risk for neonatal complications including air trapping and pneumothoraces
  - Large lesions may require extracorporeal membrane oxygenation (ECMO)
- Postnatal resection somewhat controversial in symptomatic individuals
  - Most feel risk of infection and malignancy warrants resection in all cases
- Elective resection at 1 month or older
  - Risk of anemia decreases after 4 weeks of age
  - Early resection maximizes compensatory lung growth

Diagnostic Checklist

Image Interpretation Pearls
- Large size early does not predict poor outcome
- Development of hydrops is single most important predictor of outcome

Selected References
Typical

(Left) Coronal ultrasound shows a large microcystic CCAM. The mass (arrow) is well-defined and uniformly echogenic, with only pericystic vessels. The infant (curved arrow) is displaced against the chest wall.

(Right) Gross pathology of the resected lesion shows very small cysts (arrow) within an otherwise solid mass.

Typical

(Left) Axial color Doppler ultrasound shows a cystic lung mass with vascularity supply (arrow) from pulmonary circulation compatible with a microcystic CCAM. This lesion became less obvious on follow-up scan. The infant had no respiratory distress, with only a questionable area of abnormality on chest X-ray.

(Right) Axial NECT clearly shows a residual area of abnormal lung (arrow). CT should be performed even if chest X-ray is normal.

Variant

(Left) Axial ultrasound in a second trimester fetus shows an obvious echogenic lung mass (arrow) and slight deviation of the cardiac axis (open arrow). Vascular supply was from the pulmonary circulation.

(Right) Axial ultrasound in third trimester shows complete resolution of the mass. The lesion turned a "disappearing CCAM". Despite normal appearance, a postnatal CT should be performed to evaluate for a residual mass.
TERMINOLOGY

Abbreviations and Synonyms
• Bronchopulmonary sequestration (BPS)
• Botalli's lobe

Definitions
• Bronchopulmonary tissue that does not connect to the tracheobronchial tree or pulmonary arteries
• Extraalveolar sequestration type identified in fetus
  • Fetal intralobar sequestration extremely rare

IMAGING FINDINGS

General Features
• Best diagnostic clue: Solid lung mass with arterial supply from aorta
• Location
  • 85-90% supradiaphragmatic
  • 10-15% subdiaphragmatic
  • 90% left-sided
• Size
  • Generally small to moderate size
  • Rarely can fill entire chest
• Morphology
  • Pleural investment results in well-marginated mass
  • Triangular or lobe shape

DDx: Echogenic Lung Mass

- Micronodular CCAM
- Alveolar CCAM
- Micronodular CCAM
- Pulmonary sequestration

Ultrasoundographic Findings
• Intrathoracic BPS
  • Homogeneous echogenic
    • Typically left lung base
    • Between lower lobe and diaphragm
  • Unilateral pleural effusion in 6-10%
  • May cause tension hydrothorax
  • Cysts may be seen
• Most common in hybrid lesions
• Hybrid lesions contain histologic elements of both BPS and congenital cystic adenomatoid malformation (CCAM)
• Abdominal BPS
  • Also typically left-sided
  • Stomach displaced anteriorly by an echogenic mass
  • May communicate with stomach
  • Separate from inferior vena cava
• Color Doppler
  • Prominent feeding vessel from aorta
  • May have more than one
  • Occasionally arises from left axillary artery
  • Venous drainage
  • Azygos or inferior vena cava
  • Sometimes partially drain into pulmonary veins
  • Often difficult to visualize

Spontaneous in utero regression common
BRONCHOPULMONARY SEQUESTRATION

Key Facts
- Hybrid lesion (CCAM + BPS)

Pathology
- 23% of fetal lung masses
- Associated anomalies: Seen in up to 50%
- Up to 50% of BPS have histologic features of type II CCAM

Clinical Issues
- Excellent prognosis when an isolated finding
- 50-75% regresses in utero
- May be complicated by tension hydrothorax

Diagnostic Checklist
- Postnatal work-up should be performed in all cases even if regressed in utero
- Doppler evaluation essential for making the diagnosis

MRI Findings
- T2WI
  - Well-defined high signal mass
  - Higher signal than normal lung
  - Lower signal than amniotic fluid
  - Feeding vessel not consistently visualized
  - Not necessary in most cases
  - Helpful in selected cases
  - When constrictive abnormalities are present
  - Especially congenital diaphragmatic hernia
  - Subdiaphragmatic lesion
  - Uniform high signal more suggestive of IIPS rather than neuroblastoma

Imaging Recommendations
- Use color Doppler to identify feeding vessel
- Close follow-up of lesion
- Watch for development of pleural effusion or hydrops
- May spontaneously regress
- Careful evaluation for other anomalies
  - Present in up to 50%
  - Congenital diaphragmatic hernia most common
  - Cardiac malformations
  - Other pulmonary anomalies
  - Bronchogenic cyst
  - Vascular malformations
  - CCAM
  - Gastrointestinal
  - Tracheoesophageal fistula
  - Duplication cysts
  - Neuroaxial lesions
  - Skeletal
  - Vertebral anomalies
  - Pectus excavatum

Differential Diagnosis
Congenital cystic adenomatoid malformation (CCAM)
- Micronodular type

- Feeding vessel from the pulmonary artery
- Pulmonary venous drainage
- May occur on right or left

Hybrid lesion (CCAM + BPS)
- Consider when a systemic vessel supplies a cystic lung mass
- Histology shows both lesions
- May occur in up to 50% of cases

Teratoma
- Mediastinal or pericardial
- Calculations most specific finding
- Pleural or pericardial effusions
- No aortic arterial feeder

Cystic mass of the lung and the chest
- Uniformly echogenic
- More commonly upper lobe
- Normal vasculature
- Rare to diagnose in utero

Neuroblastoma
- Most common differential for subdiaphragmatic BPS
- More often on right
- Often cystic
- No feeding vessel
- Does not present until 3rd trimester

PATHOLOGY

General Features
- General path comments
  - Embryology
  - Hypothetically early insult when tracheobronchial tree splits from primitive foregut
  - Subsequent ectopic budding of tracheobronchial tree
  - Explains high association with enteric anomalies
  - Genetics
    - Sporadic inheritance
    - No recurrence risk
  - Epidemiology

Differential Diagnosis
Congenital cystic adenomatoid malformation (CCAM)
- Micronodular type
BRONCHOPULMONARY SEQUESTRATION

- 23% of fetal lung masses
- M:F = 4:1
- Some studies show equal sex distribution
- Associated abnormalities: seen in up to 50%

**Gross Pathologic & Surgical Features**
- Pathology: cystic
- Extralobar sequestration
  - Type seen in fetus
  - Open pleural investment
  - Drains to a systemic vessel
- Intralobar sequestration
  - No pleural investment
  - Drains to pulmonary vein
  - May be acquired
- Extremely rare in utero or infancy
- > 50% present over 20 years of age
- May result from parietal infection
- Normal blood supply may be compromised with parasitization of systemic vessels
- Histology: Chronic inflammation and fibrosis

**Microscopic Features**
- Up to 50% of BPS have histologic features of type II CCAM

**Staging, Grading or Classification Criteria**
- New classification system of lung masses proposed
- Covers issue of hybrid lesions
- System is based on appearance of lung and vascular supply
- Five categories of fetal lung dysplasia
  - Type I: Agenesis
  - Type II: Normal lung with abnormal vascular supply
  - Type III: Abnormal lung with abnormal vascular supply
  - Type IV: Abnormal lung with normal vascular supply
  - Type V: Miscellaneous

**CLINICAL ISSUES**

**Presentation**
- Usually an incidental finding
- Seen as early as 16 weeks
- Pleural effusion

**Natural History & Prognosis**
- Excellent prognosis when an isolated finding
- Poorer prognosis categories
  - Largely determined by severity of associated abnormalities
  - Development of significant hydrops
  - 50-75% regressed in utero
  - May be complicated by tension hydrothorax
  - Proposed mechanism:
    - Leakage from ectatic lymphatics
    - Torsion of sequestered segment
    - Mar: progress to generalized hydrops from cardiovascular compression
  - Postnatal
- Most are asymptomatic
- May have respiratory distress or cyanosis
- May present with associated abnormality

**Treatment**
- Prenatal
  - Usually none
  - Drainage or thoracoscopic shunt for tension hydrothorax
- Postnatal
  - Contrast enhanced CT or MRI should be done in all cases
  - Chest X-ray may miss lesion
  - Embolization of feeding vessel
  - Surgical ligation and resection
  - Resection may not be necessary for regressed lesions in asymptomatic individuals

**DIAGNOSTIC CHECKLIST**

**Consider**
- When there is a lung mass with a unilateral pleural effusion
- Prenatal work-up should be performed in all cases even if regressed in utero

**Image Interpretation Pearls**
- Doppler evaluation essential for making the diagnosis
- May spontaneously regress

**SELECTED REFERENCES**

BRONCHOPULMONARY SEQUESTRATION

IMAGE GALLERY

Typical

Variant

(Left) Coronal color Doppler ultrasound shows a well-defined echogenic lung mass (arrow) being supplied by a large artery (curved arrow) arising from the aorta (open arrow). Right) Gross pathology shows the cut surface of the neoplastic sequestration. It is a solid mass with a pleural covering. The dominant feeding vessel seen on ultrasound is easily identified (arrow).

(Left) Sagittal ultrasound shows an echogenic lung mass filling the left hemithorax. A "cyst" (arrow) in was but Doppler showed arterial flow which could be traced to the aorta. Without Doppler this mass may have been mistaken for a Cyst. Right) CECT with contrast reconstruction after delivery shows two large systemic vessels entering from the aorta and supplying the mass.

(Left) Sagittal ultrasound of the normal abdomen shows an echogenic mass arising posteriorly anteriorly and displacing the stomach (arrow) anteriorly. Right) Sagittal ultrasound (upper) shows CMC as well as solid components (arrows). The arterial supply (arrow) is clearly seen. Inferiorly, this mass, histopologically, was a bronchopulmonary sequestration. CMC=Congenital Malformations.
**PLEURAL EFFUSION**

**TERMINOLOGY**

**Abbreviations and Synonyms**
- Pleural fluid
- Hydrothorax
- Chylothorax

**Definitions**
- Fluid accumulation in pleural space
- Chylothorax: Chylous fluid collection
- Hydrothorax: Serous fluid collection

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue
  - Curvilinear fluid displacing lung from chest wall
  - Lung appears to float in chest
  - Location: Pleural space
  - Size: Variable

**Ultrasonographic Findings**
- Right lung: four chamber heart view
  - Echogenic lung displaced medially
  - Coronal chest view
  - Lung displaced superiority and medially

**DDx: Cystic Chest Mass**
- Microcystic CAM
- Diaphragmatic Hernia
- Lymphangioleiomyomatosis

- "Wing-like" lungs float in fluid
- Fluid is anechoic regardless of chylothorax or hydrothorax etiology
- Chylothorax
  - Chylous fluid collection
  - Unilateral
  - R = L
  - Mass effect common
  - Mediastinal shift
  - Flattened diaphragm
  - May lead to hypovolemia when large
  - 5% with aneurysm
    - Turner syndrome
    - Trisomy 21
    - Noonan Syndrome
    - 15% resolve in fetal life
- Hydrothorax
  - Serous fluid collection
  - Bilateral and symmetric
  - Hallmark finding in hydrops fetalis
  - Immune or nonimmune
  - Asciites
  - Skin edema
  - Pericardial fluid
  - Commonly occurs with abnormalities associated with hydrops
  - Cystic hygroma (Turner syndrome)
  - Cardiac defects
PLEURAL EFFUSION

Terminology
- Chylothorax: Chylous fluid collection
- Hydrothorax: Serous fluid collection

Imaging Findings
- "Wing-like" lungs float in fluid
- Fluid is anechoic regardless of chylothorax or hydrothorax etiology
- Hallmark finding in hydrops fetalis

Top Differential Diagnoses
- Normal chest wall musculature

Pathology
- 5% with chylothorax have chromosome abnormalities
- Effusion may be first sign of hydrops

Key Facts
- Cardiac arrhythmia
- Infection
- Trisomy 21 markers and anomalies
- Fetal mass
- Goiter
- Extralobar pulmonary sequestration
- Cystic adenomatoid malformation
- Lymphangiomata
- Any mass causing fetal heart failure
- First trimester pleural effusion
  - Can be seen as early as 7 weeks
  - Associated with increased nuchal translucency
  - Poor prognosis when present before 15 wks
  - Anecdotally common
  - Turner syndrome most likely

Imaging Recommendations
- Best imaging tool
  - Routine transverse four chamber heart view
  - Coronal chest view
  - Diaphragm view
- Protocol advice
  - Look for hydrops
    - Skin edema
    - Ascites
    - Pericardial effusion
  - Look carefully at fetal heart
    - Structural defects
    - Tachycardia
  - Look for signs of fetal infection
    - Brain, liver, spleen calcifications
    - Intracranial hemorrhage
    - Intrathoracic growth restriction
  - Perform genetic sonogram
  - Sequential ultrasound
  - May resolve spontaneously
  - May progress to hydrops

DIAGNOSTIC WORKUP

Normal chest wall musculature
- Chest wall muscles are hypoechoic (not anechoic)

Clinical Issues
- 75% mortality when hydrops present
- Pulmonary hypoplasia
- Worst prognosis when present before 15 wks
- Fetal thoracentesis
- Fetal chylothorax is clear (fasting fluid)
- Thoracoamniotic shunting

Diagnostic Checklist
- Formal fetal echocardiography
- Unlike pectal笑意osis, any amount of pleural fluid is abnormal
- When isolated, frequent follow up exams necessary to look for developing hydrops

Other cystic chest masses
- Bronchogenic cyst
- Neuroenteric cyst
- Esophageal duplication cyst
- Chest wall lymphangioma

PATHOLOGY

General Features
- Genetics
  - 5% with chylothorax have chromosome abnormalities
  - Turner syndrome
  - Trisomy 13
  - Noonan syndrome
- Etiology
  - Chylothorax
    - Primary congenital lymphatic defect
    - Atea, feta, or absence of thoracic duct
    - Thoracic duct crosses from right to left at 5th thoracic level
- Level of obstruction determines R vs. L
- Chylous effusion R:L ratio is 1:1
- Hydrops
  - Effusion may be first sign of hydrops
  - Immune vs. nonimmune
    - 30% with nonimmune have abnormalities
  - Congenital infection
    - Cytomegalovirus: Most common
    - Parvovirus B19 (fifth disease)
**PLEURAL EFFUSION**

- Cardiac failure
- Anomalous heart
- Tachyarrhythmia
- Systemic cause
- Fetal anemia
- Epidemiologic cause:
  - Hydrops
  - Polyhydramnios
  - Cystic hygroma
  - Cardiac anomalies
  - Fetal anemia

**CLINICAL ISSUES**

**Presentation**
- Most common signs/symptoms:
  - Abnormal screening ultrasound
  - Fetuses presenting with hydrops

**Natural History & Prognosis**
- Bilateral effusion
  - More often associated with hydrops
  - 75% mortality when hydrops present
  - 50% mortality without hydrops
- Unilateral effusion
  - Less likely associated with hydrops
  - 20% resolve in utero
  - Near 100% survival without hydrops and normal chromosomes

**Diagnosis**
- Pulmonary hypoplasia
  - Bilateral large effusions
  - Difficult to judge severity
- Isolated pleural effusion at time of diagnosis
  - 15% resolve
  - 5% cardiac defect seen postnata
  - 5% aneuploidy
  - 36% perinatal mortality
  - Most from subsequent hydrops
  - Unknown etiology common
- First trimester pleural effusion
  - Poor prognosis
  - Worst prognosis when present before 15 weeks
  - 82% aneuploidy rate
  - Turner most common
  - 85% miscarriage rate

**Treatment**
- Reasons to treat
  - Pulmonary hypoplasia
  - Difficult to diagnose in utero
  - Hydrops
  - Treat cause of hydrops when possible
  - Aid with post delivery ventilation
  - Small pleural effusions not treated in utero
- Fetal thoracocentesis
  - Ultrasound guidance for fluid aspiration
  - Multiple aspirations often necessary
  - Fetal sent for laboratory analysis
  - Chylothorax (fluid)
  - 1 lipoprotein
  - 1 lymphocytes
  - Fetal chylosous fluid is clear/whitish fluid

**Feeding**
- Feeding tracheal chylosous fluid is "milky"
- Thoracocentesis for drainage
- Double pigtail catheter placed
- 10% calfheter failure rate
- Improved survival rates
- 80% vs. 10% with hydrops

**EXIT procedure** (ex utero intrapartum treatment)
- Cesarean section delivery
- Chest delivered for procedure
- Placental circulation maintained
- Thoracocentesis performed
- Post delivery ventilation support improved

**DIAGNOSTIC CHECKLIST**

- Ascites
- Aneuploidy
- Fetal blood sampling for anemia
- Maternal infection work-up
- Fetal echocardiography

**Image Interpretation Pearls**
- Unlike pericardial effusion, any amount of pleural fluid is abnormal
- When isolated, frequent follow-up exam necessary to look for developing hydrops
- M-mode of fetal heart to rule out tachycardia as a treatable cause

**SELECTED REFERENCES**

PLEURAL EFFUSION

IMAGE GALLERY

Typical

(Left) Axial ultrasound shows thoracocentesis in a fetus with hydrodrops. The tip of the needle (arrows) is placed into the left pleural effusion. Curved arrows point to bilateral hydrenotheorax. (Right) Sagittal ultrasound shows skin edema (open arrows) and ascites (curved arrow) in the same fetus. Although post delivery resuscitation was attempted, this baby died from pulmonary hypoplasia.

Typical

(Left) Sagittal ultrasound at 13 weeks shows a markedly increased nuchal transparancy (arrows). (Right) Coronal ultrasound of chest shows an associated pleural effusion (open arrow). Curved arrow points to the triangular lung surrounded by a rim of fluid. Findings were bilateral. This fetus was diagnosed with Turner syndrome. Early pleural effusion is often associated with aneuploidy and bad prognosis.

Other

(Left) Axial ultrasound shows normal hyperechoic chest wall musculature (arrows). This finding should not be confused with a small rim of pleural effusion. (Right) Coronal ultrasound shows normal hyperechoic diaphragm in same patient (arrows). Since any amount of fluid is considered abnormal, it is important not to mistake these hyperechoic structures with echogenic pleural effusion.
TERATOMA, CHEST

And ultrasound shows a complex, heterogeneous mass filling the chest and displacing the heart (arrow). Calcification (arrows), the most specific finding of a teratoma, and cystic areas (arrow) are present.

Conaval T2WI MR after delivery shows a mixed signal intensity mass, which has invaded the mediastinum, diaphragm, and chest wall (arrow). The treatment had malignant elements and resection was not possible.

TERMINOLOGY

Definitions
- Neoplasm composed of all three germ cell layers
  - Ectoderm, mesoderm and endoderm

IMAGING FINDINGS

General Features
- Best diagnostic clue: Calcifications within a chest mass
- Location
  - Most originate from mediastinum or pericardium
  - Most common intrapericardial mass
  - Primary lung tumors are rare
  - Site of origin difficult to discern when large
- Size
  - Variable
  - Typically large
  - May grow rapidly over short period of time

Ultrasoundographic Findings
- Heterogeneous mass
- Contains both cystic and solid components
- Calcifications most specific feature
  - Not present in all cases
- Mediastinal
  - Typically originate anteriorly

- Can cross the midline
- Difficult to differentiate from primary lung mass
- Pericardial
  - Extapericardial
  - Look for attachment to pericardium
  - Lung may be displaced by pleural effusion
  - Intrapericardial
  - Most common intrapericardial mass
  - Pericardial effusion invariably present
  - Pericardial effusion may be massive and mistaken for pleural effusion
  - At risk for cardiac tamponade
- Pleural effusions
  - Isolated or with hydrops
  - Hydrops
  - Color Doppler
  - Variable vascularity
  - No dominate feeding vessel
  - Helps differentiate from other lung masses

MR Findings
- Helpful in determining origin and extent of mass
- Not sensitive for calcifications

CT Findings
- Used in postnatal work-up
- Most sensitive modality for calcification detection

DDx: Complex Lung Mass

- Lymphangiolema
- CDH, Bowel
- CDH, Diaphragm
- Mesothelial CCM
### Key Facts
- **Sequestration**
- **Clinical Issues**
  - May have had a normal 2nd trimester scan
- **Diagnostic Checklist**
  - Other chest masses are far more likely
  - Consider when calcifications are present in chest mass
  - Most common intrapericardial mass

### Differential Diagnosis

**Congenital diaphragmatic hernia (CDH)**
- Often cystic and solid components
  - Stomach, small bowel, liver
  - Doppler confirms portal veins
  - Abdomen abnormal
    - Decreased abdominal circumference
    - Absent stomach bubble

**Congenital cystic adenomatoid malformation (CCAM)**
- Microcystic or macrocystic
  - Vascular supply from pulmonary artery

**Sequestration**
- Well-defined echogenic mass
  - Systemic vascular supply
- May have associated pleural effusion

**Lymphangioma**
- Septated cystic mass
  - May invade into chest and mediastinum
  - Largest component will be external to chest
  - Neck or axillary

**Neuroblastoma**
- Arises posteriorly
  - Rarely occurs in chest

### Natural History & Prognosis
- Variable based on size of mass and extent of local involvement

### Treatment
- Intrauterine pericardiocentesis has been performed for cardiovascular compromise
- Thoracoamniotic shunt for pleural effusion with hydrops

### Diagnostic Checklist

**Image Interpretation Pearls**
- Other chest masses are far more likely
- Consider when calcifications are present in chest mass
- Most common intrapericardial mass

### Pathology

**General Features**
- Epidemiology: < 10% of fetal teratomas occur in chest

**Gross Pathologic & Surgical Features**
- Complex masses
  - May exhibit very rapid growth
  - Does not correlate with malignancy
  - Malignant elements are uncommon

### Clinical Issues

**Presentation**
- Most present in 3rd trimester
- May have had a normal 2nd trimester scan
  - Reflects rapid growth of mass

### Selected References

### Image Gallery

(Left) Sagittal ultrasound of a teratoma demonstrates a mixed cystic and solid mass (arrows). (Right) Axial ultrasound shows that the mass located anterior to the heart and is surrounded by a pericardial effusion. There is also involvement with the anterior coronary sinus.
TRACHEAL ATRESIA

Graphic shows a high tracheal atresia (arrow) with demarcation of the distal trachea and bronchi. The diaphragm is flattened. The heart is shifted towards the midline and is crowded by the enlarged lungs.

콘알 초음파로 전반적인 확장된 폐와 기관지(라인)의 구조가 보이며, diaphragm이 평평해진다. 심장은 중앙으로 이동하고, 기관지 공간이 증가한다.

**TERMINOLOGY**

**Abbreviations and Synonyms**
- Tracheal atresia
- Laryngeal atresia
- Congenital high airway obstruction (CHAOS)

**Definitions**
- High airway obstruction caused by atresia, stenosis, or web

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue: Bilaterally enlarged, echogenic lungs

**Ultrasonographic Findings**
- Dramatic lung findings
  - Symmetric, bilateral enlargement
  - Uniformly hyperechoic
  - Homogeneous
  - Fluid-filled trachea and bronchi
  - Exact point of obstruction (larynx vs. trachea) can not usually be determined
  - Heart shifted to midline
  - Appears small

- Compressed by enlarged lungs
  - Diaphragm
    - Flattened
    - Inverted
  - Atrices common
  - May be massive
  - Hydrops
    - Not as common as isolated atresia
  - Both polyhydramnios and oligohydramnios reported
  - Associated anomalies in 30% of cases
    - Cardiac
    - Renal
    - Esophageal fistula
  - May decompress lungs in utero
  - Diagnosis may be missed until after delivery
  - May be seen with VACTERL association (vertebral anomalies, anal atresia, tracheoesophageal fistula, renal, and limb malformations)

**Imaging Recommendations**
- Protocol advice
  - Consider dedicated fetal echo
  - Heart may be difficult to evaluate because of compression
  - Cardiac anomaly worsens prognosis

**DDx: Large Echogenic Lung Mass**

- Mucinous CCAM
- Micropapillary CCAM
- Sequestration
- Sequestration
TRACHEAL ATRESIA

Terminology
- Congenital high airway obstruction (CHAOS)

Imaging Findings
- Fluid-dilated trachea and bronchi
- Heart shifted to midline
- Aspects common
- Associated anomalies in 50% of cases

Key Facts

Pathology
- Lungs more mature than expected for gestational age

Clinical Issues
- EXIT procedure (ex utero intrapartum treatment) has been successfully used to establish airway

Diagnostic Checklist
- Symmetric, homogenous lung enlargement is essentially pathognomonic
- Uterine beat is maintained while laryngoscopy is performed
- Airway secured before umbilical cord is clamped

DIFFERENTIAL DIAGNOSIS

Bilateral congenital cystic adenomatoid malformations (CCAM) or sequestrations
- Theoretically could have the same appearance
- Highly unlikely
- Trachea and bronchi would not be fluid-filled

Large single hyperaemic lung mass
- Large CCAM or sequestration can fill entire chest
- Lacks symmetry
- Heart will be shifted, not midline
- Trachea and bronchi not fluid-filled

PATHOLOGY

General Features
- Genetics: Sporadic
- Etiology
  - Mid-forgotten forms of congenital laryngeal aplasia
  - No endoderm for trachea
  - Obstruction causes retention of fetal lung fluid and subsequent overdevelopment
- Lungs more mature than expected for gestational age
- Lungs larger
- Greater number of alveoli
- Associated abnormalities
- Heart syndrome
- Tracheal atresia
- Cryptophthalmus
- Syndactyly
- Genitourinary abnormalities

CLINICAL ISSUES

Presentation
- Reported early as 18 weeks

Natural History & Prognosis
- Uniformly fatal if not recognized
- Better outcome if atresia is not complete
- Web of stenosis

Treatment
- Planning for delivery is essential
- EXIT procedure (ex utero intrapartum treatment) has been successfully used to establish airway

SELECTED REFERENCES

IMAGE GALLERY

(left) Axial 4D ultrasound show marked dilatation of tracheal lumen. The bronchi (arrows) are fluid-filled. The endotracheal tube is inserted to the midline and appears small, being almost completely obscured by shadowing from the vertebral body. (right) Coronal pathology at autopsy shows enlargement of all lobes of the lung. Note how small the heart appears in comparison. These lungs are essentially pauch without a tracheal lumen.
LYMPHANGIOMA

Graphic of a lymphangioma. Multiple cysts along the left chest, neck, and arm have formed because of congenital lymphatic obstruction. Normal lymphatic drainage instantly shown on left/right.

An ultrasound shows bilateral, large, multiloculated axillary cystic masses (curved arrow) in a second trimester fetus. The masses contain thin and thick septations (arrows).

- **Size**
  - Variable
  - Prenatal cases usually large
- **Morphology**
  - Complex cystic mass with septations
  - Septations usually thick
  - No solid component
  - Rarely unilocular

### Ultrasonographic Findings
- Gray-scale ultrasound
  - Complex cystic body wall mass
  - Sono-echoic cysts
  - Septa of variable thickness
  - No solid components
  - May enlarge during pregnancy
  - Extent of mass difficult to estimate
  - Associated anomalies rare
  - Axillary CL
  - Cystic mass between arm and chest wall
  - May extend down arm
  - Secondary lymphedema common
  - Abnormal arm positioning
  - Arm held away from fetal trunk
  - Can grow into mediastinum
  - Rib deformity common
  - Associated pleural effusion rare
  - Associated hydrops rare

### Terminology

#### Abbreviations and Synonyms
- Non-nuchal cystic hygroma
- Cystic lymphangioma (CL)
- Axillary lymphangioma
- Cutaneous lymphangioma

#### Definitions
- Benign non-nuchal cystic tumors of lymphatic system

### Imaging Findings

#### General Features
- Best diagnostic clue: Non-nuchal subcutaneous large complex cystic mass
- Location
  - ≥ 70% of non-nuchal CL are axillary
  - Often bilateral
  - May extend through chest wall
  - Mediastinal involvement common
  - ≥ 30% other sites
  - Trunk
  - Limbs
  - ≥ 80% of all lymphangioma are nuchal
- Cystic hygroma
- Different prognosis than non-nuchal CL

### DX: Cystic Body Wall Mass

- Nuchal CH
- Nuchal CH
- Aneurysm Bands
- Commotio Bands
LYMPHANGIOMA

Terminology
- Non-nuchal cystic hygroma
- Cystic lymphangioma (CL)

Imaging Findings
- 70% of non-nuchal CL are axillary
- Prenatal cases usually large
- Complex cystic body wall mass
- Arm held away from fetal trunk
- Can grow into mediastinum
- Secondary lymphedema common
- Color Doppler: No blood flow
- Follow mass size with sequential exams
- Consider 3D US or MR to assess volume

Top Differential Diagnoses
- Nuchal cystic hygroma (CH)

- Trunk CL
  - Cystic mass involving fetal trunk
  - Usually asymmetric
  - May involve lower extremity
  - Secondary lymphedema common
  - Limb held in abnormal position
  - Often transient
  - Non-localized most common
  - Often with chromosome abnormality
  - Color Doppler: No blood flow

- 3D
  - Extent of mass better seen
  - Mass volume can be calculated

MR Findings
- T1WI: Low signal
- T2WI: High signal
- Extent of mass better evaluated with MR
  - Mediastinum
  - Chest wall
  - Neurovascular structures
  - Body wall musculature

Imaging Recommendations
- Protocol advice
  - Follow mass size with sequential exams
  - Consider 3D US or MR to assess volume
  - Consider aspiration of large cysts for delivery purposes

Differential Diagnosis

Nuchal Cystic Hygroma (CH)
- Posterior lateral neck location
- Usually septated
- More common than non-nuchal CL
- 66% associated with chromosome abnormality
- Turner most common
- Noonan syndrome
- Trisomy 21
- Commonly seen in first trimester

- Non-septated more common
- Hydrops fetalis common

Anniotic Band Syndrome
- Disruption of amnion
- Entrapment of fetal parts
  - Amputation is hallmark finding
  - Lymphedema common
  - May mimic cystic mass
  - Limb body wall complex
  - Complex mass of evacuated organs

Klippel-Trenaunay Weber Syndrome
- Large cutaneous hemangiomas
  - Doppler shows blood flow in mass
  - Lesion cystic than CL
  - Hypoplasia of associated limb
  - Lower bone asymmetry
  - Uterus

Hemangioma
- Dilated vessels deep in skin
- Solitary component present
- Less cystic than lymphangioma
- Doppler shows blood flow in mass
- Scalp is a common site
- Can be inertrative
  - Chest wall involvement
  - Extremity involvement

Pathology

General Features
- Genetics
  - Second trimester not-nuchal CL not associated with chromosome abnormalities
  - First trimester axillary CL
  - Associated with trisomy 21
  - Rare finding
- Etiology
  - Axillary
LYMPHANGIOMA

- Obstruction of axillary lymph vessels at junction with jugular venous system
  - Abnormal lymphatic anlage
- Insufficient anastomoses with larger lymph channels
- Epidemiology
  - 20% of all lymphangiomas are non-nuchal
  - Axillary CL
  - 1:19,200 in early second trimester
- Associated abnormalities
  - Musculoskeletal dysmorphism
  - Secondary to mass effect
  - Hydrocoel fetsals

Gross Pathologic & Surgical Features
- Tumor with numerous cystic cavities
  - Infiltrative features
    - Skin
    - Muscle
    - Neurovascular structures

Microscopic Features
- Tumor wall
  - Endothelial lining
  - Smooth muscle fascicles
- Small compressed capillaries
- Lymphatic spaces
  - Lymphocytes
  - Rare erythrocytes

CLINICAL ISSUES

Presentation
- Most common signs/symptoms: Seen on routine screening exam
- Other signs/symptoms
  - Hydrops
  - More rare than with nuchal cystic hygroma
  - Skin edema
  - Pleural effusion
  - Ascites

Demographics
- Age
  - Not associated with advanced maternal age (AMA)
  - AMA ≥ yrs at time of delivery
- Gender: M = F

Natural History & Prognosis
- Short term
  - Obstructed labor
  - Dyspnea
  - Cesarean section delivery preferred
  - Fetal respiratory compromise
  - Delivery at tertiary care center
  - Birth trauma to mass
  - Bleeding
  - Infection
  - Skin necrosis
- Long term
  - Outcome depends on size and location of mass
  - Functional impairment common
  - Lymphedema

- Infection
  - Hemorrhage
  - Recurrence
- Microscopic components recur most commonly
- Treated with further surgery or sclerosis
- Spontaneous involution reported
  - 29% partial
  - Survival rates near 100%
  - Much better than with nuchal cystic hygroma

Treatment
- Surgical excision is treatment of choice
  - Complete excision desired
  - Inflation of vital structures common
  - Makes excision difficult
  - Post surgical recurrence common
- Sclerotherapy
  - Agents injected directly into cysts
  - Used most often for recurrences
  - Bleomycin fat emulsion
  - 40% success rate
- OK-432
- Inactivated streptococcal organisms
- Prenatal needle aspiration
  - Ultrasound guided fluid aspiration of large cysts
  - Reduce volume before delivery
- Prenatal sclerosis of fetal mass reported
  - OK-432

DIAGNOSTIC CHECKLIST

Consider
- Nuchal CL in cases of large superficial fetal mass
  - Consider fetal MR
  - Better tissue characterization
  - Extent of mass better shown

Image Interpretation Pearls
- Look for bilateral masses when one is seen
- Long view of humerus identifies early axillary CL
- Look for blood flow in mass

SELECTED REFERENCES
Typical ultrasound shows a large lymphangioma arising from the neck and extending down the chest wall (arrows). The tumor is seen to extend down the chest (arrow). Right: Oblique ultrasound shows a large lymphangioma which involves the chest wall, pectoral, and arm. As noted on prenatal, the arm is markedly ablated.

Typical T1 MRI of a newborn with bilateral anterolateral lymphangiomas diagnosed prenatally. There are large, multiloculated cystic masses involving both anterior and posterior (arrows). There was no extension into the thoracic cavity. Right: Axial CECT shows these cysts involving the chest wall and displacing much (arrows). The finding was not appreciated on the prenatal ultrasound.

Typical ultrasound shows a large lymphangioma arising from left flank (arrows). Curved arrows point to the kidney. This extensive lymphangioma extends from the lower chest to the upper left leg. Right: Axial ultrasound shows absence of blood flow in the mass. The lymphangioma did not extend into the abdominal cavity but secondary lymphatics at the leg were severe.
SECTION 6: Heart

Introduction and Overview
Cardiac Development & Imaging

Heart

- Echogenic Cardiac Focus
- Foramen Ovale Aneurysm
- Pericardial Effusion
- Situs Inversus
- Prenatal Syndromic Associations
- Ventricular Septal Defect
- Atrioventricular Septal Defect
- Hypoplastic Left Heart
- Coarctation of the Aorta
- Aortic Stenosis
- Pulmonary Valve Stenosis, Atresia
- Eisenmenger Syndrome, Tricuspid Dysplasia
- Tricuspid Atresia
- Double Outlet Right Ventricle
- Single Ventricle
- Tetralogy of Fallot
- Transposition of Great Arteries
- Truncus Arteriosus
- Hypertrophic Cardiomyopathy
- Dilated Cardiomyopathy
- Irregular Rhythm
- Tachyarrhythmia
- Bradycardia
- Rhabdomyoma
**Imaging Anatomy**

**General Anatomic Considerations**
- Fetal heart axis is 30-45 degrees, apex points left
- Fetal heart lies in an axial plane in chest
- Recognition of chambers, great vessels
  - Right atrium: Receives superior vena cava (SVC) and inferior vena cava (IVC)
  - Right ventricle
    - Trabeculated myocardiun, moderator band, triangular shape
  - Tricuspid valve leaflet attached to septum
  - Left atrium: Receives pulmonary veins
  - Fenomen oval flap seen within, flow direction right to left
  - Left ventricle
    - Smooth walled, bullet shaped
  - Mitral valve has no septal attachment
  - Aorta gives rise to head and neck vessels at apex of "candy cane" shaped arch
  - Pulmonary artery bifurcates shortly after it exits heart
  - Gives rise to ductus arteriosus

**Key Concepts or Questions**
- Fetal circulation
  - Umbilical vein brings oxygenated blood from placenta to right atrium
  - Right atrial blood is shunted to left heart through foramen ovale
  - Right atrium — left atrium — left ventricle (LV) — aorta to supply head and neck
  - SVC/IVC blood — right atrium — right ventricle (RV) — pulmonary artery
  - Ductus arteriosus takes majority of RV blood from pulmonary artery to the body; bypassing lungs
  - Blood returns to placenta via umbilical arteries for oxygenation

- Cardiac activity is seen before embryonic margins can be defined
- Absence of cardiac activity in embryos > 5 mm in size on endovaginal scan indicates demise
- Key questions
  - Is the heart size normal?
  - Is the cardiac axis normal?
  - Is there atrioventricular concordance?
  - Is there ventriculoarterial concordance?
  - Do the outflow tracts relate normally?

**Imaging Approaches**
- Indications for fetal echocardiography
  - Family history
  - Structural defect: Recurrence risk highest if mother affected
  - Syndromes: Marfan, Noonan, Holt-Oram, 22q11 deletion, Williams
  - Other heritable conditions: Tuberous sclerosis
  - In vitro fertilization pregnancy
  - Maternal indications
  - Metabolic: Diabetes melitus, phenylketonuria
  - Infections: Rubella
  - Lupus: Conduction defects
  - Teratogen exposure
  - Phenytion, isotretinoin, lithium
- Fetal indications
  - Multiple gestations (especially twin-twin transfusion)
  - Multiple anomalies
  - Abnormal nuchal translucency, even if chromosome normal
  - Anomaly detected at routine obstetric scan
  - Hydrops
  - Arrhythmia

**Imaging Protocols**
- American Society of Echocardiography
  - Establish fetus
  - Measure chambers, vessels and valves
  - Doppler interrogation of all vessels and valves
  - Examine rate and rhythm
**Cardiac Development & Imaging**

**Key Facts**

- **Embryology**
  - Critical period for heart development is from embryonic days 20-30

- **Pathology**
  - Obstructive lesions may progress
  - May result in ventricular hypoplasia or hypoplastic great artery
  - Valve regurgitation may increase
  - May cause enough chamber enlargement to pulmonary hypoplasia

**Clinical Implications**

- Early detection of CHD
  - Ultrasound in utero management
  - Allows for planning of delivery and prompt institution of postnatal therapy

**Normal Measurements**

- Area should be about equal in size
- Tricuspid valve attachment on interventricular septum offset from mitral valve attachment
- Ventricle not equal at 20 weeks, right ventricle larger by term
- Outflow tracts should be about equal in diameter
- Heart circumference ≤ 50% chest circumference
- Pericardial fluid < 2 mm

**Pathology-Based Imaging Issues**

**Imaging Pitfalls**

- S
  - Sinus venosus ASD despite detailed study
  - Atrial or ventricular septal defect (ASD, VSD)
  - Coaptation of aorta
  - Anomalous pulmonary venous return

**Embryology**

**Embryologic Events**

- Heart and blood vessel development is controlled by cascade of regulatory genes and signaling molecules
- Heart tube forms by condensations forming the atrium and ventricle
- Heart tube forms the heart tube
- New mechanism proposed based on myocardial markers, research on embryonic "fields" and use of scanning electron microscopy

- Heart develops in modular fashion with sequential addition of components to an initial primary structure
- Third week of embryonic life: Anuoplasty cords canalize and fuse to form a heart tube or primary cardiac crescent
- This primary structure forms bulk of developing LV
- Secondary (anterior) heart field gives rise to RV and outflow tract
- Tertiary field contributes cells which form atria and contribute to ventricles
- Cardiac neural crest cells + precardiac organ + aortic arches/conary vesicles
- "Sacculations" now described in primitive heart
- Sinus venosus + atrium + inlet + outlet + truncus arteriosus
- Function of inlet/outlet portion = bulboventricular foramen
- Primitive heart looping occurs by unknown mechanism, complete by end 5th embryonic week
- Normal bend is to right, D-looping
- Abnormal bend to left, L-looping → dextrocardia
- Septation
  - Paired hypocellular masses (atrioventricular/endocardial cushions) form on doral and ventral walls of looping heart tube
  - Approach each other and fuse separating primary atrium from primary ventricle
  - Atrial division is occurring at same time
  - Septum primum grows toward endocardial cushions from roof of primum atrium
  - Foramen primum lies between free edge of septum primum and endocardial cushions
  - Foramen primum closes as programmed cell death in septum primum → foramen secundum
  - Septum secundum grows right to left of septum primum
  - Partially covers foramen secundum, residual hole is foramen ovale
  - Upper septum primum atrophies, lower portion attached to endocardial cushions → flap of foramen ovale
CARDIAC DEVELOPMENT & IMAGING

Clinical Implications

Clinical Importance
- Some forms of congenital heart disease (CHD) strongly associated with aetiology

Related References
3. Anderson RP et al: Development of the heart: (3) formation of the ventricular outflow tracts, arterial valves, and truncal/ventricular arterial trunks. Heart. 89(9):918, 2003
(Left) ECHO view shows the anterior aortic wall (arrow) in continuity with the ventricular septum (curved arrow). The vessel is followed to confirm head and neck branches and vertebral arterial concordance. (Right) RIOT view shows the pulmonary artery ascension. The ductus arteriosus (arrow) turns toward the spine and descending aorta, the right pulmonary artery (curved arrow) loops around the aortic root (right arrow).

(Left) Sagittal oblique ultrasound shows the typical "candy cane" configuration of the aortic arch with the head and neck vessels (arrows) arising from the apex of the curve. (Right) Sagittal ultrasound shows the ductal arch, which has a much flatter "hockey stick" shape than the "candy cane" aortic arch. The ductus (curved arrow) bypasses the lung to connect with the descending aorta (arrows).

(Left) Sagittal ultrasound shows the superior vena cava (SVC) and inferior vena cava (arrow) draining into the right atrium (RA). One of the hepatic veins (curved arrow) is seen entering the inferior vena cava. (Right) Four-chamber view shows the inferior pulmonary veins (arrows) entering the left atrium which connects to the smooth-walled left ventricle (curved arrow). This is a biventricular concordance.
ECHOCARDIC CARDIAC FOCUS

And ultrasound shows a left ventricular echogenic cardiac focus (arrow) in a fetus with trisomy 21. The patient was at advanced maternal age and had an abnormal maternal serum quadruple test result.

Sagittal ultrasound of the fetal heart and neck in the same fetus with trisomy 21 shows no echogenic focus (open arrow) and delayed fusion of the aortic membrane (arrow below).

TERMINOLOGY

Abbreviations and Synonyms
- Echogenic cardiac focus (ECF)
- Intracardiac echogenic focus (IEF)

Definitions
- Cardiac papillary muscle echogenicity

IMAGING FINDINGS

General Features
- Best diagnostic clue: Bright as bone echogenic focus in cardiac ventricle
- Location: Left ventricle most common
- Size: Usually < 3 mm

Ultrasoundographic Findings
- Bright echogenic dot in ventricle of heart
  - Seen best when cardiac apex pointed up towards transducer
  - Should be bright as bone to be true finding
  - Often single focus in left ventricle
  - 78% left ventricle
  - 18% right ventricle
  - 4% bilateral
  - Most often incidental finding

- 3-4% of all 2nd trimester fetuses
- ECF associated with trisomy 21 (T21)
  - 1.8 likelihood ratio (LR) when isolated
  - 1.85 higher risk for T21 than a priori risk
  - Rarely turns low-risk patient into high-risk patient
  - Seek other markers for T21
  - Nuchal thickening
  - Short femur/humerus
  - Echogenic bowel
  - Renal polycystosis
  - Resolution of ECF does not change risk
  - ECF associated with trisomy 13 (T13)
    - Associated cardiac anomalies common
    - Hypoplastic left heart + ECF very suggestive of T13
    - Rarely isolated finding
    - Large and bilateral ECF
    - Risk for aneuploidy compared to single ECF

Imaging Recommendations
- Best imaging tool: Routine four chamber heart view
- Peri-protocol advice
  - Compare echogenicity with bone
  - Look carefully for T21 markers when ECF seen
  - Assess maternal a priori risk for T21 and T13
  - Maternal quadruple serum test double
  - Maternal age
  - Considered normal when isolated in low-risk patient
  - Aneuploidy not necessary

DDx: Intracardiac Echogenicities

Malignant Tumor
- N. Septal Defect
- M. Prenatal Band
- Papillary Muscle
ECHOGENIC CARDIAC FOCUS

Imaging Findings
- Bright echogenic dot in ventricle of heart
- Should be bright as bone to be true finding
- Often single focus in left ventricle
- Most often an incidental finding
- ECF associated with trisomy 21 (T21)
- ECF associated with trisomy 13 (T13)

Top Differential Diagnoses
- Rhadomyoma

Key Facts
- Normal papillary muscles
- Normal moderator band muscle

Pathology
- 3-4% of normal fetuses have ECF
- 9-12% of normal Asian fetuses have ECF

Diagnostic Checklist
- Isolated ECF in low-risk patient almost always a normal finding

DIFFERENTIAL DIAGNOSIS

Rhabdomyoma
- Homogeneous echogenic cardiac tumor
- Often involves ventricular septum
- Can originate from ventricular wall and atria
- Multiple tumors common
- 50-65% have tuberous sclerosis

Normal cardiac structures
- Normal papillary muscles
- Attach to mitral and tricuspid valves
- Not as echogenic as bone
- Normal moderator band muscle
- At apex of right ventricle
- Hyperechoic structure

Atrioventricular (AV) septal defect
- Lack of central cardiac structures
- Variable absence of atrioventricular valves
- Remains of MV and TV can mimic ECF
- Highly associated with T21

PATHOLOGY

General Features
- Genetics: ECF associated with T21 and T13
- Epidemiology
  - 3.4% of normal fetuses have ECF
  - 9-12% of normal Asian fetuses have ECF
  - 18% of fetuses with T21 have ECF
  - 39% of fetuses with T13 have ECF

Microscopic Features
- Mineralization of papillary muscle

CLINICAL ISSUES

Presentation
- Most common sign/symptoms
- Incidental finding in low-risk patient
- High prevalence in Asian patients
- Seen with other markers of T21
- Seen with severe anomalies of T13

Natural History & Prognosis
- Excellent prognosis in low-risk patients

DIAGNOSTIC CHECKLIST

Consider
- Isolated ECF in low-risk patient almost always a normal finding

Image Interpretation Pearls
- Do not diagnose ECF if echogenicity is less than bone

SELECTED REFERENCES

IMAGE GALLERY

(left) Axial ultrasound shows isolated ECF (arrow) and a small left ventricle (arrowhead in a fetus with trisomy 13; bilateral vision and palate was also seen). ECF is almost never an isolated finding with T13. (Right) Sagittal ultrasound shows three ECF (arrows) as bright as bone (open arrow) in the left ventricle. The finding was isolated and the patient was low risk based on age and serum markers; amniocentesis was not performed despite maternal age. 
FORAMEN OVALE ANEURYSM

Four chamber view shows the typical "balloonized" appearance of the foramen ovale flap (arrow) in a fetus with a foramen ovale aneurysm. There were no adverse consequences.

Color Doppler imaging shows the typical appearance of the foramen ovale flap (arrow). Red reflects atrial contraction, blue venous atrial contraction. PACs can be seen in up to 50% of fetuses with foramen ovale aneurysms.

- Look for additional structural abnormality
- Mitral valve prolapse
- Mitral and tricuspid stenosis
- Pulmonary venous obstruction
- Check rhythm
- Up to 30% will have premature atrial contractions (PACs)
- Rare case of intermittent or sustained supraventricular tachycardia (SVT)
- Cardiac evaluation of mitral valve

DIFFERENTIAL DIAGNOSIS

Normal foramen ovale flap
- Normal flap shows little mobility during cardiac cycle
- Seen projecting into left atrium on four chamber view
- Linear flap
- Not enough tissue to "balloon"
- With reversed atrial shunting flap projects into right atrium
- Seen in left heart obstructive pathology

PATHOLOGY

General Features
- Genetics: No association with aneuploidy

IMAGING FINDINGS

General Features and Synonyms
- Foramen ovale aneurysm
- Atrial septal aneurysm
- Aneurysm of septum primum
- Redundant septum primum flap

Definitions
- Redundant tissue in foramen ovale flap
- Definition of reductancy varies between series
- Flap extends at least half way across left atrium
- Flap excursion > 5 mm beyond plane of atrial septum
- Flap demonstrates abnormal mobility

TERMINOLOGY

General Features
- "Balloon" appearance of foramen ovale flap
- May make cyclic contact with left atrial wall of mitral valve
- Very redundant flap may even herniate through mitral valve

Imaging Recommendations
- Consider formal fetal echocardiography

DDx: Foramen Ovale Aneurysm

Normal flap
Normal flap
Reverse: Atrial Septum
FORAMEN OVALE ANEURYSM

Terminology
- Redundant tissue in foramen ovale flap
- Flap demonstrates abnormal mobility

Top Differential Diagnoses
- Normal foramen ovale flap

Pathology
- 5.4% of fetuses referred for arrhythmia had incidental finding of foramen ovale aneurysm

Key Facts

Clinical Issues
- No fetuses in large series (> 1,000 patients) developed significant arrhythmia

Diagnostic Checklist
- Isolated foramen ovale aneurysm is a benign entity
- If associated with PACs, very small risk of progression to tachyarrhythmia

Treatment
- Monitor for rhythm disturbance by regular auscultation
- Scattered case reports of persistent arrhythmia in children requiring resection of redundant tissue

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls
- Isolated foramen ovale aneurysm is a benign entity
- If associated with PACs, very small risk of progression to tachyarrhythmia

SELECTED REFERENCES

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
- Observed on four chamber view at routine obstetric sonography
- May be found in fetus being evaluated for PACs or arrhythmia

Natural History & Prognosis
- Associated with premature atrial contractions
- No fetuses in large series (> 1,000 patients) developed significant arrhythmia
- All infants had normal sinus rhythm by 3 months age

IMAGE GALLERY

*Left* Four chamber view shows persistent "ballooning" of the foramen ovale flap that may demonstrate the left atrial wall (reversed arrow). This is thought be a mechanical stimulus for arrhythmia. *Right* Same dropout shows extensive anteroposterior diameter. The curved arrows mark the path taken by slow pathway, similar to premature supraventricular tachycardia. The curved arrow marks the pathway to slow rhythm from circumferential and supraventricular reentry.
**TERMINOLOGY**

**Abbreviations and Synonyms**
- Pericardial fluid
- Pericardial effusion (PE)

**Definitions**
- Accumulation of fluid in pericardial space

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue
  - Fluid collection surrounds fetal heart
  - Max. thickness > 2 mm
  - Hypoechoic rim extends over atria as well as ventricles
  - If large, heart's seen beating in a "bag of water"

**Ultrasonographic Findings**
- Lenticular or oval collection of fluid adjacent to, or surrounding heart
- Seen best on standard four chamber view
- Trace of fluid along one ventricular wall is normal
  - Can be up to 2 mm
  - Majority of fetuses (50-80%) have trace of fluid if careful search done

**Imaging Recommendations**
- Pericardial effusion seen in many conditions
  - Complete fetal assessment required to exclude significant pathology
  - Look for other signs of hydrops
    - Cardiomegaly
    - Skin edema
    - Pleural effusion
    - Ascites
    - Abnormal Doppler
      - Tricuspid regurgitation
      - Reversed flow in inferior vena cava
      - Reversed flow in ductus venosus
      - Pulmonary umbilical vein flow
  - Look for signs of congenital infection
    - Liver calcifications
    - Brain calcifications
    - Echoic bowel
  - Look for anomalies
    - Measure middle cerebral artery peak systolic velocity
    - Plot against gestational age
    - Reliable indicator of fetal anomalies
      - Usually alloprenalinization
      - Parvovirus
      - Rare congenital anomalies may present with PE
  - Check growth and well-being

**DDx: Pericardial Effusion**

- Pleural Effusion
- Normal Myocardium
PERICARDIAL EFFUSION

Key Facts

Pathology
- Cardiac abnormality
- Congenital infection
- High-output states
- Fetal endocrine abnormality

Clinical Issues
- With fetus in utero overall prognosis is poor
- No treatment necessary if isolated and small
- Follow-up exams necessary when fluid is >2 mm or in high-risk patients
- Treat underlying cause where possible

Diagnostic Checklist
- Pericardial effusion may be first sign of hydrops especially if etiology is cardiac

Differential Diagnosis

Normal pericardial fluid
- Less than 2 mm
- May be transient
- Follow-up ultrasound in high-risk patients

Normal peripheral myocardium
- Outside 1-6 mm of myocardium may be hypoechoic and mimic fluid
- Seen encircling ventricles only, does not surround atria
- Circular ovals muscle fibers cause this effect
- Look for conection
- Pericardial fluid creates an immobile ring

Pleural effusion
- Usually not just adjacent to heart
- Transverse section = fluid tracks around lungs
- Sagittal or coronal sections = fluid tracks under lungs

Pathology
- Cardiac abnormality
  - Arrhythmia
  - Structural defect
  - Cardiomegaly
  - Ventricular aneurysm/diverticula

General Features

Etiology
- Cardiac abnormality
- Arrhythmia
- Structural defect
- Cardiomegaly
- Ventricular aneurysm/diverticula

Terminology
- Accumulation of fluid in pericardial space

Imaging Findings
- Fluid collection surrounds fetal heart
- Most measure >2 mm
- Seen best on standard four-chamber view
- Trace of fluid along one ventricular wall is normal
- Pericardial effusion seen in many conditions
- Complete fetal assessment required to exclude significant anomalies

Top Differential Diagnoses
- Normal pericardial fluid
- Normal peripheral myocardium
- Pleural effusion

- Severe placental insufficiency = intrauterine growth restriction
- Abnormal placental resistance = right heart strain
- Cardiac compromise = pericardial effusion
  - Look for shunt lesions as cause of high output state
  - Placental chorioangioma
  - Examine whole placental surface
  - Arteriovenous malformation (AVM)
  - Use color Doppler
  - Vein of Galen and other brain AVMs may present with PE/hydrops
  - Fetal tumors
  - Usually large and easily seen
  - In multiples check chorioangiometry and anemia
  - Monochorionic diastrophic pairs at risk for twin-twin transfusion syndrome (TTTS)
  - Risk cardiac compromise in both fetuses
  - High output in pump twin
  - Volume overload in recipient
  - Monozygotic pairs at risk for cord accidents
  - Hypoxia/sclerema = cardiac compromise
  - Twin reverse arterial perfusion (TRAP) sequence may cause cardiac compromise in pump twin
  - Anomalous aortic twin should be obvious
  - Careful search for features of aneufluency
    - One series (published in 1995) showed 30% aneufluency rate with apparently isolated PE
    - Look for specific markers: Thick nuchal fold, short humerus, absent natal bone for trisomy 21
    - Clenched fingers, cardiac defects for trisomy 18
  - Pericardial teratoma
  - Effusion often very large
  - May be mistaken for pleural effusion
  - Lung will be compressed posteriorly by pericardial effusion
  - This appearance differs from large pleural effusion
  - Circumferential pressure on lungs = lungs collapse centrally = "angiotensin" appearance
  - May have tamponade physiology
  - Mass rises from pericardium not myocardium
  - Presentation with PE also described in fetal cardiac herniamoma
PERICARDIAL EFFUSION

- **Congenital infection**
- **CMV**
- **Rubella**
- **Toxoplasmosis**
- **Parvovirus B19**
- **Syphilis**
- **High-output states**
- **TNTS/ITAP**
- **AVM**
- **Tumors**
- **Aneurysm**

- **Fetal endocardial abnormality**
  - **Fetal hypothyroidism may present as hydrops**
- **Endocrine**
  - 0.02% of fetuses in a series of 506 routine obstetric scans had isolated PE
  - **Maximum measurement 3 mm**
  - **All normal outcome**

**CLINICAL ISSUES**

**Presentation**

- incidental finding on screening exam
- in association with hydrops fetalis
- in association with cardiac anomaly

**Natural History & Prognosis**

- Variable depending on cause
  - With hydrops fetalis overall prognosis is poor
  - When PE seen early, hydrops more likely associated with cardiac abnormality
  - Some cases may be treatable (e.g., tachycardia/thrombosis)
  - When PE seen late, hydrops likely from other causes
  - Still potential to term successfully (e.g., intrauterine transfusion for fetal anemia)

- **Cardiac diverticulum**
  - Large associated PE may cause tamponade and hydrops
  - Single pericardial nodule in number of cases reports
  - No recurrence of PE
  - Normal cardiac function at birth

**Treatment**

- No treatment necessary if isolated and small
- Follow-up exams necessary when fluid is > 2 mm in high-risk patients
- May progress to hydrops
- May resolve completely

- Consider karyotype
  - Series of 35 isolated pericardial effusions (no structural cardiac defect or arrhythmia)
  - 30% had some chromosomal anomaly
  - 26% trisomy 21

- **Obstructive Screen**
  - Direct culture more reliable than maternal antibody screening

- Treat underlying cause where possible
- Medial treatment for arrhythmias
- Treat TNTS

- Laser ablation vs. serial nitroreduction
- Consider fetal surgery for tumors such as saccocoeval teratoma
- Mitral/atrial reconstruction for fetal anemia
- **Pericardial effusion**
- Benign neoplasm
- If no hydrops
  - Follow frequently
  - Postnatal resection
- If hydrops
  - Pericardiecstomy may be life-saving

**DIAGNOSTIC CHECKLIST**

- **Consider**
  - Many different etiologies for pericardial effusion
  - **Assessment** requires thorough anatomic survey
  - **Evaluation** in fetal anemia
  - May need formal fetal echocardiogram

**Image Interpretation Pearls**

- Pericardial effusion may be first sign of hydrops especially if etiology is cardiac

**SELECTED REFERENCES**

PERICARDIAL EFFUSION

IMAGE GALLERY

Typical

(left) Four-chamber view shows a small pericardial effusion (arrow) in a fetus with apparently normal tachycardia. Hydrops developed on follow-up scans despite digoxin treatment. Control was eventually achieved with digoxin plus theophylline.

(right) M-mode ultrasound from the same case shows persistent tachycardia with heart rate of 240 beats per minute.

Typical

(left) Axial oblique ultrasound of the chest shows a 5 mm pericardial effusion (curved arrow) in this infant with heterozygous, hypoplastic left heart (arrow) and critical pulmonary stenosis. Hydrops developed and the infant expired within hours of delivery.

(right) Four-chamber view shows a large pericardial effusion (arrow) in association with myocardial thickening (curved arrow) in the umbilical cord of a pregnancy complicated by twin-twin transfusion syndrome.

Variant

(left) Coronal T1W MR shows a large intrapericardial bruise (arrow) adjacent to the heart (curved arrow). It is surrounded by a massive high signal pericardial effusion. No normal lungs are visualized. Acute open (open arrow) is also present.

(right) Gross pathology shows a massively distended, fluid-filled pericardial sac (arrow) essentially filling the thoracic cavity. The tumor (curved arrow) can be seen within the sac. (Not shown in Radiographics, ref 7.)
SITUS INVERSUS

TERMINOLOGY

Definitions
- Situs inversus (SI): Heart and stomach on right (*mirror image* of normal situs)
- Situs solitus: Cardiac apex/stomach left, liver-right

IMAGING FINDINGS

General Features
- Best diagnostic clue
  - Stomach on left side
  - Cardiac apex points to right

Imaging Recommendations
- Check fetal situs in all 2nd and 3rd trimester scans
  - Never assume heart and stomach indicate fetal left side
  - Determine presenting part
  - Final longitudinal orientation of spine and relationship to maternal abdomen
- From these two, determine fetal left and right side
  - Stomach and cardiac apex on same side
  - Both left = situs solitus
  - Both right = situs inversus
  - Measure cerebral ventricles

- Mild ventriculomegaly reported as a fetal marker for Kartagener syndrome
- Careful search for other anomalies

DIFFERENTIAL DIAGNOSIS

Heterotaxy syndromes
- Left atrial isomerism
  - Complex congenital heart disease (CHD), especially left-sided obstruction and total anomalous pulmonary venous drainage (TAPVR)
  - Interrupted inferior vena cava withazygos continuation
  - Right atrial isomerism
  - Complex CHD, especially transposition/double outlet right ventricle, atrioventricular canal and TAPVR
  - Liver midline
  - No spleen

Cardiac dextroposition
- Heart displaced into right hemithorax by mass
  - Cystic adenomatoid malformation, sequestration, congenital diaphragmatic hernia (CDH)
  - May also occur with hypoplasia/agenesis right lung

Isolated dextrocardia
- Cardiac apex right, abdominal organs normal

DDx: Abnormal Heart Position

[Images of various heart positions]
Situs Inversus

**Terminology**
- Situs inversus (SI): Heart and stomach on right ('mirror image' of normal situs)

**Top Differential Diagnoses**
- Heterotaxy syndromes
- Cardiac devioposition
- Isolated dextrocardia

**Key Facts**

**Pathology**
- 20% have Kartagener syndrome

**Clinical Issues**
- Risk of CHD < 3%

**Diagnostic Checklist**
- SI not associated with aneuploidy
- Will be missed unless fetal left and right sides are determined

**Natural History & Prognosis**
- Risk of CHD < 3%
- Associated bowel malrotation increases risk for volvulus
- Prognosis excellent for isolated SI

**Diagnostic Checklist**
- SI not associated with aneuploidy
- Karyotype not necessary
- Will be missed unless fetal left and right sides are determined

**SELECTED REFERENCES**

**IMAGE GALLERY**

(Left) Axial transaxial abdominal ultrasound shows situs inversus with the liver on the left and the pancreas (arrow) on the right. This will only be appreciated at a fetal orientation is known. (Right) Axial T2 MRI shows the right-sided gallbladder (arrow) and liver (arrows) in the expected location in this fetus with situs inversus. The gallbladder is in the right upper abdomen.
HETEROTAXY, CARDIOSPLENIC SYNDROMES

Terminology

**Abbreviations and Synonyms**

- Heterotaxy
- Situs ambiguous
- Terminology is confusing with multiple terms for similar anatomic combinations
  - Listed below are terms used for certain combinations of situs, they are not necessarily synonymous
- Right atrial (RA) isomerism
  - Asplenia
  - Bilateral right-sidedness
  - Evenmark syndrome
  - Dextroisomerism
- Left atrial (LA) isomerism
  - Polyplagia
  - Bilateral left-sidedness
  - Levosomerism

**Definitions**

- Heterotaxy is any arrangement of internal organs other than situs solitarius or complete situs inversus
  - Situs solitus
    - Cardiac apex left
    - Dextrocardiac (D) loop
    - Liver/cecum right
    - Stomach left
    - Sinus inversus

- Complete mirror image of situs solitus

**IMAGING FINDINGS**

**General Features**

- Best diagnostic clue
  - Heart and stomach on opposite sides
- Abnormal relationship of abdominal aorta and inferior vena cava (IVC)
  - Complete heart block in presence of congenital heart disease (CHD)

**Ultrasonographic Findings**

- Grayscale Ultrasound
  - Intermittent IVC in LA isomerism
  - Hepatic veins drain directly to atrium
  - Enlarged azygos vein (continuation of IVC) posterior to aorta
  - IVC anterior to aorta on same side of spine in RA isomerism
  - Bilateral superior vena cavae (SVC)
  - Sessile both LA/RA isomerism
  - Abnormal stomach location
  - Right, left or central depending on liver position
  - Midline liver
  - Gallbladder may be absent in LA isomerism
  - Color Doppler
    - Look for splenic artery

**DDx: Abnormal Location Heart/Stomach**

- CDH
- CDH
- CCAM
- ECA
HETEROTAXY, CARDIOSPLENIC SYNDROMES

Terminology
- Terminology is confusing with multiple terms for similar anatomic combinations
- Heterotaxy is any arrangement of internal organs other than situs solitus or complete situs inversus

Imaging Findings
- Heart and stomach on opposite sides
- Abnormal relationship of abdominal aorta and inferior vena cava (IVC)
- Midline liver
- Cardiac anomalies occur at every level: Atrial, atroventricular, ventricular, ventriculoarterial

Top Differential Diagnoses
- Abnormal cardiac position
- Abnormal stomach bubble

- Seen with polysplenia (LA isomerism)
- Absent in asplenia (RA isomerism)
- Helpful to identify, trace course of systemic veins

Echocardiographic Findings
- Abnormal cardiac axis
- Cardiac anomalies occur at every level: Atrial, atroventricular, ventricular, ventriculoarterial
- Anomalies occur in any combination
- The commonest forms of CHD seen with each type of heterotaxy are listed below
- LA isomerism/polysplenia
  - Dextrocardia in 30-40%
  - Bilateral SVC in 40%
  - Interrupted IVC in > 70%
  - Atrial septal defect (ASD) in 80%
  - Common atrium/atrial septal defect (ASD) in 80%
  - Atrioventricular (AV) canal in 20-40%
  - Single ventricle in 10%
  - Left ventricular outflow tract obstruction in 40%
  - Conotruncal abnormalities in 15-30%
  - Pulmonary stenosis/atresia
  - Transposition of great arteries
- RA isomerism/asplenia
  - Dextrocardia in 30-40%
  - Bilateral SVC in 50-70%
  - Total anomalous pulmonary venous return (TAPVR) in 50-70%
  - Common atrium/ASD in 90%
  - AV canal in 80%
  - Single ventricle > 50%
  - Congenital abnormalities 80%
  - Double outlet right ventricle (DORV)
  - Pulmonary stenosis/atresia
  - Transposition of great arteries

Imaging Recommendations
- Protocol advice
  - Formal fetal echocardiography
  - Complete anatomic survey

Key Facts
- Isolated vena cava anomalies

Pathology
- Heterotaxy syndromes = 4% of all infants with CHD

Clinical Issues
- Depends on type and severity of associated cardiac malformation

Diagnostic Checklist
- Check situs in all fetal ultrasound scans
- Heterotaxy syndromes have worse prognosis than isolated CHD
- ≥ 2 cardiac structural defects strongly suggests heterotaxy
- Interrupted IVC strongly suggests LA isomerism
- Single ventricle + AV canal + right outflow obstruction = RA isomerism

DIFFERENTIAL DIAGNOSIS

Abnormal cardiac position
- Chest mass
  - Congenital diaphragmatic hernia (CDH)
  - Congenital cystic adenomatoid malformation (CCAM)

Abnormal stomach bubble
- Malpositioned
  - CDH
  - Look for stomach and heart on same axial scan plane
  - Look for liver in chest

Isolated vena cava anomalies
- Atrioventricular discordance of the IVC without congenital heart disease

PATHOLOGY

General Features
- Genetics
  - Majority are sporadic
  - Aneuplody rarely coexists with heterotaxy syndromes
- A number of familial cases have been described
  - X-linked (Xq26.2)
  - Autosomal dominant or recessive
- All variants of situs can occur within heterotaxy families

Epidemiology
- M/F = 1:2 in LA isomerism
- M/F = 2:1 in RA isomerism
- Heterotaxy syndromes = 4% of all infants with CHD
- Heterotaxy syndromes = 30% cardiac malpositions in infants

- LA isomerism more commonly diagnosed in affected
  - Associated complete heart block
  - Hydrops
  - Intracardiac fetal demise

- RA isomerism more common in postnatal series
  - Associated abnormalities
HETEROTAXY, CARDIOSPLENIC SYNDROMES

- LA isomerism
  - Bilateral left atrial appendages (finger-like)
  - Polydactyly in 56%
  - Both lungs inflated with hyparterial branches
  - Malpositioned stomach
  - Malarticulation of intestines with potential for obstruction in 85%
  - Centrally-placed, abnormally-shaped liver
  - Extraluminal biliary atresia
  - Absence/hypoplastic or midline gallbladder
  - Absence of a sinusoidal node-often in functional rhythm
- RA isomerism
  - Bilateral right atrial appendages (pyramidal shape)
  - Spleen in 74%
  - Both lungs trilobed with epibulbar brochus
  - Centrally-placed globular liver
  - Stomach either midline or left in 60%
  - Malarticulation of intestines with potential for obstruction in 95%
  - Presence of 2 sinusoidal nodes-often with SVT
- Broad spectrum of abnormalities fit with heterotaxy category
  - Dextrocardia + abdominal situs inversus
  - Levocardia + abdominal situs inversus
- Also documented cases of isomerism with normal spleen
- Embryology
  - Midline development field defect
  - Endocardial insult days 28-35
  - Sequence of cardiac development arrested in 5th week gestation

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - In fetus
    - Abnormal sites
    - Interrupted IVC with asynergy continuation
    - Two or more type of CHD
    - Heart block
  - Abnormality in infant
    - Cyanotic infant with respiratory distress
    - Intracardiac/vagal abnormal chest X-ray
    - Chest X-ray
    - Cardiac malposition
    - Mediastinal liver
    - Diminished or congested pulmonary vascular markings

Natural History & Prognosis
- Depends on type and severity of associated cardiac malformation
- Biventricular repair with better long-term outcome than single ventricle (60% vs. 30%)
- Increased mortality
- Obstructed pulmonary veins
- 95% in association with single ventricle
- Outflow tract obstruction
- Single ventricle malformation
- RA isomerism
- 60% overall mortality for staged single ventricle palliation
- LA isomerism
- 50% early mortality
- 40% 5 year survival
- Patients who make it to Fontan palliation have over 80% 5 year survival

Treatment
- Consider karyotype if multiple anomalies in addition to CHD
- Detailed genetic history
- Prenatal consultation with neonatology/pediatric cardiology
- Delivery in tertiary care facility
- Pulmonary arteries may be necessary for survival with duct dependent lesions
- Emergency surgery required for obstructed TAPVR
- Surgery for outflow tract obstruction necessary in first week of life
- Additional surgery for single ventricle palliation within 6 months
- Surgery for complex systemic venous abnormalities around 1 year

DIAGNOSTIC CHECKLIST

Consider
- Check situs in all fetal ultrasound scans
- Heterotaxy syndromes have some prognosis than isolated CHD

Image Interpretation Pearls
- 2 cardiac structural defects generally suggests heterotaxy
- Interrupted IVC strongly suggests LA isomerism
- Single ventricle + IV canal + right outflow obstruction = RA isomerism

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1. Cheng YJ et al. Outcome of infants with right atrial isomerism: is prognosis better with normal pulmonary venous drainage? Heart. 87(12):143-152, 2002
**HETEROXY, CARDIÓSPLÉNIC SYNDROMES**

**IMAGE GALLERY**

**Typical**

(Left) Gross pathology of the heart and lungs shows bicalveal superior vena cava (curved arrows) on either side of the great arteries (open arrow - pulmonary artery; arrow - aortic arch).

(Right) Large cava ultrasound in a fetus with heterotaxy shows a double outlet right ventricle with the pulmonary artery (arrow) parallel to the aorta (curved arrow), which is arising from the RV (open arrow).

**Typical**

(Left) Sagittal oblique ultrasound shows a large ayzygous vein posterior to the aorta, implying an interrupted inferior vena cava and probable left atrial isomerism in a fetus with congenital heart disease.

(Right) Sagittal color Doppler ultrasound confirms the great atrial impression. There is caudal flow within the aorta (curved arrow) and cephalad flow along the prominent ayzygous vein (arrow), consistent with an interrupted inferior vena cava.

**Typical**

(Left) Four chamber view shows a complete ASD. There is a common atrium. The ventricles are symmetric in size therefore this is a balanced defect. The AV valve leaflets (curved arrows) are in the closed position (arrow - ventricular septum).

(Right) Four chamber view in the same fetus shows the valve leaflets (curved arrows) in the open position. The ventricular septum is directed by the aorta. This fetus had a heterotaxy syndrome.
**VENTRICULAR SEPTAL DEFECT**

Terminology and Synonyms:
- Ventricleal septal defect (VSD)

**IMAGING FINDINGS**

General Features:
- Best diagnostic clue:
  - Defect in ventricular septum
  - Small muscular VSDs may not be visible on grayscale or with color Doppler
  - Membranous 80% Tetralogy of Fallot, truncus arteriosus
  - Muscular 10% Tricuspid, may be multiple
  - Outlet 5% Infundibular, supracristal, doubly committed subaortic
  - Often associated with aortic insufficiency
- Inlet 5% Component of an atrioventricular septal defect

Ultrasoundographic Findings:
- Grayscale Ultrasound
  - Signal drop out in septum
  - Try to image perpendicular to ventricular septum
  - Look for echogenic edge of defect

- Color Doppler
  - Color Doppler used to confirm blood flow across defect
  - Signal left ventricular pressures similar in fetus short bi-directional
  - Tri-directional shunt look for other anomalies altering balance of ventricular pressure (e.g., outflow tract obstruction)

Imaging Recommendations:
- Formal fetal echocardiography
- 50% association with additional cardiac anomaly
- Complete structural survey
- Isolated VSD with extracardiac abnormality, look for trisomy, deletion syndromes, Holt-Olmsted

**DIFFERENTIAL DIAGNOSIS**

Complete atrioventricular septal defect
- Defect involves atrial and ventricular septa
- Common AV valve straddling septal defects

DDx: Ventricular Septal Defect

![ASD Valve Closed](image1)
![ASD Valve Open](image2)
![Phenom ASD](image3)
VENTRICULAR SEPTAL DEFECT

Imaging Findings
- Defect in ventricular septum
- Small muscular VSDs may not be visible on grayscale or with color Doppler
- Right/left ventricular pressures similar in fetus ⇒ shunt bi-directional
- If unidirectional shunt look for other anomalies altering balance of ventricular pressures (e.g., outflow tract obstruction)

Key Facts
- 50% association with additional cardiac anomaly
- Top Differential Diagnoses
  - Complete atrioventricular septal defect
  - Partial atrioventricular septal defect
- Clinical Issues
  - Surgical repair if maximal medical therapy fails
  - Large VSD ⇒ risk early decompensation ⇒ consider delivery at tertiary center
  - Follow for development of hydrops. Low-risk with isolated small VSD
  - Monitor growth

PATHOLOGY

General Features
- Genetics
  - Holt-Oram syndrome: Autosomal dominant
  - TBX5 transcription factor gene mutation
- Septal defects, radial ray and other skeletal malformations
- Etiology
  - Teratogen exposure
  - Alcohol, phenytoin, rubella, diabetes, oral contraceptives, phenytoin teratogenesis
- Epidemiology
  - VSD accounts for 30% of all congenital heart disease (CHD) in newborn
  - Implies incidence of 2:3:1,000 total births
  - 6% of fetal CHD: Disparity due to demise of fetuses with more complex CHD and small, missed defects

Partial atrioventricular septal defect
- Defect involves primum atrial septum not ventricular septum
- Often associated clef in mitral valve with mitral regurgitation

CLINICAL ISSUES

Natural History & Prognosis
- Variable, depends on
  - Size of defect and degree of left → right shunt
  - Associated cardiac abnormalities (present in 50%)
  - Liveborn, isolated VSD
  > > 50% spontaneons closure, usually before age 5
  - Surgical repair if maximal medical therapy fails
  - Right atrial approach, Dacron or pericardial patch
  - Operative mortality < 2%, 5% if multiple defects
  - Device closure in cath lab is new technique
  - Recurrence risk
    - One child 3%, two 10%
  - Maternal VSD 6-10%, paternal 2%

Treatment
- Offer karyotype if extracardiac abnormalities
- Prenatal pediatric cardiology consultation
  - Large VSD ⇒ risk early decompensation ⇒ consider delivery at tertiary center

SELECTED REFERENCES

DIAGNOSTIC CHECKLIST

Consider
- Majority of VSDs missed on prenatal ultrasound
- Hemodynamically significant lesions are larger ⇒ more likely to be detected
- Those associated with complex heart disease less likely to be missed

Image Interpretation Pearls
- Look for septal continuity with aortic anulus in LVOT view to exclude VSD
- Keep sound beam perpendicular to septum: Avoids VSD mimic of "dropout" at membranous-muscular junction

IMAGE GALLERY

(Left) Ultrasound shows a high peri-membranous VSD arising from the valve with rightward to leftward shunt (Right) Gross pathology: high peri-membranous VSD arising from valve with rightward to leftward shunt
ATRIOVENTRICULAR SEPTAL Defect

Graph shows a common AV valve (cleft) spanning a central defect in the heart involving the atrial and ventricular septal. Shing of blood in the heart leads to similar situations in the aorta and A/P.

**TERMINOLOGY**

Abbreviations and Synonyms
- Endocardial cushion defect
- Atrioventricular canal
- Atrioventricular septal defect (AVSD)

Definitions
- Central defect in heart involving
  - Atrial septal defect (ASD)
  - Ventricular septal defect (VSD)
  - Atrioventricular valves
  - Abnormal course of conducting system
- Defect can be balanced or unbalanced
  - Balanced: right and left ventricles are equal
  - Unbalanced: results in equivalent of single ventricle physiology

**IMAGING FINDINGS**

General Features
- Best diagnostic clue
  - Missing "cleft" of heart in four-chamber view
  - Atrial and ventricular septum may look atrophic vs normal "cleft" of heart
  - Usual effusion of AV valves is absent
  - Presence of atrial and ventricular septal defects

**Imaging Findings**

DDX: Atrioventricular Septal Defect

**Ultrasonographic Findings**
- Strong association with trisomy 21 in fetus
  - Absent nasal bone
  - Right atrioventricular septal defect (ASD)
  - Right atrioventricular septal defect (VSD)
  - Atrioventricular valve stenosis
  - Class III/IV

**Echocardiographic Findings**
- Single AV valve makes straight line across heart in systole
  - Tricuspid insertion normally 1-2 mm offset from mitral insertion
  - Offset increases with gestational age, may be up to 7 mm at term
  - Defect in left ventricular septum
  - Defect in primum atrial septum
  - "Gossett" deformity of left ventricle (LV) outflow tract
  - Elongated, narrowed, somewhat horizontally inclined LV outflow tract

Ultrasound shows a balanced AV valve with the common AV valve equally committed to each ventricle, near the interventricular septal defect (AVSD) and the atrium of the aorta.
ATRIOVENTRICULAR SEPTAL DEFECT

Key Facts

- **Imaging Findings**
  - Missing outflow of heart in four chamber view
  - Strong association with trisomy 21 in fetus
  - Single AV valve makes straight line across heart in systole
  - Additional cardiac malformations common
  - Determine ventricular dominance (balanced or unbalanced)
  - Look for features of heterotaxy syndromes, especially interrupted inferior vena cava
  - Complete heart block (CHB) + AVSD = likely heterotaxy, specifically left atrial isomerism
  - Monitor for signs of hydrorops

- **Top Differential Diagnoses**
  - Large VSD
  - "Partial" AV septal defect

- **Imaging Recommendations**
  - Full anatomic survey for other anomalies
  - Formal fetal echocardiography
  - Condom diagnosis
  - Determine ventricular dominance (balanced or unbalanced)
  - Impacts surgical outcome
  - Evaluate associated cardiac defects
  - Look for features of heterotaxy syndromes, especially interrupted inferior vena cava
  - Check rate and rhythm
  - Conduct system involvement
  - Complete heart block (CHB) + AVSD = likely heterotaxy, specifically left atrial isomerism
  - Monitor for signs of hydrorops
  - Pericardial effusion
  - Pleural effusion
  - Ascites
  - Skin edema
  - Cardiomegaly
  - Track ratio of feet to chest circumference
  - Abnormal Doppler findings
  - Iveresed flow in ductus venous
  - Pulsatile umbilical venus flow

- **Pathology**
  - Trisomy 21 found in 40% of fetal cases
  - Other chromosomal anomalies or syndromes in 20%
  - Fetal incidence = liveborn
  - Loss rate increased association with aneuploidy/heterotaxy/additional cardiac malformations
  - Heterotaxy found in 15-20%

- **Clinical Issues**
  - Trisomy 21 not independent risk factor for adverse surgical outcome
  - 5% operative mortality
  - 20% 20 year survival rate
  - Encourage amniocentesis

Differential Diagnosis

- **Large VSD**
  - AV valves normal
  - Primum atrial septum intact

- **Large ASD**
  - AV valves normal
  - Ventricular septum intact

- "Partial" AV septal defect
  - Primum atrial septal defect
  - Complete atrial septal defect
  - Left atrial isomerism

Heterotaxy syndromes

- Multiple additional cardiac defects
- Right atrial isomerism (RAI)
  - Single ventricle
  - Bight ventricular outflow tract obstruction
  - Left atrial isomerism (LAI)
  - Interrupted IVC
  - Complete heart block

PATHOLOGY

- **General Features**
  - Genetics
    - Trisomy 21 found in 40% of fetal cases
    - Gene encoding alpha 1/alpha 2 chains of collagen VI is on chromosome 21
  - Abnormal collagen VI expression hypothesized to be causative factor in AVSD development
  - Other chromosomal anomalies or syndromes in 20%
  - Trisomy 18, 13, heterotaxy syndromes

- **Etiology**
  - Embryology
    - Endocardial cushions form too late normally
    - Primum AV canal persists after 6 weeks gestational age
  - Epidemiology
    - 1:11,000-10,000 live births
ATRIOVENTRICULAR SEPTAL DEFECT

- Partial AVSD more common than complete in liveborn
- Complexes 3-7% of congenital heart disease
- Fetal incidence > liveborn
- Loss rate reflects high association with anomieuly/heterotaxy/additional cardiac malformations
- Associated abnormalities
  - Heterotaxy found in 15-20%
  - Additional cardiac malformations such as Tetralogy of Fallot, pulmonary stenosis, left heart obstruction
  - Found in 10% with trisomy 21
  - Found in 33% in non-Down syndrome group

Staging, Grading or Classification Criteria
- Baseline classifications of AVSD
  - Type A
    - Superior bridging leaflet attached to crest of ventricular septum
  - Type B
    - Superior bridging leaflet attached to right side of ventricular septum
  - Type C
    - Superior bridging leaflet is free floating from LV free wall to RV free wall
- Additional classification of right or left dominance in unbalanced defects

CLINICAL ISSUES

Presentation
- Abnormal four chamber view detected on routine sonography
- Complete AV canal detected as early as 12-14 weeks with endovagal scanning

Natural History & Prognosis
- Markers for poor outcome
  - Multiple congenital anomalies
  - Hydrops
  - Heterotaxy syndromes
  - Defects which are unbalanced
  - Severe single ventricle palliation
  - Inherent limited life expectancy due to single ventricular pump
  - Even higher risk with trisomy 21
  - Trisomy 21 not independent risk factor for adverse surgical outcome
- Outcome is often better due to redundant AV valve tissue
- Natural history affected by high incidence of upper airway obstruction
- Resultant pulmonary hypertension
- Surgical repair
  - 5% operative mortality
  - 70% 20-year survival rate
- Recurrence risk
  - One child: 3%
  - Two children: 10%
  - Parent with AVSD and normal chromosomes: 10%
  - Higher for affected mother than father

Treatment
- Encourage antiplatelet
- Strong association with meuneplody
- Offer termination in severe cases
- With multiple additional cardiac anomalies
- With meuneplody
- With heterotaxy syndromes
- If pregnancy continues, refer to tertiary center for delivery
- Prenatal consultation with pediatric cardiologist/neonatologist
- Follow-up with valvuloplasty function and function
- Not indication for early delivery or cesarean section
- Management of birth is minimal unless additional abnormalities
- Infants tolerate oxygen saturations in 80’s
- Surgical repair takes place routinely between 4-6 months

DIAGNOSTIC CHECKLIST

Consider
- Down syndrome in > 40% of isolated AVSD
- AVSD + CHD = Left atrial isomere

SELECTED REFERENCES
ATRIOVENTRICULAR SEPTAL DEFECT

IMAGE GALLERY

Typical

(Below) Gross pathology from a fetus with an atrioventricular septal defect. The plane of section makes a direct cut view and shows a single common atrioventricular valve (arrowed arrows). There was also pulmonary hypoplasia, hence the small size of the large open arrows.

(Right) Clinical photograph shows the characteristic appearance of a child with atrioventricular septal defect. Approximately 40% of babies with atrioventricular septal defect have tetralogy of Fallot.

(Below) Color Doppler ultrasound in a fetus with AVSD shows "giant vessel" dilatation of the left ventricular outflow tract with incompetence in the aorta (curved arrow) and mitral valve regurgitation (arrow). (Right) Four chamber view shows AVSD in a fetus with left ventricle in the atrial position (open arrow - common atrium). Note two vessels behind the heart (arrows). The descending aorta is normally seen in this location, the posterior vessel is the enlarged azygos.

(Below) Four chamber view in a fetus with an unbalanced AVSD shows small left (LV) and large right (RV) ventricles. Note prominent small septal defect (arrow). (Right) Postnatal echocardiogram in the same patient confirms an unbalanced AV canal with a small left ventricle (LV). The atrial septum (curved arrow) is the mitral component and there is AVSD (curved arrow).
**TERMINOLOGY**

**Abbreviations and Synonyms**
- Hypoplastic left ventricle
- Hypoplastic left heart syndrome (HLHS)
- Endocardial fibroelastosis

**Definitions**
- Hypoplasia of left ventricle associated with
  - Mitral stenosis/insufficiency
  - Aortic stenosis/aortitis
  - Hypoplastic ascending aorta

**IMAGING FINDINGS**

**General Features:**
- Best diagnostic clue: Abnormal four-chamber view with small, non-apex-forming left ventricle

**Echocardiographic Findings**
- Left ventricle (LV)
  - Small or non-existent
  - Hypocontractile
  - May be globular
  - May see brightly echogenic LV endocardium with endocardial fibroelastosis
- Right ventricle

- Looks large
- Good function
- Apex-forming
- Atria
  - Inte-atrial septum bowed left to right
  - Only outlet for flow is LA
  - Occasionally restrictive septum
- Ascending and transverse arch very small
- Ductus arteriosus (DA) large
- Color Doppler
  - Confirms absent or minimal flow across mitral valve
  - Confirms absent or minimal flow across aortic valve
  - Left to right shunt across foramen ovale
  - Retrograde filling of LA = ductal dependence
- May see ventriculocoronary connections
- Evaluate for presence of tricuspid regurgitation
- Pulsed Doppler
  - Direction of flow through foramen ovale
  - Direction of flow in aortic arch
  - Presence of flow across mitral and aortic valves

**Imaging Recommendations**
- Formal fetal echocardiogram
- TCAP and mitral valve size and function
- Pulmonary and aortic valve size and function
- LV hypoplasia
- Endocardial fibroelastosis
- Coarctation of the aorta

DDx: Hypoplastic Left Heart Syndrome

- Double inlet LV
- Dovetail LV
- Coarctation Of Aorta
- Aortic Stenosis
HYPOPLASTIC LEFT HEART

Imaging Findings
- Best diagnostic clue: Abnormal four chamber view with small, non apex-forming left ventricle
- May see brightness echogenic LV endocardium with endocardial fibroelastosis
- Inter-atrial septum bowed left to right
- Ascending and transverse arch very small
- Ductus arteriosus (DA) large
- Left to right shunt across foramen ovale
- Retrograde filling of arch = ductal dependence
- Non-cardiac anomalies in 9% of autopsy cases

Top Differential Diagnoses
- Double inlet left ventricle
- Severe aortic stenosis
- Coarctation of aorta

Key Facts

Clinical Issues
- Most severe congenital heart lesion presenting in neonate
- Lethal in days/weeks if untreated
- 20% intrauterine fetal demise
- Long-term survival approximately 30 years
- Chromosomal abnormality in 2-10%
- Surgical intervention ⇒ planned delivery at tertiary center
- Heart transplantation ⇒ delivery at select institutions nationally
- Three-stage surgical palliation most common
- Balloon valvuloplasty of fetal aortic valve in cases of severe aortic stenosis in hopes of preventing progression to HLHS

Differential Diagnosis

Double inlet left ventricle
- Blooing of heart
- Single ventricle with bulbouventricular foramen
- Usually two normal ativoventricular (AV) valves (mitral and tricuspid)
- Usually two normal semilunar valves (aorta and pulmonar)

Severe aortic stenosis
- Antegrade flow across aortic valve
- Mitral valve may be normal in size
- LV may be apex forming

Coarctation of aorta
- Antegrade flow across aortic valve
- Mitral valve may be normal in size
- LV may be apex forming
- Flow may be R ⇒ L or L ⇒ R at atrial level
- Consider association with Turner and Shone syndromes

Pathology

General Features
- Genetics
  - Autosomal recessive transmission has been suggested
  - Multiple siblings
  - Turner syndrome (45, XO)
  - 1% of cases have HIRIS
  - Trisomy 18

- Transcription factor gene mutations
- Etiology
  - Multiple theories with no single unifying explanation
  - Multifactorial in most cases
- Structural defect early in cardiac development
  - May be secondary to transcription factor gene mutations
- "Form follows function"
  - Aortic atresia ⇒ no flow out of LV ⇒ hypoplasia
  - Mitral atresia ⇒ no flow into LV ⇒ hypoplasia
- Viral infection + myocarditis
- Embryology
  - Abnormal partitioning of primitive conotruncus into left and right ventricular outflow tracts
  - Hypoplasia/atresia of aortic valve
  - Diminished antegrade flow through aorta
  - F1 Flow = LV/aortic underdevelopment
- Epidemiology
  - 9% congenital heart disease
  - 0.161,000 live births
  - M/F = 3:1

Gross Pathologic & Surgical Features
- LV endocardium opaque, glistening, milky white in endocardial fibroelastosis
  - Diffusely thickened to 1-2 mm
- Thickening most marked in outflow tract

CLINICAL ISSUES

Presentation
- Most cases detected on routine 18-20 week scan
- Abnormal four chamber view

Natural History & Prognosis
- Most severe congenital heart lesion presenting in neonate
- Lethal in days/weeks if untreated
- Prenatal diagnosis
  - 20% intrauterine fetal demise
HYPOPLASTIC LEFT HEART

- Termination depends on many factors but
  decreasing in frequency, at least in USA
- Due to improved surgical outcomes
- Pregnancy termination rate and potential "intention
to treat" different in USA and Europe
- USA intention to treat 67%
- Europe intention to treat 34-36%, termination rate ≥ 50%

- Better perinatal stabilization = better surgical
candidates
- "Mammoth" transport
- Prostaglandin infusion started immediately
- Improving surgical techniques = increased survival
- 80% success of first stage Norwood
- Near 100% for Glenn and Fontan (2nd and 3rd stage)
- Long-term survival approximately 30 years
- May be improving in current era due to many factors
- Recurrence risk
- 2% with one sibling, 6% with two
- Familial cases with autosomal recessive pattern in
  some kindreds.
- 25% recurrence risk

Treatment
- Orbit karyotype
- Chromosomal abnormality in 2-10%
- Turner syndrome most common
- Prenatal consultation with neonatology/pediatric cardiology
- Other termination
- If pregnancy continues
- Comfort care = no intrapartum monitoring, deliver at
  any institution
- Surgical intervention = planned delivery at tertiary
  center
- Heart transplantation = delivery at select institutions
  nationally
- These-stage surgical palliation most common
  - Stage 1 (Norwood)
  - Stage 2 (Fontan)
  - Stage 3 (Glenn)
- Construction of neo-aorta from pulmonary artery, aorta and
graft
- Right heart surgery
- Pulmonary blood flow supplied by Blalock Tansig shunt or RV-pulmonary conduit (Sano modification)
- Stage 2 (Glen)
- 3-4 months
- Superior vena cava to right pulmonary artery
- Right Fontan also performed in some institutions
- Stage 3 (Fontan)
- 2-3 years
- Inferior vena cava to right pulmonary artery conduit
- Fenestration in conduit to right atrium used as a
  pop-off for systemic blood flow
- Randomized controlled trial starting in 2005 to
compare Sano modification with standard
Norwood/Blalock Taussig shunt
- Balloon valvuloplasty of fetal aortic valve in cases of
  severe aortic stenosis in hopes of preventing
  progression to HLHS

- Selection criteria
  - Prior to 20 weeks gestation if possible
  - ≤ 36 weeks gestation
  - Prior to development of endocardial fibroelastosis
  - Performed in only a few centers nationally
  - Preliminary results indicating with experience and
    selection
  - Majority end up with single ventricle
- Heart transplant
  - 15-20% mortality on transplant list
  - 70% 5 yr survival
  - Most mortality within first 30 days

DIAGNOSTIC CHECKLIST

Consider
- Fetal echocardiography very specific for this entity
  - 95% prenatal diagnosis confirmed

Image Interpretation Pearls
- Left ventricle non-specular
- Small to non-existent mitral/aortic valves

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**Typical**

- **Left**: Four chamber view showing no antegrade flow into the left ventricle (LV) and l to R shunting at the atrial level through the foramen ovale into the right atrium (arrow). 
- **Right**: Four chamber view shows a small non-separating left ventricle (LV) in a fetus with endocardial fibroelastosis. Note the high echogenicity of the left ventricular walls (arrow).

**Typical**

- **Left**: Color Doppler ultrasound demonstrates absence of flow across the mitral valve. Normal blood flow is apparent through the tricuspid valve into the right ventricle (arrow). 
- **Right**: Cross-pathology shows a hypoplastic aortic arch (curved arrow) in comparison to the pulmonary artery (open arrow) in a case of hypoplastic left heart syndrome.

**Variant**

- **Left**: DOPV view shows a very large pulmonary artery (arrow) giving rise to the ductus arteriosus (curved arrow) and right pulmonary artery. 
- **Right**: DOPV view in the same case shows a hypoplastic aorta marked by calipers. This fetus also had a Cockayne-Walker malformation, single umbilical artery and abnormal skin. Hydrops developed and the infant died shortly after birth.
COARCTATION OF THE AORTA

TERMINOLOGY

Abbreviations and Synonyms
- Coarctation of aorta (CoA)
- Interrupted aortic arch (IAA)

Definitions
- Coarctation: Narrowing of distal aortic arch
- Interrupted arch: Occlusion of aortic arch
- Aortic isthmus: That part of the aorta distal to left subclavian takeoff and proximal to insertion of ductus arteriosus

IMAGING FINDINGS

Echocardiographic Findings
- Asymmetry in ventricular size
  - Mean: right-left ventricular diameter ratio 1.69 ± 0.16 in affected fetuses
- 1.19 ± 0.08 in normal fetuses
- Pulmonary artery > aorta
- Quantitative hypoplasia, transverse arch and isthmus
  - Normal data available
  - Transverse arch measurements < 3rd percentile for gestational age in fetuses with CoA
  - Verify apparent area of narrowing from several scan planes

Color Doppler
- May show focal turbulence at narrowed area
- Left-to-right shunt across isthmus oval with left ventricular outflow obstruction
- Left ventricular (LV) pressure > left atrial (LA) pressure, flow direction at isthmus oval changes, becomes left to right

Pulsed Doppler
- May show increased velocity distal to coaractation
- Also used to assess mitral/tricuspid flow
  - Flow across tricuspid may be > 2x that across mitral valve

Interrupted arch
- Normal "candy cane" curve not seen
- Arch gives rise to one or more head and neck vessels which extend straight into neck
- Descending aorta reconstituted by ductus arteriosus

Imaging Recommendations
- Formal fetal echocardiogram for associated malformations
- Bicuspid valve
- May have associated aortic stenosis
- Conotruncal malformations
- Mitral valve disease
- Supravalvar mitral ring
- Pseudohypoplastic mitral valve
- Ventricular septal defects in 50%

DDx: Ventricular Asymmetry

- Normal At Birth
- Aortic Stenosis
- Tetralogy
- Cardiomyopathy
COARCTATION OF THE AORTA

Key Facts
- **Pathology**
  - Turner syndrome (45,XO)
  - 22q11 deletion (Di George syndrome)
  - Fetos of diabetic mother 3-5% risk

- **Clinical Issues**
  - Arch hypoplasia may progress over course of gestation
  - Goal at delivery is to maintain dactyl paclity as systemic perfusion is duct dependent
  - Definitive treatment is primary surgical repair

- **Diagnostic Checklist**
  - Coarctation is extremely difficult diagnosis in utero
  - A risk fetus with normal study still needs postnatal evaluation
  - Normal looking arch does not exclude coarctation

**PATHOLOGY**

**General Features**
- Genetics
  - Turner syndrome (45,XO)
  - 10-15% of Turner syndrome patients have CoA
  - 45% Turner syndrome fetuses have CoA
  - 22q11 deletion (Di George syndrome)
  - Present in > 50% of interrupted aortic arch cases
  - Right sided aortic arch with absent left subclavian more common

- **Etiology**
  - Fetos of diabetic mother 3-5% risk
  - Phenotype
  - Has been described in warfarin/Coumadin embryopathy

- **Epidemiology**
  - Up to 8% all congenital heart disease
  - 0.2-0.6/1,000 live births
  - M = F at birth
  - Female more common in fetuses because of Turner syndrome cases, which often have in utero demise
  - Associated abnormalities
  - Cardiac malformations in 85%
  - Bicuspid aortic valve in 20%
  - Non-cardiac 13%

- **Embryology: Three theories**
  - Aneurysm: ductal tissue encircles arch causing local constriction
  - Failure of connection 4th and 6th branchial arches to decending aorta
  - Abnormal flow patterns in developing heart
  - Aortic arch flow

**Staging, Grading or Classification Criteria**
- **CoA**
  - Isolated coarctation
  - Coarctation + ventricular septal defect
  - Coarctation + complex intracardiac anomalies
  - Interrupted aortic arch
  - Type A: Distal to left subclavian

**DIFFERENTIAL DIAGNOSES**
- Spectrum of left heart outflow obstruction
  - Aortic stenosis (AS)
    - Valve may be thickened
    - Small ascending and transverse arch due to decreased flow
    - Retrograde flow around arch in severe cases
  - Hypoplastic left heart syndrome (HLHS)
  - Left ventricle is not apex-forming
  - Severe mitral stenosis/atria
  - Severe aortic stenosis/atria
  - Endocardial fibroelastosis (EFE)
  - Highly echogenic endocardium
  - LV may be globular and dilated
  - LV may also be normal or small in size
  - Occurs as part of hypoplastic left heart syndrome

**Other causes of ventricular asymmetry**
- Right heart enlargement
  - Pulmonary valve stenosis/atria
  - Shunt lesions with increased venous return
  - Use color Doppler to look for arteriovenous malformations
  - Fetal tumors are large at presentation, easily seen
  - Incipient hydrops
  - Check for rhythm disorders
  - Check for signs of infection
  - Check for signs of aszemia
  - Placental insufficiency
  - Associated with growth restriction
  - Oligohydramnios
COARCTATION OF THE AORTA

CLINICAL ISSUES

Presentation
- Abnormal mural thickness in first trimester
- Marker for aneurysmal and congenital heart disease
- Ventricular asymmetry RV > LV
- Nonpulmonary foetal observed on four-chamber view
- Transverse arch hypoplasia

Natural History & Prognosis
- Arch hypoplasia may progress over course of gestation
- 6/7 fetuses in one series showed progressive arch hypoplasia
- 3/7 fetuses developed reversal of flow in ductus arteriosus despite antegrade flow at diagnosis
- Turner syndrome in fetus carries poor prognosis
- Progression in CoA depends on associated anomalies and timing of diagnosis
- Early arch repair straightforward with excellent outcomes
- Normal life expectancy
- Restenosis 10-15%
- Delayed diagnosis in severe cases
- Cardiovascular collapse at presentation
- Delayed diagnosis in milder cases
- Develop systemic hypertension in upper extremities
- Outcomes less favorable due primarily to added secondary morbidity
- CoA + left heart hypoplasia, midterm: follow-up = substantial growth of left heart structures after repair
- 53 fetuses with CoA + at least one hypoplastic left heart valve
- All alive and well at mean follow-up of 73 months (range 3-9 yrs)
- 69% with normal LV size and function
- 16% developed LVOT obstruction by echocardiographic criteria
- Interrupted aortic arch
- Rarely occurs in isolation
- Common associations are truncus arteriosus, transposition, double outlet right ventricle and single ventricle
- Natural history will depend on associated lesions in conjunction with arch repair
- Restenosis risk CoA
- One affected sibling 2%
- Two affected siblings 6%
- Affected mother 4%
- Affected, heterozygote 2%

Treatment
- Offer karyotype
  - Patient with interrupted aortic arch fluorescein in the hybridization (FISH) for 22q11 deletion
  - In females with coarctation for Turner syndrome
- Prenatal consultation with pediatric cardiology/neonatology
- Deliver at tertiary center
- Goal at delivery is to maintain ductal patency as systemic perfusion is duct dependent
- Prostaglandin infusion
- Avoid supplemental oxygen
- Definitive treatment is primary surgical repair
- Resolution with extended end-to-end anastomosis
- Operative repair < 1% mortality in experienced hands
- Subclavian flap aortoplasty, rare
- Patch aortoplasty, rare
- Balloon angioplasty
- Associated with restenosis
- New criteria for re-coarctation and late diagnosis with stent implantation

DIAGNOSTIC CHECKLIST

Consider
- Coarctation is extremely difficult diagnosis in utero
- At-risk fetus with normal study still needs postnatal evaluation

Image Interpretation Pearls
- Normal looking arch does not exclude coarctation

SELECTED REFERENCES
Coarctation of the Aorta

**Image Gallery**

Typical

(Left) Sagittal oblique scan in a scan with coarctation of the aorta shows marked narrowing of the isthmus (arrow). The ascending aorta (A) and aortic arch (right upper arm) are visible in the upper part of the image. The descending aorta (A) is smaller than the main pulmonary artery (P). (Right) Ultrasound scan of an interated aortic arch shows the ascending aorta (A), parallel to the superior vena cava (SVC). The vessel extends cranially without the normal curvature of the arch. Interated aortic arch has a high association with 22q11 deletion and karyotyping is recommended.

(Left) Sagittal oblique scan in a scan with coarctation of the aorta shows marked narrowing of the isthmus (arrow). The ascending aorta (A) and aortic arch (right upper arm) are visible in the upper part of the image. The descending aorta (A) is smaller than the main pulmonary artery (P). (Right) Ultrasound scan of an interated aortic arch shows the ascending aorta (A), parallel to the superior vena cava (SVC). The vessel extends cranially without the normal curvature of the arch. Interated aortic arch has a high association with 22q11 deletion and karyotyping is recommended.
**TERMINOLOGY**

**Abbreviations and Synonyms**
- Aortic stenosis (AS)
- Left ventricular outflow tract obstruction (LVOTO)

**Definitions**
- Obstruction to flow across aortic valve
  - Valve
  - Subvalvar: Fixed or dynamic
  - Supravalvar (SVAS)

**IMAGING FINDINGS**

**Echocardiographic Findings**
- Left ventricle (LV) may be large, small or normal in size
- May see concentric hypertrophy
- May see bright walls i.e., endocardial fibroelastosis (EFE)
- LV function usually decreased
- Right ventricle (RV) may be large to compensate cardiac output
- Thickened valve leaflets
- Valve often bicuspid (difficult to see in fetus)
- Subvalvar aortic (subaortic) stenosis
- Muscular: Look for asymmetric septal hypertrophy

- Fibrous Membrane from septum to mitral valve
- Turbulent flow starts below valve in subvalvar AS
- Supravalvar aortic stenosis
- Turbulent flow starts above valve in supravalvar AS
- Color Doppler
  - Turbulent flow in left ventricular outflow tract (LVOT) or across valve
  - CW Doppler: Minimal flow in aorta
  - Retrogade filling of aorta via ductus arteriosus
  - Mitral regurgitation from increased LV pressure
- Left-to-right shunt across foramen ovale
- Normal flow at foramen ovale is right to left
- Left heart outflow obstruction, left atrium to left ventricle
- Left atrial pressure ↑ → Flow direction at foramen ovale changes, becomes left to right
- Pulsed Doppler
  - Used to measure gradient across, above and below the aortic valve
- Pressure drop difficult to interpret due to presence of patent ductus arteriosus (PDA)

**Imaging Recommendations**
- Formal fetal echocardiogram
  - 30% of lesions have additional cardiac anomalies
  - Congenital/interrupted aortic arch
  - Ventricular septal defect (VSD)

**DDx: Aortic Stenosis**
- EFE
- HLHS
- Coarctation
- Cardiomyopathy
AORTIC STENOSIS

Key Facts

- Obstruction to flow across aortic valve

Imaging Findings

- Left ventricle (LV) may be large, small or normal in size
- May see concentric hypertrophy
- LV function usually decreased
- Right ventricle (RV) may be large to compensate cardiac output
- Retrograde filling of arch via ductus arteriosus
- Anti-clockwise shunt across foramen ovale
- 30% of fetuses have additional cardiac anomalies

Top Differential Diagnoses

- Hypoplastic left heart syndrome (HLHS)
- Cardiomyopathy

- Pulsed Doppler interrogation of all valves required to look for stenosis/regurgitation
- Consider Shone syndrome
- Valvar/subvalvar AS
- Coarctation of aorta
- Mitral stenosis
- Full fetal anatomic survey
- Monitor for growth restriction: 1 risk due to poor placental perfusion
- Monitor for hydrodrops
- Most likely to occur with severe mitral regurgitation, LV dysfunction
- Monitor for progression to hypoplastic left heart syndrome (HLHS)
- Postnatal management more complex than isolated AS

DIFFERENTIAL DIAGNOSIS

Hypoplastic left heart syndrome (HLHS)

- LV not apex-forming
- Typically associated with aortic and mitral atresia
- May occur as end result of critical AS in utero

Coarctation of aorta/interrupted aortic arch

- Look for isthmus hypoplasia
- AS, coarctation, HLHS all part of a spectrum of left ventricular outflow tract obstruction
- Differentiation may not be possible

Cardiomyopathy

- Intrinsinc myocardial abnormality not secondary to valve disease
- Associated with decreased LV function
- Fetuses of diabetic mothers: 1 incidence hypertrophic cardiomyopathy
- Maximum thickening seen in interventricular septum
- Resolves spontaneously by 6 months of age

Pathology

- 2-3% all congenital heart disease
- 3.5-10,000/year births

Clinical Issues

- Prognosis varies with severity of obstruction and associated anomalies
- Ballooning valvuloplasty of fetal aortic valve in cases of severe AS in hopes of preventing progression to HLHS
- Prostaglandins required at birth to maintain patency of ductus arteriosus
- Survivors need lifetime follow-up

Diagnostic Checklist

- AS may progress to HLHS in utero
- Use color Doppler to determine origin of turbulent flow

PATHOLOGY

General Features

- Genetics
  - Supraventricular AS
  - Autosomal dominant: William syndrome
  - Turner syndrome 45, XO

- Etiology
  - Valvar:
    - Bicuspid valve: Thick dysplastic leaflets
  - Subvalvar: Muscular
    - Asymmetrical septal hypertrophy
  - Elastoplastic hypertrophic subaortic stenosis
  - Hypertrophic obstructive cardiomyopathy
  - Subaortic: Membranous
  - Subaortic: Membranous
- Supravalvar: Narrowing in proximal ascending aorta
  - Williams syndrome: Gene deletion for elsin \( E N \) on \( 7 q 11.23 \)

- Epidemiology
  - 2-3% all congenital heart disease
  - 3.5-10,000/year births
  - In liveborn
    - 60-75% valvar
    - 8-20% subvalvar
    - Supravalvar: rare
  - M:F up to 4:1 for valvar/subvalvar stenosis
  - M:F = 1.1:2 for supravalvar stenosis

CLINICAL ISSUES

Presentation

- Has been detected at < 16 weeks gestational age on echocardiogram ultrasound
- Most common fetal presentation is abnormal four chamber view detected on routine antenatal screen

Natural History & Prognosis

- Prognosis varies with severity of obstruction and associated anomalies
AORTIC STENOSIS

- Mild valvular stenosis (≤ 40 mmHg) progresses slowly, intervention more common by 4th to 6th decade
- Moderate or greater valvular stenosis (> 40 mmHg) may require surgical or non-surgical intervention
- Untreated = pediatric sudden death
- Fetal cases tend to be more severe with progression to HLHS described
- Supravalvar AS rarely requires intervention in infancy but progresses with time
- Coronary artery stenoses common cause of sudden death
- Williams Syndrome has associated aortic root dilatation, "club" lacies, peripheral pulmonary stenosis
- Supravalvular AS diagnosed in childhood and usually progresses
- May be associated with isolated VSD
- Often causes aortic origination prompting earlier treatment
- Operative mortality 8% overall
- Up to 33% for neonates with critical AS
- Long term outcome
  - 10 yr survival > 90%
  - 22 yr survival 73%
- Operation rates
  - 2.4% over mean 8 yr follow-up
- Actuarial curves predict 62% lifetime free of reoperation
- Recurrence risk for valvular AS
  - One sibling 2%
  - Two siblings 6%
- Affected mother 1.3-1.8%
- Affected father 3%

Treatment
- Precise consultation with pediatric cardiologist/traumatologist
- Counsel parents regarding risk of progression
- Offer aortic root replacement
- Balloon valvuloplasty of aortic valve in cases of severe AS in hopes of preventing progression to HLHS
- Prior to 20 weeks if possible
- LV needs to be large in size
- Prior to development of EF
- Performed in only a few centers nationally
- Results improving with experience and technique
- Majority of patients still end up with single ventricle
- Prognostic factors required at birth to maintain patency of ductus arteriosus
- Balloon valvuloplasty is first line therapy if ventricle adequate in size
- Indices show usefulness: Echocardiographic scoring system taking into account
  - Body surface area
  - Mitral valve and aortic root size
  - Ratio long axis of LV to long axis of heart
- Surgical aortic valve repair/replacement or coarctation repair
- Aortic root replacement often necessary at same time if diameter > 40 mm
- Bicuspid aortic valve may be asymptomatic
- Screen family members
- Found in first degree relatives of preband
- Increased risk of bacterial endocarditis
- Eventual significant AS development possible late in life, 50 yrs of age
- Survivors need lifelong follow-up

DIAGNOSTIC CHECKLIST

Consider
- Prevalent diagnosis of valvar aortis is possible
- Subaortic valvar stenosis very rarely diagnosed, often not even clinically apparent in neonate
- AS may progress to HLHS in utero

Image Interpretation Pearls
- Use color Doppler to determine origin of turbulent flow
- SVAS: Turbocint starts above the valve
- Associated with Williams syndrome
- Supravalvar aortis: Turbulent flow starts below the valve

SELECTED REFERENCES
AORTIC STENOSIS

IMAGE GALLERY

Typical

(Left) EWS shows a dilated left ventricle (LV) with a thick, dysplastic aortic valve (arrow), which had limited motion. LV - Right ventricle.
(Right) Color Doppler ultrasound in the same view demonstrates retrograde flow in the aortic arch (blue indicates flow away from the transducer). This flow is supplying the arch vessels (blue - aortic arch). LA - left atrium, ISS - intima-media. LVOT - left ventricular outflow tract.

Typical

(Left) Transesophageal echocardiogram shows a subaortic membrane (arrow) obstructing the left ventricular outflow tract (LVOT) immediately below the aortic valve leaflets. (Right) Angiogram of the aorta shows a normal aortic valve annulus (white arrow) with significant supravalvar narrowing (arrow) at the base of the coronary arteries. Note normal brachiocephalic trunk (curved arrow).

Typical

(Left) LVOT view in postnatal echocardiogram shows thick aortic valve leaflets in a patient with a bicuspid aortic valve. LV = left atrium, LV - left ventricle, MV = mitral valve.
(Right) LVOT view with color Doppler in the same case shows turbulent flow (arrows) which starts at the valve and continues into the ascending aorta.
PULMONARY VALVE STENOSIS, ATRESIA


Four chamber view in a fetus with pulmonary atresia shows concentric hypertrophy of the right ventricular (RV) free wall and septum (arrows).

TERMINOLOGY

Abbreviations and Synonyms
- Pulmonary valve stenosis (PS)
- Pulmonary valve atresia (PA)

Definitions
- Obstruction of right ventricular outflow tract (RVOT) at level of pulmonary valve (PV)

IMAGING FINDINGS

General Features
- Best diagnostic clue
  - PS: Turbulent, high velocity flow across PV
  - PA: No intraventricular flow across pulmonary valve
- PA with intact ventricular septum (IVS) subtype
  - Abnormal four chamber view: Right ventricle (RV) small with decreased function
  - RV < left ventricle (LV) with severe hypertrophy
  - IVS cavity obliterated over time
  - Blood "must" get out = coronary cordon fistula often present
  - Coronary blood supply comes from high pressure ventricle in embryo
  - Right atrium (RA) may be enlarged
  - RVOT small or non-existent

- PA usually confluent but small
- PA with ventricular septal defect (VSD) subtype
  - Abnormal four chamber view due to presence of VSD
  - RV, LV symmetric in size
  - "Large" aorta: Receives blood from both ventricles
  - RV function usually preserved
  - RVOT small or non-existent
  - PA: often not confluent, rather major arterio-pulmonary collateral arteries (MAPCAs) supply lungs

ECHOCARDIOGRAPHIC FINDINGS
- RA normal or large
- RV size normal, large or small
- RV hypertrophy is common
- RV function normal, increased or decreased
  - Function decreased with more severe RVOT obstruction (PS or PA)
- Pulmonary valve
  - Pulmonary annulus small, with thickened valve
  - May see post-stenotic dilatation of main pulmonary artery
- Pulsed Doppler
  - Used to characterize gradient across pulmonary valve at PS
  - Used to characterize gradient across tricuspid valve to estimate RV pressure

DDx: Pulmonary Stenosis/Atresia

- Tetralogy Of Fallot
- Tetralogy Of Fallot
- HLHS - Small LV
- Tricuspid Atresia
PULMONARY VALVE STENOSIS, ATRESIA

Key Facts

Terminology
- Obstruction of right ventricular outflow tract (RVOT) at level of pulmonary valve (PV)

Imaging Findings
- PS: Turbulent, high velocity flow across PV
- PS: No antegrade flow across pulmonary valve
- RV: Hypertrophy is common
- RV function normal, increased or decreased
- JVP with intact ventricular septum, look for RV to coronary artery fistulas
- Look for features of right atrial isomerism

Top Diagnostical Differences
- Tetralogy of Fallot (ToF)
- Hypoplastic left heart syndrome (HLHS)

Pathology
- Pulmonary valve may be atretic

Pathology
- Part of 22q11 deletion syndrome
- PS accounts for 10% of all congenital heart disease (CHD)
- PA accounts for 3% of CHD

Clinical Issues
- Deliver at tertiary care facility
- Pulmonary circulation is ductus dependent in severe forms of PS and PA
- PS treatment involves balloon valvuloplasty depending on gradient

Diagnostic Checklist
- Reverse flow in ductus arteriosus = duct dependent pulmonary circulation

Reimbursement
- Medicaid

Imaging Recommendations
- Formal fetal echocardiography
- If PA with intact ventricular septum, look for RV to coronary artery fistulas
- Can supply blood to RV and LV via communications
- Course along outer wall of heart or within septum
- Look for other cardiac anomalies
- Truncus arteriosus
- Transposition of great arteries
- Double outlet right ventricle
- Look for features of right atrial isomerism
- Careful search for noncardiac anomalies

DIFFERENTIAL DIAGNOSIS

Tetralogy of Fallot (ToF)
- Pulmonary stenosis from anterior deviation of infundibulum is typical lesion
- Pulmonary atresia can occur (ToF with PA may also be classified as PA with VSD)
- VSD must be present
- Aorta overrides VSD

Hypoplastic left heart syndrome (HLHS)
- LV not apex forming
- Typically associated with aortic/mitral atresia and hypoplastic aortic arch
- Aorta looks large in PA-VSD
- Pulmonary artery branches into ductus/right pulmonary artery shortly after crossing the heart

Truncus arteriosus
- RV not apex forming
- VSD usually present

Pulmonary valve may be atretic

PATHOLOGY

General Features
- General path comments
  - Associated with small pulmonary artery and branches
  - MAFCAs in cases of PA-VSD
  - May have RV dependent coronary artery circulation
  - Presence of coronary cecal fistulas

- Genetics
  - Case reports of siblings ➔ possible autosomal recessive inheritance with 25% recurrence risk
  - Part of 22q11 deletion syndrome
  - Previously called DiGeorge/velo-cardio-facial/Shprintzen syndrome or CATCH 22
  - More commonly present with PA-VSD

- Epidemiology
  - All types 21.4:100,000 live births in United Kingdom
  - PA accounts for 10% of all congenital heart disease (CHD)
  - 1% in fetus, these cases at more severe end of spectrum
  - 1.4-8% present in infancy
  - Remainder are mild cases presenting in childhood and later
  - M = F
  - PA accounts for 3% of CHD
  - Incidence 8:100,000 live births
  - Some cases may result from in-utero progression of PS

- Associated abnormalities
  - Ebstein anomaly of tricuspid valve
  - Syndromes: Noonan, Williams and Atrigile

Staging, Grading or Classification Criteria
- Congenital Heart Surgery Nomenclature and Database Project
- PA-VSD: Classified on basis of pulmonary circulation
  - Type A: Only native pulmonary arteries (NPA)
PULMONARY VALVE STENOSIS, ATRESIA

CLINICAL ISSUES

Presentation
- Abnormal four chamber view on routine echocardiography
- PA-IVS with RV-coronary fistula reported as early as 17 weeks

Natural History & Prognosis
- PS
  - Depends on associated condition
  - In isolation = 1/3 improve, 1/3 remain unchanged and 1/3 increase in severity
- PA-IVS
  - Severe hypoxia at birth
  - Cardiomegaly = pulmonary hypertension
  - Require institution of prostaglandin
  - Require surgery within first week of life
  - 75% survivor at 1 yr
  - 67% survivor at 5 yr
  - Increased risk with prematurity and ethionamide
- PA-VSD
  - > 50% require surgery within 1 month
  - Additional 25% require surgery within 3 months
  - Survival 80% at 3 yr with unifocalization type of surgical repair
- Multiple catheter and surgical interventions necessary
- Poor prognostic markers
  - Low birth weight
  - Male gender
  - Muscular pulmonary atresia
- Discontinuous pulmonary arteries = MPAV
  - 25%; 1-5 deletion
  - 2.4% relative risk of surgical mortality for PA-VSD
- MPAVCs much more common with deletion
- Deletion is independent risk factor for surgical mortality even after correction for presence of MPAVC

Treatment
- Consider laryngectomy with fluorescent in situ hybridization (FISH) for 22q11.2 deletion
- Premature consultation with pediatric cardiology/heart genetics
- Successful total pulmonary valvulotomy has been performed
  - 28 week hypertrophic fetus with PA-IVS
- Postoperative growth of RV, pulmonary biventricular repair
- Deliver at tertiary care facility
- Pulmonary circulation is ductus dependent in severe forms of PS and PA
- Ductal closure is life threatening
- Prostaglandin infusion necessary
- 16% treatment involves balloon valvuloplasty depending on gradient
  - < 40 mmHg is mild, no intervention necessary
  - 40-70 mmHg is moderate, intervention is discretionary
  - > 70 mmHg is severe, intervention is necessary
- PA-IVS treatment
  - Transcatheter balloon valvuloplasty or radiofrequency perforation becoming first line
  - Balloon Tissue Stint palliation or RVOT reconstruction often necessary
- Few patients achieve biventricular repair
  - RV dependent coronary circulation (coronary arterial fistula) precludes decannulation of PDA
- PA VSD treatment
  - Depends on presence of native pulmonary arteries
  - Central shunt to pulmonary arteries or early unifocalization of MPAVCs often necessary
  - Unifocalization must be seen before MPAVCs together with native PA = new PA on each side
  - Currently standard of care
  - Complete repair with VSD closure and RV to pulmonary artery conduit is goal if possible

DIAGNOSTIC CHECKLIST

Consider
- Key-type with FISH for 22q11 deletion
  - Independent risk factor for adverse outcome

Image Interpretation Pearls
- Reverse flow in ductus arteriosus = duct dependent pulmonary circulation
- Prostaglandin infusion at birth to prevent ductal closure

SELECTED REFERENCES
**PULMONARY VALVE STENOSIS, ATRESIA**

**IMAGE GALLERY**

*Left*: Four-chamber view color Doppler ultrasound shows significant tricuspid regurgitation (white arrow) causing right atrial enlargement (black arrow) in a fetus with pulmonary atresia. *Right*: Four-chamber view in a perinatal study shows a hypoplastic RV with significant mild hypertrophy (arrows). There is a normal-sized left ventricle and no ventricular septal defect in this patient with PA with intact interventricular septum.

*Left*: Four-chamber view shows a thick-walled right ventricle (RV) in a fetus with pulmonary stenosis. The interventricular septum (arrow) is bowed toward the left ventricle (LV). *Right*: Pulsed Doppler ultrasound in the same fetus shows high-grade stenosis of the pulmonary valve with a gradient of 10.5 mmHg.

*Left*: RVOT view shows a small main (PA) and branch pulmonary arteries (arrow) in a fetus with pulmonary atresia. Note the large right atrium (RA) secondary to tricuspid regurgitation (A- arrow). *Right*: Clinical photograph shows typical phenotypic features in a neonate with a prenatal diagnosis of PA I at birth. Note the micrognathia (crossed arrows), prominent nose and long skin tag. (arrow).
EBSTEIN ANOMALY, TRICUSPID DYSPLAIA

TERMINOLOGY

Definitions
- Ebstein anomaly and tricuspid dysplasia both have dysplastic tricuspid valves (TV) with tricuspid regurgitation (TR).
- Ebstein anomaly has additional findings of apical displacement of septal and posterior TV leaflets and "atrialization" of the right ventricle.
  - Displaced leaflets adhere to wall, coaptation point of valve is lowered into right ventricle (RV), not atrioventricular junction.

IMAGING FINDINGS

General Features
- Best diagnostic clue for Ebstein anomaly
  - Right atrial enlargement with apical displacement of tricuspid valve.
  - Normally lower on septum than mitral valve by only 1-2 mm.

Echocardiographic Findings
- Ebstein anomaly
  - Cardiomegaly: Due primarily to right atrial (RA) enlargement.

DDx: Enlarged Right Atrium

- Pulmonary Atelectasis
- Cardiomyopathy
- Unbalanced ASD
EBSTEIN ANOMALY, TRICUSPID DYSPLASIA

Key Facts
- Ebstein anomaly and tricuspid dysplasia both have dysplastic tricuspid valves (TV) with tricuspid regurgitation (TR)
- Ebstein anomaly has additional findings of apical displacement of septal and posterior TV leaflets and "fissuration" of the right ventricle

Imaging Findings
- Color Doppler helpful to demonstrate TR, measure gradient with pulsed Doppler
- Associated structural abnormalities in 30% of Ebstein anomaly

Top Differential Diagnoses
- Pulmonary atresia
- Atrioventricular septal defect (AVSD)

DIFFERENTIAL DIAGNOSIS

Pulmonary atresia
- Tricuspid valve normally located
- RV may be hypoplastic or hypertrophied

Atrioventricular septal defect (AVSD)
- Common atrioventricular valve
- Atrial and ventricular septal defects

PATHOLOGY

General Features
- Etiology
  - Lithium has previously been implicated
  - Recent case controlled studies show no statistical difference in heart anomalies between lithium-exposed fetuses and control groups
- Epidemiology: 0.03:1000 live births, M = F
- Embryology: Ebstein anomaly
  - Inadequate separation TV leaflets and chordae tendineae from RV endocardium

CLINICAL ISSUES

Presentation
- Enlarged right atrium noted on routine obstetric scan

Natural History & Prognosis
- Large heart = compressed lungs = pulmonary hypoplasia
- Suspicious arrhythmia or development of hydrops = poor prognosis
- Recurrence risk: One child 1%, two affected 3%

Treatment
- Offer karyotype: Ebstein anomaly has been described in trisomy 21, 18
- Offer termination in severe cases (multiple anomalies, aneuploidy)
- If pregnancy continues
  - Prenatal consultation with pediatric cardiologist/neonatologist
  - Deliver at tertiary center: Early delivery does not improve prognosis
- Monitor for arrhythmia, hydrops
- Ebstein surgery

- Valve reconstruction currently procedure of choice with mortality < 10%
- Utilize anterior leaflet and annuloplasty to create new coaptation point
- Valve replacement with mechanical or porcine bioprosthesis
- Include right atrial reduction and closure of atrial septal defect
- Tricuspid dysplasia surgery
  - Tricuspid valve annuloplasty initially attempted, valve replacement often necessary

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls
- Abnormal offset of tricuspid valve is key to making diagnosis of Ebstein anomaly

SELECTED REFERENCES

IMAGE GALLERY

(left) Radiograph of a neonate with Ebstein anomaly shows cardiomegaly with a massively enlarged right atrium cavity and pulmonary oligemia. (right) Four chamber view of a fetus shows a thick, dysplastic tricuspid valve (arrow), which is not downwardly displaced, therefore this is tricuspid dysplasia, not Ebstein anomaly. Tricuspid regurgitation was present.
TRICUSPID ATRESIA

Graphic shows a absent TV (arrow), a hypoplastic RV & a ventricular septal defect (open arrow) allowing blood to enter a hypoplastic pulmonary artery (curved arrow), blood turbulence occurs in LA & LV.

TERMINOLOGY

Abbreviations and Synonyms
- Tricuspid atresia (TA)

Definitions
- Absent tricuspid valve (TV)

IMAGING FINDINGS

Echocardiographic Findings
- Atria: Inter-atrial septum bows right to left (normal)
- Ante-ventricular valves
  - Tricuspid valve appears "pliable" with no movement
  - Mitral valve functions normally
- Ventricular septal defect (VSD) usually present
- Right ventricle (RV): Small, non-aperistaltic, function variable
- Pulmonary artery: Often small depending on amount of flow from VSD
- Left ventricle (LV): Large, apex-forming with good function
- Color Doppler
  - Confirm direction of flow at atrial level
- Helps identify presence of a VSD

DIFFERENTIAL DIAGNOSIS

Pulmonary atresia-intact ventricular septum (PA-IVS)
- Tricuspid valve patent but usually abnormal
- RV small and hypertrophied

Double inlet left ventricle
- L-taping of heart
- Usually two normal atrioventricular (AV) valves but one can be stenotic
- Usually two normal semilunar valves

DDx: Tricuspid Atresia

HILVS  PA-IVS  Single Ventricle  Unbalanced AVS
TRICUSPID ATRESIA

Key Facts

Top Differential Diagnoses
- Pulmonary atresia-intact ventricular septum (PA-IVS)
- Double inlet left ventricle
- Unbalanced left dominant atrioventricular septal defect

Clinical Issues
- Unbalanced 50% mortality by 1 year
- Current surgical experience < 2% operative mortality for children who survive to Fontan repair
- Evaluate adequacy of pulmonary blood flow to determine need for surgery
- Surgical management
- Blalock-Taussig shunt if pulmonary flow is insufficient in first week
- Glenn at 4-6 months: Superior vena cava to right pulmonary artery connection
- Fontan at 2-3 years of age: Inferior vena cava to right pulmonary artery conduit
- Cardiac transplantation in rare cases

PATHOLOGY

General Features
- Genetics: 22q11 deletion in up to 8% TA
- Epidemiology
  - 1:10,000 live births, M > F
  - Third most common cyanotic congenital heart disease

Staging, Grading or Classification Criteria
- Type 1: Great artery relationship normal; 70% subtypes based on VSD
- Type 2: D-transposition 28%
- Type 3: L-transposition 2%
- Type 4: Persistent truncus arteriosus

CLINICAL ISSUES

Presentation
- Abnormal four chamber view

Natural History & Prognosis
- Untreated, 90% mortality by 1 year
- Current surgical experience < 2% operative mortality for children who survive to Fontan repair
  - 95% survival at one month, 93% at one year
  - 82% at 10 yrs
- Poor prognostic indicators
- Low birth weight
- Associated arch anomalies
- Severe RV hypoplasia

Treatment
- Prenatal consultation with pediatric cardiologists/neonatology
- Planned delivery in tertiary center
- Medical management
- Prostaglandin infusion to maintain ductal patency

IMAGE GALLERY

(left) Four chamber view with color Doppler shows (arrow) flow into the left ventricle (LV) (arrow) and flow into the small right ventricle (arrow) (arrow) cava (arrow) ventricular septal defect (VSD). (right) Bubble echo shows "plate-like" tricuspid valve (arrow) and a VSD (open arrow) opening to a hypoplastic RV.
DOUBLE OUTLET RIGHT VENTRICLE

Graphs show both great arteries (arrow) arising from the right ventricle. Presence of a VSD (arrow) allows shunting of oxygenated blood to the LV or similar saturation in the aorta and MPA.

ULTRASOUND SHOWS GLOMUS OUTFLOWS (ARROW) ARISING FROM THE RIGHT AORTIC (OPEN ARROW).

TERMINOLOGY

Abbreviations and Synonyms
- Double outlet right ventricle (DORV)

Definition
- Both great arteries arise predominantly from right ventricle (RV)
- Right atrioventricular valve is in fibrous continuity with an atrioventricular (AV) valve
- Ventricular septal defect (VSD) is usually present
- VSD represents outlet for left ventricle (LV)

IMAGING FINDINGS

General Features
- Best diagnostic clue: Outflow tracts parallel as they exit heart

Echocardiographic Findings
- Both great arteries arise predominantly from RV
- Aorta located posterior and rightward of pulmonary artery (PA)
- Aorta located to right (side-by-side with PA)
- Aorta located to right and anterior of PA
- Aorta located to left and anterior of PA
- Abnormal tricuspid dysplasticity

DIFFERENTIAL DIAGNOSIS

Tetralogy of Fallot (ToF)
- Outflow tracts relate normally (i.e., not parallel)
- Right ventricular outflow tract obstruction
- Aorta override VSD

D-transposition of great arteries (TGA)
- Outflow tracts are parallel
- Ventriculoarterial connections are key to differential diagnosis
- Aorta arises from morphologic RV
- Pulmonary artery arises from morphologic LV

DDx: Double Outlet Right Ventricle

Tetralogy Of Fallot
d-Tof-Modifier RV
Tetralogy Of Fallot
d-Transposition
DOUBLE OUTLET RIGHT VENTRICLE

Terminology
- Both great arteries arise predominantly from right ventricle (RV)
- Ventricular septal defect (VSD) usually present

Imaging Findings
- Best diagnostic clue: Outflow tracts parallel as they exit heart
- Strong association with aneuploidy if multiple anomalies

PATHOLOGY

General Features
- Genetics
  - Triad: 18, 13
  - Rare autosomal recessive cases: Multiple affected siblings in consanguineous family
- Ecology: Maternal diabetes → odds ratio 21.3
- Epidemiology
  - 1% of all congenital heart disease
  - 0.01:0.09:1.000 live births
- Embryology
  - Failure to achieve common trunk rotation
- Failure of leftward shift of aortic/pulmonary conus

CLINICAL ISSUES

Presentation
- Abnormal parallel orientation of outflow tracts

Natural History & Prognosis
- Excellent early and long term outcomes if normal chromosomes/no heterotaxy
- 73-88% survival at 5-8 yrs
- 5-10% long term survivors have no restriction on physical activities
- 36-42% of children will need operation at some point after primary repair
- More likely with outflow tract obstruction

Treatment
- Offer karyotype: 38% aneuploidy with fetal diagnosis
- Offer termination if trisomy, multiple anomalies
- Prenatal consultation with pediatric cardiology/neonatology
- Deliver at tertiary center
- Immediate management depends on associated lesions
  - Significant pulmonary stenosis: duct dependent
  - May need prostaglandins
- Corrective surgery depends on
  - Great artery relationship
  - VSD closure when side-by-side great arteries
  - Presence and type of VSD
  - Arterial switch in Tunis-Bing (subpulmonary VSD)
- Coronary artery anatomy
- Goal of correction is to reestablish LV as systemic ventricle and repair all associated lesions

Key Facts

Top Differential Diagnoses
- Tetralogy of Fallot (ToF)
- D-transposition of great arteries (TGA)

Clinical Issues
- Excellent early and long term outcomes if normal chromosomes/no heterotaxy

Diagnostic Checklist
- Parallel outflow tracts = DORV or TGA

DIAGNOSTIC CHECKLIST

Consider
- Fetal echocardiogram

Image Interpretation Pearls
- Parallel outflow tracts = DORV or TGA
- Ventriculoarterial relationship is key to differentiation
- Final diagnosis may not be possible until after delivery

SELECTED REFERENCES

IMAGE GALLERY

(Left) Angiogram shows both the aorta and MPA arising from the RV in a patient with DORV who has undergoe a PA band to limit pulmonary blood flow. (Right) Color Doppler echocardiogram shows flow exiting the RV to the aorta (A4) and main pulmonary artery (MPA). MPA dilates into the ductus arteriosus (arrow) and right pulmonary artery (curved arrow).
SINGLE VENTRICLE

Graph shows the most common single ventricle: double-outlet ventricle. Left AV valves (arrow) with the smooth-sided left ventricle. The aorta arises from an outflow chamber (open arrow).

Flow chamber view shows a single ventricle (open arrows) with LV morphology. The walls are smooth, short is oval, and the mitral valve leaflet (arrow) is attached to the free wall. The other AV valve is absent.

TERMINOLOGY

Abbreviations and Synonyms
- Single or "common" ventricle
- Univentricular heart
- Double inlet left ventricle (DILV)

Definitions
- Heart has one functioning ventricle with inflow from one or both atria
  - Often rudimentary second outflow chamber: A remnant of right ventricle is DILV
  - VSD is present (often referred to as a bulboventricular foramen)

IMAGING FINDINGS

Echocardiographic Findings
- Single ventricle
  - Left ventricular (LV) morphology 80%, may also be right-anterior or indeterminate
  - Atrioventricular valves
  - Double inlet (mitral and tricuspid), single inlet (mitral or tricuspid) or common AV valve
  - Great artery relationship is variable
  - Normal relationship: Asymmetry in size = outflow tract obstruction

DDx: Single Ventricle Heart
- Unbalanced AVSD
- HLHS
- Tricuspid Aneurysm
- Tricuspid Aneurysm

DIFFERENTIAL DIAGNOSIS

Hypoplastic left heart syndrome (HLHS)
- Usually mitral and aortic atresia/stenosis, hypoplastic ascending aorta

Unbalanced atroventricular septal defect (AVSD)
- Common AV valve, inlet VSD and primum ASD
- Two ventricles, asymmetric in size

○ Transposition
○ One atrial great artery
○ Color Doppler
○ Document flow from both atria into single ventricle
○ Document flow in one or both great arteries
○ Turbulent flow identifies outflow tract obstruction
○ Look for flow into an outlet chamber

Imaging Recommendations
- Protocol advice
  - Formal fetal echocardiography to look for associated lesions
  - Coarctation of aorta, interrupted arch, pulmonary stenosis/atrial
  - Look for features of heterotaxy syndromes
SINGLE VENTRICLE

Terminology
- Heart has one functioning ventricle with inflow from one or both atria

Imaging Findings
- Left ventricular (LV) morphology 80%, may also be right-appearing or indeterminate
- Great artery relationship is variable
- Look for features of heterotaxy syndromes

Tricuspid atresia
- Absence of tricuspid valve + right ventricular hypoplasia

PATHOLOGY

General Features
- Epidemiology: 0.05-0.1:1000 live births
- 1.7% of fetal congenital heart disease

Staging, Grading or Classification Criteria
- Complex classification based on
  - Atrioventricular connections
  - Ventricular morphology
  - Great artery position and relationship

CLINICAL ISSUES

Presentation
- Abnormal four-chamber view: Two atria, one ventricle
  - Three-chambered heart

Natural History & Prognosis
- Depends on morphology of ventricle and outflow obstruction
- Current surgical experience
  - 95% survival at 5 yrs, 80% at 15 yrs, 63% at 25 yrs
- Poor prognostic indicators
  - Need for aortic arch reconstruction, arrhythmia or need for pacemaker
- Recurrence risk if associated with right atrial isomerism: 3.4%

Treatment
- Karyotype not necessary if cardiac anomaly isolated
- Prenatal consultation with pediatric cardiologist/neonatologist
- Defect at tertiary center
- May be ductal dependent for systemic or pulmonary circulation depending on associated outflow lesions
- May require prostaglandin infusion to prevent ductal closure
- 3 stage surgical palliation
  - First stage depends on presence of outflow tract obstruction
  - Pulmonary arteries banding necessary with excessive pulmonary flow

Key Facts

Top Differential Diagnoses
- Hypoplastic left heart syndrome (HLHS)
- Unbalanced atrioventricular septal defect (AVSD)
- Tricuspid atresia

Clinical Issues
- Abnormal four-chamber view: Two atria, one ventricle = three-chambered heart
- May be ductal dependent for systemic or pulmonary circulation depending on associated outflow lesions

- Blalock-Taussig shunt necessary with diminished or no pulmonary blood flow
- Aortic arch reconstruction necessary with left ventricular (LV) outflow obstruction
- Glenn at 6 months
- Superior vena cava to right pulmonary artery connection
- Blalock-Taussig shunt taken down and/or pulmonary artery ligated
- Fontan 2-3 years: Inferior vena cava to right pulmonary artery conduit
- Cardiac transplantation is last option

DIAGNOSTIC CHECKLIST

Consider
- Formal fetal echocardiography in all cases

SELECTED REFERENCES
2. Lau YF et al: Outcome of staged surgical approach to neonates with single left ventricle and moderate-size bilateral ventricular forces. Am J Cardiol. 89(9):699-703, 2002

IMAGE GALLERY

(Left) "Four-chamber view" shows only two-chamber, two atria/ one ventricle LV. In real time, the atroioventricular (AV) valve was seen to open into the single ventricle. (Right) Color Doppler ultrasound in the same patient shows flow from both atria (A) into a single ventricle (V). The arrow points to the atroioventricular valve.
TETRALOGY OF FALLOT

Abnormalities and Syonyms
- Tetralogy of Fallot (ToF)
- TOF with absent pulmonary valve (ToF-APV)

Definitions
- Congenital heart disease with four components
  - Right ventricular outflow tract obstruction (RVOTO)
  - Ventricular septal defect (VSD)
  - Overriding aorta
  - Right ventricular hypertrophy

IMAGING FINDINGS

General Features
- Best diagnostic clue: Dilated aortic root overriding a VSD

Echocardiographic Findings
- Four chamber view normal in >95% prenatal cases
- Outflow tract assessment key to making this diagnosis
  - Large aortic outflow
  - RVOTO + VSD = flow through aorta
  - Aortic root override, perimembranous VSD
- Extent of override variable
- RVOT obstruction

DOX: Tetralogy Of Fallot

- Double Outlet RV
- Perimembranous VSD
- Pulmonary Atresia
- Transthoracic Apical

- Anterior deviation of infundibulum
- Pulmonary valve usually abnormal
- Pulmonary annulus usually small
- Turbulent flow across right ventricular outflow tract (RVOT)
- Abnormal ductus arteriosus
  - Small in 70%
  - Not visualized in 30%
  - Autopsy confirmation of absent ductus in 50% of non-visualized cases in one series
- Absent pulmonary valve (APV) complex
  - Back and forth flow across pulmonary valve seen with color Doppler
  - Markedly enlarged pulmonary artery (PA) and branches
  - May cause bronchial compression and affect lung development
  - Increased risk of hydrops
- ToF-APV = hydrops = 80% intrauterine fetal demise in one series
- Pulsed Doppler
  - Used to estimate pressure in the right ventricle (RV) and pulmonary arteries
- Color Doppler
  - Used to evaluate flow across and below (insufficiency) the outflow tract
  - Used to evaluate flow across ventricular septal defect
TETRALOGY OF FALLOT

**Key Facts**

- **Terminology**
  - Congenital heart disease with four components
  - Pulmonary atresia with ventricular septal defect (PA-VSD)
  - Right ventricular outflow tract obstruction (RVOTO)
  - Overriding aorta
  - Right ventricular hypertrophy

- **Imaging Findings**
  - Echocardiogram: Dilated aortic root overriding a VSD
  - Aortic deviation of infundibulum
  - Pulmonary valve usually abnormal
  - Pulmonary annulus usually small
  - Turbulent flow across right ventricular outflow tract (RVOT)

- **Imaging Recommendations**
  - Formal fetal echocardiogram
  - Look for additional cardiac anomalies
  - Absent pulmonary valve/pulmonary atresia → worsen prognosis
  - May be associated with atrioventricular septal defect
  - Right-sided aortic arch
  - Detailed anatomic survey
  - Increased risk of aneuploidy/syndrome if other anomalies
  - Trisomy 18/13
  - VACTERL association

- **DIFFERENTIAL DIAGNOSIS**

- **Pulmonary atresia with VSD**
  - No antegrade flow across pulmonary valve
  - Rezoned flow in ductus arteriosus
  - Abnormal four chamber view in some: Small IVS
  - VSD

- **Double-outlet right ventricle (DORV)**
  - Outflow tracts parallel as they enter heart
  - Both great arteries arise from RV
  - VSD

- **Perimembranous VSD**
  - Hole between left and right ventricles
  - Absence of pulmonary or subpulmonary stenosis
  - Normal relationship of great arteries

- **PATHOLOGY**

  - **General Features**
    - Genetics
      - Chromosomal anomalies
        - Trisomy 21 (more complicated with atrioventricular septal defect rather than simple VSD)

  - **Top Differential Diagnoses**
    - Pulmonary atresia with VSD
    - Double-outlet right ventricle (DORV)
    - Perimembranous VSD

  - **Clinical Issues**
    - Chromosomal abnormality in up to 45% of fetal cases
    - Excellent short and long term outcome in normal chromosomes and no other anomaly
    - Greater than 94% survival in liveborn
    - TOF with absent pulmonary valve worse prognosis

  - **Diagnostic Checklist**
    - 95% of patients with TOF have a normal four chamber view
    - Outflow tract assessment is key to making this diagnosis

  - Trisomy 18/13
    - Autosomal recessive conditions
    - Phenylketonuria
    - Microdeletion of chromosome 22 (22q11 deletion syndrome)
    - Previously called DiGeorge, velocardiofacial, hypocalclement syndrome or CATCH 22
    - 10% of patients with TOF have 22q11 deletion

  - **Etiology**
    - TOF also seen in developmental field defect (akin to 22q11 deletion but with normal chromosomes)
    - Malformation of ears/lips/palate
    - Apasia/hypoplasia of thymus/parathyroid glands
    - Cardiovascular malformations especially conotruncal defects
    - Some authorities refer to this field defect as DiGeorge anomaly (Di George syndrome implies 22q11 deletion)

  - **Epidemiology**
    - Commonest cyanotic congenital heart disease
    - 5-10% of congenital heart disease in liveborn
    - 0.2-0.5:1,000 live births

  - **Associated abnormalities**
    - TOF may occur in CHARGE syndrome
      - Coloboma
      - Heart disease
      - Atresia (shunt)
      - Restricted growth/development
      - Genitourinary anomalies
      - Ear anomalies
    - VACTERL association
      - Vertebral defects
      - Anorectal atresia
      - Cardiac disease
      - Tracheoesophageal fistula
      - Renal anomalies
      - Limb defects
      - 22q11 deletion syndrome (DiGeorge syndrome)
      - Apasia/hypoplasia of thymus
      - Apasia/hypoplasia of parathyroid glands
      - Mild reduction in intelligence
TETRALOGY OF FALLOT

- Complex process, mechanism contains uncertain
- Incomplete rotation of conotruncus
- Abnormal conotruncal seaption
  - Partitioning unequal = sorts larger than pulmonary artery
  - Ante- or post- or interventricular septum = VSD
- Large vessel (aorta) straddles VSD

Gross Pathologic & Surgical Features

- Infundibular stenosis
  - Anterior and cephalad deviation of infundibular septum
  - Hypertrophy of septum, free wall and septomarginal trabeculations
- Pulmonary valve
  - Unicuspid/bicuspid/tricuspid
- Valves thickened with poor mobility
- Pulmonary arteries
  - May have focal or diffuse obstruction or hypoplasia

Staging, Grading or Classification Criteria

- Three major categories
  - Traf with pulmonary stenosis
  - Traf with pulmonary atresia
  - Traf with absent pulmonary valve
- Cases with pulmonary atresia may also be categorized as "pulmonary atresia with VSD"

CLINICAL ISSUES

Presentation

- Has been detected as early as 14 week on endovaginal ultrasound

Natural History & Prognosis

- Chromosomal abnormality: In up to 45% of lethal cases
  - Prognosis will be determined by aneuploidy/syndrome
  - Extremely poor in trisomy 13/18
- Excellent short and long term outcome if normal chromosomes and no other anomaly
- Greater than 94% survival in liveborn
- Occasional palliation required prior to definitive repair
- Bullous dilatation of pulmonary valve
- Blalock-Taussig shunt
- Traf with absent pulmonary valve worse prognosis
- 32% mortality at 5 yrs
- Primarily a result of significant respiratory problems
- Associated with hydropro in fetus = poor prognosis
- Associated with oligo in fetus = poor prognosis
- Associated with oligo in fetus
- Associated with hydropro in fetus
- Associated with pulmonary atresia
- Associated with VSD

Treatment

- Encourage "kayotype"
  - Abnormal in 45% prenatal cases
  - Abnormal in 25% live born
- Offers termination if associated aneuploidy/multiple anomalies
- Prenatal consultation with neurology/pediatric cardiology
- Plan delivery at tertiary center
- Follow for postoperative RVOT obstruction
  - 2/25 fetuses in one series progress to pulmonary atresia
- Determines need for neonatal vs. after birth
- Early intervention may be required if significant RVOT obstruction/pulmonary artery hypoplasia
- Surgical repair
  - VSD closure
  - Right ventricular outflow tract reconstruction
  - Valve sparing with infundibular resection
  - Transannular patch
  - RVOT and pulmonary valve conduit
  - Anterior descending coronary artery may arise from right coronary artery
  - Surgeon needs to be aware

Diagnostic Checklist

Consider

- Formal fetal echocardiography
  - Look for associated cardiac malformations
  - Look for features predicting need for early intervention
  - Reversal of flow in ductus arteriosus
  - Failure of growth in pulmonary trunk

Image Interpretation Pearls

- 95% of fetuses with Traf have abnormal four chamber view
  - Traf is the commonest lesion missed on the four chamber view
  - Outflow tract assessment is key to making this diagnosis

Selected References

TETRALOGY OF FALLOT

**IMAGE GALLERY**

*Typical*

*Left* View of the RVOT view as a conus with VSD. Most common flow entering into the aorta from the RV via a pulmonary-ventricular septal defect (VSD). Turbulent flow (curved arrow) across the RVOT is also seen. *Right* Pulsed Doppler ultrasound shows right ventricular outflow tract/pulmonary stenosis gradient of 83.3 mmHg in a six-year-old boy with tetralogy of Fallot.

*Typical*

*Left* Ultrasound shows significant intimal thickening of the pulmonary artery and its branches (arrows) in a fetus with tetralogy of Fallot/thickened pulmonary valve annulus (TAPVR). *Right* Color Doppler ultrasound to the same fetuses shows back and forth flow (red and blue) across the right ventricular outflow tract. Severe pulmonary insufficiency and RV outflow tract obstruction are prominent features of TAPVR.

*Typical*

*Left* Dissection of the RV cavity shows a mild, dysplastic pulmonary valve (arrow) with anterior deviation of the conus (muscular band separating inferior from anterior tricuspid leaflet below the valve. *Right* Partial thrombocytopenia of a 16-week gestation with tetralogy shows a similar appearance to those in the pathological specimen. A right ventricular outflow tract (RVOT) view shows a small pulmonary valve (P. arrow) and a protruded conus (curved arrow) (deviated anteriorly).

*Note:* Abbreviations: RVOT = right ventricular outflow tract, VSD = ventricular septal defect, RV = right ventricle.
Transposition of Great Arteries

Terminology

Abbreviations and Synonyms
- Transposition of great arteries (TGA)
  - D-transposition
  - L-transposition
  - Congenital transposition of great arteries (CTGA)
  - L-transposition
  - RV-transposition

Definitions
- Ventriculoarterial (VA) discordance
  - Aorta arises from right ventricle
  - Pulmonary artery (PA) arises from left ventricle
  - Atrioventricular (AV) and VA discordance
    - Ventricular inversion
  - Right atrium → left ventricle → pulmonary artery
  - Left atrium → right ventricle → aorta

Echocardiographic Findings
- In TGA, "normal" four-chamber view
- Outflow tracts parallel as they exit heart
  - Posterior artery (pulmonary) overrides
  - Arises from left ventricle (LV)
  - Aorta (aorta) gives rise to arch/head and neck vessels
  - Arises from right (RV)
  - Associated lesions
    - Ventricular septal defect (VSD) 35%
    - Left ventricular outflow tract obstruction 10-20%
      (with VSD)
    - Coarctation of the aorta 5%
    - AV valve abnormalities 5%
- In CTGA, closer inspection reveals morphologic LV will be anterior, RV posterior
  - LV smooth walled and no choral attachments to septum
  - RV trabeculated, moderator band, choral attachments to septum
  - PA arises from aorta, left ventricle
  - Aorta arises from posterior, right ventricle
  - Associated lesions
    - VSD 60-70%
    - Right ventricular outflow tract obstruction 30-50%
    - Systemic AV valve abnormalities 90% (often without functional significance)

General Features
- Best diagnostic clue: Outflow tracts parallel as they exit heart

DDx: Transposition Great Arteries

- DORV
- Intalyst of Fallot
- Right Atrial Hypertrophy
**TERMINOLOGY**

- Various names for Transposition of great arteries (TGA) (also called D-transposition of the great arteries (DTGA) or D-TGA)
- Ventricular-arterial (VA) discordance in TGA
- Atrioventricular (AV) and VA discordance in TGA

**IMAGING FINDINGS**

- Best diagnostic clue: Outflow tracts parallel as they exit RV
- TGA “normal” 4 chamber view
- In CTGA, close inspection reveals morphologic LV will be anterior, RV posterior
- Differentiate TGA from CTGA by accurate identification of AV and VA connections

**IMAGING RECOMMENDATIONS**

- Protocol advice
- If parallel outflow tracts are seen
  - Assess ventricular morphology
  - Look for a VSD
  - Assess ventriculoarterial connections
  - Differentiate aorta from PA
  - Aim to classify TGA
  - TGA with intact ventricular septum (IVS) or small VSD 60% (so called “simple” TGA)
  - TGA with large VSD 25%
  - TGA with IVS and LV outflow tract obstruction 10%
  - TGA with intact ventricular septum and LV outflow tract obstruction 5%
  - Differentiate TGA from CTGA by accurate identification of AV and VA connections
  - Look for arterial switch
  - 80% of right atrial isomerism/asplenia have conotruncal malformations including TGA
  - Full anatomic survey for other anomalies, although rare

**DIFFERENTIAL DIAGNOSIS**

- Double outlet right ventricle
  - Normal atrioventricular connections
  - Outflow tracts are parallel but both wholly or predominantly arise from RV
- Tetralogy of Fallot
  - Normal atrioventricular connections
  - Outflow tracts not parallel

**TOP DIFFERENTIAL DIAGNOSES**

- Double outlet right ventricle
- Tetralogy of Fallot

**PATHOLOGY**

- Genetics: Rarely associated with aneuploidy
- Clinical: Examine for congenital heart disease

**CLINICAL ISSUES**

- Presentation
  - Most common signs/symptoms: Parallel outflow tracts noted on routine echo
- Natural History & Prognosis
  - Excellent short and long term outcomes
  - Arterial switch which is now procedure of choice for TGA
  - 80% survival > 90%
  - 8% incidence late coronary artery complications
  - Often have branch pulmonary stenosis and often require surgical intervention
  - Long term (20 yr plus) survival data not yet available
  - CTG survival post neonatal period > 75%
  - Survivors into 50’s without surgery
TRANSMISSION OF GREAT ARTERIES

- Even better outcome expected with new surgical techniques
- TGA circulations
  - Fetal connections are the only communications between pulmonary and systemic circulations
  - Ductus arteriosus
  - Foramen ovale
    - At birth, normal closure = dissociation of circulation = death from hypoxia
    - If present, VSD allows some admixture but also need patent foramen ovale or ductus arteriosus
  - Rashkind procedure to open atrial septum often required to improve oxygen saturation
  - Surgery required within first 2 weeks of life
  - Before development pulmonary hypertension
  - Before LV adapts to low pressure pulmonary circulation
  - Recurrence risk
    - One sibling 1.5%
    - Two siblings 5%
  - CTGA circulation
    - Oxygenated blood from lungs reaches systemic circulation
    - Associated lesions determine prognosis
      - May require early intervention
      - At-risk for conduction defect before, and following repair.
      - In one series 4/21 fetuses with CTGA had complete heart block

Treatment

- TGA
  - Not typically associated with aneuploidy. karyotype may not be necessary
  - Pelvic circulation with pediatric cardiology/radiotherapy
  - Refer to tertiary center for delivery
  - Atrial switch
    - First line of treatment is to maintain fetal shunts
    - Prostaglandin infusion to prevent ductus arteriosus closure
    - Balloon atrial septostomy (Rashkind) allows L → R atrial shunt
  - Old surgical technique: Atrial switch
    - Senning/mustard procedure
    - Significant late complications
  - New surgical technique: Arterial switch, row
    - Operation of choice
    - Great vessels transected and reconnected to appropriate ventricles
    - Coronary arteries re-planted on transposed aorta
  - Operative mortality 3-5%
  - CTGA
    - Pelvic consultation with pediatric cardiology/radiotherapy
    - Refer to tertiary center for delivery
    - No intervention necessary immediately after birth in majority
    - Without VSD: Consider no intervention
    - Long term survival reported into 50's
    - With VSD +/- pulmonary stenosis: Surgical options vary

- Atrial switch with Rastelli
- Double-switch (atrial and arterial)
- Early survival data not documented

DIAGNOSTIC CHECKLIST

Consider
- Formal fetal echocardiography
  - CTGA and TGA have different pathophysiology and treatment
  - Preterm delivery: identification of ventricular connections/arterial connections

Image Interpretation Pearls
- Normal four-chamber view does not exclude significant congenital malformations
- Parallel outflow tract = significant congenital heart disease
- 64% double outlet right ventricle
- 36% transposition of great arteries

SELECTED REFERENCES

TRANPOSITION OF GREAT ARTERIES

IMAGE GALLERY

Typical

(Ultrasound shows a smooth-walled, curved arrow) anterior ventricular chamber anteriorly and moderator (curved arrow) in the posterior ventricle. This is a case of congenitally corrected transposition of the great arteries. (Right) Color Doppler ultrasound in the same case shows parallel orientation of the coiled tracts (arrows). The pulmonary artery arises from the anterior left ventricle and the aorta from the posterior right ventricle.

Typical

(Ultrasound shows the vessel arising from the anterior ventricle (white arrow) has branches supplying the head and neck (black arrow) instead of the expected division into pulmonary artery and aorta. (Right) Another image from the same area shows the typical parietal branching (arrow) pattern of the pulmonary artery, arising from the posterior ventricle (curved arrow).

Typical

(Four chamber view shows a ventricular septal defect (arrow) in a fetus with transposition of the great arteries. A VSD is present in 35% of cases of TGA and up to 70% of cases of CTCG. (Right) Gross pathology of TGA shows the aorta arising from the anterior right ventricle, note moderator band (arrow). The pulmonary artery (PA) arises from the posterior left ventricle (LV).)
TRUNCUS ARTERIOSUS

Catheter shows the trunci vessel (curved arrow) arising over a ventricular septal defect (arrow). The pulmonary artery (open arrow) branches from the truncus shortly after it exits the heart.

IMAGING FINDINGS

General Features
- Best diagnostic clue: Single great artery (truncus) exits heart

Echocardiographic Findings
- Single great artery (truncus) exits heart, gives rise to:
  - Aortic arch, head and neck vessels
  - Left+/− branches pulmonary arteries
  - Single truncal valve with 1–6 cusps
  - Truncal valve dysplasia common
  - May cause stenosis +/− regurgitation
  - Right-sided aortic arch in 33%

- Interrupted aortic arch in 10–20%
- Ductus arteriosus
  - Agenesis = 50%
  - May be very large if arch interrupted
- Ventricular septal defect (VSD)
- Pulse Doppler
  - Useful to assess degree of truncal stenosis if present
  - Persistent forward flow in truncal vessel ⇒ run-off into low pressure system
- Pulmonary circulation is lower resistance than systemic:
  - Truncal vessel gives rise to both pulmonary and systemic vessels
- Color Doppler
  - Allows visualization of truncal stenosis and regurgitation
  - Helps with detection of VSDs
  - Shows flow pattern in aortic arch to aid in diagnosing interrupted arch

Imaging Recommendations
- Formal fetal echocardiography
- Careful anatomic survey
  - 30% of infants with truncus have syndromic
  - 10% have additional extracardiac anomalies

DX: Abnormal Outflow Tracts

| DORV | DORX | Aortic, Atresia | HLHS |
TRUNCUS ARTERIOSUS

Terminology
- Single ventricle (truncus) arises from heart

Imaging Findings
- Tubular valve dysplasia common
- Right-sided aortic arch in 33%
- Interrupted aortic arch in 10-20%
- Ventricular septal defect (VSD)
- 90% of infants with truncus are syndromic
- 10% have additional extracardiac anomalies

Top Differential Diagnoses
- Pulmonary atresia with VSD
- Tetralogy of Fallot
- Aortic atresia/hypoplastic left heart (HLHS)

Key Facts
- Pathology
  - 40% of liveborns with truncus have 22q11 deletion
  - Maternal diabetes: Odds ratio 12.8
- Clinical Issues
  - Offer karyotype and fluorescent in-situ hybridization (FISH) for 22q11 deletion
  - Early surgical repair now treatment of choice
  - Overall operative mortality ≤5% in recent series, with mean age of repair at 11 days
  - 97% of survivors very functional
- Diagnostic Checklist
  - Look for single trunk arising from heart
  - Proximal branch = pulmonary artery is diagnostic
  - Look for truncal valve with > 3 cusps

DIFFERENTIAL DIAGNOSIS

Pulmonary atresia with VSD
-orta arises from left ventricle
- Pulmonary blood flow via retrograde flow in ductus arteriosus or collateral vessels arising from descending aorta

Tetralogy of fallot
- Pulmonary artery arises from right ventricle (RV), often with small annulus
- Interior deviation of infundibular septum
- Aorta arises from left ventricle
- VSD present

Aortic atresia/hypoplastic left heart (HLHS)
- VSD not usually a component
- Only pulmonary artery seen leaving heart
- Aorta atresia = retrograde flow from duc tus arteriosus supplies the head, neck and coronary vessels
- Left ventricle not asep-forming

PATHOLOGY

General Features
- Genetics
  - 40% of liveborns with truncus have 22q11 deletion
  - Microdeletion of chromosome 22q11 deletion syndrome
  - Predisposition for Hirschsprung disease (HSCR) = CATCH 22
  - 10% of patients have truncus arteriosus
  - Right-sided aortic arch and abnormal branching are more common
- Embryology
  - Maternal diabetes: Odds ratio 12.8
  - Developmental field defect
  - Malformations of ears/jaws/lips and palate
  - Aplasia/hypoplasia thymus/parathyroid glands
  - Cardiovascular malformations, especially conotruncal defects

- Epidemiology
  - 1.2% (0.7-2.5%) congenital heart disease in infancy
  - 0.006:1,000 live births
  - M = F
- Entropy
  - Left/right signaling part of complex cascade of events
    - Cardiac neural crest cells are part of cardiac/otocerebral arrestogenic field
    - Field defects explain syndromic associations of heart and facial anomalies
  - Embryonic truncus is a normal structure which lies between the aorta and the aortic arch system
  - Truncal swelling divide the truncal lumen into two channels: Aortic and pulmonary arteries
  - As truncal septum fuses with conal septum, right and left ventricular origins are established
  - If truncal septum fails to fuse to conal septum = truncus septal defect is present
  - If truncal swellings do not divide lumen = single vessel leaves heart
  - Embryologically this form of congenital heart disease should be called "pseudotruncus arteriosus"
  - Single vessel then gives rise to pulmonary/systemic/coronary circulation

Cross Pathologic & Surgical Features
- Truncal valve usually has 3 cusps
  - Can be anywhere from 1-6 cusps
  - Classification system
  - Collett and Edwards 1949, revised in 1976 by Cotler and Van Praagh
  - Type A: Ventricular septal defect present
  - Type B: Ventricular septum intact (very rare)
  - Type A further divided
    - Subgroup or type 1
      - Short main pulmonary trunk arising from truncus, usually left-sided
      - Most common form, 90% all cases
    - Subgroup or type 2
      - Both pulmonary arteries arise separate from truncus
TRUNCUS ARTERIOSUS

- 20-30% all cases
- Subgroup or type 3
- One pulmonary artery arises from ascending aorta
- Takayasu's (thoracic) or non-collateral pulmonary arteries
- < 10% all cases
- Subgroup or type 4
- Undeveloped or hypoplastic aortic arch
- Includes interrupted aortic arch, preductal coarctation or severe hypoplasia/atrias of aortic arch
- 10-20% all cases

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - Fetus
    - Abnormal outflow tracts
    - Single great vessel leaves heart, overrides a ventricular septal defect
  - Infant or child
    - Pulmonary overcirculation early in life
  - 22q11 deletion syndrome
  - Developmental delay
  - Hypocalcemia
  - Immune deficiencies due to T-cell malfunction

Natural History & Prognosis
- Fetal series of 17 confirmed cases
  - Termination of pregnancy 24%
  - Pre-operative death 31%
  - Overall survival 42%
  - 93% mortality by end first year if untreated
  - Rarely, if ever, done
  - At birth large L- to R shunt as blood preferentially flows into pulmonary arteries
  - Untreated = pulmonary hypertension/cyanosis/heart failure/death
  - Truncal regurgitation exacerbates volume overload
  - Prognosis depends on
    - Pulmonary circulation
    - Discontinuous pulmonary arteries or only collateral vessels = worse prognosis
    - Truncal valve function
    - Septal or insufficiency affects morbidity and mortality
  - Current survival rates approaching 95% with complete repair
  - Recurrence risk
    - 0% with one sibling affected
    - 3% if two siblings affected
    - Parental karyotype required for accurate recurrence risk if child has 22q11 deletion
    - Parents may have the microdeletion but not have cardiac disease

Treatment
- Offer karyotype and fluorescent in-situ hybridization (FISH) for 22q11 deletion
- Offer termination
- Premature parental consultation with neonatology/psychiatric cardiology
  - Planned delivery in tertiary center with multidisciplinary team
  - Early surgical repair now treatment of choice
  - Before development of pulmonary hypertension
  - Overall operative mortality 4-5% in recent series, with mean age of repair at 11 days
  - 97% of survivors very functional
  - Operative repair
    - PA excised from truncus
    - Pulmonary arteries connected, if not confluent
    - Pulmonary outflow tract reconstructed using a conduit
    - VSD Closed
    - Truncal valve repaired, if necessary

DIAGNOSTIC CHECKLIST

Consider
- Fetal echocardiogram
- Evaluate for anomalies associated with 22q11 deletion

Image Interpretation Pearls
- Truncus is difficult to diagnose in utero
  - Look for single Trunk arising from heart
  - Proximal branch pulmonary artery is diagnostic
  - Look for tricuspid valves with > 3 cusps
  - Look for truncal sinusoids/septalization

SELECTED REFERENCES

TRUNCUS ARTERIOSUS

Variant:

(Right) Long-axis ultrasound shows a single outflow vessel with a thickened valve (variant). The truncus overrides a ventricular septal defect (Truncus Arteriosus).

(Right) Ultrasound shows a single large vessel or truncus (arrow) exiting the heart in a 32 week fetus. The fetus had an AV septal defect and heteronyx as well as posterior venticular valves with renal parenchymal damage. The pregnancy was terminated due to the dismal prognosis.

Typical:

(Right) Long-axis ultrasound shows the truncus overriding a ventricular septal defect (VSD). The valve (arrow) is thickened and dysplastic. Truncus arteriosus is associated with left-sided heart failure. Right Cavo pulmonary anastomosis shows a ventricular septal defect (arrow) with a single common trunk (arrow) exiting the heart. A left-sided branch (arrow) gives rise to a pulmonary artery.

Typical:

(Right) Ultrasound shows that there are cusps in the valve (arrow) of the outflow vessel, which is consistent with the diagnosis of truncus arteriosus. (Right) Sagittal oblique view. Doppler ultrasound of the truncus arteriosus (arrow) shows a distinct flow consistent with truncal stenosis. The vessel gives rise to the head and neck arteries (arrows).
HYPERTROPHIC CARDIOMYOPATHY

**TERMINOLOGY**

**Abbreviations and Synonyms**
- Cardiomyopathy (CM)
- Hypertrophic cardiomyopathy

**Definitions**
- Primary disorder of cardiac muscle
- No structural malformation
- No precardial disease
- Excludes hypertrophy and poor function secondary to outflow obstruction
- In children CM is a diagnosis of exclusion, hard to exclude some causative conditions in fetus
- Some hypertrophic CM cases progress to dilated CM if underlying condition not treated

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue: Thickened myocardium

**Ultrasonographic Findings**
- Gray-scale Ultrasound
  - Thick interventricular septum
  - Systolic anterior motion of the mitral valve in systole

- Color Doppler
  - Thickened free walls
  - Color Doppler
  - Signs of mid-ventricular obstruction
  - Tissue Doppler flow in left ventricular outflow tract
  - Synechiae with systolic retraction
  - Pulsed Doppler
  - Increased gradient in left ventricular outflow tract
  - Delayed upstroke suggesting dynamic obstruction

**Imaging Recommendations**
- Best imaging tool: Formal fetal echocardiogram
- Protocol advice
  - Exclude mechanical causes
  - Valvular stenosis
  - Ductal constriction
  - C-scantion: May not be able to exclude this in fetus
- Measure ventricular wall thickness
- Epicardial to endocardial surface
- Measure at end-diastole for minimum thickness
- Measure just below level of closed aortic and left ventricular valve leaflets
- Measure chamber dimensions in 4 chamber view
- End-diastolic diameter (EDD) is longest measurement at end-diastole
- End-systolic diameter (ESD) is shortest measurement at end-systole

**DDx: Thickened Myocardium**
- Pulmonary Stenosis
- HCM
- Rhabdomyomatisos
- Idiopathic Calcification
HYPERTROPHIC CARDIOMYOPATHY

Key Facts

- **Pathology**
  - Hypertrophic CM reported in 30% of fetuses of diabetic mothers
  - CM (all types) 0.02:1,000 live births

- **Clinical Issues**
  - Most primary/familial cases present in third trimester
  - Fetuses of diabetic mothers may show progressive increase in heart size/myocardial thickness from second trimester onward
  - Cases due to high-output state present earlier due to underlying condition
  - Postnatal treatment options may be few

- **Diagnostic Checklist**
  - Formal fetal echocardiography in all cases
  - Exclude structural malformation

- **Terminology**
  - Primary disorder of cardiac muscle
  - Some hypertrophic CM cases progress to dilated CM if underlying condition not treated

- **Imaging Findings**
  - Best diagnostic clue: Thickened myocardium
  - Turbulent flow in left ventricular outflow from subaortic stenosis
  - Exclude mechanical causes

- **Top Differential Diagnoses**
  - Outflow tract obstruction
  - Rhabdomyoma
  - Myocardial calcification

- **DIFFERENTIAL DIAGNOSIS**

  - Outflow tract obstruction
    - Left ventricular outflow tract obstruction
    - Aortic atresia/stenosis
    - Hypoplastic left heart syndrome (HLHS)
    - Pulmonary atresia/stenosis
    - Ductal constriction

  - Rhabdomyoma
    - Mimics hypertrophic CM if it involves ventricular septum
    - Usually multiple masses = easy differentiation
    - Case reports of rhabdomyoma causing diffuse myocardial thickening

  - Myocardial calcification
    - Most cases idiopathic
    - Can be seen with in utero infection
    - Associated with myocardial damage
    - Maternal cocaine abuse
    - Viral infections

- **PATHOLOGY**

  - General Features
    - Genetics
    - Autosomal recessive
    - Inborn errors of metabolism (e.g., Pompe disease)
    - Single gene disorders
    - Familial hypertrophic CM

    - Neurofibromatosis
    - Friedreich ataxia
    - LEOPARD syndrome
    - Noonan syndrome
      - Only single gene disorder likely to be diagnosed in utero
      - Familial hypertrophic CM
    - 50% have mutation of chromosome 1, 14 or 15
    - 30% missense mutation in cardiac β myosin heavy chain gene on chromosome 14q11
    - 15% mutation in cardiac troponin T gene on chromosome 1q31
    - 3% mutation in α troponin C gene on chromosome 15q2

    - Hypertrophic CM reported in 30% of fetuses of diabetic mothers
    - Higher if poor glycemic control
    - Primary hypertrophic myocardium
    - Noonan syndrome
    - Glycogen storage disease
    - Familial hypertrophic cardiomyopathy
      - Case reports of fetal diagnosis with apical hypertrophy
    - Usually does not manifest until adolescence
    - Non-compaction of ventricular myocardium
    - Pathologic entity characterized by abnormal trabeculation of myocardium
    - Thick-walled, non-dilated ventricles
    - Arrhythmia due to atrioventricular regurgitation
    - Mosaic ventricular syndactyly
    - Conotruncal type physiology with focal narrowing of abdominal aorta
    - Aortic narrowing => systolic hypertension
    - Increased work for pump twin heart, recipient has volume overload
    - Either/both may develop ventricular hypertrophy
    - If untreated, ultimately progresses to dilated end-stage heart disease
    - Other high-output states
      - Aortic
      - Aneurysmal malfunction
HYPERTROPHIC CARDIOMYOPATHY

- Twin reverse zental perfusion (TRAP)
- Tumor: Saccococcal teratoma
- Epidemiology
  - CM (FDA report) 0.02:1 1,000 live births
  - Series of 13 cases fetal CM
  - 44% dilated CM
  - 66% hypertrophic CM
  - Of 33 hypertrophic CM cases
  - 54% TTS
  - 21% fetus of diabetic mother
- Physiology
  - Ventricular walls and septum are thick
  - Thick myocardium is stiff
- Compliance = filling = cardiac output
- Hypertrophic CM may cause diastolic dysfunction
- Myocardial perfusion occurs in diastole
- Diastolic dysfunction = myocardial ischemia/myopathy
- Ischemia may = ventricular dilatation and cardiomyopathy

Microscopic Features
- Pompe disease
- Muscle fibers infiltrated with glycogen
- Individual muscle fibers massively hypertrophied

CLINICAL ISSUES

Presentation
- Most common signs/symptoms present in third trimester
- Fetuses of diabetic mothers may show progressive increase in heart size/myocardial thickness from second trimester onward
- Cases due to high-output state present earlier due to underlying condition

Natural History & Prognosis
- Depends on underlying condition
  - TTS: high mortality if untreated
  - Fetus of diabetic mother
    - Disproportionate thickening of ventricles septum or free wall
    - Progressive throughout gestation
    - Usually resolves within 6 months after birth, prognosis excellent
    - Technically not true cardiomyopathy, fetal response to maternal hypertension
- Familial forms
  - Annual risk of death 1%
- Norval fetal echocardiogram does not reliably predict free-living lifetime
  - Familial forms may not have clinical impact until adolescence or later

Treatment
- Detailed family history
- Consider echocardiography of parents if mother not diabetic
- Genetic testing possible for some types
- Ethical dilemma as presence of mutation does not = presence of disease
- Inborn errors of metabolism after neonatal resuscitative
- May require specific treatment/diagnostic measures
- Laser/radiofrequency ablation for TTS or TRAP
- Fetal surgery for tumors such as sacrococcygeal teratoma
- Intravenous transfusion for fetal anemia
- Monitor throughout pregnancy
- Hypertrophy may be progressive = secondary outflow obstruction
- Refer to tertiary center
- Delivery plan coordinated with neonatology and cardiology
- Careful postnatal evaluation
  - Accurate diagnosis important to counsel parents on prognosis, recurrence risk
  - Postnatal treatment options may be few
  - Consider implantable cardiac defibrillator in high-risk options
  - Cardiac transplantations last resort

DIAGNOSTIC CHECKLIST

Consider
- Portal fetal echocardiography in all cases
- Exclude structural malformation
- Assess baseline function

Image Interpretation Pearls
- Always check for mechanical obstruction
- In at-risk fetus may visualize ventricular shunting fraction
- Impaired systolic function, may be seen before chamber dilatation or hypertrophy

SELECTED REFERENCES

HYPERTROPHIC CARDIOMYOPATHY

IMAGE GALLERY

Typical

(left) This type with thick hypertrophy, an isolated cardiomyopathy, has a thick myocardial annulus with abnormal contractility. This typically progresses to dilated cardiomyopathy in 10 years. (right) Cineangiography shows non-compaction of the myocardium with extensive trabeculation (curved arrows) and deep intertrabecular recesses (arrows). Through cine, this can be diagnosed by the saw-tooth appearance of systolic dysfunction.

Typical

(left) Color Doppler advanced shows significant mitral regurgitation (arrow). The regurgitant jet exiting ventricular septum with the right atrium markedly (left arrow) in the ventricle. (right) Four chamber view shows abnormally thick myocardium (arrows) in the pump of a non-systolic-systolic regurgitation, complicated by TTS. POCUS demonstrates effusion (curved arrows).

Typical

(left) TTE view in a non-systolic-systolic regurgitation shows severe asymmetric systolic hypertrophy, which appears abnormal thickening of the ventricular wall (MV) causing left ventricular overload (arrows) and diastolic (LA, left arrow). (right) Color Doppler advanced in the same patient with systolic hypertrophy shows turbid left ventricular outflow (arrow) during systole, as motion of the septum and mitral valve (MV) causes "dynamic" diastolic regurgitation.
**TERMINOLOGY**

**Abbreviations and Synonyms**
- Cardiomyopathy (CM)
- Dilated cardiomyopathy

**Definitions**
- Primary abnormality of cardiac muscle
  - No structural malformation
  - No pericardial disease
  - In children CM is a diagnosis of exclusion, hard to exclude some causative conditions in fetus
- Hypertrophic CM may progress to dilated CM if underlying condition not treated

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue: Cardiomegaly

**Gray-scale Ultrasound**
- Large heart
- Poor myocardial contractility
- Myocardium often thin
- Signs of hydrops
- Pericardial effusion

**DDx: Cardiomegaly**

- Pseudo CM: CH
- Pseudo CM: TD
- Ebstein Anomaly
- Pulmonary Stenosis
DILATED CARDIOMYOPATHY

Terminology
- Primary abnormality of cardiac muscle

Imaging Findings
- Large heart
- Poor myocardial contractility
- Myocardium often thin
- Mitral/ventricular regurgitation
- Some conditions cause partial myocardial hypertrophy with a dilated heart as end-stage of process

Top Differential Diagnosis:
- Pseudocardiomegaly
- Outflow tract obstruction

Key Facts

Pathology
- Familial transmission in 20-25% of cases
- Dilated CM detected in < 1% fetal echocardiograms

Clinical Issues
- Presence of hydrops is a poor prognostic sign
- Monitors for underlying arrhythmia
- Survivors may require cardiac transplantation

Diagnostic Checklist
- Normal fetal echocardiography in all cases
- Always check for shunt lesions in fetus with apparent isolated cardiomegaly
- In at-risk fetus, measure ventricular shortening fraction
- Impaired systolic function may be seen before chamber hypertrophy or dilatation

PATHOLOGY

General Features
- Genetics
  - Familial transmission in 20-25% of cases
  - Autosomal dominant with age-related penetrance
  - X-linked: Barth, Duchenne and Becker muscular dystrophy
- Etiology
  - Major causes of dilated CM
    - High-output states
    - Myocardial damage
    - Cardiomyopathy
  - High-output states
    - Anemia
    - Shunt
    - Myocardial damage
      - Infection
      - Hypoxia/hypotension
      - Sustained arrhythmia
    - Immune complex deposition may cause myocarditis
- Epidemiology

DIFFERENTIAL DIAGNOSIS

Pseudocardiomegaly
- Heart size normal
- Chest is small
- Pulmonary hypoplasia
  - Fetal agenesis
  - Bilateral multicystic dysplastic kidney
  - Autosomal recessive polycystic kidney disease
  - Posterior urethral valves
  - Skeletal dysplasia
  - Associated with severe limb shortening

Outflow tract obstruction
- Critical aortic stenosis
- Ductal constriction
- Pulmonary atresia

Endocardial fibroelastosis
- Left ventricle may be large

Ebstein anomaly
- Marked enlargement of right atrium

- End-systolic diameter (ESD) is shortest measurement at end-systole
- Measure ventricular shortening fraction (VSG)
- VSG = EDD - EDD/EDD
- Normal right VSG 0.25
- Normal left VSG 0.30
- Look for possible causative lesions
  - Some conditions cause initial myocardial hypertrophy with a dilated heart as end-stage of process
  - Evaluate for fetal anemia
  - Middle cerebral artery (MCA) Doppler
  - Peak systolic velocity (TSV) of MCA plotted against gestational age
  - Determines when transfusion needed
  - Look for shunt lesions
  - Twin-twin transfusion syndrome (TTTS)
  - Twin reverse arterial perfusion (TRAP)
  - Aneurysm
  - Fetal tumor
  - Look for signs of intrauterine infection
  - Intracranial calcifications
  - Intrahepatic calcifications
  - Cerebral ventriculomegaly
  - Hepatomegaly
  - Absent amniotic fluid volume
  - Monitor for development of hydrops
DIAGNOSTIC CHECKLIST

Consider
- Formal fetal echocardiography in all cases
  - Exclude structural malformation
  - Congenital heart disease
  - Assess baseline function

Image Interpretation Pearls
- Always check for short extremities in fetus with apparent isolated cardiac anomaly
  - Placental chorioangioma
  - Use color Doppler for antenatal fetal evaluation
  - In at-risk fetus, measure ventricular shortening fraction
  - Impaired systolic function may be seen before chaotic hypotension or distal perfusion

SELECTED REFERENCES

CLINICAL ISSUES

Presentation
- Most common signs/symptoms: Cardiomyopathy observed on routine obstetric sonogram

Natural History & Prognosis
- Presence of hydrops is a poor prognostic sign
- Batrachomyomata is often lethal early in infancy
- Duchenne and Becker muscular dystrophy
- Develop progressive cardiomyopathy as teenagers

Treatment
- Antenatal infection screen
- Echocardiography and direct culture
- Endocarditis
- Rubella
- Hepatitis C
- Parvovirus

- Prenatal treatment options are few
- Survivors may require cardiac transplantation

MALIGNANT HYPERTROPHY

- Echocardiography: Increased interventricular septal thickness
- Echocardiographic evidence of left ventricular hypertrophy
- Cardiac catheterization: Hypertrophic cardiomyopathy
- Transcatheter aortic valve replacement
- Requirement for anticoagulation

- Surgical intervention: Myectomy or valvuloplasty
- Mortality rate is low

Diagnosis

- Electrocardiography: Sustained ventricular tachycardia
- Echocardiography: Hypertrophic cardiomyopathy
- Cardiac catheterization: Hypertrophic cardiomyopathy

- Management: Medical therapy, surgical intervention, device therapy

- Prognosis: Excellent with appropriate treatment

- Echocardiographic evidence of left ventricular hypertrophy
- Cardiac catheterization: Hypertrophic cardiomyopathy
- Transcatheter aortic valve replacement
- Requirement for anticoagulation

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DILATED CARDIOMYOPATHY

[Image Gallery]

Typical

(Left) Four-chamber view ultrasound shows significant cardiomegaly, the atria are more dilated than the ventricles. Note maximal dilatation of the right atrium (arrows). (Right) Color Doppler ultrasound in the same imaging plane shows severe bidirectional atrioventricular valve regurgitation. Blood refluxes back into the atria (arrows) along ventricular septal (V) = left ventricle, RV = right ventricle).

(Left) Four-chamber view shows significant cardiomegaly with pericardial effusion (arrows) at 23 weeks gestation. The fetus initially presented with echogenic bowel at 10 weeks. (Right) Sagittal image in the same fetus shows a dilated superior (arrow) and inferior (curved arrow) vena cava. The fetus was delivered for poor biophysical profile scores and significant hydrogyn. Congenital CHF/infarction was diagnosed by wire culture.

(Left) Four-chamber view ultrasound shows cardiomegaly with dilatation of all four chambers in this recipient twin in a pregnancy complicated by twin-twin transfusion syndrome. There is also a pericardial effusion (arrows). (Right) Ultrasound shows a large, mobile and hyperechoic RV (arrows) in a fetus with Ebstein syndrome, which progressed in infancy to a dilated cardiomyopathy.

6
**TERMINOLOGY**

Abbreviations and Synonyms
- Premature atrial contraction (PAC)
- Premature ventricular contraction (PVC)
- Atrial flutter (AF)
- Supraventricular tachycardia (SVT)

Definitions
- Irregular heart rhythm. Rate may be normal, fast or slow

**IMAGING FINDINGS**

General features
- Irregular heart rate observed on routine sonography

Ultrasonographic Findings
- Grayscal Ultrasound: Asymmetric atrial/ventricular contraction
- Pulsed Doppler
  - Conducted PAC
  - PAC associated with PAC
  - Compensatory pause
  - Sinus rhythm resumes
  - Non-conducted PAC

**DIFFERENTIAL DIAGNOSIS**

Premature atrial contraction
- Usually transient and benign

DDx: Irregular Heart Rate

- SVT
- Intermittent SVT
- 2nd degree AVB
- Atrial Flutter

- Early atrial contraction in cardiac cycle not followed by ventricular contraction
- Compensatory pause
- Sinus rhythm resumes
- PVC
- Early ventricular contraction in cardiac cycle occurring without prior atrial contraction
- Non-compensatory pause
- Sinus rhythm resumes

Imaging Recommendations
- Best imaging tool: Pulsed Doppler +/- color M-mode
- Formal fetal echocardiogram
- In fetuses with frequent PACs
- Congenital heart defects reported in up to 2% cases
- 2% risk of developing SVT, higher if multiple beats are blocked
- Atrial fibrillation or atrial flutter
- Structural defects
- Valvular incompetence
- Look for signs of hydrops
**TERMINOLOGY**

- **Premature ventricular contraction**
  - Much less common than PACs, also transient and benign

- **Supraventricular tachycardia**
  - 1:1 AV relationship
  - Characteristic rate 230-280, may be intermittent
  - Usually re-entrant pathway

- **Atrial flutter**
  - Atrial rates typically 300-500 beats per minute
  - Irregular AV block leads to irregular ventricular rate (If 2:1 block then ventricular rate is regular)

- **Second degree heart block**
  - Type 1: Progressive increase in interval from atrial to ventricular contraction with eventual dropped beat
  - Usually benign and does not progress to complete heart block
  - Type 2: Atrial to ventricular conduction interval is prolonged and constant with intermittent non-conducted atrial beats
  - May progress to complete heart block

**PATHOLOGY**

- **General Features**
  - Epidemiology
    - 1-2% of pregnancies will have arrhythmia
    - < 10% are significant, PACs/PVCs account for 90%

**CLINICAL ISSUES**

- **Presentation**
  - Abnormal heart rate or rhythm noted on physical exam

- **Natural History & Prognosis**
  - PACs and PVCs
    - Self limited: Most resolve by time of delivery
    - Extremely rare to cause problem in neonate
  - Supraventricular tachycardia
    - Usually easy to treat but 9% mortality rate
  - Atrial flutter
    - Occurs later in gestation, 8% mortality rate
  - Second degree heart block: Rare but concern for progression to complete block

**Key Facts**

- **Clinical Issues**
  - Second degree heart block: Rare but concern for progression to complete block
  - PVCs/PVCs usually require no treatment
  - Weekly auscultation to monitor for development of SVT

- **Diagnostic Checklist**
  - 90% of fetal arrhythmias due to PACs/PVCs

**Treatment**

- PACs/PVCs usually require no treatment
  - Suggest reduction of maternal caffeine/alcohol/nicotine intake
  - Weekly auscultation to monitor for development of SVT
  - SVT/atrial flutter
    - Treatment recommended to prevent hydrops
    - Digoxin first line

**DIAGNOSTIC CHECKLIST**

- Formal fetal echocardiogram

**IMAGE GALLERY**

(left) M-mode ultrasound shows atrial flutter with atrial rate of 333 bpm. The ventricular rate was variable, up to 240 bpm. (right) Pulsed Doppler ultrasound shows two types beats (arrow) followed by non-conducted premature atrial beat (arrow) and 20% occult cases, with an interesting conducted premature atrial beat with ventricular conduction (open arrow).
**TACHYARRHYTHMIA**

**TERMINOLOGY**

**Abbreviations and Synonyms**
- Sustained tachycardia
- Supraventricular tachycardia (SVT)
- Atrial fibrillation
- Atrial flutter (AF)
- PermaJet (junctional) reciprocating tachycardia (PJRT)

**Definitions**
- SVT: Heart rate > 200 beats per minute (bpm)

**IMAGING FINDINGS**

**General Features**
- Sustained fast heart rate > 200 bpm
  - M-mode tracing or pulsed Doppler must be performed to determine type of arrhythmia

**Ultrasoundographic findings**
- Color Doppler: Useful to document atrioventricular (AV) valve regurgitation
- Pulsed Doppler:
  - Curved plane in left ventricle at junction of mitral valve and left ventricular outflow tract
  - Mitral inflow = atrial rate
  - Left ventricular outflow = ventricular rate

**DDx: Tachyarrhythmias And Consequences**

- SVT
- SVT: Hypokalemic
- SVT: Hydrops
- AF

**IMAGING Recommendations**

- Best imaging tool
  - Pulsed Doppler for SVT
  - M-mode for atrial flutter
  - Formal fetal echocardiography for structural defects
  - Seen in up to 10% of tachyarrhythmias

- Look for signs of hydrops
  - Abnormal fluid location
    - Pericardial effusion
    - Pleural effusion
    - Ascite
    - Skin edema
  - Cardiomegaly
  - Track by measuring ratio of heart to chest circumference

- Look for signs of hemodynamic decompensation
  - Flow reversal in inferior vena cava
  - Flow reversal in ductus venous
  - Phlebitis flow in umbilical vein
  - Significant AV valve regurgitation
**TACHYARRHYTHMIA**

**Imaging Findings**
- Accelerated fetal heart rate > 200 bpm

**Top Differential Diagnoses**
- Supraventricular tachycardia
- Atrial flutter
- Atrial fibrillation
- Permanent junctional reciprocating tachycardia
- Ventricular tachycardia

**Pathology**
- 1-2% of pregnancies have arrhythmia
- Only about 10% clinically significant
- 1-5% of fetuses with premature atrial contractions will develop SVT
- Ventricular rates > 230 bpm ⇒ fetal central venous pressure

- Complete anatomic survey
- Surpass fetal well-being
  - Biophysical profile, daily at first

**DIFFERENTIAL DIAGNOSIS**

**Supraventricular tachycardia**
- Most common fetal tachyarrhythmia
- 1:1 AV relationship
- Characteristic rate 250-280 bpm, may be intermittent
- Usually re-entrant pathway

**Sinus tachycardia**
- May be response to maternal condition
  - Thyrotoxicosis, fever, sepsis, or drugs
- Characteristic rate 170-200 bpm
- 1:1 AV relationship

**Atrial flutter**
- Atrial rate > ventricular rate
- Atrial rate 300-500 bpm, regular
- Variable AV block
  - If 2:1 block then ventricular rate is regular
  - Variable block leads to irregular ventricular rate

**Atrial fibrillation**
- Atrial rate > ventricular rate
- Atrial rate 300-500 bpm, irregular
- Variable conduction ⇒ variable ventricular rate
- Rare in fetus

**Permanent junctional reciprocating tachycardia**
- 1:1 AV relationship
- Characteristic rate ≈ 200 bpm
- Impulse starts at AV junction and recurs along specific re-entrant pathway
- Rare and very difficult to treat

**Ventricular tachycardia**
- Ventricular rate > atrial rate
  - No characteristic rate

**Clinical Issues**
- Most reported cases present in third trimester
- Postnatal cardiac evaluation required for all
- Arrhythmias can recur/persist in neonatal period
- Hydrops present or develops in 50-75% fetuses with sustained tachyarrhythmia
- Overall fetal demise = 10%
- Digoxin first-line drug, with 60% successful conversion of SVT
- Hydropic fetus unlikely to convert to normal rhythm with digoxin monotherapy

**Diagnostic Checklist**
- SVT & concomitant fetal tachyarrhythmia
- Vital vs. differential types of tachyarrhythmia due to different therapies
- Presence/absence of hydrops impacts mortality

- 170-400 bpm recorded
- AV dissociation
- Rare in fetus, associated with
  - Ventricular ischemia/infarction
  - Ventricular aneurysm
  - Perinatal stress/ hypoxia

**PATHOLOGY**

**General Features**
- Genetics
  - Sporadic
  - Few familial pre-excitation syndromes
  - Accessory pathway identified in first degree relatives in 1.06%
  - General population prevalence 0.15%
- Etiology
  - SVT usually re-entrant pathway between atrium and ventricle
  - Atrial flutter: Single re-entry circuit within atrium
  - Atrial fibrillation: Multiple small intra-atrial re-entry circuits
- Epidemiology
  - 1-2% of pregnancies have arrhythmia
  - Only about 10% clinically significant
  - Of fetuses with tachyarrhythmia
  - SVT in 65-93%
  - Atrial flutter in 7-29%
  - Ventricular tachycardia in < 4%
  - 1-5% of fetuses with premature atrial contractions will develop SVT
- Physiology
  - Ventricular rates > 230 bpm ⇒ fetal central venous pressure
  - 1 Venous pressure ⇒ flow reversal in inferior vena cava
  - Short diastole ⇒ 1 myocardial perfusion
  - Ischemic ventricles dilate ⇒ AV valve regurgitation
  - AV regurgitation ⇒ further increase in venous pressures/hepatic congestion
  - End result is hydrops
TACHYARRHYTHMIA

CLINICAL ISSUES

Presentation
- Abnormal fetal heart rate noted on physical examination
- Most reported cases present in third trimester
  - Range 18-42 weeks

Natural History & Prognosis
- Premature cardiac stimulation required for all
- Arrhythmias can persist or persist in neonatal period
  - 48% in one series of fetuses with ventricular tachycardia
  - 8-10% of fetuses with SVT will or be diagnosed with Wolf-Parkinson-White syndrome
- Prognosis generally good for intermittent SVT
- Hydrops present or develop in 50-75% fetuses with sustained tachyarrhythmia
- Complicates treatment
- Harms to achieve therapeutic levels of medication
- Overall fetal demise ~10%
- Worse with hydrops
- Recent report indicates concern for ischemic brain injury in association with hydrops

Treatment
- Multidisciplinary team approach, most effective
- Delivery may be simplest treatment option if gestational age allows
- Internationally SVT without hemodynamic decompensation
  - Careful circulatory management
  - Daily scan and biophysical profile initially
  - Patient compliance is key, as persistent SVT with hydrops may develop within 24 hrs
  - Spontaneous resolution has been reported
  - Vagal stimulation in labor slows AV conduction may decrease rate
- Persistent SVT in evaluationetus
  - Digoxin first-line drug, with 60% successful conversion of SVT
  - May be given orally or intravenously to mother
  - Monitor maternal serum levels
  - Fetal levels approximately 80% of maternal levels
  - If failure to correct rhythm, additional medications (β-blocker) increase success rate another 25%
- Hydric fetal usually difficult to correct to normal rhythm with digoxin monotherapy
  - Response rate to digoxin alone 20%
  - Hydric fetuses do not attain base blood levels at non-hydric
- Requires additional medications or digoxin therapy to achieve success rate of 65%
- Recurrence: Potential fast response, may cause maternal proarythymia
- Amiodarone: May be successful, case reports of neonatal hypothyroidism
- Atrial Fibril
  - Digoxin monotherapy is successful in 45-53% of non-hydric fetuses
  - Add Sotalol (µlathine to convert rhythm success rate increases to 80%
  - Recommend Sotalol alone or in combination with Digoxin in hydric fetus

- May be given orally
- Fetal levels not 100% maternal level
- Concern for proarythymic effects in mother and fetes
- Success rate 60%

DIAGNOSTIC CHECKLIST

Consider
- Formal fetal echocardiogram
  - Look for associated structural disease
  - Assess baseline function
  - Look for signs of hydrops

Image Interpretation Pearls
- SVT is more common fetal tachyarrhythmia
- Vital to differentiating types of tachyarrhythmia due to different therapies
- Presence/absence of hydrops impacts mortality

SELECTED REFERENCES
3. Lammie JD et al. Differential diagnosis and management of the fetus and newborn with an irregular or abnormal heart rate. Pediatr Crit Care Med. 5(4):413-6, 2004
(Left) M-mode echocardiogram with camera placed across the right ventricle (arrows) and right atrium. Rapid atrial and ventricular rates are in a ratio with 177/180 beats per minute demonstrated by the atrial septal valve closure diagnostic feature. (Right) M-mode echocardiogram shows a faint atrial septal closure diagnostic feature in the ventricle distal to the ventricular septum (svs). Atrial fibrillation is generally good for immediate SV4 but closer monitoring is required.

(Fo) M-mode echocardiogram with color enhancement (blue ventricular wall, red ventricular lumen) shows a rapid ventricular rate with an atrial contraction (arrows) due to 180 beats. (Right) M-mode echocardiogram of a patient with atrial fibrillation shows a rapid ventricular rate (svs), measured at 180 bpm. Variable AV block resulted in a ventricular rate of 180 bpm, measured by the aortic valve motion (arrows).

(Fo) Four-chamber view shows right heart enlargement, particularly right atrial (arrows). Combination of this and other factors was poor secondary to tachycardia. This necessitates concern for development of hypotension. (Right) Four-chamber view shows severe tachycardia with rapid atrial rate (arrows) and hypotension due to sustained tachycardia. It is harder to achieve adequate systemic venous drug levels once hypotension develops.
TERMIONOLOGY

Abbreviations and Synonyms
- Sinus bradycardia
- Partial atrioventricular block
- Complete atrioventricular block
- Complete heart block (CHB)
- Trigeminal atrial contractions (PAC)

Definitions
- Abnormally slow heart rate < 100 beats per minute (bpm)
- Sinus bradycardia
  - Atrial and ventricular rates same
  - Normal conduction from atrium to ventricle
- Complete atrioventricular block
  - Atrial rate normal
  - Slow independent ventricular rate
  - Due to failed conduction from atrium to ventricle
- Partial atrioventricular block
  - First or second degree heart block
  - Long PR interval with variable ventricular conduction
- Blocked PACs
  - Early atrial beat not followed by a ventricular beat

[Image: Graphic shows Doppler curve used for evaluation of asystolia, flow during atrial contraction arrow is toward the transducer, while flow during a ventricular contraction (arrow) is away from the transducer.]

[Image: Ao = 53 bpm, showing atrial contractility is less than normal.]

IMAGING FINDINGS

General Features
- Heart rate persistently < 100 bpm

Ultrasonographic Findings
- grayscale ultrasound
  - Cardiac anatomy normal in 50%
  - Structural defects present in 50%
- Pulsed Doppler
  - Cursors placed in left ventricle at junction of mitral valve and left ventricular outflow tract
    - Mitral inflow = atrial rate
    - Left ventricular outflow = ventricular rate
- M-mode
  - Place M-mode cursor to include both atrium and ventricle
  - Evaluate atrial and ventricular rates and atrioventricular conduction
  - Is every atrial contraction followed by a ventricular contraction?

Imaging Recommendations
- Best imaging tool: Pulsed Doppler
- Normal fetal echocardiography
  - Look for structural defects commonly seen in fetuses with CHB
  - Atrioventricular septal defect

DDx: Bradycardia

[Images of Doppler waves: ΔT = 62ms, ΔT = 99 bpm, ΔT = 118 bpm]
BRADYARRHYTHMIA

Key Facts

- Risk of fetal CHB with maternal lupus up to 5%

Clinical Issues

- First trimester bradycardia associated with high pregnancy failure rate
- Poor prognosis with structural abnormality
- Normal structure/no hydrops ⇒ 50% survival
- Positive antibody screen 85% of mothers of fetuses with CHB and normal cardiac structure
- Fetal cardiac pacemaker has been achieved but did not prevent fetal demise
- Consider cesarean delivery
- Deliver at tertiary center with cardiology support

Diagnostic Checklist

- Fetus with CHB may be first presentation of maternal autoimmune disease

Complete heart block

- Independent, disassociated atrial and ventricular contractions

Partial AV block

- Second degree heart block
  - Type 1: Progressive increase in PR interval with every second beat
  - Type 2: Atrial-to-ventricular conduction time is prolonged and constant, with intermittent non-conducted beats

PATHOLOGY

General Features

- Etiology
  - 50% of cases in mothers with connective tissue disease
- Other 50% associated with cardiac malformation particularly atrioventricular septal defects
- Maternal antibodies cross placenta
- Mother has anti-SSA/Ro and/or anti-SSB/La antibodies
- Fetal/neoatal myocardium contains body’s highest concentration Ro antibodies
- Maternal antibody binds to fetal antigen
- Inflammation/fibrosis of fetal heart conduction system and myocardium
- Fibrosis inhibits repolarization
- Another, as yet unknown, cofactor may also be present
  - Majority of mothers with anti-SSA/Ro and anti-SSB/La antibodies have normal pregnancies
  - Trigger to fetal cardiac damage may be viral exogenous
- Mothers of fetuses with CHB have increased frequency of antibodies to cytomegalovirus

Epidemiology

- t-2% of pregnancies have arrhythmia
- CHB accounts for 9% of all fetal arrhythmias
- Risk of fetal CHB with maternal lupus up to 5%
- Risk of fetal CHB for antibody positive mother ≤ 2%

DIFFERENTIAL DIAGNOSIS

Transient sinus bradycardia

- May be caused by excessive transducer pressure
- Heart rate quickly returns to normal with release of transducer pressure

Blocked PAC

- Intermittent, early atrial beat without conduction to ventricle

Terminology

- Abnormally slow heart rate < 100 beats per minute (bpm)

Imaging Findings

- Cardiac anomaly normal in 50%
- Structural defects present in 50%

Top Differential Diagnoses

- Transient sinus bradycardia
- Blocked PAC
- Complete heart block
- Partial AV block

Pathology

- 50% of cases in mothers with connective tissue disease

- Atrial-ventricular discordance
- Atrioventricular dysynchrony
- Assess myocardial function
- Track by measuring ventricular shortening fraction (VVF)
- VVF = end-diastolic diameter minus end systolic diameter/end-diastolic diameter
- Assess heart size (cardiomegaly)
- Track by measuring ratio of heart to chest circumference
- Look for signs of hemodynamic decompensation
- Significant atrioventricular valve regurgitation
- Reversal of flow in vena cava
- Reversal of flow in ductus venosus
- Unbilical vein pulsation
- Look for evidence of hydrops
- Abnormal fluid accumulation
- Pericardial effusion
- Pleural effusion
- Ascites
- Sino-atrial block

- Use subclavian artery Doppler to monitor placental vascular resistance

- Risk of placental insufficiency
- Increasing placental resistance may precipitate hydrops without further decrease in heart rate
- Maternal lupus may ⇒ segmental placental infarction

- Monitor growth
- CHB = decreased placental perfusion ⇒ growth restriction
CLINICAL ISSUES

Presentation
- First trimester bradycardia noted on viability dating studies
- 2nd/3rd trimester, slow heart rate noted on physical examination
- May initially present with irregular rate from second degree heart block
- If in utero progression from second degree heart block to CHB has been described

Natural History & Prognosis
- First trimester bradycardia associated with high pregnancy failure rate
- Survivors likely to have structural disease, especially heterotaxy syndromes
- Increased mortality with heart rate < 100 bpm
- 15-25% with develop hydrops
- Intrauterine fetal demise = 75%
- Poor prognosis with structural abnormality
- Survival < 5%
- Normal structure/no hydrops = 90% survival
- Late, at-risk pregnancy monitor fetal PR interval
- Palpation may be first sign of immune-mediated disease
- If bradycardia due to maternal antibodies, significant risk for recurrent lupus syndrome
- Not equivalent to systemic lupus erythematosus, self-limiting condition
- Thrombocytopenia, anemia, low white cell count
- Hepatomegaly/cholestasis
- Skin rash/photosensitivity
- Usually resolves by 6 months as antibodies clear from infant circulation
- Syndrome resolves but damage to conducting system is permanent
- Some series show significant incidence of progression to dilated cardiomyopathy in childhood
- Survivors require close follow-up with pediatric cardiology
- Recurrence risk
- 8-16% in mother with anti-Ro/La antibodies and a previous child with CHB
- 25-64% if previous child with normal lupus manifesting CHB

Treatment
- Maternal evaluation by rheumatologist
- Positive antibody screen in 85% of mothers of fetuses with CHB and normal echocardiographic structure
- Treatment aim
- Diminish fetal inflammatory response
- Limited efficacy using steroids, plasmapheresis, and intravenous immunoglobulin
- Increase fetal heart rate
- Beta agonists (e.g., terbutaline)
- Poor maternal tolerance at dose sufficient to increase fetal heart rate
- Fetal cardiac pacing has been achieved but did not prevent fetal demise
- Consider cesarean delivery
- Stress of vaginal delivery may = acute decompensation
- Intravenous monitoring extremely difficult due to bradycardia
- Deliver at tertiary center with cardiology support
- Cardiac pacing required for definitive treatment

SELECTED REFERENCES
**BRADYARRHYTHMIA**

**IMAGE GALLERY**

**Typical**

(Left) Pulsed Doppler ultrasound shows the normal PR interval in a 23 week fetus. This is measured from the onset of atrial activity (arrow) to the onset of atrial outflow (curved arrow).

(Right) Pulsed Doppler ultrasound shows prolongation of the PR interval from onset of atrial activity (arrow) to the onset of atrial outflow (curved arrows). This may be the first sign of fetal conduction system damage. (Courtesy D. Friedman, MD).

**Typical**

(Left) M-mode ultrasound with color enhancement (red = ventricular inflow and blue = outflow) shows normal degree heart block. There is 2:1 block, with two atrial contractions (curved arrows) for each ventricular contraction (arrow). (Right) Pulsed Doppler ultrasound shows complete heart block, with the rate of atrial contraction (open arrow) independent of the rate of ventricular contraction (arrows).

**Typical**

(Left) M-mode ultrasound in the first trimester shows a heart rate of 65 bpm. The patient had a history of recurrent spontaneous abortions. This ominous finding is associated with a high pregnancy failure rate. (Right) Cocoon ultrasound of a 26 week fetus shows cardiomegaly (curved arrows), ascites (arrow) and chest plethora (open arrows). Mortality: approximately 75% when tetralogy occurs with bronchial.
Terminology

- Congenital cardiac hamartoma composed of abnormal myocytes
- Most common fetal cardiac tumor

Imaging Findings

- Well-defined, hyperechoic, intracardiac mass
  - Small masses within wall may appear as wall thickening
  - Often multiple
  - Require close follow-up to monitor growth
  - Can detect as early as 22 weeks gestation
  - May discover more as pregnancy progresses
  - Hydrops may develop from atrial or ventricular septum
  - May develop from cardiac or atrioventricular septal defect
  - May develop from adhesion or pericardial effusion
  - Skin thickening
  - Look for other findings of tuberous sclerosis
  - Subependymal nodules
  - Nodularity along ventricular walls
  - Often difficult to discern
  - Subependymal giant cell astrocytoma
  - Mass near foramen of Monro

DDX: Echogenic Cardiac Masses

- Hyperplastic CM
- Perinatal Sternum
- Pericardial Teratoma
- EFT

- May cause hydrocephalus

Echocardiographic Findings

- Tumor arising from ventricles or intraventricular septum
- Most often affects left ventricle
- May develop from atrial or ventricular septum
- Supraventricular tachycardia
- Sinus bradycardia
- Outflow tract obstruction

Imaging Recommendations

- Dedicated cardiac echo in all cases
- Follow closely for progression/hydrops
- Look for findings of tuberous sclerosis
- Fetal brain MRI recommended
  - Subependymal nodules and cortical/subcortical tubers
  - High signal intensity on T1W
  - Low signal intensity on T2W
  - Postnatal brain MRI should be done in all cases even if in utero scan is normal
  - Fetal findings may be difficult to discern
  - May use gadolinium
Rhabdomyoma

Teratoma
- Rare tumor
- Histopathologically usually benign
- Fetal echocardiography critical for diagnosis
- Pericardial (not myocardial) tumor
- Epithelial growth (will not be in cardiac chamber)
- Frequently located at right anteriose heart border
- Heterogeneous with calcification
- Solid and cystic components
- Pericardial effusion often present
- May cause heart failure due to pericardial effusion and cardiac compression
- Symptoms more related to size and location than histology
- Look for signs of hydrodrops
- Fetal pericardiocentesis can prevent cardiac tamponade
- Worse prognosis if associated with hydrodrops
- Surgical removal usually curative

Fibroma
- Usually solitary
- Benign proliferation of connective tissue
- May infiltrate normal myocardium
- Often arises from intraventricular septum or free wall of left ventricle
- Right ventricle may be involved
- Intramural solid echogenic lesion
- Occasionally can be inhomogeneous if associated with cystic degeneration
- May be associated with pericardial effusion
- Postnatal MRI
- Isointense on T1WI
- Hypointense on T2WI
- Strong enhancement

Hemangioma
- Hyperchoic
- Variable vascularity with Doppler
- Avid enhancement on postnatal CT

Key Facts
- Comprises 90% of fetal cardiac tumors
- 50-85% of fetuses have tuberous sclerosis
- Multiple in 50% of cases

Pathology
- Can be associated with pericardium
- Presents with cardiac symptoms
  - Pericardial or pleural effusion
  - Arrhythmia
  - Heart failure
- Asymptomatic lesions may be observed
- Can regress spontaneously

Myxoma
- Myxomas not typically seen in utero
- Most arise from interventricular septum/region of foramen ovale
- Left atrium > right atrium

Echogenic cardiac focus (ECF)
- Papillary muscle
- Small (usually < 3 mm)
- Very bright (similar to bone)
- 78% in left ventricle
- Associated with both trisomy 21 and 13
- Need to evaluate for other associated findings

Hypertrophic cardiomyopathy (CM)
- Thickened myocardium
- Intraventricular septum and free wall
- Fetuses of diabetic mothers at risk, especially if poor glycemic control
- Response to increased workload
  - Anemia
  - Masses (e.g., sacrococcygeal teratoma)
- Twin-twin transfusion syndrome
- Twin reverse arterial perfusion

Outflow tract obstruction
- Increased cardiac work to overcome obstruction => wall hypertrophy
- Aortic atresia/stenosis
- Pulmonary stenosis/atresia
- Ductal constriction

Endocardial fibroelastosis
- Edzegonic endocardium and papillary muscles
- Poor contractility
PATHOLOGY

General Features
- Genetics
  - Tuberculous sclerosis autosomal dominant with variable expressivity
  - About 50% of cases inherited
  - Other cases due to new mutation
- Most commonly arise on ventricular septum but may be anywhere
- Compression of adjacent lung may occur with large masses
  - Does not necessarily result in lung hypoplasia
- Critical period for lung development 18-20 weeks
  - Lung compression may be minimal at that point
- Comprises 98% of fetal cardiac tumors
  - 10-45% of fetuses have tuberous sclerosis
- Multiple in 50% of cases
  - Increases likelihood of tuberous sclerosis (> 30%)
- Features of tuberous sclerosis
  - Clinical triad
    - Seizures
    - Mental retardation
    - Cutaneous angiofibromas
  - Cardiovascular anomalies
    - RHABDOMYOMAS (most common in utero finding)
    - Brain
    - Cortical tubers
    - Subependymal nodules
    - Renal
    - Angiomyolipomas and cysts (not seen in utero)

Gross Pathological & Surgical Features
- Encapsulated intramyocardial or subepicardial mass
- Benign tumor

Microscopic Features
- Large vacuolated myocytes
- Glycogen-rich vacuoles stretch the perinuclear cytoplasm (spider cells)

CLINICAL ISSUES

Presentation
- Generally incidental finding
- Rarely presents with arrhythmia or hydrops

Natural History & Prognosis
- Most often has benign clinical course prenatally
- May grow in conjunction with gestational age or remain stable
  - Majority of growth may occur in 2nd and 3rd trimesters
  - Growth slows after 32 weeks
  - Multiple and large lesions more likely to grow in utero
  - Smaller or single lesions may remain stable or demonstrate slow growth in utero
- Usually spontaneously regresses postnatally
  - Both isolated and if associated with tuberous sclerosis
- Good prognosis if no complications in utero or first 6 months of life

- Poor prognostic indicator if associated with cardiac dysfunction
  - Arrhythmias, intracardiac flow obstruction
  - Atrioventricular valve dysfunction or regurgitation
- Seizures and impaired cognitive function may be present with tuberous sclerosis

TREATMENT
- Perinatal
  - Consider preterm cesarean section if hemodynamic obstruction identified
  - May infrequently require prenatal therapy with antiarrhythmics
  - Genetic counseling for tuberous sclerosis
- Postnatal
  - Medical management without treatment
  - Cardiac evaluation after delivery
- Medical management for heart failure may intermittently be required as neonate
- Surgical resection if adversely affecting cardiac function

DIAGNOSTIC CHECKLIST

Consider
- Fetal echocardiography to monitor cardiac function
- Fetal MRI to evaluate other signs of tuberous sclerosis

Image Interpretation Pearls
- Multiple rhabdomyomas strongly suggest tuberous sclerosis
- Rhabdomyomas less likely to cause postnatal effusions than other cardiac tumors

SELECTED REFERENCES
RHABDOMYOMA

IMAGE GALLERY

Typical

(Left) Four chamber view shows a Rhabdomyoma (arrow) in the left ventricle arising from the interventricular septum. (Right) ECG (Eco) systolic shows the mass (arrow) completely obstructing the ventricular outflow into the aorta (Ao). Follow-up scans are important to evaluate for tumor growth, progression into the outflow tract obstruction and arrhythmias.

Typical

(Left) Sagittal 3 T MRI (MRI) shows three months of life. Shows multiple high-intensity signals bilaterally (arrows) typical of tuberous sclerosis. (Right) Axial ultrasound shows multiple echogenic, intracavitary masses (arrows) involving both ventricles and the interventricular septum. Multiple rhabdomyomas have a 50% risk of developing tuberous sclerosis.

Variant

(Left) Four chamber view shows a right atrial Rhabdomyoma (arrow). This is a less common location than the ventricles. (Right) Epicardial ultrasound on a woman with adenoma shows a massive, echogenic mass (arrow) involving the cardiac apex. This appearance may be difficult to differentiate from a teratoma but the bright and uniform echogenicity makes a large rhabdomyoma more likely. Teratomas are more heterogeneous and frequently have cystic areas.
SECTION 7: Abdominal Wall

Introduction and Overview
Normal Abdominal Wall & Bowel Imaging 7-2

Abdominal Wall

Omphalocele 7-6
Gastrochisis 7-10
Body Stalk Anomaly 7-14
Bladder Exstrophy 7-18
Cloacal Exstrophy 7-20
OES Syndrome 7-22
Pentalogy of Cantrell 7-24
Imaging Anatomy

Ultrasound

- First trimester
  - Physiologic bowel herniation begins in 8th menstrual week (6 weeks post-conception)
  - Produces focal abdominal mass at umbilical cord insertion
  - Normal sonographic finding
  - Should not be mistaken for an omphalocele
  - Most prominent at 9-10 weeks menstrual age
  - Should not be visible by 12 weeks
  - Criteria for predicting possible anomaly
  - Crown-rump length > 44 mm with persistent herniation
  - Maximum diameter of abdominal mass > 7 mm
  - Premature liver is never normal

- Esophagus
  - Thoracic; portion visible in 87% of fetuses > 26 weeks
  - Cervical esophagus only visible in 19%
  - Appears as either two parallel or multiple parallel lines

- Stomach
  - Visible by 11 weeks
  - Growth charts available, however there is individual variability based on fetal swallowing and peristalsis

- Small bowel
  - May transiently see fluid in duodenum with peristalsis
  - Persistent fluid is always abnormal
  - Routinely seen in last 2nd and 3rd trimester
  - Normal < 7 mm in diameter
  - Mucosa and serosa more echogenic, muscular layers more hypoechoic
  - Fluid (succus entericus) visible in almost all cases
  - Peristalsis routinely seen at real-time examination
  - Bilateral in 2nd trimester
  - Anisotropy peristalsis in 3rd trimester

- Colon
  - Often prominent in 3rd trimester, especially agnoid colon
  - Normal < 18 mm in diameter

- Haemorrhage seen at 20-25 weeks
- Peristalsis not seen
- Meconium
- Composed of desquamated epithelium, bile, swallowed amniotic fluid and vernix
- Hypoechoic compared to bowel wall and liver
- Echogenicity increases with increasing gestational age

- Abdominal wall
  - Abdominal musculature
  - Internal oblique
  - External oblique
  - Transversus abdominis
  - Hypoechoic band beneath echogenic fetal skin
  - Seen most prominently as interface with liver
  - May potentially be confused with ascites
  - Muscles insert onto ribs
  - Anisotropy not seen posteriorly

- Liver
  - Proportionally larger in fetus than child or adult, especially left lobe
  - Fills majority of upper abdomen
  - Gallbladder
  - Right-sided, fluid-filled structure by liver edge
  - Increases in size to 30 weeks
  - Seen in 98% of cases in 3rd trimester
  - May need to use color Doppler to differentiate from umbilical vein

- Spleen
  - Lateral to stomach bubble in left upper quadrant
  - Echogenicity similar to liver
  - Pancreas
  - Usually not seen
  - May be slightly hypoechogenic compared to surrounding structures

MRI

- Valuable supplemental tool for many abdominal anomalies
  - Meconium
  - High signal intensity T1WI
  - Low signal intensity T2WI
  - Reversal
NORMAL ABDOMINAL WALL & BOWEL IMAGING

Key Facts

Abdominal Circumference
- Most variable of the biometric parameters
- If cord insertion is seen, scan is oblique
- Most important measurement for indicating growth disturbance
- Asymmetric IUGR, macrosomia

Potential Pitfalls
- Beware of missing first trimester physiologic bowel herniation & an omphalocele
- Herniation of liver is never normal
- Normal hypochronic abdominal wall musculature may mimic ascites
- Must see normal abdominal wall on either side of cord insertion
- May potentially miss gastrochisis if not seen

Anatomy-Based Imaging Issues

Imaging Protocols
- American Institute of Ultrasound in Medicine (AIUM) requirements on abdominal images
- Stomach
  - Presence
  - Size
  - Size
- Umbilical cord insertion site into fetal abdomen
- Umbilical cord vessel number
- Bile ducts

Imaging Pitfalls
- It is imperative to show normal abdominal wall on either side of the cord insertion
- May miss a defect if the abdominal wall is obscured by fetal legs or is against uterine wall

Abdominal Anatomy
- Normal physiologic bowel herniation most prominent at 9-10 weeks
- Should no longer be visible by 12 weeks
- Stomach seen by 11 weeks
- Resident fluid in duodenum never normal
- Small bowel and colon seen in 2nd trimester
- Peristalsis routinely seen at real-time examination
- MRI helpful in evaluating gastrointestinal anomalies
- Meconium
  - High signal T1WI, low signal T2WI
- Fetal bowel structures (stomach, jejunum, gallbladder)
  - Low signal T1WI, high signal T2WI
- Liver
  - High signal T1WI, low signal T2WI

- Meconium accumulates after 20 wks
- Normally at least 10 mm below bladder neck
- Anteroposterior diameter increase with gestational age
  - 2.5 mm at 24 wks
  - 9.5 mm at 35 wks
- Colon
  - Meconium in descending colon seen after 24 wks
  - Ascending and transverse colon seen in <50% before 31 wks
- Stomach and jejunum
  - Ingested amniotic fluid
  - Low signal T1WI
  - High signal T2WI
- Dial small bowel
- Appearance varies with gestational age and meconium progress
  - <32 wks often hypointense on T1WI
  - >32 wks 40% still remain hyperintense T1WI
- Liver
  - High signal intensity T1WI
  - Low signal intensity T2WI

Normal Measurements
- Routine measurement of abdominal circumference (AC) required by AIUM
- True transverse view at level of junction of umbilical vein with portal sinus
- Stomach in same plane
- BBS should be symmetrical and symmetric
- If cord insertion is in image, plane is oblique
- Abdomen appears elliptical instead of round
- Circumference should be drawn at skin/muscosic fluid line
- Important component of fetal weight determination
- Indicator of growth disturbances
- Macrosomia
- Asymmetric intrauterine growth restriction (IUGR)
- Part of gestational age calculation

Embryology

Embryologic Events
- 4th embryologic week (most conception
  - Embryonic folding results in 3 structures
    - Blind-ending cranial foregut
    - Blind-ending caudal hindgut
    - Midgut opens to yolk sac through vitelline duct
- 5th week
  - Foregut forms esophagus, stomach and proximal duodenum
  - Diverticula form proximal duodenum to form liver, gallbladder and pancreas
NORMAL ABDOMINAL WALL & BOWEL IMAGING

And ultrasound shows correct level for obtaining the abdominal circumference. The uterine body forms a loop (arrow) as it joins the pelvic vascular system. The duodenum is symmetric (arrowhead - stomach).

And ultrasound shows the fetal gallbladder (arrow) and hyperechoic abdominal wall musculature (curved arrow), seen between the fetal skin and bone. This should resolve within 6 weeks.

- Midgut forms distal duodenum, jejunum, ileum, cecum, ascending colon, and proximal two thirds of transverse colon.
- Hindgut forms distal third of transverse colon, descending colon, sigmoid colon and eventually rectum.
- Terminates at cloacal membrane at this time.
- 6th week.
- Jejunum grows faster than peritoneal cavity and herniates into umbilical cord.
- Undergoes a 90º counterclockwise rotation.
- Urogenital septum divides cloaca into rectum and urogenital sinus.
- Distal one third of urogenital sinus forms from an evagination (anal pit).
- Weeks 7–11.
- Midgut undergoes additional 180º counterclockwise rotation as it retracts into abdomen in 12th week (12th–menstrual week).
- Ascends and descending colon become retroperitoneal.
- Additional embryologic events:
  - Boundaries of gut development determined by vascular supply.
  - Foregut: Celiac artery.
  - Midgut: Superior mesenteric artery.
  - Hindgut: Inferior mesenteric artery.
- Endodermal proliferation in 6th week (oldest gut lesion).
- Over next 2.5 weeks, urocard develop and coalesce until recanalization is complete.
- Primarily involves duodenum.

Practical Implications:
- Duodenal atresia:
  - Failure of foregut recanalization.
  - Jejunal/ileal atresia.
  - Vascular injury most accepted theory.
  - One proposed mechanism is kinking of superior mesenteric artery during bowel rotation.
- Anal atresia.
- Arrest in division of cloaca into rectum and urogenital sinus.

- Omphaloceles containing small bowel.
- Failure of herniated bowel to retract into abdomen.
- High association with chromosomal anomalies.
- Gastronchisis.
  - Abnormal invagination of right umbilical vein, normally occurring in 6–7th week.
- Malrotation/non-rotation.
  - Failure of either the 30º or 180º rotation to be completed.
  - Predisposition for volvulus.

Related References:
(Left) Axial ultrasound shows a normal umbilical cord insertion. Note the normal abdominal wall (arrows) seen on either side of the insertion site. (Right) Sagittal 3D ultrasound shows the cord insertion (see arrows). This view is helpful when looking for bowel abdominal wall defects, such as bladder or choral extrophy. Open arrows point to legs.

(Left) Axial ultrasound shows an apparently unremarkable umbilical cord insertion (arrow). Note the fetal abdominal wall (a) against the uterine wall (b). When the fetus moves away from the maternal wall, a very large gastroschisis (arrow) is seen adjacent to the umbilical cord insertion site (curved arrow). This demonstrates the importance of documenting normal abdominal wall on both sides of the insertion site.

(Left) Coronal T1WI MR shows high signal necrotic (arrow) within the sigmoid and descending colon. (Right) Coronal T1WI MR shows a low signal fiber (black arrow) with high signal fluid within the stomach (white arrow), pancreas (open arrow) and bladder (curved arrow).
OMPHALOCELE

Graphic shows a median abdominal wall defect with herniation of small bowel and liver. The defect is covered by a membrane with the umbilical cord passing deeply into the sac.

Axial ultrasound shows a large, central abdominal wall defect, which contains both bowel and liver. It is covered by a smooth membrane (arrow) with the umbilical cord inserting centrally on the mass.

TERMINOLOGY

Abbreviations and Synonyms
• Enophthalmos

Definitions
• Median abdominal wall defect with herniation of abdominal contents into base of umbilical cord

IMAGING FINDINGS

General Features
• Best diagnostic clue: Color Doppler shows umbilical cord insertion on midline ventral wall mass
• Location: Central
• Size: Variable
• Morphology
  ○ Liver and small bowel most common contents
  ○ Spleen, bladder, stomach, and large bowel also reported

Ultrasoundographic Findings
• Gonadal Ultrasound
  ○ Smooth mass protruding from central anterior abdominal wall with covering membrane
  ○ Umbilical cord inserts onto membrane
  ○ Usually centrally

DDx: Omphalocele
• Occasional enterocele
• Polyhydramnios is common
• Ascites may be present
• Color Doppler
  ○ Demonstrates cord insertion onto omphalocele
  ○ May also be helpful to demonstrate intrahepatic vessels
• Associated structural abnormalities are common
  ○ Heart defects: 10% of associated anomalies
  ○ Ventricular and septal defects most common
  ○ Tetralogy of Fallot
  ○ Gastrointestinal: 40% of associated anomalies
  ○ Malrotation always present
  ○ Congenital diaphragmatic hernia
  ○ Aneurysm
  ○ Mesocolic defect
  ○ Genitourinary
  ○ Central nervous system
  ○ Umbilical cord cysts

MR Findings
• T1WI: Meconium in bowel has high signal
• T2WI
  ○ Liver dark
  ○ Fluid-filled bowel manifest as serpiginous high signal
• Midline sagittal image best shows sac and cord insertion
**OMPHALOCELE**

<table>
<thead>
<tr>
<th>Terminology</th>
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<td>Medline abdominl wall defect with herniation of abdominal contents into base of umbilical cord</td>
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<th>Imaging Findings</th>
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<td>Liver and small bowel most common contents</td>
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<td>Smooth mass protruding from central anterior abdominal wall with covering membrane</td>
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<td>Presence of 'pseudo-omphalocele' caused by scanning obliquely or by excessive transducer pressure</td>
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<th>Top Differential Diagnoses</th>
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<td>Physiologic gut herniation</td>
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<td>Gastrochisis</td>
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**Key Facts**

- Umbilical hernia
- Cloaca exstrophy
- Cord cysts

**Pathology**

- Chromosomal abnormalities in 30-40% in utero

**Clinical Issues**

- Echocardiogram for anatomic anomalies
- Serous fluid for cardiac and neural tube defects

**Diagnostic Checklist**

- Extremity from gastrochisis is essential in view of associated anomalies and outcome
- A chromosome abnormality is more likely if an omphalocele contains only small bowel

**Gastrochisis**

- Cord inserts on abdominal wall in a paraumbilical location
- No covering membranes
- Free floating loops of bowel
- Does not contain liver

**Umbilical hernia**

- Hernia covered by skin and subcutaneous fat
- A small, bowel-containing omphalocele may be difficult to distinguish from umbilical hernia but hernias are in utero

**Cloacal exstrophy**

- Omphalocele may be present
- Absent bladder
- Defect involves lower abdominal wall
- Associated anomalies
  - Genitorinary
  - Spine

**Pentalogy of Cantrell**

- Ectopia cordis in addition to high omphalocele

**Cord cysts**

- Cysts near abdominal wall may be confused with bowel herniation
- Omphalocele and cord cyst may co-exist
- Omphalomesenteric duct cyst
  - Associated with omphalocele and intra-abdominal mesenteric cysts
- Allantoic cyst
  - True cyst attached to cord
  - Always near fetal insertion site
  - Associated with patent urachus
- Wharton jelly cyst
  - Mucoid degeneration of Wharton jelly
  - Associated with omphalocele

**Bladder exstrophy**

- Absent bladder is hallmark
- Umbilical cord insert above defect

**Differential Diagnosis**

- Physiologic gut herniation
  - Bowel returns to abdomen by 11.2 weeks
  - Should not extend more than 1 cm
  - Never contains liver

**Imaging Recommendations**

- High-resolution ultrasound to evaluate membrane and contents of omphalocele
- Beware of "pseudo-omphalocele" caused by scanning obliquely or by excessive transducer pressure
- Optimal scans of fetal abdomen and cord insertion essential
- Differentiation from gastrochisis is essential
- Careful search for other abnormalities
- Dedicated cardiac echocardiography
- Cardiac anomalies most common associated finding
- Inclusion in omphalocele may cause confusion with gastrochisis
- Look for membrane and absence of bowel wall thickening
- Evaluate for possible syndromes
  - OEIS Complex
  - Omphalocele
  - Exstrophy
  - Imperforate anus
  - Spine abnormalities
  - Beckwith-Wiedemann syndrome
  - Omphalocele
  - Organomegaly
  - Macrogiotis
  - Macrogamia
  - Pentalogy of Cantrell
  - Omphalocele
  - Ectopia cordis
  - Cardiac anomalies
  - Measurement of abdominal circumference inaccurate and should be excluded from biometric calculations
Cord herniogram
- Hypoechoic cord mass
- May mimic omphalocele if close to abdominal wall

Body stalk anomaly (limb body wall complex)
- Fetus adherent to placenta
- No free-floating umbilical cord
- Sofort and limb defects

Amniotic bands
- Multiple body parts affected
- Often involves head and neck
- "Stalk" defects

PATHOLOGY

General Features
- Genetic
  - Chromosomal abnormalities in 30-40% in utero
    - Trisomy 18 (most common)
    - Trisomy 13
    - Trisomy 18
    - Turner syndrome (45, X0)
  - Chromosomal abnormalities less common at birth because of in utero demise or termination
- Epidemiology
  - 1:4,000 births
  - Gender: 3:1 M:
  - Incidence increases with advanced maternal age

Gross Pathologic & Surgical Features
- Mass covered by both peritoneal and amnion, with Wharton's jelly in between
- Proposed embryologic mechanism
  - Defect in infundibulum body folding normally occurring at 5-6 menstrual weeks
  - Liver remaining: Primary failure of body wall closure
  - Bowel containing: Persistence of primitive blood vessels beyond 12 weeks

Staging, Grading or Classification Criteria
- Categorized as having intra or extraperitoneal liver
  - Risk of chromosomal abnormality much higher if liver incarcerated
- Small omphalomesenterics
  - Often just small bowel
  - Higher association with both structural and chromosomal anomalies
- Giant omphalomesenterics
  - Large abdominal wall defect with extensive herniation of abdominal contents

CLINICAL ISSUES

Presentation
- Abdominal wall defect
- Elevated maternal serum alpha-fetoprotein (70%)

Natural History & Prognosis
- Survival as high as 80-90% if normal chromosomes and no other anomalies
- Increased prematurity and birth rate
- Stillbirth and neonatal death rates correlate with associated anomalies
  - Mortality 80-100% if associated structural and chromosomal anomalies
  - Perinatal mortality rate 19% if karyotype normal
- Transient omphalomesenterics containing bowel only have been described
- Good prognosis if no other anomalies
- In uterus rupture rate
- Difficult to differentiate from gastroschisis when ruptured

Treatment
- Amniocentesis for karyotype
- Delivery at tertiary care facility
- Protection of skin
- Nasogastric tube decompression
- Benefits of external section controversial
  - Not indicated if multiple associated anomalies
- Surgical treatment based on size
  - Primary closure if small
  - Complete resection of large omphalomesenterics can cause inadvertent elevation of intra-abdominal pressure
  - Temporary extra-abdominal suture; pouch to cover sac
  - Gradual pressure reduction with compression

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls
- Distinction from gastroschisis is essential in view of associated anomalies and outcome
- A chromosome abnormality is more likely if an omphalomesenteric only small bowel

SELECTED REFERENCES
OMPHALOCELE

IMAGE GALLERY

Typical

(Left) Sagittal abdominal ultrasound in the 1st trimester shows herniation of the bowel (arrows) through a midline abdominal wall defect. This is always abnormal, as physiologic herniation never includes bowel. (Right) Axial ultrasound in the 2nd trimester shows a very small bowel containing omphalocele (arrow) and 2 small cord-like vessels in this fetus with anomaly 13. Bowel herniation in the 2nd trimester is more normal, as physiologic herniation is complete by week 12.

Typical

(Left) Axial ultrasound of an omphalocele shows herniation of small bowel through a midline defect. It is covered by a membrane (curved arrow) and the umbilical cord inserts centrally (arrow). (Right) Clinical photograph shows the covered midline defect with the umbilical cord inserting directly on the sac. Omphalocoeles which contain small bowel are at greater risk for amnionitis, most commonly anomaly 13.

Variant

(Left) Sagittal T2 MRI shows an eccentric cord insertion (arrow) on a large, non-containing omphalocele. The insertion site is not always midline in location but is always on the sac. (Right) Clinical photograph of a giant omphalocele shows an eccentric cord insertion (arrow) on the sac. Omphalocoeles contain include small bowel, liver, and a large amount of amniotic fluid.
**TERMINOLOGY**

**Definitions**
- Bowel herniation through a right paramedian abdominal wall defect
- Rare case reports of left-sided defects

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue: Color Doppler shows umbilical cord insertion in normal location
- Small bowel always herniates through defect
- Large bowel and stomach also reported

**Ultrasoundographic Findings**
- Grayscale Ultrasound
  - Extra-abdominal bowel loops
  - No covering membrane
  - Bowel dilatation
    - Both intra- and extra-abdominal loops may be dilated
  - Greater dilatation, poorer prognosis
  - Bowel wall may become thickened, echogenic, matted and nodular
  - Secondary to chemical peritonitis from exposure to amniotic fluid

- Fibrinous, serosir deposit "pesum" covers exposed bowel
- Associated with post-operative ileus
- Resolves within 3 months of birth
- Stomach often malpositioned
- Oligohydramnios more common than polyhydramnios
- Polyhydramnios suggests associated atresia
- Intraventricular growth restriction (IUGR) common
- Color Doppler: Aids in evaluation of cord insertion
- Pulsed Doppler
  - Evaluation of superior mesenteric artery as it passes through defect has not been helpful in predicting vascular compromise and outcome
- Abnormal waveforms in the umbilical artery associated with obstructed bowel and fetal demise

**MR Findings**
- T2WI
  - High signal in extruded bowel loops, which float in amniotic fluid
  - Absence of covering membrane
- Helpful when sonographic visualization compromised
- Maternal obesity
- Oligohydramnios

**Imaging Recommendations**
- May be missed if abdominal cord insertion incompletely evaluated

**DDx:** Free Floating Loops Of Bowel

- Body Stalk Anomaly
- Amniotic Bands
- Classical Entrophy
- Anomic Bands
GASTROSCHISIS

Terminology
- Body stalk anomaly through a right paramedian abdominal wall defect

Imaging Findings
- Best diagnostic clue: Color Doppler shows umbilical cord insertion in normal location
- Small bowel always herniates through defect
- No covering membrane
- Oligohydramnios more common than polyhydramnios
- Intestinal growth restriction (IUGR) common
- May be missed if abdominal cord insertion incompletely evaluated

Top Differential Diagnoses
- Omphalocele

- Try to get fetus to move into better position by moving mother
- Imperative to see abdominal wall on both sides of cord insertion in every case
- Don’t confuse umbilical cord for exteriorized bowel loops
- MRI may add anatomic information if ultrasound inadequate
- Close follow-up for fetal distress
  - Progression bowel dilatation
  - Developing IUGR
  - Abdominal circumference is small making evaluation difficult
  - Evaluate umbilical artery (UA) and middle cerebral artery (MCA) flow
  - With developing IUGR, normal flow patterns reverse
  - As UA becomes high-resistance, the MCA becomes low-resistance (“head sparing”)
- Acute complications
  - Volvulus with resulting bowel ischemia
  - Oligohydramnios
  - Sign of fetal distress

DIFFERENTIAL DIAGNOSIS

Omphalocele
- Cord inserts on mass
- Covered by peritoneum
- Ruptured omphalocele difficult to differentiate
  - Consider if liver present
  - BGR

Body stalk anomaly (limb body wall complex)
- Tails adherent to placenta
- Extented thoracic contents and liver in addition to bowel
- No free-floating umbilical cord
- Spine and limb defects

Key Facts
- Body stalk anomaly (limb body wall complex)
- Amniotic band syndrome
- Cloacal extrophy

Pathology
- No chromosomal associations
- Higher incidence in substance use by mothers
- Incidence is increasing
- Incidence in teenage mothers is 6-10x that of mothers ≥ 25 yrs
- Association with non-gastrointestinal abnormalities is low (<5%)
- Atresias often present (7-30%)

Clinical Issues
- Bowel complications much greater than for omphalocele

Amniotic band syndrome
- Variable in presentation and severity
- Multiple body parts affected
- Often involves head and neck
  - “Slash” defects

Cloacal extrophy
- Absent bladder
  - Bowel may protrude between bladder halves
- Omphalocele
- Cord insertion low
- Genitourinary anomalies

Bladder extrophy
- Umbilical cord inserts above defect
- Absent bladder is hallmark
- No free-floating bowel

Physiologic gut herniation
- Bowel returns to abdomen by 11.2 weeks
- Should not extend more than 1 cm
- Always midline

PATHOLOGY

General Features
- Genetics
  - Most are sporadic
  - Familial cases reported
  - 3.5% recurrence risk in siblings
- No chromosomal associations
- Anomalousitis not indicated
- Etiology
  - Higher incidence in substance use by mothers
  - Particularly vasoactive substances (e.g. cocaine, nicotine, decongestants, aspirin)
- Embryology: Proposed mechanisms
  - Abnormal involution of right umbilical vein, normally occurring in 6th-7th week
  - Vascular accident involving omphalomesenteric artery (less likely)
- Epidemiology
GASTROCHISIS

- 13,000 to 50,000 births
- Incidence is increasing
- Incidence in teenage mothers is 6-10x that of mothers ≥ 25 yrs
- Associated abnormalities
  - Bowel either malrotated or non-coiled
  - Association with non-gastrointestinal abnormalities is low (< 5%)
  - Cardiac anomalies most common
  - Hypoplastic gallbladder, Medul diverticulum
  - Hydrocephaly

Gross Pathologic & Surgical Features
- Abdominal defect relatively small (< 5 cm)
- Exposed loops infarct and edematous
- Attenuation present (7-30%)
- Often long segments
- Left-sided wall defects very rare

CLINICAL ISSUES

Presentation
- Elevated maternal serum alpha-fetoprotein (95%)
- Exposed bowel results in greater elevations than
  with omphalocele
- Fetal ultrasound highly sensitive in diagnosis
- Can be diagnosed in first trimester with endovaginal ultrasound

Natural History & Prognosis
- Bowel complications much greater than for
  omphalocele
  - Vomiting
  - Torsion avascular small bowel pedicle
  - Compression of mesenteric vessels in small bowel
  - Perforation
  - Bowel obstruction
  - Dilatation of both intra- and extra-abdominal bowel
  - Significant dilatation of small bowel impacts long
    term morbidity
  - Large gaps present in utero as to whether
    diameter is "significant" (10-18 mm)
  - Perforation
  - Bowel thickening from amniotic fluid initiation
  - Associated with n-tetra and poor function
  - IUOR in up to 50%
  - May resolve on follow-up exam ("vanishing gut")
  - Associated with right defects
  - Ischemia Causes atresia
  - Short bowel syndrome
  - Premature delivery
  - Prematurity delivery
  - 90% survival
  - Deaths from prematurity, septis or bowel
    complications
  - Bowel necrosis predictor of poor outcome
  - 10-15% persistent disability
  - Mortality decreases:
    - Short gut syndrome

Treatment
- Serial ultrasound for growth evaluation and detection
  of bowel complications
- Polyhydramnios correlates with severe neonatal bowel
  complications
- Amniocentesis may improve outcome (experimental
  studies)
  - Decreases concentration of irritants in amniotic
    fluid
- Early delivery considered. If women undergoing
  dilation (convention)
  - Decision section if there is no improvement
    within value is questioned
- Delivery at tertiary care center
  - Careful control of body fluids and heat loss
  - Externally fixed, covered with sterile plastic bag to
    protect it from excessive handling and to minimize
    heat and fluid loss
  - Laparotomy surgical repair optional to decrease risk
    of sepsis and metabolic acidosis
- If return of bowel causes significant increase in
  intraperitoneal pressure, the procedure is staged
  with delayed/serial closures
- Parenteral nutrition post-operatively until intestinal
  function returns
  - May require several weeks

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls
- Polyhydramnios suggests fetal distress
- Polyhydramnios suggests bowel obstruction or atresia

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    reduced without using the fetal bowel accurately predict postnatal outcome? Ultrasound
GASTROCHISIS

IMAGE GALLERY

Typical

*Left* Axial endovaginal ultrasound of a first trimester gastrochisis (scalloped edge). The small bowel appears as tiny echogenic rings. Note the 2 vessel umbilical cord insertion. *Right* Axial ultrasound of gastrochisis in a 27-week fetus shows small bowel herniation (curved arrow) with 2 vessels to a normal cord insertion (straight arrow). It is important to follow gastrochisis cases for developing bowel dilatation. Fetal polyhydramnios and other signs of fetal distress.

Variant

*Left* Axial oblique ultrasound shows stretching of the superior mesenteric artery (twisting through the abdominal wall defect [open arrow]). Small bowel shows curved arrow - normal insertion. This is not a predictor of outcome. *Right* Axial ultrasound shows marked dilatation (calipers) of free-floating bowel loops. Significant dilatation increases risk for postnatal complications.

*Left* Axial ultrasound shows another image from the case above, which shows herniation of the stomach (SL - arrows) as well as the small bowel. *Right* Gross pathology from a case that presented because of absent fetal movement. The fetus was being followed for known gastrochisis. Ultrasound confirmed dilatation and a new (arrow) dilated bowel loop. Anteriorly, contoured vessels with bowel thrombus. A known potential complication.
Body stalk anomaly is characterized by the attachment of visceral organs to the placenta, with a short or absent umbilical cord. Imaging findings include:

- Best diagnostic clue: Abnormal fetus inseparable from placenta
- Size: Often large with complete exteriorization
- Morphology: Gross distortion, with complete loss of anatomic landmarks

Ultrasoundographic Findings:
- Complex array of multiple malformations
- Large hypoechoic-echoic wall defect
- No covering membrane
- Grossly deformed fetus
- Absent/very short umbilical cord

Imaging Recommendations:
- Fixed fetal/placental relationship essential for diagnosis
- Scan rather in different positions

DDx: Severe Body Wall Defects

- Amniotic Bands
- Amniotic Bands
- Physiologic/Anomol
- QUS
**Terminology**
- Lethal malformation characterized by attachment of visceral organs to the placenta, with a short or absent umbilical cord

**Imaging Findings**
- Complex array of multiple malformations
- Spinalis prominent feature
- May have multiple acute angulation points
- Limb defects common
- Fixed fetal/placental relationship essential for diagnosis

**Top Differential Diagnoses**
- Anomalous band sequence
- Gastroschisis
- Omphalocele

- Look for umbilical cord
- Should be free floating and obvious
- Color Doppler essential
- Often have to search carefully for fetal/placental connection
- 2D ultrasound has been described, and may be of value in defining anatomic relationship

**DIFFERENTIAL DIAGNOSIS**

**Anomalo band sequence**
- Severe cases may be indistinguishable
- Fetus may be immobile
- Normal cord
- Cord insertion site may be involved if abdominal wall defect
- Free-floating cord loops usually identified
- Variable pattern of defects
- Limb amputations
- Limb constriction
- Sallotes not a major finding
- Hands may be seen in amniotic fluid
- May extend to immobile fetus part

**Gastroschisis**
- Mobile fetus
- Small abdominal wall defect
- Normal cord
- Defect is to right of cord insertion
- Defect not covered
- Bowel float freely in amniotic fluid

**Omphalocele**
- Mobile fetus
- Normal cord
- Defect is covered by membrane
- Normal cord
- Inserts on membrane
- Generally at apex, but may be exomphalos

**OEIS complex**
- Omphalocele
- Exstrophy of bladder

**Key Facts**
- OEIS complex
- Pathology
- No known occurrence risk
- Amnion 21 continuity with fetal peritoneum at edge of defect
- Maternal umbilical cord incompletely covered in amnion
- Clinical issues
- Marked elevation maternal serum alpha-fetoprotein
- No abnormal karyotype reported
- Diagnostic checklist
- Fetus appears stuck to placenta with severe spinal and limb defects
- In first trimester, part or all of fetus is located outside the amniotic cavity

**Imperforate anus
- Spina abnormalities
- Mobile fetus

**Pentalogy of Cantrell**
- Omphalocele
- Cardiac anomalies
  - Ectopia cordis most typical of syndrome
  - Diaphragmatic hernia
  - Defect of diaphragmatic pericardium
  - Lowes sheroal defect
  - Cranial and limb defects not prominent feature
- Mobile fetus

**Cloacal extrophy**
- Mobile fetus
- Normal length cord
- Omphalocele
- Bladder extrophy
- No normal bladder seen
- Bowel may herniate out between bladder halves

**PATHOLOGY**

**General Features**
- Genetics
  - Sporadic
  - No karyotypic abnormalities
  - No known recurrence risk
  - More common in monozygotic twins
  - May be discordant
- Epidemiology
  - Reported incidence
    - 1 in 7,500 to 42,000 in United Kingdom
    - 1 in 13,000 live births in Australia
  - Risk factors
    - Alcohol, tobacco, marijuana use
    - History of prior child with congenital anomaly (amy) in 40%
    - Reported after in vitro fertilization
  - Two phenotypes described
    - No craniosfactory defects
BODY STALK ANOMALY

- 60% of cases
- Result of enterologic maldevelopment
- Malfunction of ectodermal placodes involving nephric and cardiac embryonic folding process
- Malformation of urogenital and lateral abdominal wall
- Body stalk/pelvic stalk fusion fails: Shoat or absent umbilical cord
- Anomalous/portion fusion tubs
- Anomaly does not cover cord
- Anomalous in continuity with fetal peritoneum at edge of defect
- Associated craniofacial defects
- 40% of cases
- Early vascular disruption proposed as cause
- Amniotic band present
- Also hypothesized that body stalk anomaly occurs from early amnion rupture
- Some categorize in spectrum of amniotic band syndrome
- Associated abnormalities in virtually all cases
  - Cardiac defects
  - Esophageal hernia
  - Structural defect
  - Renal anomalies
  - Hydrocephalus, agenesis, cystic dysplasia
  - Bowed femur
  - Congenital diaphragmatic hernia
  - Facial clefts
  - Gross Pathologic & Surgical Features
    - Persistence of extraamniotic coelomic cavity
    - Anterior body wall defect with excision of organs
    - Liver
    - Bowed
    - Heart
    - All organs potentially involved
    - Malformed umbilical cord incompletely covered in amnion
    - Umbilical vessels embedded in amniotic sheet connecting to skin margin of abdominal wall defect
  - CLINICAL ISSUES
    - Presentation
      - Abnormal maternal serum screen
      - Marked elevation maternal serum alpha-fetoprotein
      - Can be diagnosed at end of first trimester
      - Normal cord can be identified as early as 8 weeks
      - Abnormal ratio of crown-rump length/ cord length
      - Should normally be 1:1
      - Cord short or absent
      - Lower portion of fetus is outside amniotic cavity, upper portion may still be within amniotic cavity
    - Natural History & Prognosis
      - Lethal
      - Frequent spontaneous abortion
    - Treatment
      - Amniocentesis not required
      - No abnormal karyotype reported
      - Offer termination
      - Aim for delivery of intact fetus for autopsy
      - Psychological support to family
      - Vaginal delivery if pregnancy not terminated
      - Cesarean section avoided
      - No fetal monitoring during labor
      - No resuscitation of fetus
  - DIAGNOSTIC CHECKLIST
    - Most likely diagnosis—setting of abdominal wall defect and scoliosis
    - In first trimester, part or all of fetus is located outside the amniotic cavity
  - SELECTED REFERENCES
(Left) Ultrasound shows the typical appearance of a body stalk anomaly with gross distention of normal amniotic fluid. There is a large fetal vessel defect with extrusion of the thoracoabdominal contents. The heart (upper arrow) and liver (arrow) are adherent to the placenta (curved arrow). (Right) Ultrasound of the spine shows dramatic scalloping with 2 right-angle turns (arrows). Severe scalloping is often a prominent finding in body stalk anomaly.

(Left) Ultrasound of a 16-week fetus shows acute angulation of the fetal body (arrows). The fetal spine was flexed during the scan. There is a broad wall defect with extrusion of the bowel (open arrow). No free-floating abdominal contents could be identified. (Right) Radiograph from a similar case shows severe scalloping and extravasation of thoracoabdominal contents (arrows), which were adherent to the placenta.

(Left) Ultrasound of a dramatically shortened uterine cervix (arrow) of a gravid dissecting uterus. A new vessel (1) is a short distance from the fetus (2) to the placenta (3). (Right) Gross anatomy shows the typical features of body stalk anomaly. The fetus has been pulled away from the placenta to show the very short uterine cervix (open arrow). There is necrotic-fibrotic extravasation and severe scalloping. This case is associated with an anatomic birth defect. (Gross.)
BLADDER EXSTROPHY

TERMINOLOGY

Definitions
- Failure of closure of lower abdominal wall resulting in exposed bladder

IMAGING FINDINGS

General Features
- Variable severity
  - Mild form associated with exstrophy of urethra and external epispadias
  - Severe form associated with wide diastasis of symphysis pubis and genital defects

Ultrasonographic Findings
- Gray-scale Ultrasound
  - Absence of bladder
  - Soft tissue mass on lower anterior abdominal wall representing posterior bladder wall
  - Lower insertion of umbilical cord
- Color Doppler: Useful for identifying umbilical arteries on either side of lower abdominal wall mass

Radiographic Findings
- Widely separated pubic bones
- Everted innominate bones

Imaging Recommendations
- Protocol advice
  - Sagittal view of abdominal wall shows defect and mass best
  - Beware of misdiagnosis in cases of a normal but empty bladder
  - Rescan after an interval of 10-15 minutes
  - Any case of anuria will cause non-visualization of the bladder in utero

DIFFERENTIAL DIAGNOSIS

"Absent" Bladder
- Renal anomalies resulting in anuria
- Severe placental insufficiency
- Twin-twin transfusion syndrome (TTTS)
- Donor twin becomes anuric

Cloacal exstrophy
- Bowel herniation as well as bladder extrophy
- Other anomalies such as radioulnar synostosis and omphalocele

Omphalocele
- Midline mass is more complex than extrophy
- Cord inserts onto omphalocele
- Normal bladder

DDx: "Absent" Bladder
- Placental insufficiency
- TTTS, Donor Twin
- Cloacal Exstrophy
- Renal Agenesis
**Imaging Findings**
- Solid form associated with extrophy of urothelium and external sphincter
- Secretory form associated with wide diastasis of symphysis pubis and genital defects
- Absence of bladder
- Soft tissue mass on lower anterior abdominal wall representing posterior bladder wall

**Gastrochisis**
- Free-floating bowel loops
- Normal bladder

**PATHOLOGY**

**General Features**
- Genetics
  - Sporadic
  - Reports of trisomies 21 and 13
- Epidemiology
  - Clinical membranes covering future bladder persist, fail to retract normally
  - Prevents ingrowth of mesenchymal cells, which normally form lower anterior abdominal wall
  - Closure of lower abdominal wall does not occur and clinical membrane becomes anterior bladder wall
  - When clinical membrane ruptures, bladder mucosa is left exposed to amniotic cavity
  - Occurs after descent of the urogenital septum
- Associated anomalies
  - Limb abnormalities
  - Genitourinary anomalies
  - Epispadias and short penis in males
  - Maldeveloped testes
  - Cleft lip and palate in females
  - Psoriasis
  - Spinal dysraphism and scoliosis

**CLINICAL ISSUES**

**Presentation**
- Most common signs/symptoms
  - Absent bladder on ultrasound exam
  - Elevated maternal serum alpha-fetoprotein levels

**Natural History & Prognosis**
- Not associated with increased pregnancy complications or perinatal mortality
- Sequelae from pelvic floor defects
- Urinary and fecal incontinence
- Ureteral prolapse in females
- Infertility
- Increased risk of adenocarcinoma in extruded bladder (4%) if repair performed after infancy

**Key Facts**
- Beware of misdiagnosis in cases of a normal but empty bladder

**Top Differential Diagnoses**
- "Absent" bladder
- Cloacal extrophy

**Clinical Issues**
- Not associated with increased pregnancy complications or perinatal mortality

**Treatment**
- Amniocentesis may be considered for fetal sexing if genitalia ambiguous
- Prenatal counseling with pediatric urologist
- Cesarean section indicated for obstetric issues only
- Delivery in tertiary care center preferable
- Surgical treatment
  - Closure of bladder within first 3 days of life
  - Staged functional reconstruction
  - Sex reassignment almost never performed now

**DIAGNOSTIC CHECKLIST**

**Image Interpretation Pearls**
- Important to distinguish from cloacal extrophy, which has a worse prognosis

**SELECTED REFERENCES**

**IMAGE GALLERY**

*Left: Clinical photograph of a newborn with bladder extrophy shows a large abdominal wall defect with exposed bladder mucosa. The proximal ureters (arrows) and urethral orifice (curved arrow) are seen.*

*Right: Radiograph of an infant with bladder extrophy shows wide distention of the symphysis pubis (arrows).*
TERMINOLOGY

Definitions
- Spectrum of abnormalities resulting from abnormal development of cloacal membrane

IMAGING FINDINGS

Ultrasoundographic Findings
- Grayscale Ultrasound
  - Absence of normal bladder
  - Lower abdominal wall defect
  - Herniation of bowel between 2 halves of bladder
  - Appearance of prolapsed lumen described as looking like an elephant's trunk.
  - Omphalocele forms upper part of defect
  - Splenic symphysial pubis
  - Cloacal membrane may be intact until 22 weeks, producing a cystic pelvic mass
- Color Doppler: Useful to localize umbilical arteries and cord insertion
- Associated anomalies very common
  - Vertebrae: 40-90%
  - Myelomeningocele: 20-70%
  - Uterine tracts, up to 60%
  - Leading to oligohydramnios
  - Club feet: 20-45%

DIFFERENTIAL DIAGNOSIS

Bladder extrophy
- Absence of normal bladder with mass on lower anterior abdominal wall
- No other manifestations of cloacal extrophy

Isolated omphalocele
- Contents contained within a sac
- Abdominal wall intact inferior to defect

Gastrochisis
- Free-floating bowel loops
- Normal bladder

Anomalous heart syndrome
- Frequently involves head and neck
- Look for bands

Body stalk anomalies
- Large thoracolumbar defect
- Fetus adherent to placenta

Pentalogy of Cantrell
- Defect higher, involving upper abdomen and chest

DDx: Abdominal Wall Defects
- Omphalocele
- Gastrochisis
- Bladder Extrophy
- Pentalogy of Cantrell
CLOACAL EXTROPHY

Key Facts

- Spectrum of abnormalities resulting from abnormal development of cloacal membrane

Imaging Findings

- Absence of normal bladder
- Lower abdominal wall defect
- Ectopia vesicae: 2 halves of bladder form upper part of defect
- Associated anomalies very common

PATHOLOGY

General Features

- Etiology
  - Variable severity, depending on timing and position of disruption (membranous weeks 6-12)
  - Persistence of cloacal membrane prevents migration of mesenchymal tissue, resulting in lack of normal lower abdominal wall
  - Cloacal membrane becomes anterior bladder wall and exposes bladder lumen when it ruptures
  - Cloacal extrophy develops before the urogenital system detaches and separates urogenital sinus from hindgut
  - Disruption therefore affects both genitourinary and gastrointestinal tracts

- Epidemiology
  - Incidence: 1:200,000 to 400,000 live births
  - More frequent in monzygotic than dizygotic twins
  - More frequent after in vitro fertilization

Gross Pathologic & Surgical Features

- Spectrum ranging from epispadias to large ventral wall defect with orthogenitalia
- Exposed bladder in two halves with intestinal mucosa herniation in midline
- Dermal gut blind ending: Imperforate anus
- Genetic males have bifid penis and undescended testes
- Genetic females have duplicated Mullerian structures with duplicated, exstrophed or atretic vaginas

CLINICAL ISSUES

Presentation

- Marked elevation of maternal serum alpha-fetoprotein
- Lower abdominal wall defect

Natural History & Prognosis

- Increased rates of intrauterine death and stillbirth
- Premature labor from polyhydramnios
- Prognosis dependent on severity of defect and associated malformations
- Survival rate above 90%

Treatment

- Termination may be offered if diagnosis is made before 24 weeks, after appropriate counseling as to nature of disorder and long term sequelae

Top Differential Diagnoses

- Bladder extrophy
- Isolated omphalocele
- Gastrochisis

Diagnostic Checklist

- Suspect cloacal extrophy when there is a low abdominal wall defect and an absent bladder
- Karyotyping should be ordered to determine genetic sex
- Sex reassignment has been performed in males
- Where creation of a functioning penis is not feasible
- Delivery at tertiary care center with immediate consultation from multidisciplinary team
- Complex reconstructive surgery of gastrointestinal and genitourinary tracts

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls

- Suspect cloacal extrophy when there is a low abdominal wall defect and an absent bladder

SELECTED REFERENCES


IMAGE GALLERY

(left) Sagittal 3D MIP of a fetus with cloacal extrophy shows a low abdominal wall defect (arrows) with non-visualization of the bladder. 
(right) Clinical photograph after delivery shows marked herniation (arrows) between the two halves of the bladder (open arrows). There is also a split scrotum (curved arrows).
**TERMINOLOGY**

**Definitions**
- Full complex consists of 4 components
  - Omphalocele
  - Extrophy of bladder
  - Imperforate anus
  - Spinal deformities
- Some authors consider OEIS to be synonymous with cloacal extrophy

**IMAGING FINDINGS**

**Ultrasoundographic Findings**
- Omphalocele
  - Midline defect
  - Covered by membrane
  - Cord insert on sac
- Bladder extrophy
  - Absent normal bladder
  - Soft tissue mass in lower abdominal wall
  - Costovertebral defects of upper and lower spine
  - Hemivertebrae and segmentation defects
  - Myelomeningocele
  - Pentalgia gastroparesis
  - Imperforate anus
- Often not detected in utero

**DIFFERENTIAL DIAGNOSIS**

**Cloacal extrophy**
- Significant overlapping features
- Some consider these variations of same malformation
- May see herniated bowel between halves of extrophied bladder

**Body stalk anomaly**
- Fetus adherent to placenta
- Large gastroschisis
- Severe holoprosencephaly

**Amniotic band syndrome**
- Stalk defects not conforming to an anatomic distribution
- Craniodacrificial defects common

**Omphalocele (isolated)**
- Normal bladder
- Normal spine

**Neural tube defects (isolated)**
- Normal bladder
- No omphalocele

**DDx: OEIS Syndrome**

- Omphalocele
- Omphalocele
- Myelomeningocele
- Anomalous Enlarge
OEIS SYNDROME

Terminology
- full complex consists of 4 components
  - Omphalocele
  - Exstrophy bladder
  - Imperforate anus
  - Vertebral defects

Top Differential Diagnoses
- Cleft exstrophy
- Body stalk anomaly

Key Facts
- Anosionic hand syndrome
- Omphalocele (isolated)

Pathology
- May be most severe form of a continuum of disorders ranging from epispadias through bladder and cloacal exstrophy

Clinical Issues
- Marked elevation serum alpha-fetoprotein

PATHOLOGY

General Features
- Genetics: Sporadic
- Etiology:
  - believed to result from a single defect in development of intraembryonic mesoderm
  - a precursor to intraembryonic mesenchyme, cloacal septum and caudal vertebrae
  - here: the association of spinal defects with lower ventral wall and cloacal defects
  - may be most severe form of a continuum of disorders ranging from epispadias through bladder and cloacal exstrophy
  - severity related to timing of unknown insult
- Epidemiology: Rare. 1 in 200,000-400,000 pregnancies
- Associated abnormalities
  - Spina bifida
  - Ambiguous genitalia and müllerian defects
  - Bilateral
  - Renal anomalies
  - Horseshoe kidney
  - Renal agenesis
  - Lumbal hypoplasia and aplasia
  - Craniofacial anomalies
  - Single umbilical artery

CLINICAL ISSUES

Presentation
- Multiple malformations
- Marked elevation serum alpha-fetoprotein

Natural History & Prognosis
- Prognosis depends on structural defects
- Increased rates of intrauterine death stillbirth, patent ductus arteriosus and low birthweight

Treatment
- Prenatal counseling with multidisciplinary team
- Termination may be offered
- Karyotyping for determination of genetic sex
- Deliver at tertiary care center
- Complex reconstructive surgery required

SELECTED REFERENCES

IMAGES GALLERY

(image 1)

(image 2)
**PENTALOGY OF CANTRELL**

**TERMENOLOGY**

**Definitions**
- Complex malformation with 5 components
  - Atrioventricular septal defect
  - Hypoplastic left heart
  - Pulmonary stenosis
  - Right-sided aortic arch
  - Hypoplastic right heart

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue: Ectopia cordis with omphalocele
- Location: Medial, anterior abdominal wall

**Ultrasonographic Findings**
- Suprascapular abdominal wall defect
- Omphalocele or abdominal wall defect
- May contain stomach, liver and bowel
- May be total or partial absence of abdominal contents
- Variable displacement of heart and mediastinum from diaphragmatic/ thoracic defects
- Completely external with large defects
- Bulging of heart in small defects
- Plural or pericardial effusion

**MR Findings**
- T2WI sequences show low signal liver and heart, with high signal pleural or pericardial effusion
- Pericardium, diaphragm and liver capsule are thickened and carry difficult to separate, weft, there is increased fat or fluid
- Diaphragmatic defect may be difficult to characterize

**DIFFERENTIAL DIAGNOSIS**

**Ectopia cordis**
- Heart protrudes through a cleft sternum
- None of other components

**Cleft sternum**
- Superior cleft in sternum or absence of sternum allows heart to protrude through chest wall
- Prominent chest wall pulsations
- Associated cardiac anomalies

**Omphalocele**
- Lacks cardiac and diaphragmatic abnormalities

**Body stalk anomaly** (limb body wall complex)
- Fetus adherent to placenta
- Severely distorted fetus
PENTALOGY OF CANTRELL

Terminology
- Complex malformation with 5 components
- Complex malformation with 5 components
- Vascular ring
- Diaphragmatic hernia
- Cleft lip/palate

Key Facts
- Supraventricular septal defect
- Vascular ring
- Cleft palate
- Hypoplastic left heart syndrome
- Hypoplastic left heart syndrome

Top Differential Diagnoses
- Ectopia cordis
- Cleft lip/palate
- Hypoplastic left heart syndrome
- Hypoplastic right heart syndrome

DIAGNOSTIC CHECKLIST
- Cardiac defects
- Cleft lip/palate
- Hypoplastic left heart syndrome
- Hypoplastic right heart syndrome

SELECTED REFERENCES

CLINICAL ISSUES

Natural History & Prognosis
- Prognosis depends on severity but usually fatal when discovered prenatally

Imaging Findings
- Best diagnostic clue: Ectopia cordis with omphalocele

Amniotic band syndrome
- Frequently involves head and neck
- "Slant" defects
- Multiple limb defects
- Look for bands

PATHOLOGY

General Features
- Genetics: Sporadic
- Epidemiology
- Failure of fusion of lateral folds in thorax, with failure of development of transverse septum of diaphragm
- Other components of pentalogy are a consequence of this initial failure
- Midline developmental field defect believed to account for facial clefts and omphalocele, which are sometimes present

Epidemiology
- Rare
- M = F
- Reported in monozygotic twins

Associated abnormalities
- Cardiac anomalies
  - Atrial septal defects 50%
  - Ventricular septal defects 20%
  - Tetralogy of Fallot 10%
- Craniofacial and vertebral anomalies
- Cleft lip/palate
- Exencephaly, encephalocele
- Chromosomal abnormalities
- Trisomies 13, 18
- Turner syndrome (45, X0)
- Cystic hygroma

Cross Pathologic & Surgical Features
- Thoraco-abdominal defect with ectopia cordis, omphalocele, diaphragmatic defect, pericardial defect, and partial disruption

IMAGE GALLERY

(Left) Sagittal ultrasound shows a high diaphragmatic defect, above the level of the cord insertion (arrow), with the liver (arrowhead) behind the chest. Ectopia cordis was also present. (Right) Coron pathology in this case shows the same five regions—arrested heart (arrowhead) and heart (arrowhead)—are extracardiac. Other findings include absence of the sternum, deficiency of the diaphragm and pericardial membranes, and a persistent truncal septal defect. This constellation of findings is diagnostic of Pentalogy of Cantrell.
SECTION 8: Gastrointestinal

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ECHOGENIC BOWEL

TERMINOLOGY

Abbreviations and Synonyms
- Echogenic bowel (EB)
- Hyperechoic bowel

Definitions
- Increased echogenicity of fetal bowel

IMAGING FINDINGS

General Features
- Best diagnostic clue: Second trimester increased focal bowel echogenicity
- Morphology: Focal EB is mars-like

Ultrasonographic Findings
- Assessing bowel echogenicity
  - Compare echogenicity with liver and bone
  - Normal bowel echogenicity ≤ liver, < bone
  - Bowel echogenicity grading
    - Grade 0: ≤ liver
    - Grade 1: > liver, < bone
    - Grade 2: = bone
    - Grade 3: > than bone
  - Grades 0 and 1 are normal
  - Grades 2 and 3 are potentially abnormal

DDx: Abdominal Echogenicities

- Mecinson Resonator
- Mecinson Resonator
- Intestines
- Inflamed Bowel

- Corpus and sagittal trunk images
- Compare bowel with liver
- Compare bowel with spine
- Transverse pelvis image
- Compare bowel with iliac crest
- Transducer frequency matters
- High frequency transducer falsely increases echogenicity
- More often appears in diffuse EB
- 31% EB incidence with 8 MHz transducer
- 1.2% EB incidence with 5 MHz transducer

EB diagnosis
- 2nd trimester diagnosis
- Part of genetic sonogram
- True EB is usually focal
- Mars-like
- Lower abdomen most often
- Adverse outcome
  - 6% when isolated finding
  - 50% when not isolated
- Association with trisomy 21 (T21)
  - 6.7x the likelihood of T21
  - Compared to maternal a priori (maternal age, serum quadruple screen)
  - 1.2% of cases with EB have T21
  - More likely T21 if other markers seen
  - Nuchal thickening
  - Short femur/humerus
ECHOGENIC BOWEL

Key Facts
- 10% of EB cases from swallowed blood

Top Differential Diagnoses
- Meconium peritonitis
- Anal atresia (enterocolitis)
- Swallowed debris

Pathology
- Epidemiology: 1% of fetuses have grade 2 or 3 EB

Diagnostic Checklist
- Genetic counseling for all grade 2 or 3 EB
- Follow-up ultrasound for growth
- Focal EB is more likely pathologic than diffuse EB
- High frequency transducers falsely increase bowel echogenicity

Terminology
- Hyperechoic bowel

Imaging Findings
- Best diagnostic clue: Second trimester increased focal bowel echogenicity
- Grade 0: < liver
- Grade 1: > liver, < bone
- Grade 2: = to bone
- Grade 3: > than bone
- Grades 0 and 1 are normal
- Grades 2 and 3 are potentially abnormal
- 6.7% likelihood of T21
- More likely T21 if other markers seen
- 1.2% EB from in utero infection
- Cytomegalovirus (CMV) most common
- 10% develop IUGR

- Intracardiac echogenic focus
- Renal pelvectomy
- Clindamycin
- 2% EB from in utero infection
- Cytomegalovirus (CMV) most common
- Microcephaly
- Intracranial periventricular calcification
- Ventriculomegaly
- Hydrops
- Intratertiary growth restriction (IUGR)
- Other infections
- Toxoplasmosis
- Influenza
- Parvovirus
- Associated findings
- Hydrops
- IUGR

- EB and cystic fibrosis
- Risk of fetus with echogenic bowel having cystic fibrosis varies widely between studies (0-33%)
- Depends on population base
- Cystic fibrosis more common in Caucasians of Northern European origin
- 1% of fetuses with cystic fibrosis have echogenic bowel
- +/- Bowel obstruction
- Meconium peritonitis
- IUGR and IUGR
- UA limb atrophy
- Umbilical artery diastolic flow
- EB + IUGR + 1 Alpha fetoprotein (AFP)
- 40% increased risk for fetal demise
- Severe placental insufficiency
- 10% of EB cases from swallowed blood
- From intraamniotic blood
- Placental abruption
- Fetus swallows blood
- Blood travels through gastrointestinal tract
- Amniocentesis can be diagnostic
- Bloody fluid
- Stained fluid

- Bowel-related causes
- 1-2% of cases with EB
- Ischemia
- Atelect
- Real most common
- Other bowel findings
- Dilatation
- Ascites

Imaging Recommendations
- Best imaging tool
- Abdominal views including bowel, liver and bone
- Longitudinal views that include spine
- Transverse views that include iliac crest
- Protocol advice
- Transducer frequency
- Avoid diagnosis of EB if transducer > 8 MHz
- Switch to 5 MHz and reassess bowel
- More likely an issue when EB e diffus
- EB 2 and 3 EB need genetic sonogram
- Genetic counseling for T21
- Assessment for risk of cystic fibrosis
- Assess risk of infection
- Maternal CMV titers
- Amniocentesis for CMV

DIFFERENTIAL DIAGNOSIS

Meconium peritonitis
- Fetal bowel perforation
- Secondary peritonitis
- Peritoneal calcifications
- Linear and punctate
- Cutdowns live and bowel
- Miracil EB with focal
- Meconium pseudocyst
- Walled off bowel spill
- Hypoechocoustic fluid collection
- Often accompanied by other findings
- Ascites
- Dilated bowel
- Often from atresia
ECHOCONGIC BOWEL

• Increased risk for cystic fibrosis

Anal atresia (enterolitiasis)
• Third trimester diagnosis
• Distended colon
• Calcified intestinal mucous
  o Freen stools
  o In utero "constipation"
  o Vesico-rectal fistula
• Urine + meconium + calcification

Swallowed debris
• Fetus swallows echogenic material
  o Vernix
  o Protein
  o Intraventricular blood
  o Usually idiopathic finding
• Transient
• Dependent layering

CLINICAL ISSUES

Presentation
• Most common sign/symptoms
  o Isolated flaring on routine study
  o EB + other anomalies/markers
  o EB + IUGR
  o EB + hydrops

Demographics
• Age
  o Advanced maternal age at risk for T21
  o ≥ 35 yrs at time of delivery

Natural History & Prognosis
• Excellent when isolated in low risk patients
• Not associated with infant bowel dysfunction when isolated

Treatment
• None for EB
• May be necessary for EB associations

PATHOLOGY

General Features
• Genetics
  o T21 association
  o 1.7x 1 risk
• Etiology
  o Microvascular enzymes
  o T21, cystic fibrosis
  o Bowel motility
  o Insipidus meconium
  o Water content
  o Protein content
  o Mesenteric ischemia
• Epidemiology: 1% of fetuses have grade 2 or 3 EB
• Associated anomalies
  o T21 anomalies
  o In utero infection
  o Hydrops
  o Brain calcifications
  o Liver calcifications
  o Bowel obstruction
  o Atelectasis
  o Ischemia
  o IUGR

Staging, Grading or Classification Criteria
• Grade O (normal)
  o Bowel echogenicity = liver echogenicity
• Grade 1 (normal)
  o Bowel is minimally more echogenic than liver
  o Bowel is less echogenic than bone
• Grade 2 = EB
• Grade 3 = EB
• Bowel is more echogenic than bone
• Usually focal

SELECTED REFERENCES

(Left) Sagittal ultrasound of the fetal trunk shows fetal EB (arrows) in a case with E/E. The bowel echogenicity is greater than bone and the finding is very fatal. Fatal EB is more likely pathognomonic than benign. (Right) Axial abdomen in the same fetus confirms the presence of fetal EB (arrows) even in an unformed bladder, grade 1-II.

(Left) Coronal ultrasound of the fetal trunk shows focal grade 2 echogenic bowel (arrows) in a fetus with CMV in-utero. This pregnancy was also complicated by oligohydramnios and IUGR. (Right) Axial abdomen of the same fetus at another mosaic shows the typical prenatal/surgical calcifications (arrows) and ventriculomegaly (coronal arrows) seen with CMV.

(Left) Sagittal ultrasound of the fetal trunk obtained with 3.5 MHz transducer shows fetal EB (arrows). The spine (arrows) and EB have similar echogenicity. (Right) Sagittal ultrasound of the same fetus using a 5 MHz transducer corrects the late EB diagnosis. The bowel is more obviously echogenic (arrows) and clearly not echogenic. Soft bowel (curved arrows), 10th percentile quantifiers can give the erroneous impression of EB.
**ESOPHAGEAL ATRESIA**

**TERMINOLOGY**

**Abbreviations and Synonyms**
- Esophageal atresia (EA)

**Definitions**
- Atresia of esophagus often associated with tracheoesophageal fistula (TEF)
  - > 90% have a fistula
  - Proximal atresia with distal TEF most common type

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue: Combination of small stomach, polyhydramnios, and intrauterine growth restriction (IUGR) in late 2nd and 3rd trimester
- Diagnosis often missed before polyhydramnios develops
- Reported sensitivity of ultrasound for detection of EA < 50%

**Ultrasoundographic Findings**
- Small or absent stomach
  - Complete absence suggests either no TEF or a very small, stenotic connection
  - "Pouch" sign

- Tracheal filling with proximal esophagus with swallowing
- Frequently associated with duodenal atresia (DA)
- May not be able to diagnose combination of EA + DA prenatally if TEF present
- Stomach secretions may decompress through fistula
- If TEF not present, the distal esophagus, stomach, and duodenum form a closed "C" loop
- Normal secretions accumulate in this isolated loop
- May cause marked distention
- Has been detected in 1st trimester
- High risk for trisomy 21

- IUGR
  - Seen in up to 93%
  - Suggests amniotic fluid important for growth in latter half of gestation
  - Higher gastrointestinal (GI) obstructions cause greater growth disturbances
  - Manifests in late 2nd or 3rd trimester

- Polyhydramnios
  - Rarely develops before 20 weeks
  - Fetal swallowing not important part of amniotic fluid dynamics until that time

- Part of VACTERL association
  - Vertebral anomalies
  - Anal atresia
  - Cardiac malformation

---

**DDx: Absent Normal Stomach Bubble**

- CDH
- CDH
- CDH
ESOPHAGEAL ATRESIA

Key Facts

- Tracheo-esophageal fistula, esophageal atresia
- Renal anomalies
- Limb malformation

Top Differential Diagnoses
- Diaphragmatic hernia
- Central nervous system malformations
- Neuromuscular disorders
- Cleft lip, palate

Pathology
- Anencephaly reported in 5-44%
- Trisomy 18 (T18) most common
- EA without TEF more common in T21

Clinical Issues
- 22-75% mortality for those detected in utero

Diagnostic Checklist
- Combination of IUGR and polyhydramnios should prompt careful search for anomalies, including EA

Differential Diagnosis

Diaphragmatic hernia
- Stomach in chest
- May also have small bowel and liver in chest
- Peristalsis within chest favors pathognomonic
- Deviation of cardiac axis
- Abdominal circumference small
- Polyhydramnios

Abnormal swallowing
- Central nervous system malformations
- Neuromuscular disorders
- Cleft lip, palate
- Hialtal hernia
- Stomach partially in chest
- Tubular appearance in longitudinal plane, crosses from chest into abdomen

Pathology

General Features
- Genetics
  - Sporadic occurrence
  - No known inheritance pattern
  - Chromosomal
  - Aneuploidy reported in 5-44%
  - Trisomy 18 (T18) most common
  - Trisomy 21 (T21)
  - EA without TEF more common in T21
- Etiology
  - Embryology
  - Incomplete foregut division
ESOPHAGEAL ATRESIA

- Tracheo-esophageal septum normally divides ventral (respiratory) from dorsal (digestive) segments
- Necessity not completely understood
- Epidemiology
  - 1:2,000-3,000 live births
  - Males slightly more common than females
- Associated abnormalities
  - Reported in 63%
- Malrotation
  - Duodenal
  - Jejunal
  - Bowel malrotation
  - Cardiac abnormalities
  - Other anomalies in VACTERL association
- Case reports of biliary atresia

Staging, Grading or Classification Criteria
- Types and percentages of EA
  - Proximal atresia with distal TEF (82%)
  - Proximal and distal atresia, no fistula (9%)
  - E type fistula with no atresia (9%)
  - Atresia with both proximal and distal fistulae (2%)
  - Proximal TEF with distal atresia (1%)

CLINICAL ISSUES

Presentation
- Most common sign/symptoms
- Polyhydramnios
  - Large-for-date
  - Precipitous labor

- Abnormal serum screen (T18, T21)
- Other more obvious findings: in VACTERL association or T18
- After delivery
  - Coughing, drooling, choking
  - Recurrent pneumonia (R-type)

Demographics
- Age
  - Advanced maternal age at 1 for T21, T18
  - > 35 yrs at time of delivery

Natural History & Prognosis
- 22-75% mortality for those detected in utero
- Presence of cardiac defect greatest effect on survival in neonatal group
- Even if isolated, long term sequelae common
  - Esophageal dysmotility in nearly 10%
  - Strictures
  - Recurrent TEF
  - Aspiration

- Fistulae difficulties
- Thrombomalous
- EA without TEF more difficult to repair

Treatment
- All fistulas should be karytyped
- Aminohexadecagon for severe polyhydramnios
  - Reduce uterine irritability
  - Maternal comfort
- Predelivery consult with pediatric surgeon
- Deliver at tertiary care center
- Surgical resection and reconstruction after delivery
  - May need to be staged procedure if atretic segment is long
  - Gastrostomy tube in some cases

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls
- Ultrasound is poor in detecting EA before the onset of polyhydramnios
- Must have a high degree of suspicion and perform follow-up scans
- Combination of EGD and polyhydramnios should prompt careful search for anomalies, including EA

SELECTED REFERENCES
ESOPHAGEAL ATRESIA

**IMAGE GALLERY**

**Typical**

(left) Sagittal ultrasound of the left upper quadrant shows complete absence of a normal stomach bubble. Cervical scanning revealed what was thought to be the collapsed stomach (arrow). **(Right)** Coronal view. Doppler ultrasound focused on the fetal neck, with a distinct vessel, which showed a "swoosh sign." Arrow at the point of esophageal atresia. Observation of this blind-ending pouch showed expansion and contraction with oral swallowing.

**Typical**

(left) Frontal radiograph from the case above shows the nasogastric tube terminating in the proximal esophagus (arrow). No gas is seen in the stomach (curved arrow) consistent with esophageal atresia without a TEF. **(Right)** Lateral radiograph with non-ionic contrast shows complete atresia, with the esophagus ending in a pouch (arrow) similar to the fetal ultrasound appearance.

**Typical**

(left) Axial ultrasound at a 2nd trimester shows a stomach bubble present but smaller than expected (arrow). There is also polyhydramnios. Postnatal workup showed proximal P.E.T. with a distal TEF. **(Right)** Gross pathology from a fetus with a VACTERL association shows the dissected proximal esophagus terminating in a blind-ending pouch (curved arrow). The distal esophagus communicates with the trachea at the level of the cervical vertebrae. The stomach is small (open arrow).
**TERMINOLOGY**

Abbreviations and Synonyms
- Duodenal atresia (DA), web or stenosis

Definitions
- Lack of normal duodenal canalization leading to partial (web/stenosis) or complete obstruction (atresia)

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue: Stomach and duodenum can be connected during real-time imaging
- Duodenum most common site of intestinal obstruction
- Normal gastric incisure may mimic appearance
- Persistent fluid in duodenum is always abnormal

**Ultrasonographic Findings**
- "Double bubble"
  - Fluid-filled stomach and duodenum
  - Generally seen after 20 weeks
  - Duodenal web or stenosis may not be seen until 3rd trimester
  - Has been diagnosed in 1st trimester
  - May have worse prognosis

- Polyhydramnios
  - Usually not detected before 24 weeks
  - Present in most cases by 3rd trimester
  - May become severe
  - No fluid in distal bowel loop
  - Fetal malnutrition may intermittently decompress stomach

- Other gastrointestinal (GI) malformations common
  - Esophageal atresia (EA)
    - If a tracheoesophageal fistula is not present, fluid may accumulate in distal esophagus, stomach, and duodenum forming a "C" loop
  - Normal secretions accumulate in this closed loop
  - Accumulated secretions may cause marked dilation, much greater than typically seen with just EA
    - More likely to present in 1st trimester than isolated DA
  - Distal bowel atresia
  - Malrotation
  - Biliary atresia
  - Gallbladder atresia

- Other associated findings
  - Cardiac malformations in 37%
  - Skeletal anomalies
    - Vertebral body malformation
    - Radial ray malformation
    - Caudal regression sequence

**DDx: Other Abdominal "Bubbles"**

- Choledochocele Cyst
- Mesenteric Cyst
- Adjunal / Arterial
DUODENAL ATRESIA

Key Facts

**Top Differential Diagnoses**
- Distal atresias
- Antral web/atresia
- Choledocho cyst
- Ovarian cyst
- Duplication cyst

**Pathology**
- 5-15% of T21 cases have DA
- 50-70% of DA have other anomalies

**Clinical Issues**
- Overall mortality 15-49%
- Isolated defect, 95% survival with immediate surgical treatment
- All fetuses should be karyotyped

**DIFFERENTIAL DIAGNOSIS**

**Distal atresias**
- Jejunal, ileal, colonic, anal
- Multiple dilated distal bowel loops

**Antral web/atresia**
- Single “bubble”
- Dilated stomach
- Duodenum not seen
- Polyhydramnios

**Abdominal cysts**
- None will communicate with stomach
- Polyhydramnios not a feature
- Choledocho cyst
- Right-sided near gallbladder
- Follow bile ducts into cyst
- Ovarian cyst
- Female only
- Not usually seen until 3rd trimester
- Duplication cyst
- Duodenal duplication cyst can be difficult to differentiate from DA
- Most duplications cysts are further distal
- Beum most common location
- Mesenteric cyst

**PATHOLOGY**

**General Features**
- Genetics
DUODENAL ATRESIA

- Sporadic inheritance
- Chromosomal
  - 20% of DA cases have T21
  - 15% of T21 cases have DA
- Etiology
  - Abnormalities of duodenal morphogenesis
  - Failure of normal recanalization of duodenal lumen at 6-9 weeks (most widely accepted)
  - Vascular compromise to developing gut
  - Epidemiology: 1:3,140,000 births
- Associated abnormalities
  - 50-70% of DAs have other anomalies
  - Chromosomal
  - Cardiac
  - Skeletal
  - Other GI
  - Gastrointestinal

Gross Pathologic & Surgical Features
- Main and 3rd portions most commonly involved
- Most near ampulla of Vater
- May be incomplete (webs)
- Same risk of T21
- Antrum pancreas frequently present

Staging, Grading or Classification Criteria
- Type I (most common)
  - Entire intestinal wall and mesentery
  - Sequal or membranous luminal obstruction
  - Diameter of proximal bowel segment > distal segment
- Type II
  - Intestinal segments connected by fibrous cord
- Type III
  - Two blind ends without intervening cord
  - Wedge-shaped mesenteric defect

CLINICAL ISSUES

Presentation
- Polyhydramnios
  - Large-for-dates
  - Pretterm abort
- Abnormal scarring (T21)
- Neonatal
  - Vomiting
  - 85% bilious
  - 15% nonbilious. Proximal to ampulla of Vater

Natural History & Prognosis
- Dependent on associated abnormalities
- Overall mortality 15-20%
- Risk for 3rd trimester in utero demise, even if isolated
- Portal detect, 95% survival with immediate surgical treatment
- Recurrence rate same as general population

Treatment
- All requires should be karyotypel
- Genetic counseling
- Analodiversion for severe polyhydramnios
  - Reduce uterine irritability
- Maternal comfort
- Immediate nasogastric suction after delivery
- Plan fist after delivery
- If gas-filled 'double bubble', no water-works needed prior to surgery
- If gas present, distal to duodenal, perform upper GI exam to exclude for web or stenosis
- Surgical correction is best performed in immediate neonatal period
- Central dilations to maintain repair
- Severe cardiac malformation may require repair first
- Malnutrition unattractive respiratory insufficiency, fluid or electrolyte imbalance

DIAGNOSTIC CHECKLIST

Consider
- Coexistence EA when DA presents early in gestation, with marked dilatation ('C loop') and polyhydramnios
- High likelihood of T21

Image Interpretation Pearls
- Continuity with stomach confirms diagnosis
- Normal postnatal with prominent gastric thereby an atrium appearance of DA
- Look for location of normal 'bubble'
  - Antrum will be anteriorly located
  - Duodenum radial to stomach

SELECTED REFERENCES

1. Meagher GE et al. First trimester imaging of combined esophageal-duodenal atresia without a tracheoesophageal fistula. J. Ultrasound Med. 23(9):233, 2004
DUODENAL ATRESIA

IMAGE GALLERY

Typical

*Left:* Axial ultrasound shows a "cap" (arrows) medially to the stomach (arrow). *Right:* Axial oblique ultrasound shows the pylorus (arrow) connecting these structures, confirming the diagnosis of duodenal atresia.

Typical

*Left:* Coronal ultrasound shows a very prominent dilated bulbous duodenum and stomach, typical of DA. A thorough search for features of trisomy 21 and other associated anomalies should be performed. *Right:* Anteroposterior radiograph of a neonate with DA shows findings similar to those seen in the fetus, fluid replacement with gas, which does not extend distal to the duodenum (arrow).

Variant

*Left:* Coronal T2WI MR of a fetus with DA shows high signal fluid in the stomach, coronal arrow, and duodenum (arrow). The remainder of the bowel was normal in appearance. *Right:* Axial ultrasound of a 19-week fetus shows marked dilatation of the stomach and duodenum, which form a "C" loop (arrow). There is also polyhydramnios. These findings are typical of DA, combined with esophageal atresia. This fetus is at very high risk for trisomy 21.
JEJUNAL, ILEAL ATRESIA

Graphic shows the surgical classification system of jejunal atresia: type I - membranous type II - fibrous type II-A - "tight web", and type II-B - multiple atresias.

TERMINOLOGY
Definitions
- One or more areas of stenosis or atresia involving small bowel

IMAGING FINDINGS
General Features
- Best diagnostic clue: Hyperperistalsis within distended small bowel loops highly suggestive of obstruction
- Location
  - Roughly equal involvement between jejunum and ileum
  - 75% involve both jejunum and ileum

Ultrasoundographic findings
- Normal small bowel
  - < 7 mm diameter
  - Routinely seen in late 2nd and 3rd trimester
- Peristalsis routinely deviated/truncated
- Atresias
  - Dilated, fluid-filled loops of bowel
    - Bowel contents (tactus exterius) commonly echogenic
  - "Triple bubbles" for proximal jejunal atresia
  - "Sausage-shaped" bowel loops
- hyperperistalsis of obstructed segments often seen in real time
- Enlarging bowel 3rd trimester
- Can rarely present as cyst-like mass
- Peristalsis distinguishes atresia from other abdominal cysts
- Polyhydramnios
  - May not see before 36 weeks
  - Tandem and severity dependent on site of atresia
- Polyhydramnios seen earlier with more proximal atresias
- At risk for perforation and mesenteric peritonitis (6%) - Ascites
  - Peritoneal calcifications
  - Pseudocysts
  - More common with distal atresias
- Intravenous growth restriction (UGR)
  - Proximal atresia more likely to have IUGR
  - Ingested amniotic fluid important for fetal growth in latter half of gestation

MR Findings
- May better delineate site of obstruction
- Obstructed fluid-filled loops
- Low signal T1WI
- High signal T2WI
- Sign intensity may vary among isolated segments

DDx: Dilated Bowel Loops

- Anal Atresia
- Duodenal Atresia
- Meconium illness
**Imaging Findings**
- Gut diagnostic clue: Hyperperistalsis within dilated small bowel loops highly suggestive of obstruction
- Roughly equal involvement between jejunum and ileum
- Dilated, fluid-filled loops of bowel
- Bowel contents (sucus entericus) commonly echogenic
- "Triple bubble" for proximal jejunal atresia
- "Sausage-shaped" bowel loops
- Can rarely present as cyst-like mass
- Polyhydramnios seen earlier with most proximal atresia
- At risk for perforation and meconium peritonitis (1-6%)
- Proximal atresias more likely to have IUGR

**Imaging Recommendations**
- Protocol advice
  - Frequent follow-up scans
  - Fetal growth
  - Polyhydramnios
  - Increasing bowel dilatation
  - Perforation
  - Obtain sonographic views of rectum/anus to
    - Evaluate proximal atresia
  - Determining point of obstruction is difficult, especially when multiple loops are dilated
  - Jejunal vs. ileal atresia
  - Jejunal
    - More frequently multiple
    - Greater bowel dilatation
    - Less likely to perforate
    - Higher association with IUGR
  - Ileal
    - Usually single
    - Less distensible, with earlier perforation

**Differential Diagnosis**

**Meconium ileus**
- Obstruction from meconium impaction in distal ileum
- Often indistinguishable from atresia
- High association with cystic fibrosis
- Echogenic bowel on 2nd trimester scan

**Midgut volvulus**
- Schematic leads to infarction
- Dilated bowel segment shows no peristalsis
- Heterogeneous lumen content from hemorrhage and ascites
- May be indistinguishable early

**Colonic/anal atresia**
- Very difficult to tell urge from small bowel in fetus
- Normal hyperechoic rectum and echogenic anus (anal dimple) can not be visualized in anal atresia

**Key Facts**

**Top Differential Diagnoses**
- Meconium ileus
- Midgut volvulus
- Colonic/anal atresia
- Ureterectasis
- Normal colon

**Pathology**
- Vascular injury most accepted theory of development; multiple possible mechanisms
- Frequently associated with other gastrointestinal (GI) anomalies
- Anomalies outside GI tract uncommon

**Clinical Issues**
- Sensitivity for US detection reported as high as 100%

- Associated with VACTERL syndrome
  - Vertebral anomalies
  - Anal atresia
  - Cardiac malformations
  - Tracheo-esophageal fistula
  - Renal malformations
  - Limb anomalies

**Ureterectomy**
- Nuchal appearance may be mistaken for bowel
  - Often enlarged bladder
  - Posterior urethral valves, prune belly syndrome
  - Oligohydramnios may be present
  - Hydroureter

**Normal colon**
- Can appear prominent in 3rd trimester
  - Normal caliber 18 mm

**Ducal atresia**
- "Double bubble"
  - No bowel distalation beyond duodenum

**Abdominal cysts**
- Choledochal, duplication, ovarian, mesenteric
  - Single cysts, not tubular
  - No peristalsis
  - Not usually associated with polyhydramnios

**PATHOLOGY**

**General Features**
- Genetics
  - Most sporadic
  - Familial cases of multiple atresias reported
  - Likely autosomal recessive
  - "Apple-peel" atresia rare familial form of atresia

**Etiology**
- Vascular injury most accepted theory of development; multiple possible mechanisms
  - Rupturing of mesenteric artery during bowel rotation (16-12 weeks)
  - Fetal hypotension
JEJUNAL, ILEAL ATRESIA

- Vascular malformation
- In utero volvulus, intussusception
- Mecocceous ileum
- Associated anomalies
  - O Abnormalities of other gastrointestinal (GI) anomalies
  - O Meconium ileus
  - O Gastrostomy
  - O Volvulus
  - O Intussusception
  - O Malrotation
  - O Anomalies outside GI tract

Gross Pathologic & Surgical Features
- May occur in any segment of bowel segment

Staging, Grading or Classification Criteria
- Type I: Membranous atresia
  - O Web or diaphragm occluding bowel segment
  - O No mesenteric defect
  - O Normal bowel length
- Type II: Blind end separated by fibrous cord
  - O No mesenteric defect
  - O Normal bowel length
- Type III-A: Blind ends with complete separation
  - O V-shaped, mesenteric defect
  - O Short bowel
- Type III-B: "Apple-peel" or "Christmas tree" atresia
  - O Rectangular, size limited to ileum
  - O Remaining segments have a spiraled "apple-peel" appearance
  - O Large mesenteric defect
- Type IV: Multiple small bowel atresia
  - O Mesenteric defects
  - O Short bowel

CLINICAL ISSUES

Presentation
- Bilateral bowel and polyhydramnios in 2nd and 3rd trimester
- Sensitivity for US detection reported as high as 100%

Natural History & Prognosis
- I Ictal
  - O More likely to perforate
- Juxtoral
  - O Higher association with puncture delivery
  - O Likely secondary to polyhydramnios
  - O IUGR: more often preterm
  - O Anatomically normal colon: source for future
  - O More likely to have multiple atresias
  - O Not detectable prenatally because segments distal to obstruction are decompressed
  - O > 90% survival
- Factors negatively impacting prognosis
  - O Increasing length of stenotic segment
  - O Multiple sites of atresia
  - O Proximal worse than distal

Perforation
- O Volvulus

Treatment
- Anisequectomy to rule out cystic fibrosis
- Anisectectomy for severe polyhydramnios
- O Reduce uterine irritability
- O Maternal comfort
- O Postnatal evaluation
- O Saphenous and decubitus radiographs
- O Look for free hihi
- O Consider water-soluble contrast enema
- O Look for multiple or more distal atresia
- O Colo connected often be small caliber ("microcolon") from lack of normal meconium, especially in distal obstructions
- O Surgical resection of affected bowel
- O Long-term outcome dependent on length of resected bowel and associated malformations
- O Short gut syndrome, dysmotility and functional obstruction potential complications

DIAGNOSTIC CHECKLIST

Consider
- Testing for cystic fibrosis is recommended in all cases of distal obstruction
- O Meconium ileus may have an identical appearance to distal atresia

SELECTED REFERENCES
**IMAGE GALLERY**

**Typical**

*Left:* Sagittal ultrasound through the fetal abdomen shows a "double bubble" in this case of proximal jejunal atresia. Two dilated loops of small bowel (arrows), as well as another stomach (curved arrow) are seen. *Right:* Intra-operative photograph shows the very dilated proximal jejunum terminating in a flaccid cord (arrow). The meconium is intact (type A trauma).

**Typical**

*Left:* Axial oblique ultrasound shows a beveled, fluid-filled loop of bowel adjacent to the spine. *Right:* Neonatal abdominal radiograph taken several hours after delivery shows a dense fecal mass within the dilated bowel loops. A distal jejunal atresia was confirmed at surgery.

**Typical**

*Left:* Water-soluble contrast enema from the case above shows a small caliber colon (curved arrow). There is reflux of contrast into the duodenum (arrow). The unformed, dilated loops are gas-filled (open arrow). *Right:* Gross pathology from a different case shows the distended small bowel with abrupt termination at the point of atresia (arrows). The colon (curved arrow) is very small, which gives the "microcolon" appearance on prenatal imaging studies.
**TERMINOLOGY**

**Definitions**
- Anorectal atresia may be high (above levator sling) or low (below levator sling)
- High atresia more common

**IMAGING FINDINGS**

**Ultrasoundographic Findings**
- May go undetected prenatally
- Dilatation may not occur until 3rd trimester
- Difficult to distinguish large from small bowel
- U or V-shaped bowel in pelvis suggestive of ano-rectal atresia
- Often associated with urinary tract fistula
- May see calcified meconium "marbles" moving within bowel
- Enteroliths may also form secondary to zasia
- Part of VACTERL association
- Vertebral anomalies
- Anal atresia
- Cardiac anomalies
- Tracheo-esophageal (TE) fistula
- Renal anomalies
- Limb malformations
- Amniotic fluid usually normal

**Differential Diagnosis**

**Normal third trimester colon**
- Colon, especially sigmoid, often prominent in 3rd trimester
- Normal ≤ 18 mm

**Higher atresias**
- Present earlier than more distal atresias
- More likely to cause polyhydramnios
- Rectum is still intact

**DDx: Prominent Bowel**

- Normal Colon
- Hirschprung Disease
- High Atresia
ANAL ATRESIA

Key Facts
- Terminology: Anorectal atresia may be high (above levator sling) or low (below levator sling)
- Imaging Findings: May go undetected prenatally
  - US or V/Q/CDU bowel in pelvis suggestive of anorectal atresia
  - Often associated with urinary tract fistula
  - Part of VACTERL association
- Top Differential Diagnoses:
  - Normal third trimester colon
  - Higher atresias
- Diagnostic Checklist:
  - Normal colon in 3rd trimester may appear prominent
  - Take dedicated views of rectum/ anus when any bowel abnormality is present or associated malformations are seen
  - Consultation with pediatric surgeon
  - Feeding contraindicated until repair
  - Surgical repair
    - Timing and type dependent on site of obstruction
    - Low-lying required at birth
    - Higher atresias have diverting colostomy with repair at 3-6 months
    - Bagging continence rate
    - Less successful if missing 2 or more sacral vertebral bodies
    - Incontinence greater with higher atresias
    - Low atresias more likely to have constipation

Hiachsprung disease
- May have similar appearance, depending on extent and severity of aganglionic segment
- Usually not diagnosed prenatally

PATHOLOGY
- General Features:
  - Genetics: Autosomal recessive
  - Rare familial, autosomal recessive
  - Chromosomal: Trisomy 18, 21
- Etiology
  - Arrest in division of cloaca into rectum and urogenital sinus in 9th week
  - Teratogens: Alcohol
  - Diabetes reported risk factor
- Epidemiology
  - 1-5,000 live births
  - M:F = 3:2
- Associated abnormalities:
  - Present in >50% of cases presenting at birth
  - Present in 90% of cases diagnosed prenatally
  - Genitourinary most common
  - Skeletal malformations, caudal regression sequence
  - Other gastrointestinal anomalies, especially TF, PDA
  - Cardiac malformations

CLINICAL ISSUES
- Presentation
  - Most common signs/symptoms: Other anomalies usually seen first
  - Anal atresia generally not seen until 3rd trimester
  - Case reports of 1st trimester diagnosis
  - May be missed when isolated, especially if 2nd trimester scan is only study
- Natural History & Prognosis
  - Determined by associated malformations
  - Isolated anal atresia good prognosis
  - 1-4% recurrence risk
- Treatment
  - Amniocentesis for karyotype
- Image Interpretation Pearls
  - Normal colon in 3rd trimester may appear prominent
  - Take dedicated views of rectum/ anus when any bowel abnormality is present or associated malformations are seen

SELECTED REFERENCES

IMAGE GALLERY
- Left: Coronal ultrasound of a normal fetal rectum shows hypoechoic wall thickness and a hypoechoic vesicles (open arrows). Right: Axial ultrasound at the level of the anus (arrows) shows a normal "target" appearance.
MECONIUM PERITONITIS, PSEUDOCYST

Terminology

Definitions
- Chemical peritonitis due to intraperitoneal bowel perforation

Imaging Findings

General Features
- Best diagnostic clue: Combination of ascites, calcifications and dilated bowel & pathognomonic

Ultrasoundographic Findings
- Findings variable, according to timing and severity of perforation
- Calcifications must specific finding
- Intraperitoneal calcifications in 85%
- Impalpable on peritoneal surface
- Liver capsule often most obvious
- Must differentiate from intraperitoneal calcifications
- May also be in scrotum
- Patent prostatic utricle in fetus
- Ascites secondary to both spilled contents and incontinency response
- Often first sign of meconium peritonitis
- Meconium pseudocyst

Imaging Recommendations
- Frequent follow-up scans after initial diagnosis
- Need to plan for delivery and postnatal work-up
- May worsen with increasing bowel dilatation and abdominal distention
- May resolve completely with no sequelae
- Try to determine cause of perforation
- Dilated bowel makes a peritoneal bowel obstruction most likely
- Are bowel loops peristalsis?
- Non-peristalsis, dilated loops concerning for volvulus

DDx: Meconium Peritonitis

- Toxic Megacolon
- Gastritis
- Esophagus
- Peptic Ulcer Disease

- Meconium Bowel

- Meconium Peritonitis

- Meconium Pseudocyst

- Meconium Stasis
**Key Facts**

### Top Differential Diagnoses
- Hyperechoic bowel
- Infection
- Gallstones
- Diverticulitis

### Pathology
- Cystic fibrosis in 8% of fetal cases

### Clinical Issues
- Calciﬁcation visible 1-2 weeks after perforation
- Prognosis much better for fetus than neonate
- Spontaneous intrauterine closure of perforation may occur
- Mortality 11-14% for in utero diagnosis
- Genetic counseling for cystic fibrosis

### Differential Diagnosis

- **Hyperechoic bowel**
  - Increased echogenicity of bowel ≥ bone
  - Not calcified, so does not shadow
  - Often appears mass-like
  - Careful search for associated conditions
    - Aneuploidy (trisomy 21)
    - In utero infection
    - Intrauterine growth restriction
  - Cystic fibrosis
    - May progress to bowel obstruction from meconium ileus, which is at risk for perforation

- **Abdominal calcifications**
  - Infection
    - Scattered punctate calcifications within liver parenchyma
    - Often do not shadow
    - May be caused by a number of organisms
      - Toxoplasmosis
      - Cytomegalovirus
      - Parvovirus
      - Hepatitis B
      - Varicella
      - Herpes simplex
      - Rubella
      - Syphilis
    - Infection may be etiologic agent for jaundice, so may have signs of both perforation and infection
  - Gallstones
    - One or echogenic fecal within gallbladder
    - 3rd trimester finding

- **Fluid**
  - Small fluid collection
  - May indicate fetal bowel obstruction

- **Hypodensity**
  - Small bowel obstruction
  - Fluid only
  - May indicate fetal bowel obstruction

- **Volume**
  - Increased volume
  - May indicate fetal bowel obstruction

- **Mass**
  - Large mass
  - May indicate fetal bowel obstruction

- **Abnormal Fetal Heart Rate**
  - Decreased fetal heart rate
  - May indicate fetal bowel obstruction

- **Fetal Anomalies**
  - Presence of other fetal anomalies
  - May indicate fetal bowel obstruction

- **Fetal Death**
  - Fetal death may occur
  - May indicate fetal bowel obstruction

- **Shadowing or “comet tail” reverberation artifact may be present**

- **Usually resolve in first year of life**

- **Ectopic**
  - Calcified intraluminal meconium
  - May be seen moving within bowel lumen
  - Appears as small “marbles”
  - Described with visceralocentric fistula
  - Most often in setting of anal atresia

- **Fruits may calcify**
  - Hepatoblastoma
  - Teratoma
  - Neuroblastoma
  - All should have obvious mass

### Aspects

- **Uterine**
  - Fluid in abdomen only
  - Associated with obstructed urinary tract
  - Hydrops
  - May have a local fluid collection (urinoma)
  - Hydramnios
  - Ascites + fluid in one other area

- **Pleural effusion**
  - Skin edema
  - Pericardial effusion

- **Numerous causes**
  - Intrauterine, non-immune
  - Always check cardiac structure, rate and rhythm

### Abdominal cysts

- **Cholecystocystic**
  - Right upper quadrant cyst
  - Following bile ducts into cyst is pathognomonic

- **Enteric duplication cyst**
  - Hyperechoic wall with hyperechoic mucosa (cut signature)
  - May cause bowel obstruction

- **Mesenteric cyst**
  - Variable appearance
  - Generally smooth, thin walls
  - May be multiloculated
MECONIUM PERITONITIS, PSEUDOCYST

PATHOLOGY

General Features
- Genetics
  - Cystic fibrosis in 8% of fetal cases
- 15-40% of postnatal cases
- Autosomal recessive: 25% recurrence risk
- Delay
  - 2 proposed mechanisms: Primary ischemic event or bowel anomaly leading to perforation
  - Blood-peritonitis = meconium spills into peritoneum
  - Intestinal inflammatory reaction
  - Adhesions = "cyst" formation
  - Bowel loops may be trapped within "cyst" not
  - Calcifications secondary to inflammation
  - Bowel anomalies at risk for perforation
- Atresia (distal at greater risk, ileal proximal)
- Meconium ileus
- Volvulus
- Intussusception
- Maternal cocaine use may cause fetal bowel ischemia
- In utero infection
- Epidemiology
- Fetal incidence greater than neonatal incidence
- Reflux rectus in utero cases, which resolve without clinical sequelae

Gross Pathologic & Surgical Features
- Variable, according to severity
- May see extensive fibrous adhesions with thick, glistening bowel loops
- Pseudocysts formation around walled-off perforation
- Bowel atresias

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - Incidental note of calcification on abdominal films
  - New cystic fetus
- New cystic fetus in patient being followed for dilated bowel
- Calcification visible 1-2 weeks after perforation

Natural History & Prognosis
- Prognosis much better for fetus than neonate
- Spontaneous in utero closure of perforation may occur
- No postnatal sequelae

- Incidental note of calcification on abdominal films
- Mortality 11-14% for in utero diagnosis
- Neonatal diagnosis worse prognosis
- Mortality 40-50%
- Higher proportion of cases have cystic fibrosis
- > 50% mortality if primary bowel obstruction

Treatment
- Genetic counseling for cystic fibrosis
- Consider testing parents for carrier status
- If carriers, antenatal care is no direct treatment of gene mutations in fetus
- Simple percutaneous, calcifications only
- Routine delivery plans
- Postnatal evaluation:
  - Abdominal radiography
  - If normal, child can feed
  - Very low risk of surgical intervention
- Complex percutaneous: Dilated bowel, persistent pseudocysts, atresia
  - Deliver versus tertiary care facility
  - Evaluation by neonatologist/pediatric surgeon
  - Abdominal radiography and gastrointestinal contrast studies
  - 20-30% chance of surgery
  - Usually resection and enterostomy
- May require parenteral nutrition

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls
- Liver calcifications are on the capsular surface with meconium peritonitis, while infection causes intraparenchymal calcifications
- Consider infection as cause of perforation when calcification is seen in both locations

SELECTED REFERENCES
Typical

(Left) Coronal ultrasound early in the 2nd trimester shows a large dilated cyst (arrow). (Right) Axial ultrasound late in pregnancy shows calcifications around the liver edge (arrows) and a small amount of amniotic fluid (outlined arrow). The pseudocyst has completely resolved. In utero perforations may spontaneously heal and have no postnatal sequelae.

Typical

(Left) Coronal ultrasound in a 2nd trimester fetus shows liver calcifications (arrow), which multiple scans showed continued to resolve. These were also noted with dilated bowel loops (curved arrow). No pseudocyst was seen in this case (open arrow - bladder). (Right) Radiograph after delivery shows bone calcifications (arrow) over the face, which represents the reportage of accretionary peritonitis. The infant began feeding without difficulty.

Variant

(Left) Axial ultrasound shows an unusually large irregular pseudocyst (arrow), which invaded the retroperitoneum on surrounding structures and enlarged the abdominal circumference. (Right) Sagittal/axial view of a fetus with exomphalos, periumbilical skin defects, and an opening to the umbilical cord. This appearance could potentially be confused with exomphalos. 
**VOLVULUS**

Axial ultrasound shows a single dilated segment of bowel (arrows) within the upper abdomen. It is filled with echogenic debris and no peristalsis was seen during real-time examination.

ERoscopic photograph shows the twisted loop of volvulus small bowel (arrows), confirming the prenatal diagnosis of volvulus.

**TERMINOLOGY**

**Definitions**
- Bowel loop twisted on its mesentry, resulting in vascular compromise
- Fetal cases generally involve small bowel

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue: Dilated, non-peristaltic bowel loop

**Ultrasoundographic Findings**
- Dilated bowel loops
  - A single “kinked” loop is very suggestive
  - May see multiple dilated loops from proximal obstruction
- May have had a normal scan earlier in gestation
- Volvulus is infrequent event
- Echogenic intraluminal contents from infection and necrosis
- Ascites
- May be seen with or without bowel perforation
- Hydrops may develop as overall fetal condition worsens

**MR Findings**
- In utero diagnosis of volvulus has been described
- Dilated, low signal intensity bowel on T2WI from intraluminal hemorrhage

**Imaging Recommendations**
- Real-time evaluation important
  - Infected bowel loses ability for peristalsis
  - Obstructed, but viable, bowel loops often have hyperperistalsis
- Attempt to evaluate mesenteric vessels with Doppler
  - May have a “swirled” appearance
  - Often technically difficult

**DIFFERENTIAL DIAGNOSIS**

**Duodenal atresia**
- “Double bubble”
- Able to connect stomach and duodenum during real-time examination
- Dilated bowel is normal
- Associated with T-tube 21

**Jejunal/ileal atresia**
- Hyperperistalsis often seen in obstructed loops
- Dilatation of loops may remain stable or progress over time

**DDx: Dilated Bowel**

**Duodenal Atresia**

**Jejunal Atresia**

**Ileal Atresia**

**Rect Atresia**
VOLVULUS

Terminology
- bowel loop twisted on its mesentery, resulting in vascular compromise

Imaging Findings
- Best diagnostic clue: Dilated, non-peristaltic bowel loop
- A single "kinked" loop is very suggestive
- May have had a normal scan earlier in gestation

Intussusception
- Difficult to make diagnosis in utero
- As with aneurysm, prenatal ultrasound should be performed

PATHOLOGY

General Features
- Genital tract
  - No chromosomal association
  - Embryology: Most related to malrotation with a short, unstable mesenteric attachment
  - Epidemiology: Incidence in neonatal series inversely proportional to maternal age
  - Associated abnormalities
    - Jejuno-ileal atresia may co-exist with volvulus
    - Malrotation generally present
    - Congenital diaphragmatic hernia, gastroschisis, omphalocele and abdominal heterotaxy are described in neonatal series

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - Dilated bowel
  - Reported as early as 16 weeks

Natural History & Prognosis
- May cause in utero demise
- Outcome is generally poor
  - Related to length of gausversegment and gestational age at time of volvulus
- Those with late presentation and immediate resection have better prognosis

Treatment
- Consider early delivery if lungs are mature
- Consult with pediatric surgeons for urgent evaluation upon delivery
- Surgical resection of infarcted segment

Key Facts
- Etiologic intraluminal contents from infarction and resection
- Top Differential Diagnoses
  - Jejuno-ileal atresia
  - Intussusception

Diagnostic Checklist
- Ultrasound findings reflect vascular compromise with bowel infarction

DIAGNOSTIC CHECKLIST

Consider
- In setting of a new dilated loop of bowel in a previously normal gestation

Image Interpretation Pearls
- Lack of peristalsis in a dilated, echogenic bowel loop is very suspicious
  - Ultrasound findings reflect vascular compromise with bowel infarction

SELECTED REFERENCES

IMAGE GALLERY

(left) Axial echogenic ultrasound from the live case shows normal, decompressed, distal bowel (curved arrows) as well as the markedly enlarged loop (arrow). A small amount of calcification present. (right) Radiograph taken before surgery shows a dilated abdomen with abrupt termination of bowel (arrows) at the site of obstruction.
ASCITES

TERMINOLOGY

Definitions
- Fluid in peritoneal space

IMAGING FINDINGS

Ultrasonographic Findings
- Anechoic fluid in abdomen
  - Outlines intraperitoneal structure
    - Solid organs
    - Bowel
  - Echogenic features
  - Falciform ligament may also be visible
  - Must distinguish from pseudocysts
    - Perihepatic/perihepatic fat peripherally around fetal abdominal cavity
    - Anterior location
    - Just under skin surface
    - Between fetal skin and liver margin
    - Represents normal abdominal wall musculature
    - Internal oblique
    - External oblique
    - Transversus abdominis
  - Muscles project onto ribs, therefore sonolucency not seen posteroanteriorly
  - Luency may occur posteriorly adjacent to dorsal ribs
  - Pseudocysts cannot outline umbilical vein
  - True ascites can be seen in other parts of abdomen
- Look for signs of hydrops
  - Pleural effusion
  - Pericardial effusion
  - Skin oedema
  - Polyhydramnios
  - Placentomegaly
  - Placental measurement > 4 cm

Imaging Recommendations
- Discovery of ascites requires work-up for etiology
  - Determine if isolated or part of generalized hydrothorax
  - Look for pleural fluid, pericardial effusion, skin thickening
  - If isolated, most likely from perforated viscus; gastrointestinal or urinary tract obstructions
  - Source may be difficult to determine after perforation and decompression
  - Careful screening ultrasonogram warranted
  - Check for anatomic abnormalities
  - Carefully evaluate peritoneal surfaces for calcifications
  - Merocentium peritonitis from bowel perforation
  - Oligohydramnios suggests a urinary tract anomaly

DDx: Abdominal Fluid Collections
- Met Pseudo-cyst
- Ovarian-Cyst
- FCU
- Symphysis pubis
Differential Diagnosis

**Gastrointestinal**
- Bowel anomaly with perforation
  - Diverticulosis
  - Melanoma
  - Appendicitis
  - Intussusception
  - May be difficult to diagnose when bowel loops are collapsed
  - Malrotation with volvulus
  - Perforation of obstructed loop
  - Perforation leads to meconium peritonitis
  - Look for other signs
  - Periportal calcifications
  - Meconium pseudocyst
  - Meconium plug syndrome
  - Consider cystic fibrosis

**Genitourinary**
- Urinary ascites
  - Perforation of an obstructed system
  - Oligohydramnios may be present
  - Persistent urethral valves (PUV)
  - Typical "keyhole" appearance of bladder
  - Hydrothorax
  - Male fetus
  - Oligohydramnios may be severe
  - Bladder may rupture into peritoneal cavity
  - Ureteropelvic junction (UPJ) obstruction
  - Hydrothorax
  - Echogenic thinned renal parenchyma
  - Renal pelvis may rupture
  - Urinary ascites
  - Focal hydronephrosis
  - Look for contralateral renal anomalies
  - UPJ obstruction (bilateral is 10–30%)
  - Multicystic dysplastic kidney
  - Renal agenesis
  - Ureterovesical obstruction
  - Ovarian cyst rupture
  - Ovarian cyst may be large and extend into abdomen

**Immune hydrops**
- Fetal anemia
  - Kernicterus (hyperbilirubinemia)
  - Maternal anti-D titers
  - Mother has maternal antibodies
  - Middle cerebral artery (MCA) Doppler
  - Measure peak systolic velocity
  - Check for presence and severity of anemia
  - Assess for need to transfuse

**Nonimmune hydrops**
- Wide range of etiologies
  - Cardiac malformation
  - Structural anomaly resulting in poor contractility
  - Fetal anemia
  - Atrioventricular canal
  - Arrhythmias
  - Tachycardia
  - Treatments available
  - Conversion to normal rhythm may reverse hydrops
  - Narrowing of infants
  - More often associated with a structural anomaly
  - Chromosomal anomaly
  - Turner syndrome
  - Trisomy 18
  - Trisomy 13
  - Fetal edema
  - Hydrops from either high-output failure or mass-effect with impaired venous return
  - Cystic adenomatoous malformation
  - Multiple large cysts seen if macrocystic
  - Microcystic type is echogenic

**Top Differential Diagnoses**
- Bowel anomaly with perforation
- Urinary ascites
- Immune hydrops
- Nonimmune hydrops

**Clinical Issues**
- May be earliest sign of hydrops
- Diagnostic fetal paracentesis considered when etiology is unclear
- Consider fetal echocardiogram to exclude cardiac etiology

**Diagnostic Checklist**
- Therapeutic paracentesis prior to delivery may be warranted
ASCITES

• May spontaneously regress in utero
• Bronchopulmonary sequestration
• Hecothoracic pulmonary mass
• Look for systemic seeding vessel with Doppler
• Occurs at lung bases, left > right
• May have unilateral pleural effusion
• May spontaneously regress in utero
• Congenital high airway obstruction sequence (CHAOS)
• Unilaterally echogenic, calcified lungs
• Flattened diaphragm
• Ascites common
• Saccocoesyolec teratomatous
• Mixed cystic and solid mass
• Solid masses more likely to develop hydrodrops
• Echoplastic with intrapleural/abdominal extension
• Can be completely intrathoracic

Infection
• Look for scattered calcifications
• Brain
• Liver, spleen, peritonum
• Varzea B19
• Most common infectious cause of hydrodrops
• CMV
• Varicella
• Toxoplasmosis
• Syphilis
• Hematologic disorders
• Homozygous X-thalassemia
• Placental chorioangioma

Congenital chyloous ascites
• Malformation of lymphatic duct
• May require lymphatic duct ligation

CLINICAL ISSUES

Presentation
• Intraperitoneal fluid
• Abdominal circumference above of other growth parameters

Natural History & Prognosis
• May be earliest sign of hydrodrops
• Associated with lower survival rate if present with hydrodrops
• Gestational age at presentation is an important prognostic factor
• Higher fetal loss rate if seen before 24 weeks gestation
• Close sonographic follow-up recommended
• Isolated ascites has variable prognosis
• Associated anomalies may not be readily apparent perinatally
• If massive can compress thoracic cavity
• May lead to pulmonary hypoplasia
• Can cause abdominal distention during delivery

Treatment
• Test mother and/or fetus range from noninvasive
  • invasive
  • TORCUL procedure
  •Mother

• Fetus may be positive even if maternal titers normal
• Antibiotics
• Karyotype
• Diagnostic fetal paracentesis considered when etiology is unclear
• Platelet count
• Sympathetic count
• Urea nitrogen
• Creatinine
• Mecromia
• Fetal ceroidosis
• Consider fetal echocardiogram to exclude cardiac etiology
• Sonographic follow-up warranted
• Monitor abdominal girth
• May require in utero therapeutic paracentesis

DIAGNOSTIC CHECKLIST

Consider
• Therapeutic paracentesis prior to delivery may be warranted
• May allow vaginal delivery

Image Interpretation Pearls
• Distinguish true ascites from pseudoascites
• Exclude hydrodrops as underlying etiology for ascites

SELECTED REFERENCES
ASCITES

IMAGE GALLERY

Typical

(Left) Sagittal ultrasound shows ascites (curved arrows), skin edema (open arrows) and pleural effusion (arrow) in a third trimester fetus with hydroptic feta. When ascites is seen, always look for other signs of hydroptic. (Right) Axial ultrasound of the abdomen shows ascites with decompressed bowel loops (arrows). Initially this fetus presented with dilated bowel. Prenatal exam showed fetal ascites. Ascites resolved later in utero after perfusion.

Typical

(Left) Sagittal T2WI MR shows urinary ascites with hydrocephalus and a tortuous hypogastric (open arrows). The markedly distended abdomen (arrow) is compressing the thoracic cavity (curved arrow) pushing the fetus at risk for pulmonary hypoplasia. (Right) Axial ultrasonic ultrasound of the fetal abdomen is another cause of urinary ascites. Hydrothoracic (arrows) and a dilated bladder (open arrow) are evident, as well as oligohydramnios.

Typical

(Left) Coronal ultrasound shows ascites and sonolucent echogenic peritoneal loci (arrows). This suggests that the ascites is from a bowel perforation with subsequent ascites peritonitis. (Right) Axial color Doppler ultrasound shows ascites excluding the umbilical arteries. Fetal heart rates were normal and no obvious abnormalities were seen. When the etiology of ascites is indeterminate, fetal peritoneal fluid may be considered.
ENTERIC DUPLICATION CYST

TERMINOLOGY

Definitions
- Enteric duplication cyst: Enteric lining with muscular wall
- Enteric cyst: Enteric lining with fibrous wall
- May either be cystic (80%) or tubular (20%) 

IMAGING FINDINGS

General Features
- Best diagnostic clue: Thick-walled cyst with hyperreflective mucosa and a hypoechoic wall
- Often difficult to differentiate from other cystic abdominal masses

Ultrasoundographic Findings
- Fluid generally anechoic but can be echogenic
- Findings vary according to location
  - Small bowel
  - Solitary abdominal cyst
  - Jejunum most common site
  - Stomach
  - Appendiceal cyst within gastric lumen
  - Esophagus
  - Mediastinal cyst

- Vertebral anomalies commonly associated, especially hemivertebrae
- Rarely bowel dilatation from obstruction
- Polyhydramnios may develop
- Tubular duplications communicate with bowel and are usually not detected in utero
- Peristalsis within cyst has been described

Imaging Recommendations
- Confirm cyst is intraperitoneal and separate from urinary tract
- Most cystic abdominal masses are related to urinary tract
- Obtain enlarged, high-resolution images looking at wall thickness and morphology
- Proscend wall more easily evaluated
- Follow-up for bowel dilatation, polyhydramnios

DIFFERENTIAL DIAGNOSIS

Ovarian cyst
- Females only, seen in 3rd trimester
- Most common abdominal cystic mass in female
- Ovarian stromal luteoma can be anywhere in abdomen

Mesenteric cyst
- May be unicellular or multicellular
- Appearance may be identical

DDx: Abdominal Cysts

Mesenteric Cyst
Mesoneum Pseudocyst
Ovarian Cyst
Cholelithiasis Cyst
ENTERIC DUPLICATION CYST

Key Facts

**Imaging Findings**
- Best diagnostic clue: Thick-walled cyst with hyperechoic mucosa and a hypoechoic wall
- Generally anechoic but can be echogenic
- Rent most common site
- Rarely bowel dilatation from obstruction
- Obtain enlarged, high-resolution images looking at wall thickness and morphology

**Top Differential Diagnoses**
- Ovarian cyst
- Mesenteric cyst
- Choledochal cyst
- Meconium pseudocyst

**Clinical Issues**
- Excellent prognosis

- Most present in childhood
- Infraumbilical, abdominal pain

**Natural History & Prognosis**
- Excellent prognosis

**Treatment**
- Work-up after delivery to confirm diagnosis
- Surgical resection

**DIAGNOSTIC CHECKLIST**

**Image Interpretation Pearls**
- Always look at wall for a ringed appearance created by a hyperechoic mucosa and hypoechoic wall

**SELECTED REFERENCES**

**IMAGE GALLERY**

*Left* A high-resolution image of an abdominal cyst shows a hyperechoic mucosa (arrow) surrounded by a hypoechoic wall (open arrow), a lining described with enteric duplication cyst. *Right* Intraoperative photograph shows the cyst attached to a loop of small bowel (arrow). Histology confirmed an enteric duplication cyst.
MESENTERIC CYST

TERMINOLOGY
Abbreviations and Synonyms
- Cystic lymphangioma
- Lymphangioma

IMAGING FINDINGS
General Features
- Location
  - Small bowel mesentery most common
  - Jejunum
  - Retropertitoneum
- May also occur in solid organs
- Size: Variable but often large

Ultrasoundographic Findings
- Variable appearance
  - Thin-walled
  - Does not have muscular wall as seen with duplication cysts
  - May be unilocular
  - Can be large enough to mimic aneurysm
  - Bowel displaced, not floating in fluid
  - Often multilocular, with one to multiple septations

Imaging Recommendations
- Can be very complex, displacing around organs and extending out of abdomen
- Variable echogenicity of fluid, but usually anechoic

DIFFERENTIAL DIAGNOSIS
Enteric duplication cyst
- Can appear identical to unilocular mesenteric cyst
- Often has thick wall
- Look for hyperechoic mucosa surrounded by hypoechoic muscular wall
- More likely to cause obstruction and in utero bowel dilatation
- More common

Ovarian cyst
- Females only, 3rd trimester
- Most common abdominal cystic mass in female
- Ovarian ligament lax so can be anywhere in abdomen

DDx: Other Lymphangiomas
- Chest
- Chest
- Neck, Cystic Hygroma
- Retropertitoneal
MESENTERIC CYST

Terminology
- Cystic lymphatic malformation
- lymphangiom

Imaging Findings
- Thin-walled
- May be unicellular
- Often multilocular, with one to multiple septations
- May extend out of peritoneal cavity to involve retroperitoneum and lower extremities

Key Facts

Top Differential Diagnoses
- Enteric duplication cyst
- Ovarian cyst
- Meconium pseudocyst
- Urachal cyst

Diagnostic Checklist
- Most likely diagnosis for a large, multiloculated abdominal mass separate from the urinary tract

Meconium pseudocyst
- Thick, irregular wall
- Can calcify
- Often sequelae of meconium peritonitis
- Peritoneal calcifications
- Dilated bowel

Urachal cyst
- Midline
- Between bladder and cord insertion

Choledochal cyst
- Right upper quadrant
- Look for bile ducts entering cyst

PATOLOGY

General Features
- Etiology
  - Thought to be proliferation of ectopic lymphatics
  - Lack normal communication with lymphatic system
  - Lymph accumulates forming a cystic mass
  - Epidemiology: Rare

Microscopic Features
- Has endothelial lining
- Dissected lymphatic spaces
- Fluid may be proteinaceous, serous, chylous or hemorheologic

CLINICAL ISSUES

Presentation
- In utero
  - Incidental cyst seen on routine scan
- Childhood
  - Palpable mass
  - Abdominal distention and pain
  - May cause bowel obstruction
  - Less likely to do so than duplication cysts because they are of mesenteric origin, rather than bowel wall
  - May rupture reported

Natural History & Prognosis
- Excellent prognosis

Treatment
- Postnatal workup usually requires CT or MRI to see full extent of large masses
- Surgical excision
  - May rarely recur after resection
  - More likely with retroperitoneal lymphangiom

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls
- Most likely diagnosis for a large, multiloculated abdominal mass separate from the urinary tract
- May involve retroperitoneum and extremities

SELECTED REFERENCES

IMAGE GALLERY

(Left) Axial ultrasound through the abdomen of a newborn with a palpable abdominal mass shows a very complex cystic mass lying just above the abdomen and abutting the liver edge (arrows). (Right) Gross pathology shows multiple crypts with clear fluid (arrows) within the lumen. Histology confirmed an abdominal lymphangioma, which was attached to the liver capsule.
**GALLSTONES**

**TERMINOLOGY**

**Abbreviations and Synonyms**
- Fetal cholethiasis

**Definitions**
- Stones with shadowing
- Echogenic bile ("sludge")

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue: Third trimester fetal gallbladder (GB) with echogenic material

**Ultrasoundographic Findings**
- Normal fetal GB
  - Ovoid or tear drop shaped
- Intrahepatic early, then becomes subhepatic
- Gallstones
  - Third trimester finding
  - GB size variable
  - Enlarged, contracted or normal
  - One or more echogenic foci in gallbladder
  - Most often multiple
  - Shadowing
  - > 3 mm stones more likely to shadow

**Imaging Recommendations**
- Protocols: Confirm foci are within GB lumen

**DIFFERENTIAL DIAGNOSIS**

**Liver echogenicities**
- Calcifications from infection
  - Toxoplasmosis, cytomegalovirus, varicella
- Tumors + calcification
  - Hepatoblastoma, teratoma, neuroblastoma
- Hemangiomata
  - Echogenic mass without calcification

**DDx: Focal Liver Echogenicities**
- Meconium Retention
- Toxoplasmosis
- Varicella
GALLSTONES

Imaging Findings
- Best diagnostic clue: Third trimester fetal gallbladder with echogenic material
  - >3 mm stones more likely to shadow
- Coloret tail artifact
- Wall-echo-shadow sign
- Protocol advice: Confirm foci are within GB lumen
- Top Differential Diagnoses
  - Liver echogenicities

Mechonium peritonitis
- Fetal bowel perforation
- Calcifications form on peritoneal surfaces, including liver capsule
- Often accompanied by other findings
  - Aciets
  - Dilated bowel
  - Meconium pseudocyst

PATHOLOGY
- General features
  - Genetics: Not associated with aneuploidy
  - Etiology
    - Maternal estrogen effect on fetal bile
    - 1 Cholesterol, bile acids
    - Placental abruption
    - 1 Indirect bilirubin
    - Other maternal causes
    - Maternal narcotic use
    - Maternal hemolytic anemia
    - Blood group incompatibility
    - Epileptology: 1:200 3rd trimester fetuses
    - Associated abnormalities
      - Choledochal cyst
      - Congenital dilatation of bile ducts

CLINICAL ISSUES
- Presentation
  - Most common signs/symptoms
    - Almost always asymptomatic
    - Infant cholestasis more often symptomatic
    - Cholestatic jaundice, acholic stools, sepsis
- Demographics
  - Gender: M:F
- Natural History & Prognosis
  - Excellent prognosis
  - Usually completely resolve in first year of life
- Treatment
  - Usually none needed
  - Bilary drainage if obstructive

Key Facts
- Mechanism peritonitis

Pathology
- Epidemiology: 1:200 3rd trimester fetuses
- Clinical Issues
  - Usually completely resolve in first year of life

Diagostic Checklist
- Fetal gallstones do not always shadow
- Sludge may be hypoechoic or echogenic

DIAGNOSTIC CHECKLIST
- Consider
  - Sludge when gallbladder appears diffusely echogenic

Image Interpretation Pearls
- Fetal gallstones do not always shadow
- Sludge may be hypoechoic or echogenic
- Obtain follow-up exams after baby is born until resolution

SELECTED REFERENCES

IMAGE GALLERY
- Left: Long axis ultrasound shows shadowing (arrows) internal to the fetal gallbladder (curved arrow). On this image, it is difficult to tell whether this is one large stone or multiple small stones. (Right) Long axis ultrasound in another fetus shows at least a large echogenic foci within the gallbladder (arrows). These are do not shadow but were seen moving freely within the gallbladder.
HEPATIC CALCIFICATIONS

TERMINOLOGY

Definitions
- Liver-associated calcification
  o May be intraparenchymal, capsular or vascular

IMAGING FINDINGS

Ultrasoundographic Findings
- Determination of intraparenchymal vs. capsular location-key factor in determining etiology
- Bowel perforation with meconium peritonitis most common cause of capsular calcifications
- Parenchymal calcifications indicate more systemic process
- Acoustic shadowing may or may not be present

DIFFERENTIAL DIAGNOSIS

In utero infection
- Scattered punctate echogenic foci diffusely throughout liver
- Toxoplasmosis
- Cytomegalovirus
- Varicella zoster
- Herpes simplex

DDx: Right Upper Quadrant Echogenic Foci
- Meconium Peritonitis
- Acalculous Cholecystitis
- Infected Calculi
- Angiomyolipoma

Hepatic neoplasms
- Rare
  o Congenital hepatocelestoma
  o Hemangioma
  o Hemangioendothelioma
  o Hamartoma
  o Teratoma
  - More likely in younger patients
  - Metastatic
  - Neuroblastoma
HEPATIC CALCIFICATIONS

Key Facts

Pathology
- Malformations reported in 21% of fetuses with parenchymal calcifications
- Associated with abnormal karyotype

Clinical Issues
- Isolated, single hepatic calcifications are generally of no consequence
- Multiple calcifications more likely to have associated abnormalities adversely affecting prognosis
- Multiple calcifications more likely to have associated abnormalities adversely affecting prognosis
  - Malformations
  - Chromosomal
  - Infection

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls
- fetus at increased risk for chromosomal abnormalities
- Careful anatomic survey warranted
- Look for other calcifications to assess for evidence of in utero infection
  - Intracranial
  - Other intraabdominal locations

SELECTED REFERENCES

IMAGE GALLERY

(Left) Axial ultrasound shows multiple calcifications along the liver capsule (arrows). Multiple loculi of dilated biliary ducts are also seen in the abdomen. (Right) Coronal ultrasound shows calcifications outlining the surface of the liver (arrows). Peripheral calcifications are less likely to represent true parenchymal calcifications.
**HEPATOMEGALY, SPLENOMEGALY**

**TERMINOLOGY**

Definitions
- Enlargement of fetal liver and/or spleen

**IMAGING FINDINGS**

Ultrasoundographic Findings
- Liver and/or spleen occupies a significant portion of abdomen
  - May extend into pelvis
  - Normative values for splenic circumference have been described
- Enlarged abdominal circumference in relation to other growth parameters

**DIFFERENTIAL DIAGNOSIS**

Hydrops
- Immune
  - Splenomegaly
    - Can aid in assessing for presence of severe anemia in initially nonhydropic fetuses
    - Could be secondary to extramedullary hematopoiesis
- Nonimmune

**DDx: Upper Abdominal Mass**

- Congenital twine
- Teratoma
- Hemangiopericytoma
- Hepatoblastoma

- Sonographic findings
  - Skin edema
  - Pleural/perihepatic effusions
  - Ascites
  - Hepatosplenicomegaly

Infection
- Cytomegalovirus
  - Most common in utero infection
- Toxoplasmosis
- Parovirus B19
  - With associated hydrops
- Human immunodeficiency virus (HIV)
  - If mother is infected, interventional procedures not indicated including amniocentesis
  - Increases exposure risk to fetus
- Syphilis
  - Dilated bowel
  - Bowel lacerations

Trisomy 21
- Myeloproliferative disorders
  - Transient myeloproliferative disorder
  - May show spontaneous recession
  - May not have any detectable sonographic findings in utero
  - Variable spectrum of severity
  - Congestive heart failure
  - Usually presents as acute myelogenous leukemia
HEPATOMEGALY, SPLENOMEGALY

Key Facts

- Myeloproliferative disorders
- Glycogen storage disorder
- Beckwith-Wiedemann syndrome

Diagnostic Checklist

- Toxoplasmosis, other, rubella, cytomegalovirus and herpes (TORCH) titers for infection
- Annulocytosis for karyotype
- Look for other signs of hydrops

CLINICAL ISSUES

Presentation

- Most common signs/symptoms: Enlarged abdominal circumference

DIAGNOSTIC CHECKLIST

Consider

- Toxoplasmosis, other, rubella, cytomegalovirus and herpes (TORCH) titers for infection
- Annulocytosis for karyotype

Image Interpretation Pearls

- Look for other signs of hydrops

SELECTED REFERENCES


IMAGE GALLERY

(Left) Sagittal T2W H and IR shows a markedly enlarged liver (arrow) with a hypointense mass centered in the spleen (arrowhead) with hypointense mass centered in the spleen.

(Right) Sagittal ultrasonogram shows a hypechoic lesion (arrow) and hepatomegaly in a 22 week fetus with prominent cardiomegaly. Autopsy confirmed hepatomegaly, edema, ascites and intrahepatic lesions.
CHOLEDOCHAL CYST

TERMINOLOGY

Definitions
- Congenital cystic dilatation of the common bile duct. Note the anomalous pancreaticobiliary junction (arrow), with the pancreatic duct joining into the common bile duct proximal to the sphincter of Oddi.

IMAGING FINDINGS

General Features
- Best diagnostic clue: Following bile ducts into cyst confirms diagnosis
- Size: Variable, often large if seen prenatally

Ultrasonographic Findings
- Unilocular, cysts right upper quadrant masses
  - Echogenic contents in cyst seen been described
  - May see thin, tubular bile duct, entering cyst
  - More extensive intrapancreatic dilatation not reported

MR Findings
- bile high signal on T2WI
- MR cholangiogram may prove helpful

Imaging Recommendation
- Follow bile contour
  - Coronal view most helpful
  - Subhepatic, immediately adjacent to capsule

DDx: Cystic Mass By Liver

- Duodenal Atresia
- Umbilical Vein Varix
- Umbilical Liver Varix
- Duplication Cyst

Differential Diagnosis

- Umbilical vein varix
  - Color Doppler to rule out umbilical vein varix
- Duodenal atresia
  - Connects to stomach

Enteric duplication cyst
- Located anywhere in abdomen, ileum most common

Gallbladder duplication
- Same biliary shape as normal gallbladder

Ovarian cyst
- Females only, seen in 3rd trimester
  - Ovarian ligaments may be anywhere in abdomen

Liver cyst
- Within liver parenchyma, rare

Mesenteric cyst
- Located anywhere in abdomen, may be multilocular

Meconium pseudocyst
- Thick, irregular wall
Imaging Findings
- Choleocele, cystic right upper quadrant mass
- May be subtle, tubular bile ducts entering cyst

Top Differential Diagnoses
- Unbilical vein varix
- Duodenal atresia
- Enteric duplication cyst
- Gallbladder duplication

Key Facts

Pathology
- 1/3 of all cases from Japan

Clinical Issues
- Untreated leads to cholestasis, biliary cirrhosis and eventual liver failure

Diagnostic Checklist
- Right upper quadrant cyst communicating with bile ducts is pathognomonic

PATHOLOGY

General Features
- Etiology
  - Possible mechanisms (likely multifactorial)
    - Strong association with anomalies of pancreato-biliary junction
    - Insertion of pancreatic duct into common bile duct (CBD) above sphincter complex
    - Reflux of pancreatic enzymes into bile duct with weakening of wall
    - Does not completely explain very early cysts
    - Alveolar thickenings
      - Abnormal recanalization during organogenesis
      - Abnormal epithelium resulting in wall weakness

Epidemiology
- Rare in western population
- More common in Asia
- 1/3 of all cases from Japan
- M < F
- Associated abnormalities: Biliary atresia

Staging, Grading or Classification Criteria
- Type 1: Saccule or fusiform dilatation of CBD
- Type 2: CBD diverticulum
- Type 3: Cholecdocholeal fistula
- Type 4: Intrahepatic and extrahepatic dilatation
- Type 5: Intrahepatic dilatation (Caroli disease)

CLINICAL ISSUES

Presentation
- Incidental finding in utero
- Diagnosed as early as 15 weeks
- Childhood presentation
- Jaundice (most common), pain, right upper quadrant mass

Natural History & Prognosis
- Untreated leads to cholestasis, biliary cirrhosis and eventual liver failure
- Risk factor for cholangiocarcinoma

Pathway
- Good outcome with early treatment before irreversible damage

Treatment
- Complete work-up in neonatal period
- Surgical resection with choledochojjunalostomy or hepaticejjunalostomy
- May delay up to 6 months of age if asymptomatic

DIAGNOSTIC CHECKLIST
- Right upper quadrant cyst communicating with bile ducts is pathognomonic

SELECTED REFERENCES

IMAGE GALLERY

(i) Color Doppler ultrasound shows a mass-like cystic mass communicating with dilated bile ducts (arrows). This finding is pathognomonic for a choledochal cyst. (Right) Ultrasound of the liver after delivery confirms a dilated bile duct (arrow) entering the choledochal cyst.
LIVER TUMORS

TERMmology
Definitions
- Variety of benign and malignant tumors derived from both endodermal and mesenchymal tissues

IMAGING FINDINGS
General Features
- Best diagnostic clue: Well-defined, right upper quadrant mass
- Size: Generally large
- Morphology
  - Most tumors are well-defined, large liver masses
  - Leukemia in the exception and most commonly presents as hepatomegaly
  - Generally solid, but cystic masses occur

Ultrasoundographic Findings
- Infantile hemangioendothelioma
  - Variable echogenic appearance
  - Hyperechoic, hyperechoic, or mixed echogenicity
  - Detected as early as 16 weeks
  - Vascular masses
  - Increased flow on color Doppler
  - Flow void described on fetal MRI
  - Hydrol can develop from

- Hemangioblastoma
  - Solid, echogenic masses
  - Pseudocapsule around lesion creates well-defined borders
  - "Spike-wheel" described with alternating hypo- and hypechoic areas
  - Moderate vascularity by color Doppler
  - Calcifications occasionally seen
  - Can have spontaneous hemorrhage
  - Hydrol potential complication

- Leukemia
  - Hepatomegaly most common finding
  - Hydrol may develop from
    - Fetal anemia
    - Leukemic infiltration of myeloid tissue
    - Vascular fibrosis with increased vascular resistance

- Metastases
  - Neuroblastoma

Dx: Hepatomegaly

Leukemia

Leukemia

Hydrol

Neuroblastoma Met
KEY FACTS

Imaging Findings

- Most tumors are well-defined, large liver masses
- Leukemia is the exception and most commonly presents as hepatosplenomegaly
- Generally solid, but cystic masses occur

Top Differential Diagnoses

- Nonmalignant hydrops
- Immune hydrops
- Infection

Pathology

- 15-20% increased risk of leukemia in trisomy 21
- Benign primary tumors (hemangiendothelioma, mesenchymal hamartoma) are more common than malignant ones (hepatoblastoma)

- Most common primary fetal tumor to metastasize to liver
- 25% of neuroblastoma cases have liver metastases
- Solid primary tumors are more likely to metastasize than cystic ones
- Liver is most common site of metastases
- May be either infiltrative or focal
- Other metastatic fetal tumors exceedingly rare

Keywords

- Protocol advice
- Confirm mass is within liver
- Large renal, adrenal and retroperitoneal masses may be mistaken for liver tumors
- Careful Doppler analysis
- Significant vascularity with arteriovenous malformations favors hemangiendothelioma
- Follow-up scans
- Monitor site of tumor
- Development of hydrops
- In-utero treatment or early delivery may be considered if mass is rapidly growing and/or signs of impending cardiovascular compromise

Differential Diagnosis

Conditions Causing Hepatomegaly

- Most conditions cause splenomegaly as well as hepatomegaly
- Most tumors are well-defined liver masses (except leukemias)
- Large number of causes
- Nonimmune hydrops
- Skin edema
- Pleural/pericardial effusions
- Acute
- Hepatosplenomegaly
- Multitude of causes, including cardiac, multiple types of masses, cholangioleidal and placent
- Immune hydrops
- HIV/AIDS (HPV) immunocompromise
- Other autoimmune syndromes (Kelley-Duffy, C, E, and others)
- Splenomegaly may be prominent feature
- Infection
- Cytomegalovirus
- Toxoplasmosis
- Parovirus B19
- Gaucher disease
- Perinatal-lethal subtype
- Hepatosplennomegaly
- Hydrops
- Hypokinesia/arthrogryposis
- Ichthyosis
- Facial dysmorphism
- Prenatal testing available
- Beckwith-Wiedemann syndrome
- Macroglossia
- Nephromegaly
- Omphalocele
- Hepatosplennomegaly
- Predisposition to rhabdomyosarcoma

PATHOLOGY

General Features

- Genetics
  - Sporadic
  - 15-20% increased risk of leukemia in trisomy 21
- Epidemiology
  - Rare
  - <= 5% of fetal tumors occur in liver
  - Benign primary tumors (hemangiendothelioma, mesenchymal hamartoma) are more common than malignant ones (hepatoblastomas)
- Associated abnormalities
  - 10-15% of hemangiendotheliomas have hemangioendotheliomas elsewhere
  - Liver, spleen, cutaneous most common
- Leukemia associated with Down syndrome

Microscopic Features

- Intractile hemangiendothelioma
- Other autoimmune syndromes (Kelley-Duffy, C, E, and others)
- Splenomegaly may be prominent feature
- Infection
- Cytomegalovirus
- Toxoplasmosis
- Parovirus B19
- Gaucher disease
- Perinatal-lethal subtype
- Hepatosplennomegaly
- Hydrops
- Hypokinesia/arthrogryposis
- Ichthyosis
- Facial dysmorphism
- Prenatal testing available
- Beckwith-Wiedemann syndrome
- Macroglossia
- Nephromegaly
- Omphalocele
- Hepatosplennomegaly
- Predisposition to rhabdomyosarcoma
LIVER TUMORS

- Lesion composed of large endothelial-lined vascular channels
- Mesenchymal hamartoma
  - Large fluid-filled cysts
  - Loosely organized mesenchymal tissue containing small bile ducts
- Hepatoblastoma
  - Malignant tumor classified histologically as epithelial or mixed (epithelial + mesenchymal)
  - Leukemia
    - Acute myelogenous leukemia
    - Possibly due to defective granulocyte maturation
    - Erythroid peripheral leukocyte counts with circulating blasts

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - Large right upper quadrant mass
  - Hydrops
  - Fetal
  - Unexplained congestive heart failure
  - Pale/hypothermic

Natural History & Prognosis
- Variable according to histologic type
- Hemangioblastoma
  - Rapid, proliferative growth in first 6 months of life
  - Significant vascular shunting may lead to congestive heart failure
- Tumor commonly regresses and involutes after 6 months
- Hepatic endophytic hemangioma is benign and surgery is curative
  - Not always possible, depending on size and location of mass
- Hepatoblastoma
  - Malignant neoplasm
  - Poor prognostic for those diagnosed in perinatal period
- Leukemia
  - Variable spectrum of severity
  - Transient myeloproliferative disorder
  - Described in Down syndrome
  - May spontaneously resolve
  - Congenital leukemias may rapidly progress and be fatal
  - Much poorer prognosis than those presenting later in childhood

TREATMENT
- If diffuse hepatosplenomegaly consider concomitance
- Diagnosis of leukemia is based on white blood cell analysis
- Erythrotype of triose 21
- Pediatric surgery consult prior to delivery
- Delivery at tertiary care facility
- Consider cementan section
- Instillation, tumor rupture has been reported
- Hemangioblastomas
  - May not require treatment if asymptomatic
  - May spontaneously regress
- Corticosteroids first line of treatment
  - Thought to cause vasocstriction of aberrant vessels
- Corticosteroids have been successfully used in cases with rapidly growing masses
  - Both maternal administration and direct uterine vein injection have been described

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls
- Hemangioblastomas are most likely diagnostic for a vascular intraperitoneal mass
- Mesenchymal hamartoma is less likely diagnosis for a multicystic, cystic liver mass
- May be rapidly expanding
- Hepatic-blastomas are well-defined, solid masses, which may exhibit a "spoke-wheel" pattern of echogenicity
- Consider leukemia in setting of diffuse hepatosplenomegaly, especially if fetus has Down syndrome
- Metastatic neuroblastoma may cause either local liver mass or diffuse infiltration; diffuse infiltration may be difficult to diagnose

SELECTED REFERENCES

LIVER TUMORS

IMAGE GALLERY

Typical

(Left) Axial ultrasound of a heterogeneous hepatocellular carcinoma shows a large, irregular, heterogeneous mass (arrows) essentially replacing the liver. (Right) Axial ultrasound of the liver after ablation shows the area is very heterogeneous with a hypoechoic rim (arrow) and an irregular hypoechoic center (open arrow).

Typical

(Left) An anteroposterior radiograph in the same case shows diffuse intrahepatic biliary dilatation with periportal edema. Also note the dilatation in the right upper quadrant and displacement of bowel loops (arrows) by the enlarged liver. (Right) CT scan shows areas of fluid (arrows) and hemorrhage (open arrow). Histology confirmed a hepatocellular carcinoma. (All shown in Radiographics, ref 1).

Typical

(Left) Axial ultrasound of a metastatic hepatic lesion shows a large, heterogeneous mass (arrow) associated with the liver. No flow was seen in these cystic spaces. (Right) Cross-sectional pathology of the resected mass shows the typical large cystic spaces in a background of thornigonal myxoid stroma. (Also shown in Radiographics, ref 1).
SECTION 9: Genitourinary

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Terminology
Definitions
- Components of genitourinary system
  - Kidneys, ureters, bladder, urethra
  - Adrenal glands
  - Internal and external genitalia

Anatomy-Based Imaging Issues
Key Concepts or Questions
- Are there two kidneys?
  - Bilateral renal agenesis → anhydramnios → pulmonary hypoplasia → lethal anomaly
  - Unilateral renal agenesis → normal amniotic fluid volume → non-associated with pulmonary hypoplasia
- Must follow for contralateral reflux, uropelvic junction obstruction
- Is renal size and echogenicity normal?
  - Bilateral large kidneys
    - Autosomal recessive polycystic kidney disease (ARPKD)
    - BeckWith-Wiedemann Syndrome
    - Multicystic dysplastic kidneys (MCDK)
  - Unilateral large kidney
    - MCDK, mesoblastic nephroma
    - Increased renal echogenicity
    - ARPKD, cystic dysplasia
  - Are there obvious renal cysts?
    - Macroscopic cysts → MCDK, cystic renal dysplasia, autosomal dominant polycystic kidney disease
  - Are the ueters visible?
    - Normal ueters never seen sonographically
    - If ureters are dilated consider obstruction, reflux, primary megaureter
  - Is the bladder visible?
    - "Azerty" bladder most commonly due to failure of urine production
  - Some structural malformation prevent normal bladder development

Imaging Approaches
- Ultrasound (US)
  - Endovaginal scans useful in early gestation with low fluid
  - Kidneys can be identified by 12.14 weeks gestation
  - Internal architecture seen as early as 16-18 weeks
  - Hyperechoic medullary pyramids arranged symmetrically around renal sinus
  - Sezal sinus appears as fluid-filled "slit" in center of kidney
  - Cortex is thin in early gestation

- Soft tissue mass in midline, inferior to cord insertion
  - Bladder extrophy
  - Looks for bifid scrotum/penis with bladder/colon extrophy
- Is the bladder normal in size?
  - Should fill and empty during course of a scan
  - If bladder is too large
    - Posterior urethral valves, urethral atresia, prune belly syndrome

- Are the adrenal glands normal in morphology and position?
  - Normal adrenals have characteristic "ice-cream sandwich" appearance
  - Hypernephroma cortex → "sandwich"
  - Hyperechoic medulla → "ice-cream" filling
  - Normal adrenal is triangular or Yolched
  - Flat, "lying down" adrenal useful sign that kidney is not in renal fossa
  - Pseudocyst, enlarged adrenals seen in congenital adrenal hypoplasia (look for visualization of fetal testes)

- Unilateral adrenal mass has narrow differential diagnosis
  - Neuroblastoma
  - Adrenal hemorrhage
  - Extralobar sequestration

- Are the genitalia normal?
  - Anomalies genitalia seen in structural malformation sequences that affect bladder development, aneuploidy, syndromes
**Key Facts**

**Fetal Kidneys Have Little Impact On**

**Renal Fluid Volume < 16 Wks Gestation**
- Normal fluid volume in early pregnancy does not include significant renal pathology

**Bladder Should Be Visible On Every 2nd/3rd Trimester Scan**
- Fluid-filled structure that changes volume during scan
- Absent, evaluate cause
  - Lack of urine production
  - Look for renal anomalies, IUGR, TTTS
  - Structural malformation of bladder
  - Look for calcified meconium - mixing of urine with meconium - cloacal malformation, aneuploidy with fetus

- By 3rd trimester renal silhouette/perihepatic fat deposition → increased complexity
- Doppler ultrasound to identify renal arteries
- Amniocentesis a setting of oligohydramnios
- Fluid instilled around fetus to provide acoustic window for imaging
- Invasive: Modern approach is non-interventional use of MRI

- MRI
  - T2WI essential for evaluation of renal anatomy
  - Kidneys parenchyma intermediate in signal < fluid, > liver or muscle
  - Renal collecting system, bladder should contain high-signal urine
  - Adrenal glands seen best in later gestation, low signal similar to liver on T2WI
  - May be helpful in ovarian cyst evaluation
  - Cysts are high signal on T2WI, arise from adnexa
  - T1WI
  - Helpful to look at course of colon, return if concern for associated cephalic, bowel anomalies
  - May allow differentiation of adrenal hyalinosis (high signal blood products) from fetal megalohypotonia (intermediate signal)

**Imaging Protocols**
- American Institute of Ultrasound in Medicine guidelines
  - Document presence of kidneys/bladder in all 3rd/3rd trimester scans
  - Assess fluid volume
  - MRI
    - Very helpful when US visualization is limited
    - Oligohydramnios/oligohydramnios, large maternal body habitus
    - Lack of amniotic fluid less of an issue for MRI than for US

**Imaging Pitfalls**
- "Lying down" adrenals
  - Fetal adrenals are relatively large compared to kidney → mislead for kidneys
  - Adrenal hypertrophy described in renal agenesis
  - Adrenal/lumbar arteries confused with renal arteries
  - On color Doppler evaluation
  - Bladder pitfalls
    - No urine production → bladder not seen
    - It is anatomically present but not visible as fluid-filled structure, may contain mucous secretions
    - Renal agenesis, severe growth restriction (IUGR), discordant twin in twin-transfusion syndrome (TTTS)
    - Must see change in volume of fluid-filled structure to verify urine production
    - Beware other fluid-containing entities (e.g. ovarian, cyst, persistent cloaca)
  - Normal amniotic fluid does not always indicate normal renal function
  - Renal function has no significant impact on fluid volume before 16 weeks
  - Ambiguous genitalia
    - Gender determination important in X-linked conditions
    - Ambiguous genitalia associated with aneuploidy, syndromes

**Normal Measurements**
- Normative data available for renal size throughout gestation
  - Ratio of renal circumference to abdominal circumference stable throughout pregnancy
  - Normal pelvis AP diameter
    - < 4 mm at gestational age < 22 weeks
    - < 7 mm from 30 weeks to term
  - Largest collecting system concerning for obstruction or reflux
  - Infants need postnatal evaluation
    - Do not scan < 72 hours of age: Postnatal fluid shifts → dehydration → risk for underestimation of collecting system dilution
Embryology

Embryologic Events
-Renal development
  -Intermediate mesoderm → renal primordium
  -Mesonephros, metanephros
  -Urogenital sinus → urethra, urogenital plate
  -Ectopic vesical unclosed
  -Kidneys functional in 10 weeks
-Bladder development
  -Anterior cleft forms part of bladder neck, prostatic urethra
  -Bladder separated from rectum by urorectal septum

Adrenal development
-Neural crest cells → sympathoadrenal ganglia → adrenal medulla

Gonad development
-Primordial germ cells → genital ridges → primitive gonads
-Male/female differentiation occurs at 8th week
  -In male: Primitive gonad → testis, mesonephric ducts → vas deferens
  -In female: Primitive gonad → ovary, mesonephric ducts atrophy, paramesonephric (müllerian) ducts develop → fallopian tubes, uterus, superio vagina

External genitalia
-Cloacal folds fuse anteriorly → genital tubercle by 5th week

Clinical Implications

Clinical Importance
-Androblastoid cell fluid required for normal lung development
-Any cause of severe oligohydramnios carries poor prognosis
-Important to recognize conditions, which are definitely lethal e.g. renal agenesis, bilateral MCPD for proper counseling and pregnancy management

Related References
(Left) Axial ultrasound in a third trimester shows the typical "ice-cream sandwich" appearance of the adrenals (arrow). The cortex is hypoechoic and the medulla hyperechoic. This is quite different from the normal kidney. (Right) Coronal 12 MV MR shows the low signal, triangular adrenal (white arrow) superior to the kidney (black arrow) and medial to the stomach (curved arrow) and spleen (open arrow).

(Left) Axial oblique color Doppler ultrasound shows a normal bladder being flanked by the umbilical arteries (arrows). The bladder should change appearance during the exam, as it fills and empties. (Right) Coronal 12 MV MR shows a normal fetal bladder (open arrow) containing high signal urine. The liver (curved black arrow), spleen (black arrow), small bowel (curved white arrow) and lungs (white arrow) are well seen.

(Left) Axial ultrasound shows normal male genitalia with the penis (curved arrow) and scrotum (arrow) seen in an image obtained through the fetal pelvis. The open arrow indicates the bladder. (Right) Axial ultrasound shows the normal appearance of female genitalia. The labia create multiple parallel echos (arrows).
Renal developmental variants include unilateral renal agenesis (A), pelvic kidney (B), crossed fused renal ectopia (C) and horseshoe kidney (D). Errors of formation, fusion and ascent lead to these anomalies.

Renal ultrasonogram shows crossed renal ectopia with fusion. The left and right kidneys are fused and form a bladed single kidney (arrow). In this case, the right kidney has crossed and fused with the left.

**TERMINOLOGY**

- **Definitions**
  - Causes of developmental variants
  - Absent renal tissue
  - Icteric renal tissue
  - Abnormal fusion
  - Abnormal ascent
  - Unilateral renal agenesis
  - One kidney does not form
  - Pelvic kidney
  - Kidney located in pelvis
  - Horseshoe kidney
  - Kidneys fused in horseshoe configuration
  - Lower > upper pole fusion
  - Isotamix = bridging tissue
  - Crossed renal ectopia
  - Both kidneys on one side
  - 95% of cases are fused. Crossed fused renal ectopia

**IMAGING FINDINGS**

- **General Features**
  - Best diagnostic clue
  - Empty renal fossa
  - Abnormal renal morphology
  - Location

**DDx: Poorly Visualized Kidneys**

- Oligohydranmios
- Prominent Adrenal
- Cystic Dysplasia
- Mesoblastic Nephroma

- **Left > right**
  - 57% empty renal fossa on left

**Ultrasonographic Findings**

- Unilateral renal agenesis
  - Empty avascular fossa
  - Best seen on axial view
  - Confirmed on longitudinal view
  - Compensatory renal hypertrophy
  - Normal kidney compensates for absent kidney
  - Size > 95th percentile
  - Seen in 44% of cases, as early as 22 weeks
  - Color Doppler confirms diagnosis
  - Coronal acta view
  - Absent renal artery
  - Adrenal gland lies empty renal fossa
  - "Laying down" appearance
  - Globular instead of triangular
  - Can mimic kidney
  - Colon in empty renal fossa may mimic kidney
  - Pelvic kidney
  - Empty renal fossa
  - Kidney in fetal pelvis
  - Located superior to bladder
  - Often difficult to see
  - Echogenicity similar to bowel
  - Contralateral kidney is normal-sized
  - No compensatory hypertrophy
RENAL DEVELOPMENTAL VARIANTS

Key Facts
- Renal cystic dysplasia
- Renal agenesis

Imaging Findings
- Empty renal fossa
- Abnormal renal morphology
- Adrenal gland fills empty renal fossa
- Look for pelvic veins if one kidney missing
- Use color Doppler to find renal arteries
- Consider MRI if visualization is limited

Top Differential Diagnoses
- Normal adrenal gland
- Severe oligohydramnios (normal kidneys)

- Color Doppler brain
- Fellows renal artery to pelvic kidney
- Adrenal gland in renal fossa
- Horsehoe kidney
- Kidney lower poles connected by ischium
- Parenteral or fibrous connection
- Ischium is anterior to aorta
- Seen best on axial and coronal views
- Kidneys more inferior than normal
- Ischium "snag" on inferior mesenteric artery during ascent
- Malrotation common
- Median deviation of lower poles
- Anteriorly directed extra-renal pelvis
- Uppper pole fusion is rare variant
- Inverted horsehoe morphology
- Associations
- Turner syndrome
- Trisomy 18
- Other genitourinary anomalies
- Crossed renal ectopy
- Icteric kidney located in opposite flank
- 95% are fused
- Left passes to right most often
- Large bifid kidney
- One renal fossa is empty
- Other contains atypical lage kidney
- Color Doppler
- 2 renal arteries
- One normal and one low
- Associations
- Vertebra segmental anomalies
- Scoliosis
- Spina bifida
- Causes of unilateral empty renal fossa
- Unilateral renal agenesis (51%)
- Pelvic kidney (37%)
- Horsehoe kidney (5%)
- Crossed renal ectopia (4%)

MR Findings
- May be modality of choice with oligohydramnios
- Useful for differential diagnosis

MR Findings
- Large field-of-view
- Better able to find pelvic kidney
- Improved contrast in some cases
- Fibrous ischium of horseshoe kidney
- Pelvic kidney vs. power

Imaging Recommendations
- Test imaging tool
- Careful assessment of renal fossa
- Axial and longitudinal views
- Renal morphology assessment
- Look for fusion
- Protocol advice
- Look in fetal pelvis if one kidney missing
- Use color Doppler to find renal arteries
- Consider MRI if visualization is limited
- Look at renal orientation on coronal view
- Horseshoe kidney low poles point medial

DIFFERENTIAL DIAGNOSIS

Normal adrenal gland
- Prominent in early 2nd trimester
- May be mistaken for kidney
- Globular morphology if kidney absent
- Laying down" adrenal
- Long axis parallel to spine

Severe oligohydramnios (normal kidneys)
- Poor visualization in utero agenesis
- Consider MRI
- Color Doppler
- Identify renal arteries
- Amniocentesis
- Sajnol placed in uterus
- Improve visualization for safe of diagnosis

Renal cystic dysplasia
- Multifacial etiology
- Obstructive
- Multicystic dysplastic kidney
- Aneuploidy
RENAL DEVELOPMENTAL VARIANTS

- Syndromic
  - Oligo results in small kidney
  - May mimic renal agenesis
- Acute cystic dysplasia with bizarre morphology
  - Liver, renal, or complex anomalies
- Minicysts fused kidneys

Renal or adrenal mass
- Rare in prenatal life
- Mesoblastic nephroma most common
  - Solid, large, heterogeneous mass
  - Distinct margins
- Neuroblastoma
  - Arterial mass
  - Displaces normal kidney inferiorly

PATHOLOGY

General Features
- Genetics
  - Aneuploidy/syndromes common in other anomalies
  - Turner syndrome
  - Horsehoe kidney + other anomalies
- Embryology
  - Normal renal embryology
  - Kidneys arise from mesonephric blastema (MB)
  - MB develops on either side of dorsal body wall
  - Ureteric bud (UB) arises from mesonephric duct
  - UB penetrates MB + induces kidney formation
  - UB divides into collecting system and ureter
  - Kidney develops at 6-9 wks
  - Kidneys function by 10 wks
  - UB fails to reach MB
  - Renal agenesis
  - Failure/poor ascent
  - Pelvic kidney
  - Horsehoe kidney
  - Fusion of MB
  - Crossed fused ectopia
  - Horsehoe kidney
  - MB or UB cross median
  - Ectopic kidney
- Epidemiology
  - M > F
  - Horsehoe kidney
  - 1:400 in general population
  - Pelvic kidney
  - 1:700
  - Unilateral renal agenesis
  - 1:1,000
  - Crossed renal ectopia
  - 1:17,000

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - Isolated anomaly
  - Incidentally noted during antenatal survey
  - Often associated with other anomalies
  - Other signs/symptoms
    - Oligohydramnios
  - Suggests bilateral process
  - Anomaly + obstruction

Natural History & Prognosis
- Long term complications
  - Infection
  - Obstruction
  - Stones
  - Vesicoureteric reflux
- Uralate renal agenesis
  - 1: Renal insufficiency and proteinuria
  - 2: 50% develop hypertension as adults
  - Horsehoe kidney
  - Excellent prognosis when isolated
  - Often with other genitorinary anomalies
    - Hypoplasia/cryptorchidism
    - Duplex collecting system

Treatment
- Postnatal ultrasound to confirm diagnosis
  - Include uroeters in females
  - Urinary anomalies associated with renal anomalies, especially renal agenesis
  - Treat for complications

DIAGNOSTIC CHECKLIST

Image Interpretation
- Pearls
  - Empty renal fossa is not always renal agenesis
  - Look for pelvic kidney
  - Look on opposite side for ectopic kidney
  - Horsehoe kidney may be missed if thighs are thin
  - Better clue may be lower pole medially orientation
  - Routinely obtain longitudinal views of kidneys
  - Adrenals minic kidney on axial views
  - Measure normal kidney if only one kidney found
  - Compensatory hypertrophy suggests agenesis
  - Normal bladder/anatomic (fluid important prognostic indicators)

SELECTED REFERENCES


**Typical**

- **Left**: Axial ultrasound through the right flank shows a single kidney (arrows). Open arrow points to the kidney. A causal vessel for a second kidney missed.
- **Right**: Coronal oblique ultrasound shows a second kidney in the pelvis (arrows) above the partially healed lateral fission area. fission kidneys are often difficult to see and the term may be misdiagnosed as having only one kidney.

**Typical**

- **Left**: Coronal oblique ultrasound shows a horseshoe kidney (arrows). The inferior portion of the kidneys are connected by an inflexion (open arrow) of renal pelvis. These kidneys are also dysgenic from a curve dystasia, and the term had no high other anomalies as well. **Right**: Coronal gross pathology view shows the horseshoe morphology. The anterior (arrows) gave mentally and travel anterior to the aorta.

**Typical**

- **Left**: Axial ultrasound shows one kidney (arrows). Pelvic ultrasound of the pelvis shows a duplicated stroma (open arrow) with three endobulbar vena. 

- **Right**: Coronal ultrasound (Piptil ultrasound shows unilateral renal agenesis. Only one way other (arrows) arises from the body. Open arrow points to the single kidney.
DUPLICATED COLLECTING SYSTEM

TERMINOLOGY

Definitions
- Renal collecting system split into separate upper and lower pole moieties

IMAGING FINDINGS

General Features
- Best diagnostic clue: Dilatation of upper pole collecting system + ureteroceles is diagnostic
- Upper and lower pole moieties separated by band of renal parenchyma
- Two separate ureters drain upper and lower poles
  - Upper pole drained by ectopic ureter
  - Ureteroceles usually present at distal end
  - Ureter often dilated from obstruction
  - Lower pole drained by normotopic ureter
  - Ureterosigmoidoscopy of normotopic ureter distended by ectopic ureteroceles
  - Vesicoureteral reflux may occur
- Cranial association in 10-20%
- Weigert-Meyer rule
  - Ectopic ureter inserts inferior and medial to normotopic ureter, in trigone of bladder
  - Upper pole obstructs
  - Lower pole refluxes

Ultrasoundographic Findings
- Kidney
  - Asymmetric renal size
  - Affected kidney larger than contralateral side
  - Unilateral renal enlargement may be only clue that duplication is present
  - Dilatation of upper pole collecting system
  - May appear "cyst-like"
  - Reflux can intermittently dilate lower pole
  - Severe obstruction may result in dysplastic changes
  - Upper pole parenchyma may be replaced with large cysts that displace lower pole
  - Cysts may shrink over time - kidney starts to appear more normal
- Ureters
  - Often dilated
  - Ectopic: Dilated from obstruction
  - Normotopic, may be dilated from reflux
  - Ectopic ureter: Most commonly inserts into bladder
  - Extravesical insertion sites also possible
  - Ejaculatory ducts
  - Vas deferens
  - Epididymis
  - Seminal vesicles
  - Uterus
  - Vagina
  - Urethra (least common)

DDx: Renal Duplication

UPI Obstruction
Vesicoureteral Reflux
Mesodermal Nephroma
Multicystic Dysplastic
DUPLICATED COLLECTING SYSTEM

Terminology
- Renal collecting system split into separate upper and lower pole moieties

Imaging Findings
- Best diagnostic clue: Dilatation of upper pole collecting system + ureteroecele is diagnostic
- Upper and lower pole moieties separated by band of renal parenchyma
- Upper pole drained by ectopic ureter
- Lower pole drained by nonmotopic ureter
- Ectopic ureter inserts inferior and medial to normal ureter, in trigone of bladder
- Evaluate kidney in both transverse and longitudinal planes
- Transverse views alone can lead to erroneous diagnosis of ureteropelvic junction (UPJ) obstruction

Bladder
- Ureteroecele associated with ectopic ureter
- Ureteroecele + thin-walled, "balloon-like" structure in bladder
- Obstetric
- May cause bladder outlet obstruction
- May obstruct contralateral kidney
- May prolapse in and out of bladder
- Oligohydramnios can occur if ureteroecele obstructs bladder outlet

Imaging Recommendations
- Protocol advice
  - Always search for other signs of duplication in presence of hydronephrosis
  - Normal lower pole moiety
  - Asymmetric renal size
  - Dilated ureter(s)
  - Ureteroecele
- Evaluate kidney in both transverse and longitudinal planes
  - Transverse views alone can lead to erroneous diagnosis of ureteropelvic junction (UPJ) obstruction
  - Lower pole moiety may be displaced inferiorly and difficult to see
  - Measure length
  - > 95% for gestational age
- Evaluate bladder: several different times during study
  - Ureteroecele may be misinterpreted as bladder; if bladder is empty
  - Distended bladder may compress ureteroecele
- Follow collecting system in realtime
  - Renal pelvis -> ureter -> ureteroecele
- Whenever one anomaly found, look for others
- Contralateral renal malformation
- May change prognosis and management
- Multiple anomaly syndrome (e.g., VACTERL sequence)

Key Facts

Top Differential Diagnoses
- Ureteropelvic junction (UPJ) obstruction
- Reflux

Pathology
- Gynecological abnormalities in 50% of affected females

Clinical Issues
- Excellent prognosis with early correction
- In utero treatment not usually indicated
- Complete work-up after delivery

Diagnostic Checklist
- Always evaluate for duplication in presence of hydronephrosis (unilateral or bilateral)

DIFFERENTIAL DIAGNOSIS

Ureteropelvic junction (UPJ) obstruction
- Pelvis dilated
- Uterus not seen
- No ureteroecele

Reflux
- Entire collecting system dilated
- No ureteroecele
- Findings may vary between scans

Simple ureteroecele
- Simple ureteroecele insert in normal location
- Not associated with renal duplication
- Not usually seen in utero

Congenital Megaureter
- Upright dilatation of ureter
- Hydronephrosis variable
- Usually unilateral (left > right)
- May affect males
- Nonsmaller bladder

Other causes of renal enlargement
- Multicystic dysplastic kidney
- Mesoblastic nephroma
- Beckwith-Wiedemann syndrome
- Associated with omphalocoele, macrocephaly
- Autosomal recessive polycystic kidney disease
- Bilateral, cystic kidneys

PATHOLOGY

General Features
- Genetics: Sporadic
- Etiology
  - Duplication with ectopic ureteroecele
    - 1:9,000 live births
    - Duplication without ureteroecele (partial, incomplete)
**DUPLICATED COLLECTING SYSTEM**

- Ureters, join into single ureter before bladder insertion
- 1:3:50 in general population
- Not statistically significant
- Incidence of ureteroceles parallels that of duplication
- Associated abnormalities
  - Gynecological abnormalities in 50% of affected females
  - Renal anomalies (including duplications) are commonly present with other anomalies
- Embryology
  - Accessory ureteric bud inserts separately into metanephric blastema
  - Unusual bud divides or duplicates prematurely

**CLINICAL ISSUES**

**Presentation**
- Most common signs/symptoms: Usually incidental finding at routine 2nd trimester ultrasound
- Other signs/symptoms: Evaluation of hydrouretonephrosis

**Natural History & Prognosis**
- Progress depends on degree of renal damage from reflux and obstruction
- Prenatal diagnosis decreases risk of urosepsis and renal damage
- Obstructed upper pole moiety prone to infection due to urine stasis
- When diagnosis is known prophylactic antibiotics administered from birth
- Decrease rate of intrauterine tract infection
- Improved outcome with prenatal vs. postnatal diagnosis
- Much lower incidence of perioperative infection
- Much lower recurrent infection after correction
- Higher rate of resolution with reflux
- Younger age at correction
- Early surgical intervention preserves renal function
- Excellent prognosis with early correction
- If not diagnosed in utero, duplication with obstruction/reflux usually presents in infancy
- Recurrent urinary tract infections
- Urinary retention
- Unsuccessful toilet training in girls, epididymitis in boys
- From ectopic insertion

**Treatment**
- In utero treatment not usually indicated
- Consider excision of ureteroceles if causing bladder outlet obstruction and oligohydramnios
- Complete work-up after delivery
- Urology consult
- Ultrasonogram of kidneys and bladder
- Volding cystourethrogram (VCUG) to visualize dynamic nature of uretercele
- "Dropping Bly" sign on VCUG
- Reflux into lower pole moiety via nonanatomic ureter
- Obstructed upper pole moiety pushes lower pole calyces inferiorly

- Radioisotope scan to assess renal function
- Intravenous pyelogram not usually necessary
- Delayed nephrogram and pyelogram of upper pole moiety due to obstruction
- Helpful to evaluate extravesical ureteric urethral insertion sites
- MRI
  - May be helpful in complex cases
  - Used in females to evaluate associated gynecological abnormalities
- Potential surgical options based on severity of abnormality
  - Endoscopic incision of ureteroceles
  - Particularly if severe obstruction
  - May convert obstructing ureterocoele into refluxing one
  - Uretal reimplantation
  - Ureteroureterostomy
  - Ureteropyelostomy
  - Mitral pyeloureterostomy
  - Performed if poorly functioning upper pole

**DIAGNOSTIC CHECKLIST**

**Consider**
- Always evaluate for duplication in presence of hydrouretonephrosis (unilateral or bilateral)
- Prenatal MR in females to search for associated gynecological malformations

**Image Interpretation Pearls**
- Dilated upper pole moiety + cystic mass in bladder is diagnostic for duplication = ureterocoele
- Majority of duplicated kidneys are > 95th percentile in length

**SELECTED REFERENCES**
(Left) Coronal oblique view of a renal duplication shows bifid ureteropelvis at the upper pole moiety (arrow). There is mild calicectasis in the lower pole (open arrow). This finding should prompt a search for an associated ureteroceles. (Right) Axial ultrasound shows a ureteroceles as a thin-walled, cystic lesion (arrow) within the lateral aspect of the bladder.

(Left) Ultrasound shows dilatation of the upper calyces (arrow), which prompted a careful evaluation of the bladder via a ureteroscopy (curved arrow) was inserted. (Right) Axial image through the upper pole of the kidney (arrow) shows dilatation of the calyces (calipers). This could easily be mistaken for a UPJ obstruction unless longitudinal views are obtained. A coronal view (bottom) shows a duplicated kidney (calipers).

(Left) Coronal oblique view shows marked dilatation of the upper pole moiety (arrows), discordance the minimally dilated lower pole (open arrows). The lower pole may not be visible if upper pole hydronephrosis is severe. (Right) Coronal view (arrows) shows severe parenchymal thinning in the upper pole (arrows). This obstruction with mild dilatation of a lower pole calyces (open arrows).
MILD PELVIECTASIS

Terminology
Abbreviations and Synonyms
- Mild pelviectasis (MP)
- Pyelectasis
- Transient hydronephrosis

Definitions
- Renal pelvis distended with urine

Imaging Findings

General Features
- Best diagnostic clue
  - Enlarged fluid-filled renal pelvis
  - No collection (distention of renal calyces)
  - Renal pelvis diameter (RPD) > 4 mm (2nd trimester)
    - RPD > Anteroposterior (AP) diameter of pelvis
    - RPD > 7 mm (3rd trimester)
  - Location
    - Most often bilateral
    - R > L when unilateral

Imaging Findings
- Normal 2nd/3rd trimester kidney
- Echogenicity
- Renal parenchyma initially homogeneous

DDx: Hydronephrosis

- Hyperechoic pyramids can mimic caliectasis
- Echogenic renal hilum
- Transverse kidney view
- Axial view through spine and flank
- Two symmetric kidneys easily seen
- Best view to measure RPD
  - Normal RPD < 3 mm
  - Longitudinal views
- Sagittal and coronal kidney views
- Best view to rule out caliectasis
- Can measure renal length
- Renal vessels at hilum can mimic pelviectasis
- Color Doppler helpful

- Mild pelviectasis
  - Fluid-filled renal pelvis
    - "Ballooned" renal pelvis
  - Measure RPD on x-ray image
  - Longitudinal views helpful
  - Rule out hydronephrosis
  - Look for distended ureter

- Ultrasound criteria for MP diagnosis
  - RPD should not measure > 8.28 renal diameter
    - > 3 mm in first trimester
    - > 4 mm at 14-22 wks
    - > 5 mm at 22-32 wks
    - > 7 mm after 32 wks
    - > 10 mm always pathologic
MILD PELVIECTASIS

**Key Facts**

- **Top Differential Diagnoses**
  - Hydroureteric junction (UPJ) obstruction
  - Lower tract obstruction
  - Renal hilum vessels

- **Pathology**
  - 0.46% fetuses with isolated MP have aneuploidy

- **Clinical Issues**
  - Prognosis depends on degree of pelviectasia
  - Postnatal follow-up if RPD > 7 mm after 32 wks

- **Diagnostic Checklist**
  - Most cases of MP are transient and idiopathic
  - Postnatal work-up essential if MP persists/progresses
  - Increased risk of subsequent fetus also having MP

- **Protocol advice**
  - Rule out hydronephrosis when MP is seen
  - Look carefully for caliectasis
  - Look for distended ureter
  - Look for normal bladder filling and emptying
  - Follow-up ultrasound
  - Repeat scan in 4 weeks to look for progression
  - Some progress to hydronephrosis and require postnatal evaluation
  - Look for additional anomalies
  - At time of diagnosis and at follow-up
  - Consider amniocentesis
  - Determine maternal risk for aneuploidy

**DIFFERENTIAL DIAGNOSIS**

- **Urateropic junction (UPJ) obstruction**
  - Obstruction at junction of ureter and renal pelvis
  - Most common cause of congenital hydronephrosis
  - Renal pelvis distention
  - May be massive
  - Calyceal distention variable
  - Rarely presents early as MP

- **Lower tract obstruction**
  - Ureter distention
  - Ureterovesical junction obstruction
  - Duplex collecting system
  - Ureteral breech
  - Lower pole with reflux
  - Bladder outlet obstruction
  - Markedly distended bladder
  - Posterior urethral valves (PUV)
  - Signet-shaped hydronephrosis
  - +/- Ureteral distention
  - +/- Renal cystic dysplasia
  - Urethral atresia
  - Rarely presents initially as MP

- **Renal hilum vessels**
  - Renal artery and vein
MILD PELVIETASI S IS

Treatment
- Postnatal follow up if BPD > 7 cm after 32 wks
- Follow-up ultrasound
  - Not earlier than 72 hrs after birth
  - Neonatal dehydration minimizes obstruction
  - Voiding cystourethrogram
  - Rule out reflux
  - Renal nuclear medicine scan may be considered to assess function
  - Obstructive lesions often need surgical intervention

DIAGNOSTIC CHECKLIST
Consider
- Assess maternal risk for aneuploidy
  - Maternal age
  - Serum screening biochemistry results

Image Interpretation Pearls
- Most cases of MP are transient and idiopathic
- Measure BPD when fetal bladder is empty
- Some cases of MP are associated with aneuploidy
- Determine if MP is isolated finding
- Determine maternal risk profile
- Use "hyperdysplasia" term sparingly
- Renal pelvis ± calyceal distention
- Often obstructive process
- Any amount of caliectasis is abnormal
- May suggestive of obstruction than MP alone
- Follow-up antenatal ultrasound after 32 wks
- Postnatal work-up not necessary if BPD < 7 mm
- Reduce number of postnatal tests
- Postnatal work-up essential if MP persists/progresses
- Renal function preservation depends on early diagnosis of renal obstruction/reflux
- Increased risk of subsequent fetus also having MP

SELECTED REFERENCES
MILD PELVIECTASIS

IMAGE GALLERY

Typical

(Left) Axial ultrasound shows bilateral, mild pelvicactas in a fetus with normal chromosomes. The kidneys are located on either side of the spine (open arrows) and the fluid-filled renal pelvis (arrow) is easily seen.

(Right) Sagittal ultrasound confirms that only the renal pelvis (arrow) is dilated. Hypoechoic renal pyramids (solid arrows) should not be confused with calyceal distention.

Typical

(Left) Axial ultrasound shows second trimester isolated mild pelvicactasis (arrow). Follow-up ultrasound was recommended.

(Right) Axial (upper) and sagittal (lower) images at 35 weeks shows the right UPJ resolved (curved arrows) but the left progressed to hydronephrosis. The left renal pelvis (arrows) and calyces (open arrows) are clearly dilated. Postnatal ultrasound confirmed hydronephrosis from UPJ obstruction.

Typical

(Left) Axial ultrasound shows mild pelvicactasis (arrows) in a fetus with trisomy 13. The kidneys are also slightly enlarged and echogenic.

(Right) Sagittal ultrasound of the face in the same fetus shows a premaxillary "straw" (arrows) secondary to bilateral cleft lip and palate. A cardiac anomaly was also seen, although no 6p is associated with trisomy 13. It is almost never as isolated finding.
**TERMINOLOGY**

**Abbreviations and Synonyms**
- Ureteropelvic junction (UPJ) obstruction
- Pelviureteric junction obstruction
- Congenital hydronephrosis

**Definitions**
- Renal pelvis obstruction
  - At point where pelvis meets ureter

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue: Hydronephrosis without hydronephrosis or bladder dilatation
- Location: 10% bilateral

**Ultrasoundographic Findings**
- Moderate to severe hydronephrosis
- Dilated renal pelvis
- Hydronephrosis
- Central renal fluid collection
- Can become massive
- Caliectasis
- Disoriented renal calyces
- May appear cyst-like

**DDx: Hydrourephrosis**
- Calyces connect with renal pelvis
- Seen best on sagittal views
- Enlarged kidney
- Flap fold length
- +/- Cortical thinning
- Distention ends abruptly at UPJ
- Blurred or ‘bullet shaped’ renal pelvis
- Seen best on coronal view
- Normal ureters
- < 5 mm, if seen at all
- Normal bladder if UPJ obstruction is unilateral
- Rises and empties every 20–30 minutes
- Thin wall
- Small or absent bladder with bilateral UPJ obstruction
- Renal pelvis measurement
  - Kidney imaged in transverse plane
  - Renal pelvis anteroposterior (AP) diameter
  - Renal pelvis AP diameter, diagnostic criteria
- Vanish numbers given in literature
- $\geq 10$ mm always considered abnormal
- $\geq 7$ mm after 33 weeks needs follow-up
- $\geq 4$ mm before 20 weeks needs follow-up
- Renal pelvis/kidney ratio $>3.28$
- Caliectasis abnormal, regardless of AP diameter
- Secondary renal dysplasia
- Obstruction causes renal damage
- Renal echogenicity
URETEROPELVIC JUNCTION OBSTRUCTION

Terminology

- Congenital hydronephrosis

Imaging Findings

- Most diagnostic clue: Hydronephrosis without hydronephrosis
- Distention ends abruptly at UPJ
- Bilateral UPJ obstruction in 10%
- Contralateral renal abnormality in 25%
- Extrarenal anomalies in 10%
- Polyhydramnios in 1/3
- Hydroureteronephrosis if obstruction is bilateral and severe

Top Differential Diagnoses

- Multicystic dysplastic kidney (MCDK)
- Bladder or ureter obstruction
- Mild renal pelviectasis

Key Facts

- Normal renal pyramids

Pathology

- Isolated UPJ obstruction not associated with aneuploidy
- 1/3 of UPJ obstructions have an accessory crossing vessel
- 1,200 live births

Clinical Issues

- Overall excellent prognosis
- Risk of renal impairment if prenatal AP diameter > 10 mm
- Ultrasound > 72 hrs after delivery
- Prenatal intervention rarely indicated

Diagnostic Checklist

- UPC obstruction often progressive

Differential Diagnosis

- Multicystic dysplastic kidney (MCDK)

- Kidney tissue replaced by cysts
  - Cysts do not communicate
  - Renal parenchyma often lost
  - Large kidney in fetal life
  - Atrophy with time
  - May be sequelae of early obstruction
  - Poor or absent renal function
  - "Hydronephrotic form" of MCDK can mimic UPJ obstruction

- Large central cyst < cortical cysts
- Cysts do not communicate

Bladder or ureter obstruction

- Distended ureter
  - Serpiginous, redundant morphology
  - Can mimic MCDK or hydronephrosis
- Ureterovesicle junction obstruction (UVJ)
- Duplication ureter
  - Superior ureter with ureterocele
  - Inferior ureter with reflux
  - Vesicoureteral reflux
  - Diagnosis rarely made prenatally

Bladder outlet obstruction

- Enlarged bladder
- Often thick-walled
- Posterior urethral valves
  - "Key-holed" morphology
  - Unusual urethra
- Variable degrees of hydronephrosis

Mild renal pelviectasis

- Mild renal pelvis distention in 2nd trimester
  - > 4 mm before 22 wks
  - Often bilateral
  - No calyceal distention
  - Often idiopathic and non-obstructive
  - Seen in 2-3% of prenatal cases
URETEROPELVIC JUNCTION OBSTRUCTION

- Minor marker for aneuploidy
- Trisomy 21 most often
- Look for other markers/neoplasms
- Abnormal renal tracts in low-risk patients
- May progress to UPJ obstruction
- Follow-up ultrasound

Normal renal pyramids
- Hypoechoic parenchymal structures
- Titanium more than round
- Can mimic hydronephrosis
- Do not coalesce with calyces
- Pyramids superficial to calyces
- Pyramid "point" ends in calyx

PATHOLOGY

General Features
- Genetics
  - Sporadic
  - Isolated UPJ obstruction not associated with aneuploidy
- Urology
  - Abnormal interwoven muscularis layer of wall
  - Impairs distensibility
  - 2nd to crossing vessel
  - 1/3 of UPJ obstructions have an accessory crossing vessel
  - Vessel lies anterior to UPJ
  - Perhaps waves fibrous scar
  - Abnormal neural innervation at UPJ
  - "Hitchsprunl equivalent"
- Epidemiology
  - 1:2,000 live births
  - M:F
  - Associated abnormalities
    - 25% with contralateral renal anomaly
    - 10% with bilateral UPJ obstruction
    - 10% with non-genitourinary anomalies

Gross Pathologic & Surgical Features
- Junction of pelvis with ureter usually patent
- Complete atresia

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - Incidental finding
  - In association with contralateral renal anomaly
  - In association with amniotic fluid abnormality

Natural History & Prognosis
- Overall excellent prognosis
- Risk of renal impairment if prenatal AP diameter > 10 mm
- Factors associated with poor prognosis
  - Bilateral renal anomalies
  - Early oligohydramnios
  - Pulmonary hypoplasia
  - Other non-genitourinary anomalies
  - Postnatal symptoms
- Abdominal mass
- Urinary tract infection
- Hematuria
- Abdominal or flank pain
- Neonatal work-up
  - Ultrasound < 72 hrs after delivery
  - Nuclear medicine renal scan for renal function
  - Voiding cystourethrogram to evaluate for reflux
  - CT angiography
  - Look for crossing renal artery
  - Failing treatments affect plan
  - Replaced digital subtraction angiography

Treatment
- Prenatal intervention rarely indicated
- Corrective surgery if renal function impaired
- Pyeloplasty
- Open surgery
- Resection of narrow UPJ segment
- Endopyelotomy
- Must know if crossing vessel present
- Perioperative drainage
- Temporizing measure
- Infection control
- Postnatal follow-up
- Pelviectasis persists for years
- Even with successful surgery
  - Follow renal growth
  - Suggests successful therapy
- Nuclear medicine renal scans
  - Assess renal function
  - Assess renal drainage

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls
- Severe UPJ obstruction may look like renal cyst
- Document that "cyst" connect with renal pelvis
- Obtain follow-up ultrasound
- UPJ obstruction often progressive

SELECTED REFERENCES
URETEROPELVIC JUNCTION OBSTRUCTION

IMAGE GALLERY

Typical

(left) Coronal ultrasound shows bilateral UPJ obstruction. The renal poles (arrows) communicate with the calyces (open arrows). In this case, the acoustic field volume was normal. UPJ obstruction is bilateral in 10% of cases. (right) Coronal CT urography shows obstructive renal bands at the UPJ (arrows). In a child with bilateral hydronephrosis, typical UPJ obstruction is not complete.

Typical

(left) Axial ultrasound shows severe UPJ obstruction presenting as an abdominal cyst. With careful scanning, "kinking cysts" representing calyces can often be seen. (right) Axial CT shows severe UPJ obstruction in the renal sinus. There is marked distention of the renal pelvis (arrows) and calyces (open arrows) as well as significant renal cortical thinning.

Typical

(left) Axial ultrasound shows a fetal cystic lesion (arrow) of one kidney and cystic dysplasia of the other (open arrows point to the echogenic cystic kidney). The bladder (curved arrow) is empty, and there is oligohydramnios. (right) Parasagittal radiograph shows mass effect from the dilated renal pelvis (arrows) and lateral pneumaturia (open arrow) from pulmonary hypoplasia. The presence of early severe oligohydramnios is a bad prognostic sign.
OBSTRUCTIVE CYSTIC DYSPLASIA

TERMINOLOGY

Abbreviations and Synonyms
- OBSCUTrive cystic dysplasia (OCD)
- Cystic renal dysplasia
- Obstructive urethropy
- Potter type IV

Definitions
- Genitourinary tract (GU) obstruction → renal cysts

IMAGING FINDINGS

General Features
- Best diagnostic clue
  - Renal macronodules + GU obstruction
  - Hydronephrosis, hydroureter, bladder distension
- Location
  - Unilateral
  - Bilateral
  - Segmental (rare)
  - From obstruction of duplicated uroter
- Morphology: Reniform shape maintained

Ultrasoundographic Findings
- Renal cyst;
  - Variable number of cysts

- None to few cysts
- Kidney completely replaced by cysts
- Variable-sized cysts
- Many small cysts
- Few large cysts
- Cortical cysts common
- "Biliary" beads
- Subcapsular cyst
- Interferring renal parenchyma often discernible
- Kidney maintains reniform shape
- Cortical echogenicity often increased
- Microscopic cysts
- Renal dysplasia
- Renal size may be 1, 1, or normal
- Enlarged kidneys
  - Associated hydronephrosis
  - Large cysts
  - Small kidneys
- Long-standing obstruction
  - Often diffusely echogenic
- Urethral obstruction
  - Distended bladder is cardinal finding
  - +/- Bladder wall thickening
  - +/- Hydroureter
- Cystic kidneys
  - Small or large
  - +/- Hydronephrosis
  - Common causes

DDx: Renal Cysts And Mimics

- MCCK
- MCDK
- UPI
- Normal Pyramids
# OBSTRUCTIVE CYSTIC DYSPLASIA

## Terminology
- Cystic renal dysplasia
- Renal macrocysts + GU obstruction
- Intrarenal cysts common
- Intervening renal parenchyma often discernible
- Severe OCD from early obstruction
- Bilateral may show OCD development
- Bilateral OCD → oligohydramnios

## Differential Diagnoses
- Multicystic dysplastic kidney (MCDK)
- Hydroureter
- Renal cystic dysplasia 2nd to aneuploidy/syndromes

<table>
<thead>
<tr>
<th>Key Facts</th>
<th>Pathology</th>
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<tbody>
<tr>
<td>* Unilateral process with normal fluid</td>
<td></td>
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<tr>
<td>* Bilateral OCD → oligohydramnios</td>
<td></td>
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<tr>
<td>* Depends on severity of obstruction</td>
<td></td>
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<tr>
<td>* Kidney function</td>
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## Imaging Recommendations
- Look carefully for OCD when GU obstruction seen
- Renal views
- Longitudinal
- Transverse
- Measure anterior-posterior diameter of renal pelvis
- Adequate bladder imaging
- Size
- Wall thickness
- Voiding
- Sequential ultrasound necessary
- OCD may develop during pregnancy
- Assess amniotic fluid objectively
- Follow amniotic fluid index
- Sex determination for PUV
- Males only

## DIFFERENTIAL DIAGNOSIS

### Multicystic dysplastic kidney (MCDK)
- Renal tissue replaced by cysts
  - From ureter/vesicovasal bypass atresia
  - < 10 weeks gestation
  - Kidney/loops nephrostomy
- Associated ureter/bladder dilatation not seen
- Helps differentiate from OCD
- 95% without renal function
- Survival depends on function of contralateral kidney
- 20% bilateral MCDK
- 40% with contralateral renal anomaly

### Hydroureter
- Renal collecting system distention
  - UFI obstruction most common cause
  - Distended calyces may appear "cyst-like"
- Calyces connect with renal pelvis
- Longitudinal views best


**OBSTRUCTIVE CYSTIC DYSPLASIA**

- Severe UPI obstruction often associated with OMD

**Renal Cystic Dysplasia**

- **General Features**
  - **Pathology**
    - **General Features**
      - **Bilateral cysts in upper tract**
      - **Obstructive uropathy in nephrons**
      - **Secondary cyst formation**
      - **Distal nephron tubular dilatation**
    - **Autosomal recessive polycystic kidney disease (ARPKD)**
      - Bilateral, large echogenic kidneys
      - **Renal pyramids**
        - **Hyperechoic renal parenchyma**
        - **Adjacent to calyx**
    - **Gross Pathologic & Surgical Features**
      - **Cysts are often cortical**
      - **Form in mesonephric nephrogenic zone**
    - **Microscopic Features**
      - **Cysts can develop in any portion of nephron**
      - **Glycocalyx**
      - **Tubuli**
      - **Collecting ducts**
      - **Islands of normal nephrons, between cysts**
    - **Clinical Issues**
      - **Presentation**
        - Most common signs/symptoms
        - **Unilateral/OCD most often noted on routine exam**
        - **Hydronephrosis + renal cysts**
        - **Preonset + renal cysts**
        - **Bilateral OCD**
        - **Glycocalyx**
        - **Distended bladders + bilateral cysts**
        - **Small for dates**
        - **Other signs/symptoms**
        - **Non-OB anomalies**
  - **Risk for aneuploidy/syndromes**
  - **Demographics**
    - **Gender:** M>F
  - **Natural History & Prognosis**
    - **Prognosis depends on renal function**
    - **Number of healthy nephrons**
    - **Early vs. late obstruction**
    - **Severity of obstruction**
    - **Bilateral OCD has a grim prognosis**
    - **Early oligohydramnios**
    - **Pulmonary hypoplasia**
    - **Severe renal insufficiency**
  - **Treatment**
    - **Newborn**
      - **Ultrasound to confirm diagnosis**
      - **Nephrectomy for renal scarring**
      - **Assess renal function**
      - **Treat cause of GU obstruction**
      - **Surgery for severe UPI obstruction**
      - **Posterior urethral valves**
      - **Ureteroureterostomy**
      - **Antenatal cyst drainage can be considered**
      - **Pressure on adjacent tissue**
    - **Renal dysplasia**
      - **Improve renal function**

**DIAGNOSTIC CHECKLIST**

- **Consider**
  - Look for renal cysts when GU obstruction diagnosed
  - Perform careful follow-up exam
  - **Image Interpretation Pearls**
    - May be impossible to differentiate OCD from MCDK
    - **Hydronephrosis/hydronephrosis suggests OCD**
    - **May not be important to differentiate**
    - **Similar presentation**
    - **Poor/no renal function for both**
    - **Look carefully for other anomalies once OCD seen**
  - **Genetic testing recommended if OCD is not isolated**

**SELECTED REFERENCES**

OBSTRUCTIVE CYSTIC DYSPLASIA

IMAGE GALLERY

Typical

(Left) Ultrasound shows bilateral OCDs. At least 5 cysts (arrows) are seen within the left kidney. Some normal interposing renal parenchyma is present (curved arrows). Calyces resemble the normal right kidney. (Right) Bladder ultrasound through the fetal bladder in the same case shows a large ureteric stone (arrows). The distal ureter is “beaked” into the bladder and causes severe obstruction in this case.

Typical

(Left) Avid ultrasound shows bilateral, severe OCD in a fetus with associated renal vein anomalies. Nontypical small cysts have replaced the kidney (arrows), however, subcortical cysts are most numerous. (Right) Coronal ultrasound in the same case shows a markedly distended, thick-walled urinary bladder (open arrow) and bilateral hydronephrosis (curved arrows). Severe oligohydramnios was also seen.

Typical

(Left) Coronal ultrasound shows postnatal OCD from posterior urethral valves. The kidney is hydrourephrosis (curved arrow points to distended calyces) and there are scattered renal cortical cysts (curved arrow). (Right) Sagittal oblique radiograph performed during voiding cystourethrography in the same case shows a dilated posterior urethra (arrows), with an abrupt caliber change at the level of the valve (curved arrow) (open arrow - bladder).
RENEAL AGENESIS

TERMINOLOGY

Abbriviations and Synonyms
- Potter syndrome
  - Anhydramnios associated with abnormal facies, limb deformities

Definitions
- Absence of renal tissue
  - Bilateral is lethal
  - Unilateral compatible with normal life expectancy

IMAGING FINDINGS

Ultrasonographic Findings
- Bilateral renal agenesis
  - Anhydramnios
  - "Absence" bladder
    - No urine being produced, so bladder can not be visualized
  - "Lying down," flattened adrenals
  - Adrenal gland does not fold into "Y" or "tricorner hat" configuration if no kidney
  - Renal adrenals glands are relatively large, almost same size as kidneys normally in gestation
  - Occupies renal fossa in absence of kidneys
  - Pyriform hypoplasia

- Measure ratio of chest/diaphragm
- Ureter, bladder and/or bowel position
- Congenital heart disease in 14%
- Color Doppler
- No demonstrable renal arteries
- Normal amniotic fluid volume
- Bladder seen to fill and empty
- One kidney seen
- May see "lying down" adrenal ipsilateral to absent kidney
- 2 vessel cord seen in many renal anomalies

MR Findings
- Normal urinary tract
  - Renal kidneys well seen by 12 weeks gestation
  - Uterine pelvis in intermediate signal
  - Ureter in collecting system is high signal on T2WI
  - Adrenal glands lower signal than normal renal parenchyma
- Signal approximates that of skeletal muscle
- Bilateral renal agenesis
  - No demonstrable renal tissue
- Flattened, discordant adrenals in renal fossa
- No urine in fetal bladder
- Anhydramnios
- Unilateral renal agenesis
  - One normal-appearing kidney

DDx: No Urine In Fetal Bladder
- Bilateral MCDK
- Septen JUGR
- ARPKD Disease
- Bladder +171 Dopper
RENAL AGENESIS

Imaging Findings
- Polyhydramnios
- "Absent" bladder
- "Flying down" flattened adrenals
- Fetal hydrops
- Clubfoot, other joint contractures
- Congenital heart disease in 14%

Top Differential Diagnoses
- Premature rupture of membranes
- Severe intrauterine growth restriction (IUGR)
- Sirenomelia

Pathology
- Potter sequence (oligohydramnios sequence)
- Physical findings secondary to lack of movement and compression by uterine wall

Key Facts
- Characteristic facies: Broad, flattened, braked nose, low-set ears, receding chin, widely separated eyes with prominent infraorbital folds

Clinical Issues
- Amniotic fluid volume is normal in first trimester, even with bilateral renal agenesis
- Renal contribution to amniotic fluid is minimal before 17 weeks
- Bilateral agenesis is lethal
- Recurrence risk 3%

Diagnostic Checklist
- Adrenal gland can be mistaken for kidneys
- Adrenal gland has an "ice-cream sandwich" appearance

In cases of apparent unilateral agenesis
- Look for pelvic kidney
- Look for anomalous second kidney (e.g. multicystic dysplastic)

DIFFERENTIAL DIAGNOSIS

Premature rupture of membranes
- Fetal bladder will fill and empty
- Kidneys present and normal
- Talk to the patient
  - Can usually give history of "gush" of fluid
  - Sterile speculum examination for diagnostic

Severe intrauterine growth restriction (IUGR)
- Kidneys present and normal
- Fetal bladders will fill and empty
- Umbilical artery Doppler likely abnormal

Sirenomelia
- Bilateral renal agenesis
- Need to look at extremities carefully
  - Fused lower extremities
  - Cardiac/abdominal wall defects

Autosomal recessive polycystic kidney disease (ARPKD)
- Kidneys present, often very large, hypechoic

Bilateral multicystic dysplastic kidneys
- Kidneys present
- Variably-sized cysts are dominant imaging feature

Differential diagnosis for "absent" bladder
- No urine formation
  - Either poor renal perfusion or abnormal/absent parenchyma
- Ig twin twin transfusion syndrome (TTTS) ‘donor’ twin showing blood to ‘recipient’
- Donor renal perfusion is decreased

Imaging Recommendations
- Aware pitfalls in diagnosis of bilateral renal agenesis
- Differentiate kidneys from adrenal glands
- Fetal adrenals very prominent, especially early in gestation
  - Adrenal hypertrophy described in pathologic series of renal agenesis
  - Echogenic adrenal medulla between layers of hypoechogenic cortex
  - In renal agenesis, adrenals have flattened, diskoid, "flying down" appearance
  - Kidneys do not have a layered appearance
  - Kidneys are "bean-shaped" in long axis, oval or round in cross section
  - Corticomedullary differentiation is evident, with hypoechogenic pyramids (becomes more obvious with advancing gestation)
  - Color Doppler shows flow in multiple abdominal vessels, which may be confused for renal arteries
  - Celiac axis, superior mesenteric artery are present
  - Adrenal arteries are present and may be enlarged with adrenal hypoplasia
  - Lumbar arteries may also be mistaken for renal arteries
- The bladder is anatomically present but not seen when empty
  - May see small bladder containing mucus secretion especially with MRI
  - Do not mistake for urine production
  - Watch for changes of bladder size and shape; if seen, there must be some urine production
  - Use endovaginal ultrasound
  - Fetal kidneys can be seen as early as 12 weeks
  - Consider fetal MRI
  - Preferable to amniocentesis for better anatomic visualization
  - Non-invasive

- Perform all three scan planes to avoid false positive diagnosis
- Check for pelvic kidney or other anatomic variant
RENAL AGENESIS

PATHOLOGY

General Features
- Genetic
  - Trisomy 7, 10, 21, 22
  - Branchio-oto-renal dysplasia (BOR) syndrome
- Autosomal dominant with variable expression
- Renal anomalies, including agenesis
- Deafness/uniformed ear/branchial cysts
- Cardio-oculo-facial syndrome
- Autosomal recessive
- Micrognathia, joint contractures, renal anomalies

- Embryology
- Failed induction of metanephric blastema by ureteric bud
- No nephron formation

- Epidemiology
  - Bilateral: 1/3,000 births
  - M > F
  - Unilateral: 1/1,300 births

- Associated abnormalities
  - Poor sequelae (oligohydramnios sequence)
  - Physical findings: secondary to lack of movement and compression by uterine wall
  - Characteristic facies: broad, flattened, beaked nose, low-set ears, receding chin, widely separated eyes with prominent infraorbital folds
  - Clubbed hands and feet
  - Renal agenesis may be part of VACTERL association
  - Vertebral, anorectal, cardiac anomalies, tracheoesophageal fistula, renal and limb anomalies

CLINICAL ISSUES

Presentation
- Amniotic fluid volume is normal in first trimester, even with bilateral renal agenesis
- Renal contribution to amniotic fluid is minimal before 12 weeks
- Fluid comes from deficiencies, gastrointestinal tract

Natural History & Prognosis
- Bilateral agenesis is lethal
- 30% stillbirth
- Survivors die of respiratory failure due to pulmonary hypoplasia
- Largest documented survival: 39 days

- Unilateral agenesis associated with
  - Genital anomalies
  - Males: bilateral vesicoureteral reflux in single kidney 30%
  - Females: Mullerian duct anomalies
  - Vescoureteral reflux in single kidney 30%
  - Increased incidence of vesicoureteric/ureterocecal junction (VUJ) obstruction
  - Recurrence risk 3%

Higher if part of multiple anomaly complex

Treatment
- Bilateral
  - Offer termination
- If pregnancy continues
  - Do not monitor in labor
  - Stress importance of non-invasive at birth

- Unilateral
  - Follow regularly with special emphasis on single kidney, fluid volume
  - Progressive VUJ obstruction may change delivery timing

DIAGNOSTIC CHECKLIST

Consider
- Any condition with early onset severe oligohydramnios carries poor prognosis
- Bilateral renal agenesis is lethal
- Aim to make specific diagnosis in order to counsel parents appropriately

Image Interpretation Pearls
- Adrenal gland can be mistaken for kidneys
- Adrenal gland has an "ice cream sandwich" appearance
- Use MRI in difficult cases

SELECTED REFERENCES
Typical

(Left) axial T2W MR shows normal liver (curved arrow), gallbladder (white arrow), ureters (black arrows), and nephro-pectoral fluid (open arrow) in the renal canal. The kidneys are absent and there is hydronephrosis. (Right) axial T2W MR of a normal fetal abdomen (for comparison) shows obvious kidneys (white arrows) as well as the liver (curved arrow), renal canal (open arrow) and an extremity (black arrow).

Typical

(Left) Gross pathology shows the relatively large size of the fetal adrenal (curved arrow) compared to the kidney (arrow). This can lead to the erroneous assumption that kidneys are present, when in fact, the visualized tissue is actually an adrenal gland. (Right) Axial ultrasound shows the fetal adrenal gland with its “ice-cream sandwich” appearance (arrow), compared to the kidneys (curved arrows), which are more round and have hypochoic pyramids.

Typical

(Left) Ultrasound focused on the fetal adrenal gland (curved arrow) shows the characteristic “lying-down” appearance seen with renal agenesis. A pituitary T2W MR shows the cinematic appearance of absent kidneys and elongated, discoid iliacus (arrow). (Right) Coronal color Doppler ultrasound shows multiple hilar arterial arteries (arrow) in the case of renal agenesis. This is a potential pitfall in attempted identification of the renal arteries.
MULTICYSTIC DYSPLASTIC KIDNEY

Surgical abdomen shows a unilateral MCDK. Multiple multicellular cysts of variable size are seen throughout the kidney (arrows). Intrarenal renal parenchyma is echogenic.

Gross pathology shows the kidney replaced by multiple cysts of varying size. Minimal intrarenal dysplastic tissue is seen and the Weiner is absent.

TERMINOLOGY

Abbreviations and Synonyms
- Multicystic dysplastic kidney (MCDK)
- Renal cystic dysplasia
- Potter type II

Definitions
- Renal tissue replaced by cysts

IMAGING FINDINGS

General Features
- Best diagnostic clue: Multiple variable-sized cysts in renal fossa
- Location
  - Unilateral in 80%
  - Bilateral in 20%
- Size: Overall kidney size in 90%
- Morphology
  - Variable appearance of both cysts and kidney
  - Cystic: do not communicate

Ultrasoundographic Findings
- Paraginous mass with macroscopic cysts
  - Reniform shape is lost

- Normal renal parenchyma not discernible
- Multiple cysts of variable size and shape
- Cysts may 1 or 1 during pregnancy
- Rarely require prenatal drainage
- Overall kidney size is enlarged
- Renal length > 55th percentile in 90%
- Bilateral MCDK in 20%
- Bilateral cystic kidneys
- No amniotic fluid
- No fluid-filled bladder seen
- Anomalies associated with restricted space
  - Club feet
  - Abnormal posturing
  - Small chest
- Glen malformation from pulmonary hypoplasia
- MCDK is rarely segmental
- Only upper pole cystic change
- Suggests duplex collecting system
- MCDK may be part sequelae of total obstruction
- Hydronephrosis initially seen
- Early and severe
- Renal parenchymal cysts appear secondarily
- Nephrostomy offering renal tissue still present
- Cysts predominate by 3rd trimester
  - No normal renal parenchyma
  - Appearance identical to 1st MCDK
- Costalateral renal anomaly (pap-MCDK) in 40%
  - Vesicoureteral reflux most common

DDx: Genitourinary Obstructive Cystic And Cyst-Like Lesions

- Hydronephrosis
- Hydromecephalus
- Megaoesten
- Obstructive Cystic Dysplasia
MULTICYSTIC DYSPLASTIC KIDNEY

Key Facts
- Genetics: Isolated MCDK not associated with aneuploidy

Pathology
- M/C: F: M = 2:1
- Unilateral MCDK has excellent prognosis
- Bilateral MCDK in 90%
- MCDK usually involutes with time
- Rare development of Wilms tumor
- Bilateral MCDK almost always fatal
- Conservative management
- Surgical excision reserved for complications

Clinical Issues
- Amniocentesis, if any other anomalies seen
- Beware of "hydro nephrotic type" of MCDK

Differential Diagnosis

Hydronephrosis
- Renal collecting system distension
  - Urinary tract obstruction
- Enlarged calyces may appear "cyst-like"
- Bilateral hydronephrosis
- Cystic pararenal cyst change from obstruction
- Hydronephrosis → cortical cysts
- Often see some normal renal tissue
- Reniform shape often retained
- Rarely can appear identical to MCDK
- Early obstruction (<10 wks)

Simple renal cyst
- Isolated unicocular renal cyst (rare)
- Vast majority resolve during pregnancy
- 4% progress to MCDK
- Not associated with aneuploidy

Autosomal recessive polycystic kidney disease
- Bilateral large echogenic kidneys
- Rare or no macroscopic cysts
- Oligohydramnios
- Most often fatal in neonatal period if severe involvement

Autosomal dominant polycystic kidney disease
- Rarely seen in fetal life

Terminology
- Multicystic renal dysplasia
- Renal tissue replaced by cysts

Imaging Findings
- Paraspinal mass with macroscopic cysts
- Overall kidney size is enlarged
- Bilateral MCDK in 20%
- Contralateral renal anomalies (non-MCDK) in 40%
- Non-renal anomalies in 5%
- Yellow amniotic fluid volume carefully measured

Top Differential Diagnoses
- Hydronephrosis
- Obstructive cystic dysplasia

- Postnatal diagnosis
- Ureteropalvic junction (UPJ) obstruction
- Hydronephrosis
- Renal agenesis
  - Color Doppler confirms absent renal artery
  - Renal hypoplasia
- MCDK and amniotic fluid
  - Unilateral MCDK most often with normal fluid
  - Normal bladder
- Bilateral MCDK = severe oligohydramnios
  - Bladder not visualized
  - Meckel-Gruner syndrome
  - Encephalocoele
  - Postaxial polydactyly
  - Triosomy 13
  - Intrauterine growth restriction
  - Holoprosencephaly
  - Facial anomalies
  - Cardiac defects
  - Polydactyly
  - Triosomy 13
  - Intracranial growth restriction
  - Cardiac defects
  - Clefted hands
  - Choroid plexus cysts
  - Bowel-containing omphalocele
  - Non-renal anomalies in 5%
  - Amniocentesis recommended

Imaging Recommendations
- Protocol advice
  - Kidney documentation part of every 2nd/3rd trimester exam
  - Longitudinal views vs transverse views
  - When MCDK present, look at contralateral kidney carefully
  - Follow-up ultrasound every 3-4 wks
  - Contralateral renal problem can develop
  - MCDK cysts can enlarge dramatically
  - Follow amniotic fluid volume carefully
  - Objective measurements preferable
  - Amniotic fluid index (AFI)
  - Maximum vertical pocket (MVP)
  - Determine if MCDK is isolated
  - Careful fetal anatomic survey
  - Genetic counseling for non-isolated MCDK
MULTICYSTIC DYSLASTIC KIDNEY

- Few unicystic cysts
- Liver/pancreatic cysts
- Familial history important
- Scan parents for occult disease
- Normal fluid

Dilated ureter
- Often from obstruction
- Posterior urethral valves
- Ureteral reflux
- Serpiginous course of dilated ureter
- Can mimic MCDK
- Careful urograms shows separate kidneys

PATHOLOGY

General Features
- Genetics: isolated MCDK not associated with nephropathy.
- Ectodystrophy: normal metanephrine embryology
- Early ureter obstruction/atria
- Metanephrine tissue does not form nephrons
- End result is dysplastic cystic tissue
- Segmental MCDK
- Atelesia or diplegic ureter
- Most often upper poles ureter
- Epithelium: 1:3:000 live births
- Associated abnormalities: 5% with non-renai anomalies

Gross Pathologic & Surgical Features
- Enlarged kidney replaced by cysts
- Non-uniform shape
- Intervening dense fibrotic stroma
- Ureter and renal pelvis atresia

Microscopic Features
- Smooth-walled cysts

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
- Unilateral MCDK
- Incidentally seen during prenatal scan
- Bilateral MCDK
- Severe oligohydramnios
- Neonatal presentation
- Palpable mass
- Symptoms of contralateral UPJ obstruction

Demographics
- Gender
  - M/F = 1.1
  - Female febrile has worse prognosis
  - 2x more likely to have bilateral MCDK
  - 4x more likely to have aneuploidy

Natural History & Prognosis
- Unilateral MCDK has excellent prognosis
  - Non-functioning kidney in 90%
- Determined by nuclear medicine renal scan
- MCDK kidney usually involutes with time
  - 20% in 1st yr of life
  - 50% by 5th yr of life
  - May take up to 20 yr
- Compensatory hypertrophy of contralateral kidney
- Rare complications
- Infection
- Hypertension
- Miss effect
- Rare development of Wilms tumor
- MCDK + contralateral renal abnormality
- Bilateral MCDK almost always fatal
- Severe contralateral anomaly
- Often fatal
- Renal insufficiency
- Malignant contralateral anomaly
- Often correctable, with excellent prognosis

Treatment
- Conservative management
  - Neonatal work-up required in every case
  - Ultrasound to confirm diagnosis
  - Vaginal ultra sound to evaluate for reflux
  - Postnatal renal scan for function
  - Ultrasound surveillance
  - Every 6 months for 1 year
  - Yearly until involution
  - Surgical excision reserved for complications
  - Recurrent infections
  - Hypertension
  - Wilms tumor

- Pregnancy termination offered for bilateral MCDK

DIAGNOSTIC CHECKLIST

Consider
- Careful evaluation of contralateral kidney
- Follow-up ultrasound indicated
- Follow APF
- Reflects renal function
- Amniocectesis if any other anomalies seen

Image Interpretation Pearls
- Beware of "hydroureter type" of MCDK
- Large central cyst with small peripheral cysts
- Careful scan shows cysts do not communicate

SELECTED REFERENCES

MULTICYSTIC DYSPLASTIC KIDNEY

IMAGE GALLERY

Typical

(left) General ultrasound shows an enlarged left-sided MCDK (open arrow) at 10 weeks. The kidney extends from the stomach (curved arrows) to the diaphragm (open arrow). (Right) General ultrasound performed 5 weeks later shows the cysts have enlarged and there is mass effect upon the diaphragm (curved arrow) and abdominal vessels (color Doppler Image). MCDK tends to grow during pregnancy.

Typical

(left) General TVMI MRI shows bilateral MCDK in a neonate who died shortly after birth. The kidneys are enlarged with cysts (arrows) and are more "soft-tissue" than renal. (Right) Gross pathology of bilateral MCDK (kidneys are bisected in the coronal plane) shows innumerable cysts. MCDK do not function and therefore, the bladder (arrow) is atretic. Bilateral MCDK is almost always fatal.

Variant

(left) Axial ultrasound shows a left-sided MCDK (open arrow) and right-sided UPJ obstruction (curved arrow – distended renal pelvis). The lower image shows a hypoplastic left renal pole (arrow). MCDK is associated with both contralateral renal and non-renal anomalies. (Right) General ultrasound shows a MCDK on the right (open arrow) with a central cyst (arrow) and multiple peripheral cysts, a pattern which mimics hydronephrosis (open arrow – normal left kidney).
AUTOSOMAL RECESSIVE POLYCYSTIC KIDNEY DISEASE

Terminology

Abbreviations and Synonyms
- Autosomal recessive polycystic kidney disease (ARPKD)
- Infantile polycystic kidney disease

Definitions
- Single gene disorder resulting in bilateral, symmetric, cystic renal disease
- Involves distal convoluted tubules + collecting ducts (i.e. medulla)
- Cortex is spared

Imaging Findings

General Features
- Best diagnostic clue: Enlarged, hyperchoic kidneys

Ultrasoundographic Findings
- Kidney size > 2 standard deviations (SD) above mean for gestational age (GA)
- By late fetal life, kidneys may be anywhere from 3-4x normal size
- Renal enlargement may not occur until mid 2nd trimester
- Kidneys are diffusely hyperchogenic
- Cysts may be visible but do not predominate

- Normal hypechoic cortex is present
- May be difficult to discern with severe disease
- Oligohydramnios
- Fetal bladder not visible
- Musculoskeletal abnormalities
- Oligohydramnios limits movement = contractures

MR Findings
- Large kidneys of uniformly high signal intensity on T2WI
- Small, discrete cysts may be visible
- Look for low signal rim of cortex
- Bladder with little or no urine
- Oligohydramnios
- Thorax looks small in relation to abdomen

Imaging Recommendations
- Obtain renal renal measurements in at-risk fetuses
- Parents are known carriers
- Measure ratio of renal circumference to abdominal circumference
- > 2 SD above mean is abnormal
- Monitor amniotic fluid volume
- Early onset oligohydramnios = poor prognosis
- Look for signs of pulmonary hypoplasia
- Thorax looks small in relation to large abdomen
- Measure thoracic circumference

DDx: Renal Anomalies And Oligohydramnios

- Bilateral MCCK
- Renal Agenesis
- Posterior UV
- Meckel-Gruber
- Bilateral MCCK
- Renal Agenesis
- Posterior UV
- Meckel-Gruber
AUTOSOMAL RECESSIVE POLYCYSTIC KIDNEY DISEASE

Key Facts
- Most kidneys look normal up to 25 weeks
- Milder cases may not be apparent on prenatal ultrasound
- Renal enlargement may not occur until mid 2nd trimester
- Top Differential Diagnoses
  - Bilateral multicystic dysplastic kidney (MCDE)
  - Trisomy 15
  - Meckel-Gruber syndrome
- Pathology
  - Ecstatic distal convoluted tubules and collecting ducts
- Clinical Issues
  - Diagnosis reported at 15 weeks in at-risk fetus

- Normative data available
- Measure acceleration time/ejection time (AT/ET) ratio in pulmonary artery
- Prediction of pulmonary hypoplasia
- Consider MRI
- Helpful with difficult maternal habits
- Image quality less compromised by lack of amniotic fluid than ultrasound

DIFFERENTIAL DIAGNOSIS

Bilateral multicystic dysplastic kidney (MCDE)
  - Macroscopic renal cysts are a dominant feature
  - Anhydramnios

Trisomy 13
  - Cystic dysplasia seen in 50%
  - Kidneys usually echogenic, enlarged, cysts may be visible
  - Holoprosencephaly
  - Polydactyly
  - Facial anomalies
  - Cyclops, proboscis, cleft lip/palate, midline facial cleft

Meckel-Gruber syndrome
  - Ectopia choanae/Macrocephaly is a clue if oligohydramnios limits “view”
  - Polydactyly
  - Cystic renal dysplasia
  - Usually macroscopic cysts
  - Enlarged hyperplastic kidneys, have been described

Tuberous sclerosis
  - Family history
  - Autosomal dominant transmission in 2/3 of cases
  - Neurofibromas
  - Rhabdomyomas: Echogenic cardiac mass
  - Tubers: Subependymal nodules
  - Renal cysts/solid masses not usually seen in utero

Beckwith-Wiedemann syndrome
  - Macrodactyly, often associated with polyhydramnios
  - Omphalocele
  - Macroglossia

Autosomal dominant polycystic kidney disease
  - Check family history, scan parental kidneys
  - Hypertensive renal enlargement
  - Rarely presents in fetus. Cysts may be visible late 2nd trimester
  - Renal echogenicity generally normal but hypertrophic kidneys have been described
  - Amniotic fluid normal

PATHOLOGY

General Features
- General path comments
  - Ectopic distal convoluted tubules and collecting ducts
  - Increased volume of medulla → renal enlargement
  - Increase in reflective interfaces → high echogenicity on ultrasound
  - Increased “water” content in multiple tubules/cysts = high-signal intensity T2WI

- Genetics
  - Autosomal recessive
  - Mutation of PKHD1 gene which maps to chromosome 6p12
  - Mutations are “private” (i.e. specific to individual families)
  - HNF1b transcripts factor regulates expression of PKHD1 in kidney
  - HNF1b mutations also cause ARPKD

- Epidemiology
  - 1:20,000 to 50,000 births
  - M: F = 1

- Associated abnormalities
  - Potter sequence secondary to oligohydramnios
  - Pulmonary hypoplasia
AUTOSOMAL RECESSIVE POLYCYSTIC KIDNEY DISEASE

CLINICAL ISSUES

Presentation
- Majority detected < 24 weeks
- Diagnosis reported at 16 weeks in at-risk fetus
- Most cases occur normal up to 20 weeks
- Milder cases may not be apparent on prenatal ultrasound

Natural History & Prognosis
- Disease has variable phenotype
  - Prenatal, neonatal, infantile and juvenile forms described
  - Disease expression may vary widely within affected families
- Fetal diagnosis
  - Oligohydramnios = pulmonary hypoplasia = majority stillborn or neonatal death
- Prenatal form 30-50% death
- Severe renal disease
- Polycystic hyperechogenity
- Minimal hepatic fibrosis
- Juvenile form
  - Most renal disease, marked hepatic fibrosis
- Liver disease more relevant in survivors
- Neonatal survivors
  - 1 yr survival 85%
  - 10 yr survival 82%
- Need for artificial ventilation at birth strongly correlates with mortality
- Mean age of diagnosis of chronic renal failure 4 yrs
- Actual renal survival (end point defined as start of dialysis or death from renal failure) 85% at 5 yrs
- 71% at 10 yrs
- 47% at 20 yrs
- 75% develop systemic hypertension
- 44% develop portal hypertension
- Incidence increases with age, no correlation with onset chronic renal failure/insufficiency
- Severity and outcomes vary within affected families
- Cannot predict outcome of future children based on severity of index case
- Recurrence risk 25%

Treatment
- Genetic counseling
  - Family history
  - Increased incidence of occult renal disease in family members
  - Offer termination
- If pregnancy continues, plan delivery at tertiary center
  - Infants may require respiratory support
- Monitor abdominal circumference
  - Risk of abdominal distoacy
- May influence timing of delivery
  - Avoid cesarean section for non-viable fetus
- Encourage autopsy confirmation for intrauterine or neonatal death
- Prenatal diagnosis is an area of continued research
- Chronic renal insufficiency/anaemia is the most common cause of death
- Specific mutation in family known from tissue or blood of affected child
- Much more complicated with confirmed diagnosis in prior child

DIAGNOSTIC CHECKLIST

Consider
- Phenoype expression, highly variable within individual families
- Cannot exclude juvenile form on basis of prenatal US alone
- Prenatal diagnosis is possible if specific mutation is known
- Strongly encourage autopsy/renten biopsy in lethal cases

Image Interpretation Pearls
- MRI can be helpful to refine diagnosis of renal anomalies associated with renal hypodensities

SELECTED REFERENCES
AUTOSOMAL RECESSIVE POLYCYSTIC KIDNEY DISEASE

**IMAGE GALLERY**

**Typical**

*Left:* Axial ultrasound in a 15-week foetus, of a couple with one affected child, shows increased echogenicity of the kidney (arrow). Anatomic fluid volume is normal but that does not (left) normal renal function at this gestational age. *(Right)* A4D colour Doppler ultrasonogram shows a very smoothlooking turned around between the quadrilateral arteries (arrow).

**Typical**

*Left:* General ultrasound from the case above at 22 weeks shows severe oligohydramnios. The chest is small (arrow) and the kidneys are large and echogenic (calipers). *(Right)* Sagittal ultrasound in a different case of ARPKD shows an enlarged, hyperechogenic kidney (calipers). There is preservation of the normal hyperechogenic cortex (arrows). This is a characteristic finding but may be difficult to discern on prenatal scans.

**Typical**

*Left:* General 3D postnatal MR shows a tiny thymic cavity (white arrow). The kidneys (black arrows) are massively enlarged with no normal remaining parenchyma. High signal intensity is caused by the dilated tubules. *(Right)* Cross-pathway from the amniotic fluid shows massively enlarged kidneys (arrows). The thymic cavity is small and the lungs (white arrow) are severely hypoplastic.
TERMINOLOGY
Abbreviations and Synonyms
- Congenital mesoblastic nephroma
- Fetal renal hamartoma
- Leiomyosarcoma hamartoma
- Mesenchymal hamartoma
- Bola-like tumor

Definitions
- Benign mesenchymal renal tumor composed predominately of spindle cells

IMAGING FINDINGS
General Features
- Best diagnostic clue: Solid renal mass + polypoid mass
- Morphology
  - Variable growth pattern
  - May see distinct, well-defined, intrarenal mass
  - Infiltrative growth pattern
  - Smaller masses retain reniform shape
  - Larger masses may fill abdomen, displacing bowel

Ultrasonographic Findings
- Generally solid

MR Findings
- Helpful for confirming renal origin of mass
- Solid mass with uniform signal intensity
- Mild increased signal on T2WI

Imaging Recommendations
- Confirm renal origin of mass
- Look for normal kidney and adrenal on side of mass
- Adjacent mass may fill renal fossa and be confused for renal mass
- Look for displaced kidney

DIAGNOSIS: Enlarged Kidneys

- Cystic Fused Kidney
- Beckwith-Wiedemann
- Duplication
- Aortic Coarctation
**MESOBLASTIC NEPHROMA**

**Key Facts**
- **Pathology**
  - Most common renal neoplasm in fetus and newborn
  - In utero polyhydramnios (amniotic fluid accumulation) is most likely cause of polyhydramnios

- **Clinical Issues**
  - Perinatal complications in 7%
  - Acute fetal distress requiring emergency cesarean section
  - Neonatal hypertension
  - Neonatal hypercalcemia
  - Surgical resection usually curative

- **Diagnostic Checklist**
  - Mesoblastic nephroma has an excellent oncologic outcome but is at high-risk for perinatal complications

**Terminology**
- Benign mesenchymal renal tumor composed predominately of spindle cells

**Imaging Findings**
- Best diagnostic clue: Solid renal mass + polyhydramnios
- Variable growth pattern
- Generally solid
- Polyhydramnios in ≥ 70%
- Vascular mass

**Top Differential Diagnoses**
- Wilms tumor
- Crossed fused ectopy
- Adrenal lesion

- Consider MRI if ultrasound cannot determine if mass is renal
- Color Doppler
- Assess vascularity
- Look for renal artery
- Confirms mass in renal

- Calculate amniotic fluid index (AFI)
- Polyhydramnios if AFI > 24
- Frequent follow-up exams
- Worsening polyhydramnios
- May become severe, resulting in preterm labor
- Enlarging abdominal circumference
- Rarely complicated by hydrops

**DIFFERENTIAL DIAGNOSIS**

**Renal Tumors**
- Wilms tumor
- Ultrasound appearance identical to mesoblastic nephroma
- Extraordinarily rare in utero
  - Average age at presentation: 3.6 years
  - Bladder tumor also reported

**Crossed fused ectopy**
- Unilateral enlargement
- Fixed kidneys not cross midline
- Opposite renal fossa is empty

**Renal collecting system duplication**
- Unilateral renal enlargement
- Ureter pole often hydrophthalmic
  - Drained by ectopic ureter
- Often obstructs
- Lower pole may or may not be dilated
- Drained by orthotopic ureter
- Often refluxes
- Look in bladder for uretercele

**Autosomal recessive polycystic kidney disease (ARPKD)**
- Bilateral, symmetric renal enlargement

- Diffusely hypechoic kidneys
- Scattered small cysts may be seen, but not a dominant feature
- May have oligohydramnios

**Beckwith-Wiedemann syndrome**
- Oligohydramnios including enlarged kidneys
- Macroglossia
- Macrocephaly
  - Tongue protruding
- Hemihypertrophy
- Polyhydramnios
- Hypoglycemia in neonatal period
- At risk for neonatal tumors
  - Wilms tumor, hepatoblastoma

**Multicystic dysplastic kidney**
- Cystic, not solid
- Multiple, non-communicating cysts of various sizes

**Adrenal Lesions**
- Neuroblastoma, adrenal hemorrhage, extrahepatic sequestration
- Suprarenal location
- Kidney displaced inferiorly
- Normal adrenal gland not identified

**Retroperitoneal teratoma**
- May be large
  - May be difficult to evaluate displaced kidney
- Point of origin difficult to discern
- Heterogeneous masses
  - Mixed cystic and solid
  - Calcifications are most specific diagnostic feature

**PATHOLOGY**

**General Features**
- Genetics
  - Sporadic
  - Has been reported in siblings
- Epidemiology
  - Rare, overall
MESOBLASTIC NEPHROMA

- Most common renal neoplasm in fetus and newborn
- 5% of perinatal tumors arise from kidney
- Majority are mesoblastic nephroma
- Rare reported cases of Wilms or rhabdoid tumor
- M > F
- Associated abnormalities: Polyhydramnios and hypercalcemia
- Theories of polyhydramnios
  - Polyuria
  - Often seen in neonates with mesoblastic nephroma and is associated with hypercalcemia
  - "in utero polyuria" from hypercalcemia most likely cause of polyhydramnios
  - Bowel obstruction
  - May contribute but does not explain all cases
  - May set significant polyhydramnios without bowel obstruction
  - Mass causes increased blood flow to kidney ⇒ ↑ urine output
  - Impaired concentrating ability of affected kidney

Gross Pathologic & Surgical Features
- Whorled appearance
- Similar to uterine fibroid
- No capsule
- Still appears well-defined by ultrasound

Microscopic Features
- Benign mesenchymal tumor
- Spindle-shaped cells infiltrate normal renal parenchyma
- Cellular variant may be more aggressive

CLINICAL ISSUES

Presentation
- Fetal
  - Rapid, acute onset of polyhydramnios in 3rd trimester
  - Large for dates
  - Preterm labor
  - Increased abdominal circumference
  - Solid abdominal mass
- Neonatal
  - Obvious palpable mass on exam
  - Hypertension
  - Increased renal production
  - Hypercalcemia
  - Associated with parathyroid and hyperplastic gland
  - Both hypercalcemia and hypertension resolve after resection

Natural History & Prognosis
- Can show rapid growth despite benign histology
- Perinatal complications in 71%
- Severe polyhydramnios
- Hydrops
- Acute fetal distress requiring emergency cesarean section
- Premature delivery
- Respiratory distress
- Neonatal hypertension
- Neonatal hypercalcemia
- Large abdominal circumference may result in dystocia at delivery
- Surgical resection usually curative
- Surgical complications reported in 26%
- Rare local recurrence or metastases for cellular mesoblastic nephroma
- Liver most common site

Treatment
- Referral to tertiary care center for close monitoring
- Antenatal reduction for polyhydramnios for patient comfort or preterm labor
- Tocolytics for preterm labor
- May require cesarean section
- Referral to pediatric urologist
- Reexamination in neonatal period
- Nephrectomy with wide margins usually curative

DIAGNOSTIC CHECKLIST

Consider
- MRI to confirm mass is renal and not from surrounding structures
- Mesoblastic nephroma has an excellent oncologic outcome but is at high-risk for perinatal complications

Image Interpretation Pearls
- Mesoblastic nephroma is the most likely diagnosis of a unilateral, solid renal mass

SELECTED REFERENCES

**Typical**

*Left:* Coronal oblique ultrasound of the kidney shows a markedly enlarged lower pole (calyces), extending into the pelvis and shifting the bladder (arrow). The upper pole of the kidney (upper arrow) is preserved.

*Right:* Gross pathology; after resection, shows a well-defined, gray, lower pole mass with dense stromal architecture. (Also shown in Radiographics, ref 1.)

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*Left:* Axial ultrasound through the renal dimensions is most striking for severe polyhydronephrosis. There is a large solid mass in the region of the right kidney (arrow). The left kidney is normal (arrow). (Right:) Axial CECT after delivery shows dramatic enlargement of the right kidney with essentially complete replacement by the tumor. Despite its large size, mesoblastic nephroma is generally benign and can be cured with resection. (Also shown in Radiographics, ref 1.)

*Left:* Axial ultrasonogram shows a mass (calyces) in the left renal fossa with no identifiable normal kidney on that side. The right kidney (arrow) is normal. (Right:) Gross pathology of the resected kidney shows only a small Crescent of remaining renal parenchyma (arrow). The kidney has otherwise been replaced by a large mass. Histology confirmed a mesoblastic nephroma.
**NEUROBLASTOMA**

**TERMINOLOGY**

**Definitions**
- Maligant tumor composed of neuroblasts, arising within sympathetic neural plexus or adrenal medulla.

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue:
  - No identifiable adrenal gland on side of mass
  - Kidney is displaced inferiorly
- Location
  - May occur anywhere along sympathetic chain
  - > 50% occur in adrenal gland
- Cervical and thoracic tumors also reported
- 60% are right-sided
- Morphology
  - Approximately 50% are cystic
  - May represent involuting tumor
  - Remnants are solid or complex
  - Solid masses are more likely to metastasize

**Ultrasoundographic Findings**
- Variable appearance

**MR Findings**
- Confirm anatomic location
- Signal characteristics, variable depending on cystic or solid composition
- Cystic: Marked increased signal on T2WI
- Solid: Moderate increased signal on T2WI
- Can help exclude adrenal hemorrhage from differential
- Useful for staging and evaluating metastases
- Diffusely infiltrating liver metastases may be missed

**Imaging Recommendations**
- Confirm adrenal origin of mass
- Document mass is separate from kidney
- Look for normal adrenal

**DDx: Neuroblastoma**

- Sequestration
- Sequestration
- Teratoma
- Hemorrhage
NEUROBLASTOMA

Key Facts

Terminology
- Tumor or tumor component of neuroblasts, arising within sympathetic neural plexus or adrenal medulla

Imaging Findings
- > 90% occur in adrenal gland
- Approximately 50% are cystic
- Solid masses are more likely to metastasize
- Liver most common location for metastases
- Diffusely infiltrating liver metastases are difficult to diagnose

Top Differential Diagnoses
- Extrarenal sequestration
- Duplication renal collecting system
- Adrenal hemorrhage

Pathology
- Most common congenital malignancy
- Tumors may "nurse" to more benign histologic type
- > 90% of fetal have a favorable stage (I, II and IV-S)

Clinical Issues
- Prognosis affected by stage and biologic markers
- Most fetal tumors have both invasive-stage and markers
- > 90% overall survival
- 70% mortality rate if mother presents with preeclampsia from placental metastases

Diagnostic Checklist
- Only half of suprarenal masses are neuroblastomas, so must carefully evaluate for other causes, especially extrarenal sequestration

Adrenal hemorrhage
- Reported in utero but uncommon
- Will involute over time
- No color flow within mass
- MRI can confirm blood products

Teratoma
- May infiltrate retroperitoneum and appear similar to stage II or IV neuroblastoma
- Often large, so usually can not identify normal adrenal gland
- Complex, mixed cystic-solid masses
- Calcifications most specific finding

Mesoblastic nephroma
- Renal mass
- Adrenal gland is normal

PATHOLOGY

General Features
- Genetics: Rare familial cases
- Epidemiology
  - Normal fetal adrenal contains neural-likely nodules
  - Histologically indistinguishable from neuroblastoma
  - Peak number of nodules 17-20 wks gestation
  - Nodules involute over time
  - Seen in 100% of fetal adrenals in 2nd trimester
  - Preserved in only 0.5-2.5% of newborn adrenal glands
  - Fetal neuroblastoma may represent temporary defect in growth of these nodules that are destined to involute over time
  - May explain non-aggressive nature of fetal tumors
  - When compared to those in pediatric age group
- Neuroblastoma:
  - Most common congenital malignancy
  - 30% of all fetal tumors
  - 2nd only to teratomas

DIFFERENTIAL DIAGNOSIS

Extrarenal sequestration
- More likely than neuroblastoma as cause of left-sided suprarenal mass, especially if solid
- 10-15% occur below diaphragm
- 90% on left
- Uniformly echogenic solid mass
- Stomach is displaced anteriorly
- Present earlier (2nd trimester)
- Dominant feeding vessel from aorta
- Separate adrenal gland may be identified
- Radiologically may be hybrid lesion
- Sequestration + congenital cystic adenomatoid malformation

Duplicated renal collecting system
- Hydronephrotic upper pole may be mistaken for cystic suprarenal lesion
- Need to examine kidney carefully in both axial and longitudinal planes
- Look for ectopic ureteroceles in bladder
- Separate adrenal gland may be identified
Gross Pathologic & Surgical Features
- Approximately half of all fetal tumors are cystic
  - Cystic change may indicate ongoing involution
  - Cystic tumors have small aggregates of neuroblasts
  - Solid tumors have sheets of tumor cells

Microscopic Features
- Derived from primitive neural crest cells
- Tumors may "mature" to more benign histiologic type
  - Neuroblastoma: Malignant tumor composed of neuroblasts
  - Ganglioneuroblastoma: Malignant tumor with both immature and mature elements
  - Ganglioneuroma: Benign tumor composed of mature ganglion cells
- Biologic markers
  - MYCN amplification
  - Proto-oncogene on chromosome 2p
  - Multiple copies (> 10) in aggressive tumors
  - DNA index
  - Tumors with an increased DNA content (index > 1) have a more favorable prognosis.
  - Most fetal neuroblastomas have a favorable DNA index (index < 1) and no MYCN amplification

Staging, Grading or Classification Criteria
- Stage I: Confined to adrenal gland
- Stage II: Extension beyond adrenal but does not cross midline
- Stage III: Extension across midline
- Stage IV: Distant metastases
- Stage IV S: Unique grouping of metastases, with an excellent prognosis
  - Skin, liver, and < 10% of bone marrow (not bone)
  - > 90% of fetal have a favorable stage (I, II, IV-S)

Treatment
- Consider early delivery if rapidly growing or metastases detected.
- Surgical resection after delivery
- Chemotherapy in most cases
- Given early childhood course, some advocate more conservative postnatal approach
  - Monthly monitoring for 8-12 months (less than 3 cm)
  - Cystic tumors
  - Biopsy solid masses
  - If favorable biologic markers and stage, surgery
  - Post biologic markers/tumor or failure to involute → surgery

DIAGNOSTIC CHECKLIST
Consider
- Overall prognosis for fetal neuroblastoma is excellent
- Majority of tumors have favorable stage and biologic markers

Image Interpretation Pearls
- Only half of suprarenal masses are neuroblastoma, so must carefully evaluate for other causes, especially extralobar sequestration
  - Neuroblastoma
  - More likely cystic
  - More often on right
  - Usually seen within 3rd trimester
  - Extralobar sequestration
  - Solid
  - Significantly more common on left
  - Usually seen by 2nd trimester
  - May see feeding vessel from aorta

SELECTED REFERENCES
NEUROBLASTOMA

IMAGE GALLERY

Typical

(Left) Coronal ultrasound of a cystic neuroblastoma shows a complex cystic mass (arrows). (Right) Sagittal ultrasound performed on day 1 of life for a cystic mass seen in utero. Thick septations are present within the mass. The mass was resected and neuroblastoma was confirmed. About half of all typical neuroblastomas are cystic and have an excellent prognosis.

Typical

(Left) Coronal ultrasound shows a very large, solid mass (arrows) above the kidneys (open arrows). (Right) Solid ultrasound shows the adrenal mass (thick arrows). In addition, the ureter is heterogeneous, with several discrete nodules (open arrows) and there is ascites (white arrows). Solid tumors are more likely to metastasize than cystic ones. (Also shown in Radiographics, ref 1).

Typical

(Left) Gross pathology of the liver from the above case shows diffuse metastatic disease. (Right) Solid ultrasound in another case of metastatic neuroblastoma shows a complex cystic and solid mass infiltrating the abdomen and obscuring normal anatomy. There is biding, with skin thickening (arrows) and ascites (open arrows). The mother presented with preeclampsia from placental metastases. This carries a very poor prognosis, and the infant died shortly after birth.
TERMINOLOGY
Abbreviations and Synonyms
- posterior urethral valves (PUV)

Definitions
- Urethral membrane acts as valve, resulting in bladder outlet obstruction
  - Posterior urethra obstructed by valves
  - Obstruction is usually partial
  - Occurs exclusively in males

IMAGING FINDINGS
General Features
- Best diagnostic clue
  - "Keyhole" sign
  - Distended bladder "funnels" into dilated, posterior urethra

Ultrasonographic Findings
- Male fetus
  - May be difficult to determine gender if severe oligohydramnios
- Findings vary with degree of obstruction
- Renal findings
  - Ureterectasis

DDx: Dilated Bladder
- Caliectasis
- Hydro nephrosis
- Renal dysplasia
- Cortical cysts
- Bladder findings
  - Variable degree of bladder distention
  - May fill entire abdomen
  - Thick-walled
  - May not see with severe dilatation
  - Dilated "keyhole" appearance of posterior urethra
  - If present, strongly suggests diagnosis of PUV
  - Not always seen
  - Urethral aresia can potentially give similar appearance
- Renal dysplasia
  - Echogenic parenchyma thought to be due to fibrosis
  - Suggests, but is not diagnostic of, dysplasia
  - Likely due to back pressure from outflow obstruction
  - Irreversible
  - Persist in spite of intervention to relieve obstruction
- Degree of hydronephrosis does not necessarily correlate with degree of dysplasia
  - May have severe dysplasia with no hydronephrosis
  - Fetal-vascular, dysplastic kidney
  - Fetal hydroureter, renal dysplasia
  - Dysplasia → decreased urine production
  - Renal cortical cysts

Gross pathology show same cases show marked obstruction of the abdomen due to the greatly distended bladder. Note the very small chest cavity. Early oligohydramnios result in fetal pulmonary hypoplasia.
**Key Facts**

**Terminology**
- Urethral membrane acts as valve, resulting in bladder outlet obstruction
- Occurs exclusively in males

**Imaging Findings**
- "Keyhole" sign
- Diverted bladder "funnels" into dilated, posterior urethra
- Hydroureter
- Hydrenephrosis
- Renal dysplasia
- Oligohydramnios
- Urinary ascites
- Follow all fetuses with large bladder
- Evaluate for poor prognostic signs:
  - 100% predictive for dysplasia
  - Seen in 44% of dysplastic kidneys
  - Indicate irreversible damage
  - Fetus unlikely to benefit from in utero intervention if present
  - Usually suggests a fatal outcome
  - Described as early as 20 weeks gestation
  - Renal atrophy is a poor prognostic sign
  - Oligohydramnios
  - Small, bell-shaped chest → pulmonary hypoplasia
  - Poor prognosis
  - 80% mortality rate
  - Associated malformations in 43%
  - Cardiac malformations
  - May be seen with VACTERL association
  - Bladder rupture → urinary tract decompression
  - Favorable prognostic sign, relieves pressure on kidneys
  - Urinary ascites
  - Echogenic kidneys
  - Peritoneal calcifications
  - May also see ruptured collecting system
  - Perinephric fluid collection = urinoma

**MRI Findings**
- Potential role in evaluating renal parenchyma for dysplastic changes
- May help confirm diagnosis in certain cases
- Severe oligohydramnios
- Large maternal body habitus

**Imaging Recommendations**
- Follow all fetuses with large bladder
- Likely transient finding if otherwise normal urinary tract and amniotic fluid volume
- Evaluate for poor prognostic signs:
  - Echogenic kidneys (with or without cysts)
  - May precede abnormal urine chemistries
  - Worsening bilateral hydrenephrosis
  - Unilateral "protects" other kidney (better prognosis)
POSTERIOR URETHRAL VALVES

Presentation
- Bladder distention
- Oligohydramnios
- Has been detected in 1st trimester

Natural History & Prognosis
- Wide range of severity
- Overall mortality 25-50%
- > 80% with oligohydramnios
- Mild and moderate cases in utero = best prognosis
- Very severe cases may remain undetected until childhood
- Need to rule out PUV postnatally in all males with persistent bladder dilatation and/or hydrourephrosis in utero
- Degree of fetal renal damage affects survival
- Characteristic phenotypic features, if severe oligohydramnios
  o Polyhydramnios
  o Fetal tachycardia
  o Flexion contractures
  o Pulmonary hypoplasia
- Vesicoureteral reflux may persist in childhood
- Renal insufficiency develops in up to 45% of survivors

Treatment
- Karyotype fetus with either aneuploidy or bladder tap
- Prognosis worse with aneuploidy
- Can also evaluate sex chromosomes if fetal sex entertained
- Termination may be offered
- > 32 wks, worsening oligohydramnios = deliver = endoscopic valve ablation
- < 32 wks, serial renal function
  o Perform 3rd trimester bladder drainage over 3-4 days
  o Third sample most useful ("fresh" urine)
- Normal fetal urine is hypotonic
- Isotonic urine = poor renal function
- Good prognostic indicators
  o Na < 100 mEq/L
  o CI < 90 mEq/L
  o Osmolality < 210 mosm/L
  o B2 microglobulin < 4 mg/L
  o Ca < 8 mg/dL
- Sonographically normal kidneys (normal echogenicity, no cysts, preserved corticomedullary differentiation)
- Beta 2 microglobulin

- Found in fetal serum
- Filtered by glomerulus, reabsorbed by proximal tubule
- Large amounts in fetal urine = renal damage
- Consider intervention for those in good prognostic category with worsening oligohydramnios and/or hydrourephrosis
  o Vesicostomy
  o Goal is to prevent pulmonary hypoplasia
  o May achieve or migrate
  o Often pulled out by fetus
  o Anterior placentation related to contralateral
  o Vesicostomy insufficient fail
  o Shown to potentially improve pulmonary function, but no effect on renal outcomes
  o Generally no intervention if amniotic fluid volume normal
  o No improvement in outcome for intervention late in pregnancy
  - Experimental studies are ongoing using in utero endoscopic valve ablation
  - Long term sequelae from poor bladder function may necessitate urinary diversion surgery

DIAGNOSTIC CHECKLIST

Consider
- Early oligohydramnios = poor prognosis regardless of cause
- Early diagnosis of PUV allows consideration of intervention
  o Type and timing of intervention very controversial
  o UCSF series 1986 to 1999: Fetal mortality rate 43%
  o Intervention may result in live births but 43% of survivors still have renal insufficiency

Image Interpretation Pearls
- Dilated bladder + oligohydramnios in male fetus highly suspicious for PUV
- Some findings in a female, likely to be urethral agenesis

SELECTED REFERENCES

POSTERIOR URETHRAL VALVES

IMAGE GALLERY

Typical

(Left) Ultrasound shows a thick-walled (arrow), distended bladder. The "keyhole" sign is created by funneling of the bladder into the dilated posterior urethra (open arrow). (Right) Ultrasound shows a needle (arrow) in the bladder for urine aspiration. This allows karyotype analysis, as well as assessment of urinary osmolality and electrolyte concentration. The latter provide an indirect measure of renal function.

Typical

(Left) Axial oblique ultrasound shows a markedly dilated bladder (open arrow) and bilateral hydronephrosis (arrows) in a fetus with posterior urethral valves. (Right) Coronal ultrasound in the same fetus after urography: Shunting illness urinary stasis surrounding the liver (arrows) and bowel (curved arrow). This was attributed to short migration with urine leak through the bladder puncture site.

Typical

(Left) Sagittal ultrasound shows typical findings of PUV with obstruction of the bladder (arrow), a dilated posterior urethra (open arrow), and megalourethra (curved arrow). (Right) Coronal ultrasound in a 16-week male fetus with PUV shows a portion of the bladder (arrow) and bilateral hydronephrosis (open arrow). Renal parenchymal echogenicity is present due to normal, increasing suspicion for renal dysplasia.
PRUNE BELLY SYNDROME

TERMINOLOGY

Abbreviations and Synonyms
- Posterior urethral valves

Definitions
- Rare congenital disorder characterized by dramatic collecting system dilatation, deficiency of abdominal musculature and cryptorchidism

IMAGING FINDINGS

Ultrasonographic Findings
- Gross dilatation of collecting system
  - Large, thin-walled bladder
  - Bilateral hydronephrosis
  - Entire urethra dilated
  - No obvious point of obstruction
  - May be difficult to visualize
  - Oligohydramnios often present

Imaging Recommendations
- Very difficult to differentiate from posterior urethral valves (PV)
- Need to focus scan on urethra
- PCV has dilatation of proximal portion of urethra

DIFFERENTIAL DIAGNOSIS

Posterior urethral valves
- May appear identical
- Some cases of prune belly syndrome may be end result of early obstruction from valves
- Look for dilated posterior urethra (‘keyhole’ sign)
- Hydronephrosis/ureter not always present
- Thick-walled bladder

Megacystis-microcolon
- Massive dilatation of urinary bladder with hydronephrosis
- Normal amniotic fluid volume
- More common in females (8:1)

DDx: Obstruction Causing Hydronephrosis

UP Definition

PV

PUN

Duplicated System
PRUNE BELLY SYNDROME

Terminology
- Rare congenital disorder characterized by dramatic collecting system dilatation, deficiency of abdominal musculature and cryptorchidism

Imaging Findings
- Large, thin-walled bladder
- Bilateral hydronephrosis
- Entire urethra dilated

Pathology
- Bladder aspiration shows normal renal function
- No other malformations
- Neonatal renal transplant may be required

Key Facts
- Need to focus scan on urethra
- Scan genitalia, looking for undescended testes

Top Differential Diagnoses
- Posterior urethral valves
- Megacystis-microcolon

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls
- Consider prune belly syndrome when there is massive dilatation of the entire collecting system

SELECTED REFERENCES

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
- Massive collecting system dilatation
- Polyhydramnios
- Postnatal
- Flaccid, "doughy" abdomen
- Wrinkled appearance resembles a prune
- Potter facies may be seen if severe polyhydramnios

Natural History & Prognosis
- Depend on severity of polyhydramnios and renal damage
- Renal failure common in survivors

Treatment
- Serial sonography required throughout pregnancy
- Monitor degree of dilatation and urinary fluid volume
- Vesicocutaneous stent may aid in decompressing bladder and improving urinary fluid status
- Consider early intervention for best possible outcome
- Perform only if certain criteria met
- Karyotype normal

IMAGE GALLERY

(a) Gross pathology shows the thin abdominal wall, with no musculature (arrow), a dramatically dilated bladder (open arrow) and a portion of a very flattened, dilated urethra (curved arrow). Undescended testes were also present. (right) Cryoablation of an infant with prune belly syndrome shows a greatly dilated bladder (open arrow), with reflux into an invisible ureteric system (arrow). The contrast appears less dense than normal urine, as it is diluted by the large amount of urine within the collecting system. (Courtesy C.L. Cowgill, M.D.)
**TERMINOLOGY**

Definitions
- Congenital dilatation of intravesical segment of ureter
  - Dilated segment prolapses into bladder lumen
  - Variable type: simple, ectopic and exoureterocele
- Simple
  - Occur at normal ureterovesical junction
  - Located at trigone of bladder
  - Not usually seen in utero
- Ectopic
  - Almost always associated with renal duplication
  - Inserts medial and inferior to trigone, near bladder base
  - Ectopic ureter usually has a stenotic opening into bladder
  - Ectopic ureter may potentially insert outside of bladder
    - Females: Vagina, uterus
    - Males: Epididymis, seminal vesicles, ejaculatory ducts, vas deferens
    - Directly onto perineum
    - Urethra
- Exoureterocele
  - Uncharacteristic type of ectopic ureterocele
  - Dissects submucosally into urethra
  - Can cause intermittent bladder outlet obstruction

**IMAGING FINDINGS**

General Features
- Best diagnostic clue
  - Thin-walled, cystic mass inside bladder lumen
  - Hydrostatic cysts predominately involving upper pole of kidney
- Weight-Meyer rule in renal duplication
  - Upper moiety ureter inserts inferior and medial to normal ureteric insertion site
- Ectopic implantation = upper pole obstructs
- Lower renal pole moiety inserts normally in bladder trigone
- Distortion of orifice by adjacent upper moiety ureterocele may result in reflux

Ultrasoundographic Findings
- Blackout findings
  - Anechoic, "balloon-like", thin-walled cyst inside bladder lumen; represents ureterocele
  - May prolapse in and out of bladder
- If ureterocele obstructed = hydronephrotic
  - Look for Connection of "cyst" to distal ureter
- "Color Doppler may show ureteral jet"
- If ureterocele is large
  - May obstruct contralateral kidney
  - May cause bladder outlet obstruction
  - Ureteral findings

**DDx: Abnormal Bladder Or Collecting System**

- Posterior IV
- UPI Obstruction
- UPI Obstruction
URETEROCELE

Key Facts
- Congenital dilatation of intramural segment of ureter
- Dilated segment prolapses into bladder lumen
- Affected always associated with renal duplication
- Ectopic ureter may potentially insert outside of bladder

Imaging Findings
- Thin-walled, cystic mass inside bladder lumen
- Hydro nephrosis predominantly involving upper pole of kidney
- Ureteroceles omits inferior and medial to normal ureteral insertion site
- Lower renal pole moiety inserts normally in bladder trigone

- If fluid-filled tube connects to renal pelvis
- May 'touch' spine (dilated bowel loops tend to be more central)
- May see peristalsis
- Both upper and lower pole ureters can be dilated in renal duplication
- Ureteroceles with obstructed ectopic ureter
- Neonatal ureter dilated from reflux

- Renal findings
  - Hydro nephrosis usually worse in upper pole (obstructed system)
  - Lower pole may also have hydronephrosis from reflux
  - Kidney large relative to contralateral, non-duplicated kidney
  - Obstructive cystic dilatation of upper pole renal parenchyma if obstruction severe
  - Dilated collecting system/cyst may replace upper renal parenchyma = displaces normal lower pole
  - Mass effect → lower pole pushed down
- Oligohydramnios
- May develop if ureteroceles obstructs bladder outlet

Imaging Recommendations
- Protocol advice
  - When hydro nephrosis present, always search for other signs of renal duplication
  - Normal lower pole moiety (i.e. dilated collecting system upper pole only)
  - Ureterectasis
  - Ectopic ureteroceles
  - Ureteroceles + dilated upper pole collecting system + duplication
- Evaluate bladder several times during any fetal ultrasound
  - Ureteroceles best seen when bladder partially full
  - If is bladder empty, ureteroceles may be misinterpreted as bladder
  - When distended, bladder may compress ureteroceles
  - Examine kidney in both transverse and longitudinal view

- Transverse view alone may mimic ureteropelvic junction (UPJ) obstruction
- Lower pole moiety may be displaced inferiorly and difficult to see
- Follow collecting system in real-time
- Renal pelvis → ureter → ureteroceles

DIFFERENTIAL DIAGNOSIS

Bladder mass
- Rhabdomyosarcoma
  - Solid mass
  - Lacks communication with distal ureter
  - Bladder hemangioendothelioma
    - May be solid or cystic
    - No communication with distal ureter
    - Extremely uncommon in fetus

Mass effect from sigmoid colon
- Distal bowel dilation → multiple low echogenic structures in pelvis
- Urine is anechoic, meconium produces low-level echoes
- Look for changing shape as bladder fills and empties
- Colonic loops do not undergo significant peristalsis

Vesicoureteral reflux
- Dynamic changes may be observed
  - Common
- Normal bladder

Congenital megaureter
- Uniform dilatation of the ureter
- May have hydro nephrosis
  - Usually unilateral (left > right)
  - May affect males
- Normal bladder

UPJ obstruction
- Collecting system dilatation
  - Uter not dilated
  - No ureteroceles
Bladder “Hutch” diverticulum
- Teratocutaneous defect of bladder
- Extrinsic, does not prolapse into bladder lumen
- Separate from distal ureter

PATHOLOGY

General Features
- Genetics: Sporadic
- Etiology
  - Steroids of distal ureteric orifice
  - Distal ureteric lumen expands between mucosa and muscle of bladder wall
- Ectopic ureterocele occurs adjacent normal ureteral orifice allowing reflux into lower pole moiety
- Embryology theories
  - Delayed canalization of Chiavalle neobladder during embryogenesis
  - Accessory ureteric bud inserts separately into metanephric blastema
- Epidemiology
  - Incidence of ectopic ureterocele parallels that of renal duplication
  - Renal duplication with ectopic ureterocele
  - 1:7,000 live births
  - Familial (duplication without ureterocele spatial duplication)
  - 1:150 in general population
- Ureters are before bladder insertion
- Partial duplication less likely to have ureterocele
- No clinical significance
- Ectopic simple ureterocele = 5:1
- Associated abnormalities
  - Gynecological abnormalities in 30% of females with duplication
  - Contralateral duplication in 10-20%

CLINICAL ISSUES

Presentation
- Incidental finding in urology
- Found in workup of hydronephrosis
- Typical presentation in infancy
  - Hematuria, urinary tract infection
  - Hydronephrosis, urinary retention
  - Boys with extravesical insertion
  - Epididymitis or renal symptoms
  - Girls with extravesical insertion
  - Unsuccessful toilet training
  - Underwear always damp
- Simple ureterocele may be asymptomatic

Natural History & Prognosis
- Prognosis depends on degree of obstruction
  - Excellent if no obstruction or reflux
  - Variable outcome if high grade reflux or prolonged obstruction

Treatment
- In utero treatment not usually indicated
  - Consider incision of ureterocele if bladder outlet obstruction/polyhydramnios
  - Postnatal work-up in all cases
  - Ultrasonogram of bladder and kidneys
  - Voiding cystourethrogram (VCUG)
    - Filling defect in bladder best seen on early filling image
    - Vesicoureteral reflux into lower pole
  - "Dropping lily" sign: Obstructed upper pole pushes lower pole calyces inferiorly
  - Intravenous pyelogram is usually necessary
  - Delayed nephrogram and pyelogram of upper pole moiety due to obstruction
  - May see extravesical ureteric insertion site
  - Delineate associated gynecological abnormalities
  - Radiourodynamics scan to assess function
- Surgical options based on consequences of ureterocele
  - Endoscopic ureterocele incision
    - Particularly if infected or obstructed
  - Ureteral reimplantation surgery
  - Heminephrectomy
  - Performed if poorly functioning upper pole

DIAGNOSTIC CHECKLIST

Consider
- Cystic mass in bladder is overwhelmingly likely to be an ectopic ureterocele
- Examine kidneys in both axial and longitudinal planes to look for duplicated collecting system
- Always consider collecting system duplication as a cause of hydronephrosis

Image Interpretation Pearls
- Dilated upper pole moiety + cystic mass in bladder = ureteral duplication with ureterocele

SELECTED REFERENCES
**URETEROCELE**

**IMAGE GALLERY**

**Typical**

(B) Axial view (Doppler ultrasound shows a cyst (arrow) within the bladder) is a typical appearance for a ureterocele. (Right) Coronal ultrasound of the kidney shows hydromeum (arrow) at the upper pole moiety (arrow) of the renal duplication. The lower pole shows normal calyces (open arrow). In a duplicated system, the upper pole obstructs secondary to the ectopic ureterocele and the lower pole may reflux.

**Variant**

(B) Axial ultrasound shows a dilated, ectopic ureterocele (arrow) within the bladder. Both the upper (red arrow) and lower poles (open arrow) of the kidney were dilated. (Right) Coronal view from a VCUG shows a large, smooth filling defect (arrow) at the bladder base, created by an ectopic ureterocele.

(B) Axial ultrasound shows a large ureterocele (arrow) in the bladder. (Right) Coronal oblique ultrasound of the kidney shows multiple cystic areas within the left kidney (arrow). Chronic urinary obstruction associated with the ureterocele results in obstructive cystic dysplasia of the kidney. The right lower calyx (open arrow) is normal.
**URACHAL ANOMALIES**

**TERMINOLOGY**

**Definitions**
- Group of disorders resulting from incomplete inversion of allantois
  - Patent urachus
  - Most common form seen in utero
  - Urachal cyst
  - Urachal diverticulum
  - Urachal sinus

**IMAGING FINDINGS**

**General Features**
- Location
  - Midline, anterior pelvis
  - Urachus lies in space of Retzius, between transversalis fascia and peritoneum

**Ultrasoundographic Findings**
- Cystic mass above bladder
- Communication with bladder confirms patent urachus
- May extend into base of umbilical cord
- Associated with allantoic cord cysts

**Differential Diagnosis**

**Other Abdominal Cysts**
- Location most important in differentiating from urachal anomaly
- Other cystic masses are not restricted to anterior midline
- Ovarian cyst, enteric duplication cyst, mesenteric cyst
- Bowel obstruction, meconium pseudocyst

**Bladder Outlet Obstruction**
- Dilated bladder may extend up to umbilicus
- Hydronephrosis, hydroureter, cystic kidneys
- Look for ‘key hole’ appearance with posterior urethral valves (PUV)
- Oligohydramnios

**Omphalocele**
- Potential source of confusion if urachus communicates with umbilical cord cyst

**DDx: Pelvic Fluid Collections**
- Ovarian Cyst
- Ovarian Cyst
- PUV
- Duplication Cyst
URACHAL ANOMALIES

**Terminology**
- Group of disorders resulting from incomplete involution of allantois

**Imaging Findings**
- Cystic mass above bladder
- Communication with bladder confirms patent urachus
- May extend into base of umbilical cord
- Associated with allantoic cord cysts

**PATHOLOGY**

**General Features**
- **Embryology**
  - Allantois forms from caudal end of yolk sac
  - Functions as primitive bladder and early blood forming organ
- **Evolution to become median umbilical ligament**
- **Are persistent segments are termed urachal remnants**
- **Bladder outlet obstruction is risk factor**
- **Urachus serves as “pop-off valve” to decongest bladder**

**Epidemiology**
- **Patent urachus 1:40,000 live births**
- **M:F = 2:1**
- **Associated abnormalities**
  - Usually an isolated finding
  - umbilical cord cyst or thickening
  - Thickening may be from urine absorption into Wharton jelly
  - **Association with aneuploidy reported**
  - Other genitourinary anomalies
  - PUB, cryptoepithelial, renal anomalies
  - Omphaloleia

**CLINICAL ISSUES**

**Presentation**
- Most common signs/symptoms: Incidental cystic abdominal mass
- Other signs/symptoms
  - Umbilical cord cyst
  - Postnatal
  - Persistent drainage from umbilicus
- Urinary tract infection

**Natural History & Prognosis**
- Cystic mass may spontaneously close in utero
- Patent urachus or urachal sinus may remain
- Excellent prognosis with repair
- Risk of infection and malignancy if not resected

**Treatment**
- Complete postnatal work-up, even if anomaly appears to have evolved in utero
- VCUG best test to document patency of urachus

**Top Differential Diagnoses**
- Other abdominal cysts

**Pathology**
- Bladder outlet obstruction is risk factor
- Usually an isolated finding

**Diagnostic Checklist**
- Anterior, midline location most important diagnostic finding
  - Ultrasound appearance depends on type and amount of persistent remnant
  - Typically thick, well-defined wall
  - Resection of entire tract
  - May need to be done as a staged procedure if presenting with infection/inflammation
  - Patent urachus with bladder outlet obstruction
  - Correct obstruction first
  - Urachus may spontaneously close when pressure relieved

**IMAGE GALLERY**

(left) A VCUG after delivery, in the same infant from the preceding page, shows the bladder (arrow) in direct continuity superiorly with the patent urachus (arrows). (right) Interpretative photogaph in another case shows an allantoic cyst (arrows) within the base of the umbilical cord. The cyst is filled with urine, and communicates with the bladder via a patent urachus.
AMBIGUOUS GENITALIA

Terminology
Abbreviations and Synonyms
- Ambiguous genitalia (AG)
- Normal genital morphology
- Intersex conditions

Definitions
- Continuum appearance of external genitalia
- Cannot determine if fetus is male or female
- AG is morphologic diagnosis with many cases

Imaging Findings
General Features
- Best diagnostic clue: Perineal region seen well and gender is indeterminable
- Morphology: Extremely variable
- General AG issues
  - Cannot differentiate penis from clitoris
  - Early phallic structure similar in males and females
  - Mild clitoromegaly normal in fetal life
  - Cannot differentiate scrotum from labia
  - Cryptorchidism (non-descended testes)
  - Empty scrotum resembles labia
  - Fusion labia resembles scrotum

Ultrasound Findings
- AG findings in XY fetus
  - Hypospadias
  - Abnormal ventral penile urethral opening
  - Penoscrotal, scrotal, penile are most severe
  - Distal penile hypospadias is least severe
  - Blunt-ending penis
  - +/− Small penis
  - +/− Chordee (ventral curvature of penis)
  - +/− 10% with cryptorchidism
- Epispadias
  - Abnormal dorsal urethral opening
  - More rare than hypospadias
  - Small hypospadias
  - Associated with bladder exstrophy
- Microepispadias
  - Small penis
  - +/− Cryptorchidism
- Clefts
  - Ventral curvature of penis
  - Penis is foreshortened
- Cryptorchidism
  - Undescended testes

DDx: Normal Genital Morphology

- Normal Male
- Normal Female
- Normal Labia
- Normal Scrotum
AMBIGUOUS GENITALIA

Key Facts

Pathology
- Torsomy 13
- Triploidy
- Congenital adrenal hyperplasia
- Female pseudohermaphroditism (46,XX)
- Male pseudohermaphroditism (46,XY)
- Mixed gonadal dysgenesis (45,XO/46,XY)
- Pure gonadal dysgenesis
- True hermaphroditism (rare)
- 1:5,000 live births

Clinical Issues
- Congenital adrenal hyperplasia may be fatal if not treated

Diagnostic Checklist
- Do not assign gender prenatally if AG

- Can not diagnose if < 32 wks
- Scrotum mimics labia
- Bigh ending vagina
- Rarely seen prenatally
- AG findings in XX fetus
- Citrorganomaly
  - Can mimic penis
  - Can mimic hypoplasia + cryptorchidism
- Fusion of labia
  - Posterior most often
- Mimics emptiness
- Prominent labial folds
- Redundant labia minora
- Normal variant
- AG + other anomalies
- Anencephaly
- Trisomy 13
- Triploidy
- Many syndromes
  - Smith-Lemli-Opitz
  - Pander-Willi
- Vebocardiofacial syndromes
- AG and congenital adrenal hyperplasia
- Important treatable cause of AG
- AG secondary to virilized female (XX)
- Citrorganomaly
  - +/- fused labia
- Congenital adrenal hyperplasia
  - Bilateral enlarged adrenal glands
  - Discol morpholgy
  - Indistinct cortex/medullary differentiation
  - Normal adrenal glands are triangular with an "ice cream sandwich" appearance (hyperplastic cortex and hypoplastic medulla)
- Other causes of adrenal gland size or suprarenal mass are usually unilateral
  - Neuroblastoma
  - Hemorrhage
  - Extralobar sequestration

Imaging Recommendations
- Best imaging tool
  - Evaluate genitalia in axial + sagittal planes

- Penis resembles clitorises on axial view
- Clitoris points caudal on sagittal view
- Penile points cranial on sagittal view
- Look for testes in scrotum after 25 wks
- Use color Doppler to see urine stream
- Consider 3D ultrasound
- Multiplanar capacity
- Surface rendered views helpful

Protocol advice
- Look for testes in scrotum after 25 wks
- 97% descend by 32 wks
- Use color Doppler to see urine stream
- Find extrarenal office (tep vs. ventral vs. dorsal)
- Genetic counseling
- Anencephaly
- Do not assign gender during fetal life if ambiguous
- Event when karyotype is known
- Best done after full physical exam
- Family must see significant counseling
- Look carefully for other anomalies
- AG associated with anencephaly and syndromes

DIFFERENTIAL DIAGNOSIS

Normal female genitalia
- Labia
  - 2-4 parallel eczhecahine lines
- Clitoris
  - Between labia on transverse views
  - Points caudal on sagittal views
- Urethra
  - Can often be seen after 20 wks
- Echogenic mass between bladder and rectum
- Ovaries
  - Rarely seen unless with cyst (3rd trimester)

Normal male genitalia
- Normal scrotum
  - Testes descend at 25-28 wks
  - Small hydroses common
  - Often transient
- Normal penis
  - Tapered end
  - Urethra from tip
AMBIGUOUS GENITALIA

PATHOLOGY

General Features
- Genetics
  ○ Trisomy 13
  ○ Triploidy
  ○ Klinefelter (47XXY)
- Many duplication and deletion syndromes
- Congenital adrenal hyperplasia
  ○ Autosomal recessive (29% recurrence)
- Biology
  ○ Heterogeneous group with many etiologies
    ○ Congenital adrenal hyperplasia
    ○ Carbohydrate aldosterone synthase enzyme defect
    ○ > 90% from 21-hydroxylase defect
    ○ Female pseudohermaphroditism (46,XX)
    ○ Fetus has 2 ovaries
    ○ Excess androgenesis
    ○ Congenital adrenal hyperplasia
    ○ Maternal ingestion of androgens
    ○ Mاد pseudohermaphroditism (46,XY)
    ○ Fetus has 2 testes
  ○ 1 End organ testosterone response (80%)
  ○ Testosterone production
  ○ 1 Mullerian inhibiting factor
- Mixed gonadal dysgenesis (45,X/46,XY)
- Mosaicism
- Stearoyl CoA desaturase deficiency
- Female phenotype common
- Pure gonadal dysgenesis
- Variable karyotype (46,X, + variable Ychromatin)
- Variable external genitalia
- Epidemiology
  ○ 1:5,000 live births
  ○ 1:150,000 live births with congenital adrenal hyperplasia

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  ○ Incidentally noted during routine ultrasound
  ○ Parents desire to know gender of child
  ○ In association with other anomalies
- Prior child with congenital adrenal hyperplasia
- Amenorrhea/chorionic villus sampling to rule out congenital adrenal hyperplasia in first child
- Molecular analysis for CY21ZI gene
- Other signs/symptoms
  ○ Material hormone ingestion during 1st trimester
  ○ Premenarche for threatened abortion
  ○ Anzoemias for endohormones

Natural History & Prognosis
- Congenital adrenal hyperplasia may be fatal if not treated
  ○ Aldosterone/cortisone
  ○ Salt wasting
  ○ Hypertension, hyperkalemia
  ○ Progressive virilization
  ○ AG in females

Treatment
- Consultant team approach best for family
- Genetics, urology, psychiatry
- Gender assignment only after neonatal work-up
  ○ Physical examination
  ○ Laboratory tests (including endocrine function)
- Surgical treatment often necessary
- Congenital adrenal hyperplasia treatment
  ○ Premarin desamethasone

DIAGNOSTIC CHECKLIST

Consider
- AG diagnosis only if perineum is seen well
- Beware of false normal histology
- Amniocentesis
  ○ Determine genetic sex
  ○ Rule out androgenesis
  ○ Rule out congenital adrenal hyperplasia

Image Interpretation Pearls
- Do not assign gender prematurely if AG
  ○ Even when amniocentesis results are available
- Generic sex not always followed
- Examine fetal urothelial glands if virilized female seen
  ○ Rule out congenital adrenal hyperplasia

SELECTED REFERENCES
AMBIGUOUS GENITALIA

**IMAGE GALLERY**

**Typical**

(Left) A doll's head shows a small, bean-shaped renal sac (arrow) which may be a 3rd trimester fetus with a normal Nk language (path - open arrow). Preliminary diagnosis of cryptorchidism was suggested. (Right) A doll's head shows bilateral empty scrotum (arrow). One testis was found in the inguinal canal and the other was intra-abdominal.

**Variant**

(Left) A doll's head shows ambiguous genitalia (arrow) in a child with multiple other anomalies and growth restriction. The genital mound is amorphous. Chromosomal studies were made subsequently. (Right) Clinical photograph of the same fetus shows a amorphous (arrow) and “fetal-like” scrotum, consistent with cryptorchidism. AG is common with trisomy 13 and trisomy 18 but not in an isolated finding.

(Left) A doll's head shows continued genital morphology in a 3rd trimester fetus. The echocardiographic lines (arrows) suggest fetal but we were unsure and therefore, 3D ultrasound was performed. (Right) 3D views and 3D reconstruction (bottom) show labia majora (arrow) and labia minora (open arrow) folds. The baby was born with prominent labial folds, considered a normal variation.
**HYPSAPADIAS**

**Terminology**

**Definitions**
- Urethra open on ventral side of penis, not tip

**Imaging Findings**

**General Features**
- Best diagnostic clue: "beak-ended" penis
- Location: Anywhere along expected course of urethra

**Ultrasoundographic Findings**
- Tip of penis is blunt instead of pointed
  - "Squashed cone"
  - Often see 2 echogenic lines at tip
- Prepuce lateral folds
- Small penis (nonspecific)
- Chordee (ventral curving of penis)
- Abnormal stream (color Doppler)
  - From ventral penis instead of tip
  - Fan-shaped instead of linear
- "Tulip sign" of severe hypospadias
  - Small beak-ended penis between 2 scrotal folds
  - Undescended testicles (cryptorchidism)
- Associated penile cyst (rare)
- Cyst from urethrocystaneous fistula

- Fills and empties with micromanipulation
- Associated anomalies
  - 40% with other urogenital anomalies
  - 10% with cryptorchidism
  - 7-9% with extra-urogenital anomalies

**Imaging Recommendations**
- Fetal sex determination
  - Accuracy is > 90% after 20 wks
- Look at morphology of penis

**Differential Diagnosis**

**Ambiguous Genitalia**
- Can not determine sex based on morphology
- Heterogeneous disorders
  - Chromosomal defect
  - Hormonal influence
  - Common diagnoses
    - Citroomegaly
    - Cryptorchidism
    - Hypospadias
- Associated anomalies needed helpful

**Micropenis**
- Small penis with normal shape
- Normal stream
- Many different causes

**DDx: Ambiguous Genitalia**

- Citroomegaly
- Cryptorchidism
- Micropenis

**Clinical photograph shows that the urethral opening (arrow) is ventral in the penis tip. Lateral fields of the prepuce (open arrow) and ventral curve of the penile shaft (closed arrow) are classic findings of hypospadias.**

**Ultrasound shows short penile hypospadias. The tip of the penis is not tapered but instead ends bluntly (arrow). Note the "squeezed cone". Two echogenic lines (open arrow) represent prepuce lateral folds.**
HYPOSPIADAS

Terminology
- Preputial opening on ventral side of penis, not tip

Imaging Findings
- Best diagnostic clue: "Blunt-ended" penis
- Often see 2 echogenic lines at tip
- Crooked (ventral curving of penis)
- Abnormal stream (color Doppler)
- 50% with other urogenital anomalies

- Associated cryptorchidism common

Normal early male genitalia (< 20 wks)
- Fusion of labioscrotal folds not complete
- Testes may not descend until > 26 wk

PATHOLOGY

General features
- Genetics
  Most often, normal chromosomes
  XXY and XXXY syndromes
  Trisomy 13, trisomy 18, triploidy
- Embryology
  Failure of complete urethral groove fusion
  Fusion fails short of tip of glans
  Hormone etiology theory
  Organ testosterone insensitivity
  17-hydroxysteroid dehydrogenase
  Can not convert testosterone to androsterone
dihydrotestosterone
- Epidemiology
  Most common congenital defect of genitalia
  0.2-4.1 per 1,000 births
  4-12% recurrence risk for male fetuses

Staging, Grading or Classification Criteria
- Classification based on scrotal position
  > 50% anterior (glans)
  > 30% midline (penis)
  > 20% posterior (penoscrotal, scrotal, perineum)

CLINICAL ISSUES

Presentation
- Most common signs/symptoms: Incidental finding at
  time of sex determination
  Other signs/symptoms
  Associated with many syndromes
  Cryptorchidism, Smith-Leitn, Optiz, 4p-,
  Aniridia-Wilms

Demographics
- Age: 1 risk with advancing maternal age

Natural History & Prognosis
- Early complication
- Meatal stenosis
- Late complications

Top Differential Diagnoses
- Ambiguous genitalia
- Microprosperm
- Normal early male genitalia (< 20 wks)

Pathology
- 0% anterior (glans)
- 30% midline (penis)
- 20% posterior (penoscrotal, scrotal, perineum)

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IMAGE GALLERY

(left) Ultrasound shows a penis cyst termed. Severe posterior
hypospadias can be associated with urinary colonic tissue and
penis cyst. The finding is rare and in this case caused bladder
obstruction. (right) Sagittal ultrasound through the fetal penis in
the same case shows a large fluid collection, which communicates
posteriorly with the rectum cavum. The fluid had multiple
anomalies, including high renal stones. Extraprostatic anomalies
occur in 7-9% of cases.
HYDROCELE

TERMINOLOGY

Definitions
- Fluid in scrotal sac

IMAGING FINDINGS

General Features
- Best diagnostic clue: Fluid surrounds testis
  - Location
    - Most commonly unilateral
    - Bilateral in 1/3
  - May be asymmetric
- Morphology
  - "Half moon" crescent around testis
  - Large hydrocele may completely surround testis

Ultrasoundographic Findings
- Simple hydrocele (common)
  - Anechoic fluid
  - Normal testis
  - Homogeneous echotexture
  - Symmetric size
  - Normal epididymis
  - Often transitory
  - 50% resolve by 37 wks
  - Most resolve by birth
- Complex hydrocele (rare)
  - Fluid with linear/focal echo
  - Suggests a secondary process
  - Herniorrhage
  - Testicular infection/torsion
  - Associated testicular abnormality
  - Acutely enlarged, followed by atrophy
  - Heterogeneous echotexture
  - Exostatitc testis (rare)
  - Enlarged epididymis
  - Skin thickening
  - Meconium peritonitis is rare cause
  - Complex peritoneal fluid enters scrotum
  - May see calcifications
  - Normal testis

Imaging Recommendations
- Protocol advice: Look carefully at testes if complex hydrocele seen

DIFFERENTIAL DIAGNOSIS

Testicular torsion
- Testis twists upon vascular pedicle
  - Testis almost never viable at birth
  - Acutely enlarged, heterogeneous testis
  - Hydrocele often an early finding
  - Complex > simple

DDx: Abnormal Scrotal Morphology

- Testicular Torsion
- Testicular Tumor
- Inguinal Hernia
- Cryptorchidism
Terminology
- Fluid in scrotal sac

Imaging Findings
- "Half moon" crescent around testis
- Simple hydrocele (common)
- Complex hydrocele (rare)

Top Differential Diagnoses
- Inguinal hernia
- Testicular torsion

Inguinoscrotal hernia
- Peritoneal contents herniate into scrotum
- Multilocular scrotal mass is bowel
- Look for peristalsis
- Associated hydrocele common

Cryptorchism (undescended testes)
- Hydrocele; empty sac may mimic hydrocele
- Can not make diagnosis before 32 wks

PATHOLOGY

General Features
- Biology
  - Normal testicular descent by 25-32 wks
  - Perineal testicular veins form from extension of perineal cavity
  - Aids in descent of testis
  - Normally obliterated and becomes utricle vaginalis
  - Hydrocele forms if persistent patent processes vaginalis or fluid not resorbed
- Epidemiology
  - 15% of male fetuses > 27 wks
  - 21% at 27-32 wks
  - 11% > 32 wks
- Associated abnormalities
  - Inguinal hernia
  - Hydrocoele testis
  - Meconium peritonitis
- Testicular infarction/torsion

Staging, Grading or Classification Criteria
- Communicating hydrocele (patent processes vaginalis)
- Fluid communicates with peritoneum
- Non-communicating hydrocele
- Fluid confined to scrotum

CLINICAL ISSUES

Presentation
- Most found on newborn exam
- Painless and transillumination
- Light shine on scrotum shows intra-sac contents
- Communicating hydrocele
- Cannot move fluid from scrotum into peritoneum

Natural History & Prognosis
- Most often physiologic and transient

Key Facts
- Inguinoscrotal hernia

Pathology
- 15% of male fetuses > 27 wks
- Communicating hydrocele (patent processes vaginalis)
- Non-communicating hydrocele

Clinical Issues
- Most often physiologic and transient
- Surgery if hydrocele not resolved by 12-18 months
- Hydrocele sac repaired
- Muscle wall reinforced to prevent hernia

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls
- Many simple hydroceles resolve by birth
- Consider hematocoele, if fluid is complex

SELECTED REFERENCES

IMAGE GALLERY

(C) Coronal ultrasound shows a complex, right scrotal hydrocele with fluid locules (arrows) and scrotal skin thickening (open arrow). A small simple hydrocele is seen on the left (curved arrow).
(right) Sagittal ultrasound of the right testis after birth shows a large, hydronephrosis, varicocele and testicular cysts as mentioned previously. Interestingly, the hydrocele was anechoic after birth, suggesting that the prenatal fluid contained hemorrhage that subsequently reabsorbed.
**TESTICULAR TORSION**

Ultrasound of a left inguinal sperm shows an enlarged left testicle (arrows) and a normal-sized right testicle (curved arrows). The left hydrocele contains few linear echoes (open arrows), secondary to hemorrhage.

**TERMINOLOGY**

Definitions
- Twisting of spermatic cord → testicular infarction

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue: Asymmetric testis size + complex scrotal fluid
- Location: L > R, rarely bilateral
- Size: Testis may be either large (acute) or small (chronic)

**Ultrasonographic Findings**
- Normal scrotum
  - Testes descend at 25-32 wks
  - Symmetric testicular size
  - Homogeneous echotexture
  - Transient anechoic hydroceles
- Acute torsion:
  - Enlarged testis + epididymis
  - Appears as single undifferentiated mass
  - Variable echotexture
  - Diffusely hypoechoic from edema
  - Heterogeneous from infarction
  - Scrotal edema

- Complex hydrocele
  - Hemorrhage
  - Linear and focal echoes
  - Contralateral simple hydrocele
- Chronic torsion
  - Small testis
  - Echogenic capsule
  - "Echogenic halo"
  - Intracapsular calcification
  - +/- Hydrocele
  - "Double ring hemorrhage" variant
  - Tests surrounded by 2 concentric fluid layers
  - 2nd to hemorrhage into 2 spaces
  - Between visceral and parietal tunica vaginalis
  - Between tunica vaginalis and scrotum
  - Doppler rarely helpful
  - Difficult to show flow if < 1 cc volume

**Imaging Recommendations**
- Careful evaluation of testes when complex hydrocele seen
- Doppler not helpful unless flow seen on normal side

**DIFFERENTIAL DIAGNOSIS**

Unilateral cryptorchidism
- One undescended testis
- Scrotal asymmetry can mimic mass

**DDx: Enlarged Scrotum**

- Cryptorchidism
- Inguinal Hernia
- Hydrocele
- Hydrocele
TESTICULAR TORSION

Terminology
- Twisting of spermatic cord \(\Rightarrow\) testicular infarction

Imaging Findings
- Enlarged testis + epididymis
- Complex hydrocele
- Echogenic capsul
- "Double ring hematoma" variant
- Doppler rarely helpful

Inguinal hernia
- Abdominal contents herniate through inguinal canal
- Cystic/echogenic mass in scrotum
- Look for peristalsis

Large simple hydrocele
- Fluid remains anechoic
- Can be easily sign of torsion
- Torsion unlikely if testis is normal

Testicular tumor
- Extremely rare in prenatal life
- Solid mass
- Testis sac tumor most common

PATHOLOGY

General Features
- Biology
  - Spermatic cord torsion
    - Venous flow affected before arterial
  - Epidemiology: 1-4,000 newborn males

Staging, Grading or Classification Criteria
- Extravaginal torsion (almost all fetral/pediatric cases)
  - Spermatic cord + tunica vaginalis twist as a unit
- Intravaginal torsion (adults)
  - Spermatic cord twists inside tunica vaginalis

CLINICAL ISSUES

Presentation
- Difficult prenatal diagnosis
- Enlarged testis surrounded by a hydrocele
- Hydrocele usually complex
- Scrotum may be swollen and dusky on newborn physical exam
- Acute torsion: Enlarged, painful testis
- Chronic presentation: Hard, shrunken testis

Natural History & Prognosis
- Fetral/neonatal torsion has low salvage rates

Treatment
- Fetus not delivered emergently for unilateral torsion
- Salve rates are abysmal
- Consider emergency delivery if torsion is bilateral
- Chronic torsion

Key Facts

Top Differential Diagnoses
- Unilateral cryptorchidism
- Inguinal hernia
- Large simple hydrocele

Pathology
- Extravaginal torsion (almost all fetral/pediatric cases)

Clinical Issues
- Fetral/neonatal torsion has low salvage rates

- Orchiectomy and contralateral orchiopexy
- Acute torsion
- Surgery to untwist spermatic cord
- Bilateral orchiopexy

DIAGNOSTIC CHECKLIST

Consider
- Testicular torsion diagnosis with complex scrotal fluid seen

Image Interpretation Pearls
- Doppler is not very helpful
- Simple hydrocele is much more common than torsion
- Torsion is rarely saved when diagnosed in utero

SELECTED REFERENCES


IMAGE GALLERY

[Image 1]: Scrotal ultrasound from the same case as the preceding page. Performed immediately after delivery, shows marked heterogeneity of the left testis. No blood flow was demonstrated. (Right) Ultrasound of the testes, in another case, shows bilateral torsions diagnosed almost after birth. The right testis and epididymis (curved arrow) are swollen and heterogeneous, consistent with an acute event. The left testis is shrunken and contains calcific foci (arrows), consistent with chronic torsion.
**TERMINOLOGY**

**Definition:**
- Benign functional cyst within fetal ovary

**IMAGING FINDINGS**

**General Features:**
- Best diagnostic clue: Abdominal cyst containing “daughter cyst” in a female fetus
- Most unilateral
- Can be bilateral
- Vary in size but may be large
  - Up to 10 cm
- Ascites develops if cyst ruptures
- Usually found in lower lateral abdomen or pelvis
  - Occasionally found in upper abdomen
- Supporting ligaments are lax, allowing for displacement
- Very hard to differentiate a displaced ovarian cyst from other intra-abdominal cysts
- May cleave from ovary
- Position in abdomen changes between scans
- Polyhydramnios may develop
  - 10% of cases
- Cause unknown
- Proposed theories

**Ultrasoundographic Findings:**
- Single
  - Generally anechoic
  - Unilocular
  - Imperceptible walls
  - May have occasional septations
  - "Daggers sign"
    - Small cyst along the wall of cystic mass
    - Highly specific (up to 100%) and sensitive (62% sensitive)
  - Small cyst represents an ovarian follicle
  - Well-circumscribed
  - Avascular
- Complex
  - Internal echos indicate hemorrhage
  - Usually secondary to torsion
- Appearance varies based on age of blood products
  - Differently echogenic with acute hemorrhage
  - Fluid-fluid level seen with repeat bleed, as clot separates from serum
  - Crescentic or rounded echogenic "mass" formed by clot retraction
  - Apparent septations due to fiber strands
  - Appears solid if organized hematoma

**DDx: Intra-Abdominal Cystic Mass**

- MCDK
- UPT obstruction
- Enteric Duplication
- Patent Urachus
**OVARIAN CYST**

**Terminology**
- Benign functional cyst within fetal ovary

**Imaging Findings**
- Most diagnostic clue: Abdominal cyst containing “daughter cyst” in a female fetus
- Most unilateral
- Rarely, one but may be large
- Ectopic develops if cyst ruptures
- Internal echos indicate hemorrhage
- Ectopic suspected by presence of new fluid-fluid level
- Consider MRI in difficult cases

**Top Differential Diagnoses**
- Urachal Cyst
- Enteric duplication cyst
- Mesenteric Cyst

- May develop thin echogenic wall from cysticificication
- Cyst portion
  - Condition in uterus: Reported as high as 40%
  - Increased risk if cyst > 6 cm
- May occur even with smaller cysts
- Torsion suggested by presence of new fluid-fluid level
- Suggested if previously anechoic or hypechoic cyst becomes hypechoic
- Consider if new fetal echinocole
- Due to peritoneal irritation
- Cyst may be extremely mobile
- Torsion + necrosis of cyst pedicle or fallopian tube
- Cyst may break loose and float in peritoneal cavity
- Doppler not helpful
- Ectopics
- Result of fluid transudation or cyst rupture

**MR Findings**
- Cyclic mass separate from uterine tract
- Septations or hemorrhage may be visible
- Look for high signal contents on T1WI

**Imaging Recommendations**
- Look at fetal gender
  - Most intra-abdominal cysts occur in either sex
  - Ovarian cyst can be confidently ruled out if fetus is male
- Confirm normal urinary tract
  - High number of cystic abdominal masses are related to urinary tract
- Confirm normal appearance of GI and hepatobiliary system
- Use high-resolution transducer to look for “layered” cyst wall
- Characteristic of enteric cyst: “Gut signature”
- Look for cyst complications
  - Torsion
  - Hemorrhage
  - Necrosis

- Rupture
- Bowel obstruction
- Monitor for development of polyhydramnios
- Monitor cyst size: Look of dystocia if large enough to cause abdominal distortion
- Consider MRI in difficult cases
- Useful to confirm normal renal/liver anatomy if maternal habitus limits tomographic image quality

**DIFFERENTIAL DIAGNOSIS**

**Intra-abdominal cysts**
- Urachal Cyst
  - Between dome of bladder and clom insertion
  - Occurs in both male and females
- Enteric duplication cyst
  - Presents earlier, in 2nd trimester
  - Occurs in both males and females
  - Look for “gut signature”
  - May appear identical to ovarian cyst
- Mesenteric Cyst
  - Occurs in both males and females
  - May appear identical to ovarian cyst
  - Much less common
- Choledochal Cyst
  - Right upper quadrant
  - Associated with liver, look for bile ducts

**Gastrointestinal abnormalities**
- Dilated Bowel
  - Tubular configuration
  - Contents echogenic
  - Peptibalts confirmatory
  - Meckel’s Pseudocyst
  - Often ill-defined contour
  - Vital sign calcify
  - Other sequelae of meckel’s peritonitis
  - Peritoneal calcifications
  - Dilated bowel

**Renal abnormalities**
- Hydrenephrosis/UTI obstruction
OVARIAN CYST

- If severe, hydrourephrosis can appear as a cystic mass
- No ipsilateral "normal" kidney
- Surrounded by fetal parenchyma
- Multicystic dysplasia kidney
- Usually multiple cysts present
- Replaces normal renal parenchyma
- Normal kidney cannot be identified

Intra-abdominal neoplasms
- Cystic teratoma
- Lymphangioma

Hydrocolpos
- Midline pelvic mass
- Posterior to bladder

PATHOLOGY

General Features
- Etiology
  - Result from fetal ovarian response to increased hormone levels
  - Placental human chorionic gonadotropin
  - Maternal estrogen
  - Fetal gonadotropins
- Associated with fetal hypothyroidism
- Check for goiter
- Increased incidence with certain maternal conditions
- Diabetes
- Rheus isoimmunization
- Toxemia of pregnancy
- Epidemiology
  - 1/3 of infant girls have ovarian "cysts"
  - Most microscopic
  - Rarely large enough for sonographic detection
- Most common cause of intra-abdominal cyst in female fetus

Gross Pathologic & Surgical Features
- Most are follicular in origin
- Other types reported
  - Theca lutein
  - Corpus luteum
  - Simple cyst, origin unknown
- No malignat potential

CLINICAL ISSUES

Presentation
- Usually incidental finding in 3rd trimester female
  - Very unlikely cyst is ovarian if seen before 3rd trimester

Natural History & Prognosis
- May resolve spontaneously in utero
- Large cyst >6 cm associated with increased risk of:
  - Hydrops
  - Torsion
  - Infarction
  - Intestinal obstruction
  - Rupture
- In uterus or during delivery
- If cyst large enough to disrnet abdomen, may cause dystocia
- Most show substantial regression by 6 months of age
- Postnatal decrease in hormone stimulation
- May take up to 2 years for complete resolution
- Prognosis excellent, if no torsion

Treatment
- Prenatal cyst drainage
  - Controversial
  - Effects other/temporary, cyst may recur
  - Can result in intrauterine bleeding
  - May increase risk of infection
  - May increase risk of preterm labor
  - Usually only done for large cysts with bowel obstruction
  - Some authors advocate aspiration for cysts >4 cm to prevent torsion
  - Elevated progesterone and estradiol in fluid is diagnostic of ovarian cyst
  - Consider elective cesarean section if large cyst
  - Or aspiration prior to induction of labor
- Prenatal ultrasound
  - Confirm cyst is truly ovarian
  - Follow monthly until resolution
- Indications for surgical resection
  - Evidence of torsion
  - Bowel or urinary tract obstruction
  - Surgery should aim to preserve ovarian parenchyma
  - Fetal retention with ovarian preservation
  - Oophorectomy may be necessary if hemorrhagic infarction from torsion

DIAGNOSTIC CHECKLIST

Consider
- MRI to help further define anatomy and cyst origin

Image Interpretation Pearls
- Precise prenatal diagnosis of ovarian cyst may not be possible
- 'Daughter cyst' sign is highly specific for ovarian origin

SELECTED REFERENCES
OVARIAN CYST

IMAGE GALLERY

Typical

Variation

Sagittal T2WI MR shows a large ovarian cyst filling the left adnexa and dilating the fallopian tube. The cyst is heterogeneous, with low signal areas (arrows) representing hemorrhage. Hydrosalpinx with thin walls (open arrows) is also seen. (Right) Intraoperative photograph shows a large, hemorrhagic ovarian cyst. Hemorrhage was noted to be caused by inimina from the hemorrhage. No invasion was present in this case, but should always be considered when hemorrhage is present.
SECTION 10: Musculoskeletal

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**ACHONDROGENESIS**

Ultrasound shows nearly absent ossification of the spine (correct arrows) in the case of type II achondrogenesis. The small arrows indicate normal ossification and a large size proportion to the body.

Kilograph in the 3rd trimester shows a “floating head” (arrow) is a fetus with type II achondrogenesis. The rib are barely visible (correct arrows) and the spine is completely unossified (open arrows).

**TERMINOLOGY**

**Abbreviations and Synonyms**
- T1a achondrogenesis (Horton-Harris)
- T1b achondrogenesis (Fraccaro)
- T2 achondrogenesis (Lange-Saldino)

**Definitions**
- Group of lethal osteochondrodysplasias due to failure of cartilaginous matrix formation
- Characterized by severe microsomia, unossified spine, short trunk and disproportionately large head
- 2nd most common lethal short-limb chondrodysplasia

**IMAGING FINDINGS**

**General Features**
- **Type IA**
  - Most severely affected
  - Poorly ossified skull
  - Complete unossified spine
  - Short ribs with multiple fractures
  - Proximal femurs with metaphyseal spikes
  - Arthrocleisis with hypoplastic ilium
- **Type IB**
  - Poorly ossified skull
  - No rib fractures
  - Posterio pelvis of spine may be ossified
  - Creased ilium
  - Distal femurs with metaphyseal irregularities
  - Type II
  - Normal skull ossification
  - Deficient spine mineralization
  - Hypoplastic ilium with medial spine
  - Flared metaphyses

**Ultrasonographic Findings**
- Severe microsomia
- Lack of vertebral ossification
- Disproportionately large head with either normal or deficient ossification
- Small thorax with protuberant abdomen
- Short flared ribs with or without fractures
- Polyhydramnios
- Cystic hygroma
- Hydrops in 1/3 of cases
- Micrognathia
- Hypoplastic palate

**Other Modality Findings**
- Fetal skeletal survey findings
  - Type II: “Floating head”
  - Only skull ossified well enough to be seen

**DDx: Short Limb Chondrodystrophies**

- Hypochondroplasia
- Of Type B
- TD Type I
**ACHONDROGENESIS**

### Key Facts
- Can be diagnosed as early as 12-14 weeks
- Top Differential Diagnoses
  - Hypophosphatasia
  - Osteogenesis imperfecta (OI)
  - Atelestogenesisis II
  - Hyperchoondrogenesis
  - Thanatophoric dysplasia (TD)

### Diagnostic Checklist
- Pelvic radiography in 3rd trimester to confirm abnormal ossification, evaluate spine
- Rib fractures in absence of long bone fractures in type IA
- No rib fractures in type IB
- Absent spine ossification with normal calvarium in type II achondrogenesis

### Imaging Recommendations
- Best imaging tool
  - 1st trimester endovaginal ultrasound
- Can be diagnosed as early as 12-14 weeks
- Diagnosis repeated at 9 weeks with positive family history
- Protocol advice
  - Careful evaluation of skeleton
  - Ossification of spine, calvarium
  - Morphology of long bones
  - Radiographs in 3rd trimester
- Directed fluoroscopic images focused on spine, cranium and long bones

### Homozygous achondrogenesis
- Normal calvarial ossification

### Thanatophoric dysplasia (TD)
- Normal ossification
- Micromelia less extreme
- Hydrops uncommon
- Cloverleaf skull

### Short rib-polydactyly syndrome
- Polydactyly
  - Both preaxial and postaxial
  - May appear hydropic

### PATHOLOGY

#### General Features
- Genetics
  - Types IA and IB: Autosomal recessive
  - 25% recurrence risk
  - Type IA: Molecular basis not known
  - Type IB: Mutations in diastrophic dysplasia sulfate transporter gene (DTDST)
  - Results in abnormal sulfation of chondroitin sulfate-containing proteoglycans
  - Achromatidogenesis IB and diastrophic dysplasia are allelic disorders
  - Prenatal diagnosis possible by chorionic villus sampling (CVS) if specific mutation known
  - Type III Sporadic
  - Mutations in type II collagen gene COL2A1
  - Negligible recurrence risk
  - Recurrence in case of siblings attributed to germline mosaicism

### Epidemiology
- 1:40,000-50,000 live births
- May account for 1.650 retinal deaths
- Associated abnormalities
  - Type II with occipital cleft soft palate
  - Hydrops in 1/3
  - Polyhydramnios

---

**Differential Diagnosis**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypophosphatasia</td>
<td>Skull demineralized</td>
</tr>
<tr>
<td></td>
<td>Fractures uncommon</td>
</tr>
<tr>
<td></td>
<td>Diffuse under ossification of all bones</td>
</tr>
<tr>
<td>Osteogenesis imperfecta (OI)</td>
<td>Fractures are predominant finding in OI types II-IV</td>
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<td></td>
<td>Skull porosity mineralized in OI</td>
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<tr>
<td></td>
<td>Rib fractures severe in type II</td>
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<td>Long bone bowing in types III-IV</td>
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<td>Abnormal type I collagen</td>
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<tr>
<td>Atelestogenesisis II</td>
<td>Thoracic platyspondyly</td>
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<td>Sowed radius, ulna, tibia</td>
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<tr>
<td></td>
<td>Clubfeet</td>
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<td></td>
<td>Better ossification of vertebrae</td>
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<tr>
<td>Hypochondrogenesis</td>
<td>Findings less severe with better ossification of vertebral bodies</td>
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<tr>
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<td>Tubular bones less short</td>
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<tr>
<td></td>
<td>Mild cases of achondrogenesis II and severe hypochondrogenesis difficult to distinguish</td>
</tr>
</tbody>
</table>
ACHONDROGENESIS

- Type IA: occasional enchondrocytes

Microscopic Features
- Disorganization of chondrocytes
- Failure of alignment in columns
- Cartilage matrix varies irregularly in microsclerotinized bodies

Staging, Grading or Classification Criteria
- Definitive diagnosis of subtype possible with histopathologic studies
- Type IA: Pathognomonic period acid-Schiff-positive hypertrophic inclusion bodies
- Type IB: Decrease in type II collagen
- Fibers in cartilage matrix anastomized in zigzags around chondrocytes
- Type II: Structurally abnormal type II collagen
- Electron microscopy: retention of type II collagen within vacuoles
- Increased amount of types I collagen seen in cartilage

CLINICAL ISSUES

Presentation
- Most common signs/symptoms: Severe microscrotic skeletal dysplasia associated with deficient spine realignment
- Other signs/symptoms: Polyhydramnios

Demographics
- Age: No ascertainment with increased parental age
- Gender: recorded cases show excess of males
- Consanguinity found in families affected with type I

Natural History & Prognosis
- Lethal
- Increased incidences of prematurity
- Majority stillborn or die in first few weeks due to pulmonary hypoplasia
- Longest survivor less than a month

Treatment
- No prevent or postnatal treatment
- Older pregnancy termination
- If pregnancy continued and diagnosis certain
- Avoid fetal anesthetics in labor
- No intervention for premature labor
- Psychological support for family
- If diagnosis unclear and live born infant, observation appropriate until confirmatory tests performed
- Deliver in tertiary center with expertise in fetopathology and skeletal dysplasia
- Steer important of full genetic evaluation
- Recurrence risk
- Genetic counseling
- Anticipation important for final specific diagnosis
- Complex set of X-rays
- Absent mineralization of spine
- Large skull with wrinkled bones
- Bell-shaped chest cage
- Short, abnormally long bones with variety of abnormalities
- Cell culture
- Bone/cartilage biopsy
- Rarely type generally low yield
- International Skeletal Dysplasia Registry at Cedars-Sinai for atypical cases

DIAGNOSTIC CHECKLIST

Consider
- Pelvic radiographs in 3rd trimester to confirm abnormal ossification, evaluate spine

Image Interpretation Pearls
- Rib fractures in absence of long bone fractures in type IA
- No rib fractures in type IB
- Absent spine ossification with normal calcification in type II achondrogenesis
- Transverse view shows less than 3 ossification centers per spinal segment

SELECTED REFERENCES
**ACHONDROGENESIS**

**IMAGE GALLERY**

**Typical**

(left) Radiograph shows poor skull ossification (arrow) and thin, wavy ribs (arrow) in type I achondrogenesis. Lack of spine ossification is apparent (open arrow).

(right) Radiograph shows a well ossified calvarium (arrow) with lack of spine ossification (curved arrow) in type II achondrogenesis. This results in the "floating head" appearance on fluoroscopy. Note the absence of rib fracture (open arrow).

**Typical**

(left) Ultrasound shows severe micrognathia and chestnut (arrow) in a midtrimester fetus with achondrogenesis. Note the severely deficient long bone ossification (open arrow).

(right) Axial ultrasound shows the calvarium is normally shaped and exhibits near normal ossification (curved arrow) typical of type II achondrogenesis. A cystic hydramnion (open arrow) is also present, which is a described association.

**Typical**

(left) Clinical photograph shows a premature, adrenalectomized infant with type II achondrogenesis. Note the hypoplastic midface (arrow) and the hydroptic thorax.

(right) Postural photograph shows the body of the same infant. Note the extreme micrognathia (arrow), prominent abdomen (curved arrow), and the marked edema (open arrow).
ACHONDROPLASIA

TERMINOLOGY

Definitions
- Most common heritable, non-lethal skeletal dysplasia
- Characterized by disproportionately short limbs (short stature), large head with frontal bossing, depressed nasal bridge, and short digits
- Homozygous achondroplasia is lethal
  - Occurs when mutation inherited from each of 2 affected parents

IMAGING FINDINGS

General Features
- Best diagnostic clue: Normal early scan, with long bone shortening noted after 32 weeks
- Morphology
  - Oligoamelia
  - Pyramidal limb shortening

Ultrasonographic Findings
- Gray-scale ultrasound
  - Normal ossification without fractures
  - No bowing or angulation seen prenatally
  - Progressive macrocephaly with frontal bossing
  - May be a late finding
  - Depressed nasal bridge with upturned nasal tip

DDx: Short Limb Chondrodysplasias

- DD Type I: Thalas
- DD Type II: Formos
- DD Type III: Skiff
- DD Type IV: Ribus
**ACHONDROPLASIA**

### Terminology
- Most common heritable, non-lethal skeletal dysplasia
- Characterized by disproportionately short limbs (rhizomelia), large head with frontal bossing, depressed nasal bridge, and short digits
- Homozygous achondroplasia is lethal

### Imaging Findings
- Best diagnostic clue: Normal early scan, with long bone shortening noted after 22 weeks
- Radiographs may be taken in 3rd trimester to better evaluate bone morphology and ossification
- Normal ossification without fractures
- No bowing or angulation seen prenatally
- Progressive macrocephaly with frontal bossing
- Prominent thoracolumbar kyphosis

#### Radiographic Findings
- Radiography
  - Radiographs may be taken in 3rd trimester to better evaluate bone morphology and ossification
  - Positioning under fluoroscopy with spot films better than frontal film
  - Fetal bones often overlap maternal spine

#### Imaging Recommendations
- Best imaging tool: Late 2nd to early 3rd trimester ultrasound
- Protocol advice
  - Follow-up sonogram if femur lagging behind other measurements
  - Heterozygous form becomes obvious in 3rd trimester
  - Rule out lethal skeletal dysplasia
  - Micromelia
  - Small chest
  - Severe polyhydramnios
  - Consider radiography in 3rd trimester

### DISEASE FACTS
- Follow-up sonogram if femur lagging behind other measurements
- Heterozygous form becomes obvious in 3rd trimester
- Rule out lethal skeletal dysplasia

### Top Differential Diagnoses
- Hypochondroplasia
- Thalassemic dysplasia (TD)
- Homozygous achondroplasia
- Osteogenesis imperfecta (OI)

### Pathology
- Autosomal dominant single gene disorder
- Fibroblastic growth factor receptor-3 (FGFR3) mutations
- 80% of cases are new mutations (sporadic)

#### RADIOGRAPHIC FINDINGS
- Lethal disorder
- Occurs in 25% of offspring when 2 parents affected with achondroplasia
- Severe limb shortening
- Pulmonary hypoplasia
- SADDAN syndrome
- Severe Achondroplasia with Developmental Delay and Acanthosis Nigricans
- Bony changes as severe as TD
- Differentiation from TD and achondroplasia may be difficult without molecular analysis

#### Type I collagen abnormalities
- Osteogenesi imperfecta (OI)
- Fractures dominant feature
- Decreased ossification

#### Cartilage oligomeric matrix protein (COMP) associated disorders
- Pseudoachondroplasia
  - Disproportionate short stature
  - Abnormal joints
  - Osteoarthritis requiring joint replacement
- Spondyloepiphysial dysplasia
- Rhizomelic dysplasia with similar long bone features
- No frontal bossing
- Micrognathia +/- Robin sequence (cleft palate)

### PATHOLOGY
#### General Features
- Genetics
  - Autosomal dominant single gene disorder
  - Fibroblast growth factor receptor-3 (FGFR3) mutations
  - 97% of cases involve a glycine to arginine substitution in codon 380 of FGFR3 transmembrane domain (G380R)
  - Results in receptor overactivation
  - FGFR located on short arm of chromosome 4
  - 80% of cases are new mutations (sporadic)
  - Homozygous achondroplasia is lethal
ACHONDROPLASIA

- Recurrence risk: 1 affected parent
  - 50% of offspring with achondroplasia
  - 50% of offspring unaffected
- Recurrence risk: Both parents affected
  - 25% of offspring with achondroplasia
  - 25% with lethal (autosomous) achondroplasia
- Recurrence risk: Both parents unaffected
  - Sporadic: No increased risk

- Lesions:
  - FGFR tyrosine kinase expressed by chondrocytes in the growth plate of developing long bones
  - Overactivity of FGFR3 signaling may impair chondrocyte function within the epiphyseal growth plates
  - Decreased endochondral ossification
- Epidemiology:
  - Heterozygous: 20,000-22,000 live births
  - Homozygous: Rare
  - Both parents must be affected or one parent + new mutation

CLINICAL ISSUES

Presentation
  - Most common signs/symptoms: Long bone shortening in late 2nd, 3rd trimester

Demographics
  - Age: Associated with increased paternal age
  - Gender: No gender predilection
  - Ethnicity: Found in all ethnic groups

Natural History & Prognosis
  - Generally normal lifespan
  - Some studies suggest risk of premature death compared with general population
  - Increased incidence of death in first year of life
  - Often sudden and unexpected
  - Associated with acute terminal compression of cervical spine or brainstem
  - Normal intelligence
  - Increased incidence of orthopedic and neurologic complications
  - Cerebral anomalies, stenosis
  - Limb bowing
  - Thoracolumbar kyphosis
  - Midface hypoplasia with upper airway obstruction
  - Pregnancy in women with achondroplasia
    - Cesarean delivery necessary even if fetus affected due to inadequate pelvic proportions
    - Inverted breech position
    - Cord entanglement and back pain may worsen
    - Affected fetus in unaffected mother
    - Cesarean delivery often necessary due to macrocephaly
    - Polyhydramnios in 3rd trimester

Treatment
  - Genetic counseling
    - One or both parents affected
    - Significant recurrence risk with each pregnancy
    - Prenatal or antenatal diagnosis of affected infant
  - Prenatal diagnosis available
    - Diagnosis suspected by ultrason or prenatal radiography
    - Molecular analysis of FGFR3 mutations
    - Amniocentesis
    - Cordocentesis
    - Prenatal ultrasound
    - Prenatal imaging, genetic diagnosis (PGD) if mutation known
    - Prevent homozygous lethal form in cases of 2 affected parents
  - Pregnancy termination in cases of homozygous achondroplasia
  - Postnatal treatments
    - Limb lengthening and softening procedures
    - Cervicomedullary decompression in cases of spinal stenosis
    - Bowing and spinal fusion procedures
    - Facial distraction for midface hypoplasia, airway obstruction

DIAGNOSTIC CHECKLIST

Consider
  - 3rd trimester radiography

Image Interpretation Pearls
  - Normal 2nd trimester scan does not rule out achondroplasia
  - Progressive limb shortening, in late 2nd and 3rd trimester

SELECTED REFERENCES
ACHONDROPLASIA

IMAGE GALLERY

Typical

(G) Left: Ultrasound shows the typical appearance of a "battered" hand of a fetus with achondroplasia. Note the beak-shaped, similar lengths of all the digits, and mildly spade-shaped appearance of the first metacarpal. Right: Radiograph shows typical hand findings of an infant with achondroplasia. Note the significant beak-shaped, with hypoplasia of the distal phalanges (arrows).

Typical

(G) Sagittal ultrasound shows the thoraco-abdominal profile of a fetus with achondroplasia. Note the slightly small chest (arrow) with a prominent abdomen (open arrows). Right: Sagittal ultrasound shows the spine in a 2nd trimester fetus with achondroplasia. There is a very prominent kyphosis of the lumbar spine (arrows). A finding common in achondroplasia.

Typical

(G) Ultrasound shows the femur (arrows), of a 3rd trimester fetus with achondroplasia. The length is less than the 5th percentile. But the morphology and ossification is relatively normal. These are important differentiating factors when evaluating skeletal dysplasia. Right: Chart shows normal length (FL) and head circumference (HC) plot. Initially the FL is normal with shortening becoming obvious in the 3rd trimester. HC plot shows an enlarged head.
AMELLA, MICROMELIA

TERMINOLOGY

Abbreviations and Synonyms
- Phocomelia

Definitions
- Amyelia: Absence of 1 or more limbs
- Micromelia: Shortening of both proximal and distal segments of limb
  - May further subdivide into mild or severe micromelia
- Phocomelia: Shortening of the limb with hand/foot arising near trunk
- Limb reduction defect (LRD): Absence of any portion of skeletal structures or soft tissues of limb
  - May be a transverse, longitudinal or intercalary deficiency
- Hemimelia: Absence of distal limb

DIFFERENTIAL DIAGNOSIS

Amelia
- Roberts syndrome/Roberts SC syndrome
  - SC-phocomelia considered rare syndrome
- Clinical characteristics
  - Tetraphocomelia: 90% (only upper limbs affected in 10%)
  - Facial clefts in 80%
  - Severe pre- and postnatal growth restriction
  - Dysmorphic features
  - Other anomalies: Genitourinary (GU), cardiac, syndactyly, ear and nose, anterior encephalocele, microphthalmia
- Autosomal recessive
- Most die in utero or shortly after birth
- Rare report of longer term survivor
- Characteristic cytogenetic features: Premature centromere separation

IMAGING FINDINGS

Imaging Recommendations
- Protocol advice
  - Pattern of involvement key in formulating differential diagnosis
  - Symmetric vs. asymmetric limb anomalies
  - Upper or lower limbs more severely affected?

U0X: Short Limbs

- Transverse
- Amniotic Bands
- CLEFT Type Leg
- Ulnar Deficiency
Key Facts
- Thrombocytopenia-absent radius (TAR) syndrome
- Thalidomide embryopathy
- Achondrogenesis
- Osteogenesis imperfecta type II

Clinical Issues
- Most common signs/symptoms: Missing or severely shortened extremities on 1st or 2nd trimester ultrasound
- Most chondrodysplasies with severe micromelia lethal in perinatal period

Diagnostic Checklist
- Which segment of limb affected and symmetry of involvement important in determining differential diagnosis
- Ultrasound
- Fetal MRI

Terminology
- Amelia: Absence of 1 or more limbs
- Micromelia: Shortening of both proximal and distal segments of limb
- Phocomelia: Shortening of the limb with hand/foot arising near trunk
- Limb reduction defect (LRD): Absence of any portion of skeletal structures or soft tissues of limb

Imaging Findings
- Careful search for associated anomalies, especially cardiac, neural tube defects, and skeletal abnormalities

Top Differential Diagnoses
- Roberts syndrome
- Robert SC syndrome
- Tetra-amelia
- Aneuploidy

- Autosomal recessive tetra-amelia due to mutations in WNT1 gene
- Isolated phocomelia/amelia of 1 or more limbs
- Amniotic bands
- Asymmetric Single or multiple limbs involved
- Bizarre orofacial clefting
- Body wall schisis defects
- Strands of amnion may be seen in amniotic fluid on ultrasound or by gross examination of placenta
- Constriction rings around extremities, digits
- Thrombocytopenia-absent radius (TAR) syndrome
- Upper limb phocomelia, may be severe
- Lower limb anomalies in 50%
- Hypomagnesemia/ectopic thrombocytopenia
- Facial capillary hemangioma
- Autosomal recessive
- Distinct from Fanconi anemia
- No abnormality of thumb
- No increased chromosome breakage in TAR

- DE-phocomelia
- Von Voss-Cheney syndrome
- Phocomelia, enchephalocele, thrombocytopenia, GU anomalies

- Autosomal recessive
- Thalidomide embryopathy
- Common sedative, morning sickness drug used in Europe in the 1950s and early 1960s
- Removed from market in 1962: Recognition of severe limb anomalies in offspring of mothers treated with thalidomide in early pregnancy
- Mechanism of action: Interference with angiogenesis
- Characteristic pattern of anomalies: Tetraphocomelia, cardiac, GU, facial, nervous system
- Approved by FDA in 1998 for treatment of complications of leprosy
- Experimental treatment of human immunodeficiency virus (HIV), ulcerative diseases and inflammatory conditions
- Single dose in a pregnant woman confers full risk of embryopathy

Micromelia
- Achondrogenesis
- Lack of vertebral ossification
- Disproportionately large head with normal or deficient ossification
- Short ribs +/− fractures
- Micrognathia
- Hydrops common
- Autosomal recessive 1A, 1B, 2 sporadic
- Arthrogryposis
- Macrocephaly, micrognathia, cleft palate
- Short trunk with small chest, protuberant abdomen
- Clumpert, “fishhook” thumb
- Short tubular bones with metaphyseal flaring
- Wide gap 1st and 2nd toes
- Autosomal recessive: Mutations in diastrophic dysplasia sulfate transporter gene (DTDST)
- Dysegmental dysplasia
- Irregular vertebral bodies with multiple ossification centers (anisopondyly)
- Short spine, small thorax with short ribs
- Short, thick ischial and pubic bones
- Short, wide, angulated tubular bones
AMELIA, MICROMELIA

- Autosomal recessive
- Fibrochondroplasia
- Wide forehead and cheeks with protuberant eyes
- Short tubular bones with bulbous ends
- Vertebral osteofibrosis
- Convex posterior fontanelle
- Broad ribs with medial and lateral spurs
- Autosomal recessive
- Osteogenesis imperfecta type II
- Short stature
- Cleft palate
- Small feet
- "Skeletal" thumbs
- Increased perinatal mortality: normal life span if no severe spinal complications
- Autosomal recessive

PATHOLOGY

General Features
- Genetics
  - Autosomal recessive: Roberts, TAR, DK-phenocopies
  - Micromelia: Mertens autosomal recessive
  - Cases of recurrent tetra-amelia in consanguinous families
- Familial: Pseudoxanthoma elasticum
- Etiology
  - Mutations of WNT3 genes in autosomal recessive tetra-amelia
  - Mutations in LIMD1 gene involved in diastrophic dysplasia, achondroplasia, and osteogenic I
  - Mutations in COL2A1, IIA, IA in I II
- Associated abnormalities: Tetra-amelia with other visceral anomalies very rare

CLINICAL ISSUES

Presentation
- Most common signs/symptoms: Measuring or severely shortened extremities on 1st or 2nd trimester ultrasound
- Other signs/symptoms
  - Robert syndrome: Osteocle clipping with phocomelia/amelia
  - Evidence of skeletal dysplasia with micromelia

Natural History & Prognosis
- Most chondrodysplasias with severe micromelia lethal in perinatal period

Treatment
- No prenatal treatment
- Survivors need orthopedic surgical management of progressive spinal, limb abnormalities

DIAGNOSTIC CHECKLIST

Consider
- Cytogenetic analysis of chromosome separation in suspected Roberts syndrome

Image Interpretation Pearls
- Vertebral or limb affected and symmetry of involvement important in determining differential diagnosis
- Evaluation of bone morpholonomy of bones of extremities to exclude skeletal dysplasia
- Careful search for other structural anomalies

SELECTED REFERENCES
**AMELIA, MICROMELIA**

**IMAGE GALLERY**

**Typical**

(Left) Ultrasound of the pelvis shows hypoplastic ilia (arrows) and absent lower extremities in fetus with intra-uterine. (Right) Antemortem x-ray graph shows a stillborn fetus with intra-uterine. Note the absence of all 4 limbs and the hypoplastic clavicles (arrow) and pelvis (open arrow).

**Typical**

(Left) Close-up photograph shows absence of the lower extremity with a slightly protrusive (arrow). Perpendicular structures are normal. (Right) Clinical photograph of the opposite side shows a cutaneous dimple (arrow) over area of the missing extremity.

**Typical**

(Left) Ultrasound shows severe upper extremity micromelia (arrow) to a mid-patellar fetus with achondrogenesis. (Right) Clinical photograph shows severe micromelia (arrow) in a premature stillborn infant with achondrogenesis.
ASPHYXIATING THORACIC DYSPLASIA

Central abdominal shows a mid-gastric facies and
encephaly. The long, narrow thorax is evident
(arrow).

Congenital lung: shows a very long and
narrow thoracic configuration of a newborn with
syndrome. The ribs are short with a horizontal
configuration (arrow).

TERMINOLOGY

Abbreviations and Synonyms
- Jeune syndrome
- Jeune asphyxiating thoracic dystrophy
- Thoracic-pelvic-phalangeal dystrophy

Definitions
- Rare autosomal-dysplasia
  - Characterized by a severely constricted, long, narrow
    thorax and cystic renal dysplasia
  - Speculation exists that Jeune and short rib-polydactyly
    syndrome type III (Verma-Naumoff) are variants of
    same disorder

IMAGING FINDINGS

Ultrasonographic Findings
- Small chest with short ribs
  - Thoracic circumference < 5th percentile with normal
    abdominal circumference
- Cystic kidneys
- Short tubular bones
- Increased nuclear thickness reported
- Oligohydranmios if severe renal disease
- Postaxial polydactyly

Radiographic Findings
- Abnormalities most marked in infancy, tend to
  normalize in childhood
- Short, horizontal ribs with small thorax
- Short iliac, pubic, and pubic bones
- Medial and latera] iliac spurs
- Short extremities
- Cone-shaped epiphyses
- Postaxial polydactyly

DIFFERENTIAL DIAGNOSIS

Short rib-polydactyly syndrome (SRPS)
- SRPS type III (Verma-Naumoff)
- Severe short, horizontal ribs
- Small iliac bones
- Micromelia with metaphyseal spurs
- Small vertebral bodies
- Perinatal lethal

Ellis van Creveld syndrome
- Cataracts, cardiac anomalies, and
  polydactyly
- Pelvic configuration is difficult distinguishable
  from Jeune
- Less severe thoracic involvement
- Cardiac defect in 50%
- Postaxial polydactyly
- Progressive distal shortening of extremities

DDx: Similar Findings in Short-Rib Polydactyly

Short Rib-Polydactyly
Short Rib-Polydactyly
Short Rib-Polydactyly
Terminology
- Jeune syndrome
- Rare osteochondrodysplasia
- Charactized by a severely constricted, long, narrow thorax and cystic renal dysplasia

Imaging Findings
- Abnormalities most marked in infancy, tend to normalize in childhood

Key Facts
- Lifespan potentially normal with normal intelligence
- Biliary atresia
- Small thorax, small pelvis, laryngeal stenosis
- Rib shortening milder than Jeune syndrome
- Absence of iliac spurs, renal disease
- Autosomal dominant

Uniparental disomy 14 (paternal)
- Recognizable phenotype with thoracic dystrophy
- Characteristic "coat hanger" rib sign (caudal anterior rib bowing) on radiograph

PATHOLOGY
General Features
- Genetics: Autosomal recessive
- Etiology
  - Specific gene(s) unknown; maps to 15q13
  - Ellis van Creveld region on 4p excluded
  - Epidemiology: Rare; 1/70,000 births
  - Associated abnormalities: Hepatic fibrosis, pancreatic fibrosis, retinal degeneration

Microscopic Features
- Irregular, patchy enchondral ossification
- Pulmonary hypoplasia with marked reduction in number of alveoli
- Cystic renal dysplasia
- Periportal hepatic fibrosis

CLINICAL ISSUES
Presentation
- Most common signs/symptoms
  - Prematurity is highly variable
  - Long narrow thorax
  - Brachydactyly, short limbs
  - Cystic renal dysplasia
  - Postaxial polydactyly in 14%

Natural History & Prognosis
- Neuonatal and infantile deaths due to pulmonary hypoplasia in 70%
- Survival associated with growth of thoracic cavity
- Mild cases present in childhood with short stature and renal disease
- Renal insufficiency, renal failure by late childhood

Top Differential Diagnoses
- Short rib-polydactyly syndrome (SRPS)
- Ellis van Creveld syndrome
- Barnes syndrome

Pathology
- Genetics: Autosomal recessive
- Clinical Issues
  - Phenotype is highly variable

- Severe liver involvement → biliary cirrhosis → portal hypertension

Treatment
- Genetic counseling should be offered
- Rib/thoracic cage expansion procedures
- Urosecoxylic acid: Stabilize hepatic function
- Renal transplantation

SELECTED REFERENCES

IMAGE GALLERY
(Left) Sagittal ultrasound shows a fetus in the third trimester with Jeune syndrome. Severe constriction of the thorax is noted (arrows) when compared with the normal abdomen (curved arrow). (Right) Axial ultrasound shows a significantly shortened rib as the mid-clavicular (arrow). The heart appears large and the cardiothoracic ratio is mildly increased, reflecting the small thoracic size.
CAMPOMELIC DYSPLASIA

Terminology

Abbreviations and Synonyms
- Campomelic dysplasia (CD)
- Campomelic syndrome
- Campomelic dystrophy
- Campomelic dysplasia

Definitions
- Campomelia = bowed limbs
- Raze, semi-ilethal osteochondrodysplasty
- Characterized by bowed extremities with absence of fractures, cutaneous dimpling, hypoplastic scapulae, sex-reversal in males.

Imaging Findings

Ultrasoundographic Findings
- Severe angular deviations of femora, tibiae, fibulae
- Ambiguous genitalia
- NT sex reversal (male to female)
- Genotypic males appear phenotypically as females
- Hypoplastic scapulae
- No fractures
- Bell-shaped chest
- 1st trimester increased nuchal translucency or cystic hygroma

Radiographic Findings
- Normal ossification without fractures
- Anterolaterally bowed femora, tibiae
- Thoracic kyphoscoliosis
- Absent/ delayed ossification of thoracic pedicles
- Hypoplastic scapulae
- 11 pairs of ribs

Imaging Recommendations
- Best imaging tool: Mid-trimester ultrasound

Differential Diagnosis

Osteogenesis imperfecta (OI)
- Decreased mineralization of skull, long bones
- Fractures are prominent feature

Typhomelic dysplasia
- Scapulae are normal
- Predominantly femoral involvement

Acampomelic campomelic dysplasia
- Absence of bowing of extremities
- Hypoplastic scapulae

Femur-fibula-ulna complex
- Short limb dwarfism

DDx: Bowed Extremity Syndromes

- OI Type IV
- IV involved
- Fibular Hemimelia
- Kyphoscoliotic
CAMPOMELIC DYSPLASIA

Key Facts

- **Top Differential Diagnoses**
  - Osteogenesis imperfecta (OI)
  - Kyphomelic dysplasia
  - Acampomelic campomelic dysplasia
  - Femur-fibula-ultra complex

- **Clinical Issues**
  - 3/4 of males are sex-reversed (appear phenotypically female) or have ambiguous genitalia
  - Occasional longer term survivors

Treatment

- **No prenatal treatment**
- **Delivery in tertiary care facility**
  - Risk of respiratory insufficiency
  - Expertise in genetic fetopathology, skeletal dysplasias
- **Orthopedic treatment of musculoskeletal abnormalities in survivors**

DIAGNOSTIC CHECKLIST

- **Image Interpretation Pearls**
  - Prenatal diagnosis centers around ultrasound findings with postnatal radiographic confirmation

SELECTED REFERENCES


IMAGE GALLERY

(Left) Radiograph shows the chest of a newborn with campomelic dysplasia. Note the hypoplastic scapulae (arrows). Bony fusion of the sternum and ribs is normal.

(Right) Radiograph shows the right leg of the same infant shows mid-shaft angulation of the femur, tibia and fibula (arrows). Osseous fusion is normal.
**HYPOPHOSPHATASIA**

**TERMINOLOGY**

**Definitions**
- Rare osteochondroplasia with deficient mineralization and deficiency of tissue nonspecific alkaline phosphatase (ALP)
- 3 subtypes
  - Perinatal lethal
  - Microsomia and severe hypomineralization
  - Infantsile
- Rickets-like skeletal changes, fractures, premature shedding of teeth
- Late onset (adult form)
- Often limited to biochemical findings
- Bowing, pseudofractures, ectopic calcifications in spiral ligaments and joint cartilage, rachitic changes in ribs

**DIAGNOSTIC FINDINGS**

**General Features**
- Best diagnostic clue: Perinatal lethal type; Microsomia and severe undermineralization of bones and calcification on mid-trimester ultrasound

**Ultrasoundographic Findings**
- Pelvalatal [enmal type

**DIAGNOSTIC FINDINGS**

**General Features**
- Best diagnostic clue: Perinatal lethal type; Microsomia and severe undermineralization of bones and calcification on mid-trimester ultrasound

**Ultrasoundographic Findings**
- Pelvalatal [enmal type

**DIFFERENTIAL DIAGNOSIS**

**Osteogenesis Imperfecta (OI)**
- Fractures predominate finding in OI types II/IV
- Rib fractures seven in type II
- Poor skull mineralization
- Serum alkaline phosphatase normal

**Achondrogenesis type IA**
- Absent spine ossification

**DDx: Hypomineralization**

- OI Type II
- OI Type IV
- Achondrogenesis
### HYPOPHOSPHATASIA

**Terminology**
- Rare osteochondrodysplasia with deficient mineralization and deficiency of tissue nonspecific alkaline phosphatase (ALP)

**Imaging Findings**
- Best diagnostic clue: Perinatal lethal type: Micromelia and severe undermineralization of bones and calvarium on mid-trimester ultrasound

- Affects vertebral body to greater extent than neural arch
- Multiple rib fractures
- Poor calvarial ossification
- Tubular bones short and thick

**PATHOLOGY**

**General Features**
- Genetics
  - Perinatal lethal/Infantile: Autosomal recessive
  - 25% recurrence risk
  - Adult form is both autosomal recessive and dominant
- Carriers have 1 serum ALP/1 urinary phosphoethanolamine
- Biology
  - Mutations in tissue nonspecific ALP (TNSALP or ALPL) gene
  - Decreased enzyme activity impairs bone mineralization, dentinogenesis
  - Degree of deficiency correlates with severity of clinical features
- Epidemiology: 1/100,000 births (perinatal lethal type)

**CLINICAL ISSUES**

**Presentation**
- Most common signs/symptoms: Hypomineralization, bowed limbs
- Other signs/symptoms
  - In infancy
    - Premature shedding of teeth
    - Decreased/absent serum ALP activity
    - ↑ Plasma pyridoxal 5'- phosphate
    - Hypercalcemia and hypercalcuria
    - ↑ Serum phosphate in 50%

**Natural History & Prognosis**
- Perinatal hypophosphatasia: lethal
- Infantile hypophosphatasia
  - Hypercalcemia: Irritability, poor feeding, vomiting, failure to thrive
  - Craniosynostosis: ↑ intracranial pressure
  - Nephrocalcinosis
  - Increased mortality: Cardiomyopathy, ↑ intracranial pressure
  - Delayed walking, abnormal gait
- Spontaneous improvement in limb bowing may occur
- Late onset
  - Bowing, joint pain from fractures, crystal deposition
  - Foot pain from metaphyseal stress fractures may be first sign of late onset disease
  - Short stature common
  - Osteopenia, fractures after menopause

**Treatment**
- Perinatal diagnosis: Measure ALP activity in chorionic villi, cultured amniocytes or fetal blood
- Direct mutational analysis possible
- Aggressive dental care to preserve teeth
- Hypercalcaemia responsive to dietary restriction
- Intravenous bisphosphonates may stabilize fractures
- Disappointing results with enzyme therapy, calcitonin
- Avoid vitamin D supplements (hypercalcemia)
- Bone marrow transplantation

**SELECTED REFERENCES**

**IMAGE GALLERY**

(Left) Ultrasound shows a short, underdeveloped radius (arrow) and club in an affected fetus with hypophosphatasia. (Right) Sagittal radiograph shows the hypomineralized skull of an infant with infantile hypophosphatasia (arrows).
OSTEOGENESIS IMPERFECTA

TERMINOLOGY

Abbreviations and Synonyms
- Osteogenesis imperfecta (OI)
- 'Brittle bone disease'
- OI type I: Osteogenesis imperfecta tarda
  - Van der Hoeve syndrome
- OI type II: Perinatal lethal
- OI type III: Woflk/track bone type of lethal OI
- OI type IV: Progressively deforming OI
- OI type V: Lobstein disease/Emmer-Lobstein disease

Definitions
- Connective tissue disorder due to abnormalities in type I collagen (COL1A1, COL1A2) associated with osseous fragility and fractures

IMAGING FINDINGS

General Features
- Best diagnostic clue: Presence of fractures distinguishes OI from other skeletal dysplasias

Ultrasoundographic Finding:
- Extremities
  - Long bone shortening/angulation secondary to fractures

DDx: Short Limb Skeletal Dysplasias; Femurs
- Hypochondroplasia
- TD Type 1
- Caminofolic
- Achondroplasia

- Pseudoarthrosis formation
- Callus formation gives bones a "crumpled" appearance
- Decreased mineralization
- May see posterior cortex (i.e., no shadowing from anterolateral cortex)
- Chest
  - Small circumference
  - Multiple rib fractures (‘beading’)
- Brain
  - Anomaly 'too well seen'
  - Poorly mineralized skull
  - No cerebellar artifact
  - Skull deformation from transverse pressure ('soft' bones)

Radiographic Findings
- Radiography
  - Fractures may be better demonstrated on fetal skeletal survey
- Major radiographic features
  - Generalized osteoporosis
  - Delayed articular bone formation with wormian bones
  - Tubular bone with thin cortex, thin shafts
  - Severe cases with collapsed vertebral bodies, rib fractures, broad tubular bones due to compression fractures
OSTEOGENESIS IMPERFECTA

Terminology
- Connective tissue disorder due to abnormalities in type I collagen (COL1A1, COL1A2) associated with osseous fragility and fractures

Imaging Findings
- Best diagnostic clue: Presence of fractures distinguishes OI from other skeletal dysplasias
- Callus formation gives bones a "crumpled" appearance
- Decreased mineralization
- Multiple rib fractures ("beading")
- Skull deformation from transducer pressure ("soft" bones)

Top Differential Diagnoses
- Hypophosphatasia

Key Facts
- Achondrogenesis
- Camptomelic dysplasia
- Thanatophoric dysplasia (TD)

Pathology
- Most autosomal dominant
- Type I: Fractures rare at birth
- Type II: Most severe form, multiple fractures, lethal
- Type III: Multiple fractures at birth; progressive severe deformity of limbs, spine, skull
- Type IV: Delayed presentation, clinical and radiographic spectrum between type I and type III

Diagnostic Checklist
- Severe limb shortening with limb and rib fractures, most likely lethal OI

Imaging Recommendations
- Best imaging tool
- Mid-trimester ultrasound (US)
- 1st trimester endovaginal US in high-risk patients
- Protocol advice
- Monitor all long bones/assess for fractures
- Severe shortening in OI type II
- Look for scapulae
- If visible, camptomelic dysplasia unlikely
- Compare chest to abdominal circumference
- Small chest → more risk for pulmonary hypoplasia
- Normal ultrasound does not exclude OI in high-risk patient

DIFFERENTIAL DIAGNOSIS

Hypophosphatasia
- Generalized hypomineralization of all bones
- Fractures uncommon
- Low serum alkaline phosphatase in neonate

Achondrogenesis
- Spine mineralization absent in type II
- Hydrops, cyclic hypoglycemia common
- Skull ossification variable
- Severe microsomia

Camptomelic dysplasia
- Hypoplastic scapulae
- Sharp angulation of femur, tibia/fibula
- Normal skull ossification

Thanatophoric dysplasia (TD)
- Ossification generally normal
- Severe long bone shortening, bowing may be mistaken for fractures

PATHOLOGY

General Features
- Genetics

- Mutations in COL1A1, COL1A2 genes of type I collagen
- Most autosomal dominant
- Most recurrences of type II attributed to germlinal mosaicism
- Recurrence risk up to 3%
- Autosomal recessive inheritance suspected in some cases of type II
- Epidemiology
  1/20,000-1/60,000 live births
  Incidence of maternal CM in pregnancy
  1/20,000-1/30,000
- Associated abnormalities
  - Dextrocardia imperfecta
  - Hearing loss

Gross Pathologic & Surgical Features
- Of type II (perinatal lethal type)
  - Thin cortical bone, sparse trabecular bone
  - Increased osteoclasts/osteocytes
  - Thin osteoid with thin collagen filibrils
  - Patchy mineralization

Staging, Grading or Classification Criteria
- Severity Classification: Based on phenotype
  - Type I: Fractures rare at birth
  - Type II: Normal teeth; IB with dextrocardia imperfecta (60%)
  - Type III: Normal teeth; IB with dextrocardia imperfecta (60%)
  - Increased capillary fragility
  - Bone fragility improves with adolescence; may recur after menopause
  - Worn down bones
  - Type II: Most severe form, multiple fractures, lethal
  - IB with blue sclerae; short, thick tubular bones
  - IB neonatal form of type III
  - IC with blue sclerae; slender/twisted tubular bones
  - Small chest with "beaded" ribs
  - Severe limb shortening
  - Prematerialization of skull
OSTEONECROSIS IMPERFECTA

- Type III: Multiple fractures at birth, progressive severe deformity of limbs, spine, skull
  - Detectable by 2nd trimester
  - Generalized osteopenia
  - Scoliosis or kyphosis
  - Triangular facets
  - Severe stunted stature
  - Spinal cord compression
  - Osteoporosis common
  - Curved non-ambulatory
- Type IV: Delayed presentation, clinical and radiographic spectrum between Types I and Type III
  - Scoliosis or kyphosis
  - Short stature
  - Delayed bone maturation or deformity
  - Generalized desmin localization
- Types V, VI, VII
  - Non-type I collagen defects
  - Recognized provisionally due to severe clinical data

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - Multiple fractures on mid trimester ultrasound
    - Cases of type III/IV OI reported with isolated bent femurs in utero
- Other signs/symptoms
  - 1st trimester cystic hygroma, increased nuchal
    - Alkaline phosphatase
  - Detected as early as 12-14 weeks

Demographics
- Age: Tendency towards mildly increased paternal age in lethal OI
- Gender: Females > males

Natural History & Prognosis
- Variability according to type
  - Type I/IV: Normal to slightly decreased life span
  - Type II: Perinatal lethal
  - Type III: Significantly shortened life span
- Pregnancy in women with OI
  - Increased uterine atony
  - Increased bleeding tendencies
  - Increased amniotic fluid volumes, large babies
  - Premature delivery
  - Respiratory difficulties very short stature
  - Possible association with malignant hyperthermia with general anesthesia
  - Scoliosis, delivery controversial
  - Triangular individual cases
  - Maternal pelvic fractures
  - Case reports of uterine rupture with vaginal delivery, attributed to decreased total collagen in myometrium

Treatment
- No prenatal treatment for fetus
- Experimental bisphosphonate therapy in maternal OI (preconception)
- Genetic counselling indicated in all cases
- Biochemical/collagen analysis from cutaneous villous sampling (CVS) or amniocentesis
  - Molecular analysis possible in some cases
  - Postimplantation genetic diagnosis (PGD) reported in type I, IV
- Suspected lethal or severe OI
  - Pregnancy termination in option
  - Confirmation of diagnosis important for genetic counseling
- Delivery in center with expertise in genetic fetopathy, skeletal dysplasia
  - No benefit from cesarean section
  - No increase in survival in lethal OI
  - No increase in perinatal deaths in non-lethal OI
  - Autopsy with cesarean section
  - Tissue for biochemical, molecular confirmation
  - Postnatal
    - Intravenous therapy to straighten and stabilize long bones in severe OI
    - Cyclic bisphosphonate therapy in severe OI
      - Increases bone turnover and increases bone density
      - Decreases fracture frequency, pain

DIAGNOSTIC CHECKLIST

Consider
- Fetal skeletal survey at 3rd trimester
- Image Interpretation. Pears
  - Severely limb shortening with limb and rib fractures most likely lethal OI

SELECTED REFERENCES
OSTEONEOSIS IMPERFECTA

IMAGE GALLERY

Typical

[Images of ultrasound and radiographs showing typical features of osteogenesis imperfecta, including bowed femurs, fractures, and thin cortices.]

Typical

[Images showing another case with similar features, emphasizing the varied presentation.]

Typical

[Images of an axial ultrasound and photograph of a mother and her infant, highlighting the varied presentation across different types and stages.]
**TERM I N O L O G Y**

**Abbreviations and Synonyms**
- Short rib (polydactyly) syndrome (SRPS)
- Short rib syndrome
- Polydactyly with neonatal chondrodysplasy

**Definitions**
- Group of nine lethal autosomal/polydactyls characterized by severe microelia, short horizontal ribs, polydactyly, visceral anomalies
- Four subtypes described
- Controversy exists over whether types I and II are distinct entities or represent a spectrum of the same disorder given very similar radiographic findings

**IMAGING FINDINGS**

**General Features**
- Salcido-Nieman and Verna-Nieman types (SRPS types I and II)
- Preaxial polydactyly
- Hydrops
- Cardiac: Septal defects, coarctation, transposition of great vessels
- Urogenital: Renal cysts, cloacal anomalies, vaginal atresia, vaginal fistula
- Anorectal: Imperforate anus, cloacal anomalies
- Radiographic findings: Fibroplastic iliac bones with flattened acetabular roofs, rounded vertebrae with coronal cleft, long bones with pointed metaphyses, central area with lateral metaphyseal spikes/thrusted appearing ends
- Macleod type (SRP type III)
- Pre- and postaxial polydactyly
- Hydrops
- Orofacial clefts, often midline
- Ambiguous genitalia
- Central nervous system (CNS) abnormalities
- Radiographic findings: Short horizontal ribs, short tubular bones with smooth ends, short and thin bones (shorter than fibers), normal iliac bones
- Bearn's longer type (SRP type IV)
- Pre- and postaxial polydactyly in 50%
- Visceral anomalies: Osteopetrosis, cardiac, cystic/hypoplastic kidneys, lobulated tongue, oval fontanel
- Median oral facial cleft
- CNS: Hydrocephalus, holoprosencephaly, hemihypertrophy
- Ambiguous genitalia
- Radiographic findings: Short horizontal ribs, small iliac bones, short tubular bones with smooth metaphyses, bowed radii, and ulnae

**DDx: Similar Findings In Jeune Syndrome**

- Jeune Syndrome
- Jeune Syndrome
- Jeune Syndrome
SHORT RIB-POLYDACTYLY

Terminology
- Group of rare lethal osteochondrodysplasias characterized by severe micromelia, short horizontal ribs, polydactyly, visceral anomalies
- Four subtypes described

Top Differential Diagnoses
- Jeune syndrome (asphyxiating thoracic dystrophy)
- Ellis van Creveld syndrome
- Mohr-Majewski syndrome

Key Facts
- Genetics: Autosomal recessive

Pathology
- Diagnosis possible by 15-16 weeks gestation based on micromelia, very short ribs
- Consider 1st trimester endovaginal ultrasound in at-risk pregnancies
- Prenatal/neonatal lethal

DIFFERENTIAL DIAGNOSIS
- Jeune syndrome (asphyxiating thoracic dystrophy)
  - Thoracic long and narrow with short horizontal ribs
  - Thoracic constriction improves with age
  - Cystic renal dysplasia
  - Polydactyly less common (14%)
  - Long bones less severely affected with more normal tibiae
  - Spina bifida exists that Jeune and SIF, type III are variants of same disorder

Ellis van Creveld syndrome
- Chondroectodermal dysplasia
- Rare: Incidence in Amish
- Less severe thoracic involvement
- Cardiac defect in 50%
- Postaxial polydactyly
- Progressive distal shortening of extremities
- Survival with normal intelligence

Mohr-Majewski syndrome
- Osteochondrodysplasia (OFD) type IV
- Distinction between SPS and OFD IV is unclear: May be part of a single spectrum
- Severe rib involvement, ribs longer
- Neonatal survival possible

Natural History & Prognosis
- Prenatal/neonatal lethal

Treatment
- Genetic counseling should be offered
- No treatment available
- Option of pregnancy termination
- Prenatal confirmation of diagnosis crucial for recurrence risk counseling

SELECTED REFERENCES

PATHOLOGY

General Features
- Genetics: Autosomal recessive
- Etiology: Genetic basis unknown

Microscopic Features
- Loss of synchrony in cartilage removal and osteogenic differentiation at all growth plates

CLINICAL ISSUES

Presentation
- Diagnosis possible by 15-16 weeks gestation based on micromelia, very short ribs
  - Consider 1st trimester endovaginal ultrasound in at-risk pregnancies

IMAGE GALLERY

(Left) Radiograph shows metaphyseal bone spurs (curved arrows) in Venna-burnet SPS. Radio-density is apparent (open arrows).
(Right) Radiograph shows posteriorly directed (arrows) of the facet in a fishes bubble with SPS. Physeal plates are short, rounded (open arrows) and skeletal phalanges are hypoplastic (curved arrows).
THANATOPHORIC DYSPLASIA

TERMINOLOGY

Abbreviations and Synonyms
- Thanatophoric dysplasia (TD), lethal skeletal dysplasia, thanatophoric dwarfism, lethal osteochondrodysplasia

Definitions
- Lethal skeletal dysplasia due to mutation of fibroblast growth factor receptor 3 gene (FGFR3)
- Divided into 2 subtypes based on morphologic findings
- Thanatophoric is Greek for "death-bearing"

IMAGING FINDINGS

General Features
- Best diagnostic clue
  - TD type 1: "Telephone receiver" femur
  - TD type 2: Kleeblattschädel ("cloverleaf") skull

Ultrasoundographic Findings
- Type 1
  - Long bones severely affected
  - Micromelia
  - All measure well below the 5th percentile for gestational age
  - Prominent bowing

- TD type 2
  - "Telephone receiver" femur
  - Normal calcification
  - No evidence of fractures
  - Progressive shortening observed throughout gestation
  - Head
    - Macroecephalic, relatively normal-shaped skull
  - Depressed nasal bridge
  - Short, upturned nasal tip
  - Hypoplastic maxilla
  - Frontal bossing, severe in 2nd trimester
  - Thorax
    - Small, narrow
  - Short horizontal ribs
  - Abnormal cardiothoracic ratio
  - Spine
    - Platy spondyly
  - Fusion of lumbar vertebrae
  - Normal ossification
  - Hands
    - Very short phalanges
  - Trident shaped hands
  - idiosyncrasies
    - Polyhydramnios, often severe
  - Limb reduction in joint mobility noted
- Type 1
  - Kleeblattschädel ("cloverleaf") skull
  - Femurs longer, less curved

DDx: Other Short Limb Conditions

- Achondrogenesis
- Achondroplasia
THANATOPHORIC DYSPLASIA

**Terminology**
- Lethal skeletal dysplasia due to mutation of 5th osteoblast growth factor receptor 3 gene (FGFR3)
- Divided into 2 subtypes based on morphologic findings

**Imaging Findings**
- TD Type I: "Telephone receiver" femur
- TD Type II: Kleinhalsköfchen ("cloverleaf") skull
- Long bones severely affected
- Normal ossification
- Trident shaped hands

**Top Differential Diagnoses**
- Achondrogenesis
- Homozygous achondroplasia
- Camptomelic dysplasia

- Prominent lumbar kyphosis
- Pelvis
- Hypoplastic with spicules
- Accessory pelvic ossification centers
- Long bones
- Micromelia
- Prominent bowing, especially TD I
- Flared irregular metaphyses
- No fractures

**Imaging Recommendations**
- Measure, assess morphology of all long bones
- Carefully assess calvarium shape, profile
- Consider fetal skeletal survey if 3rd trimester
- 3D US may be additive in select cases
- Useful for spatial relationships
- Evaluation of facial dysmorphism
- Relative proportion of appendicular skeletal elements
- Images aid in counseling parents

**Key Facts**
- Osteogenesis imperfecta (OI)
- Very low recurrence risk
- Most common type of lethal osteochondrodysplasia

**Clinical Issues**
- Can be diagnosed as early as 14 weeks
- 75% severe polyhydramnios by 2nd trimester
- Lethal within first few hours to days of life
- Molecular testing for FGFR3 mutations
- Autopsy important for final specific diagnosis
- X-rays even if prenatal ultrasound performed
- Bone/cartilage biopsy
- Deliver in tertiary center with expertise in fetal genotypic pathology/skeletal dysplasia

**Homozygous achondroplasia**
- Look at parents
- May not be apparent until > 20 weeks

**Camptomelic dysplasia**
- Hypoplastic scapula
- Short mid-shaft-tibial angulation
- Lower extremities more severely affected

**Osteogenesis imperfecta (OI)**
- Bones accutely angulated from fractures
- Decreased ossification, especially calvarium
- Ribs appear "beaded" due to multiple fractures

**Fibrochondrogenesis**
- Cloverleaf skull common
- "Thumb bell" shaped long bones
- Hypoplastic posterior vertebrae with clefts

**Carpenter syndrome**
- Cloverleaf skull
- Polyhydramnios
- Cardiac abnormalities
- Umbilical hernia
- Limbs straight, not as short

**PATHOLOGY**

**General Features**
- General path comments: Defective differentiation of chondrocytes in cartilage growth plates
- Genetics
- Sporadic, new, dominant mutation of FGFR3 gene on short arm of chromosome 4
- Identifiable mutation found in all cases
- TD I involves a lysine-to-arginine substitution at position 288 in approximately 22% of cases
- TD II involves a lysine-to-glutamine substitution at position 650
- Very low recurrence risk
- Has occurred in monozygous twins
- Discordance for kleinhalsköfchen skull reported

DIFFERENTIAL DIAGNOSIS

**Achondrogenesis**
- Absent spine ossification
- Only skull ossifies well enough to be seen
THANATOPHORIC DYSPLASIA

- Prenatal Diagnosis
  - Ultrasound
  - Amniocentesis or chorionic villus sampling (CVS) for molecular analysis of FGFR3 mutations
  - 3rd trimester radiography
- Biological
  - No FGFR3 member of tyrosine kinase receptor family
  - Tyrosine kinase important in cell growth and differentiation
  - Not due to simple haploinsufficiency
- Epidemiology
  - Most common type of lethal osteochondrodysplasia
  - First described as a distinct entity by Mureactes in 1967
  - 1:10,000 live births in USA
  - No ethnic or gender predilection
  - Advanced paternal age:
    - 50% occur with paternal age over 55 years
  - Associated abnormalities:
    - Club palate
    - Heterotopias
    - Polymicrogyria
    - Other microscopcic central nervous system (CNS) abnormalities

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - Usually found on routine screening ultrasound
  - Carries diagnosed as early as 14 weeks
  - 1st trimester associations
    - Increased nuchal thickness
    - Reversed diastolic flow in ductus venosus
  - Other signs/symptoms
    - May be diagnosed late when polyhydramnios causes increased uterine size
    - 75% severe polyhydramnios by late 2nd trimester
  - Natural History & Fetal Compromise
    - Lethal within first few hours-to-days of life
    - Small thorax Pulmonary hypoplasia
    - Central agenesis also a primary cause of death
    - Abnormal skull:time/small fontanels magnus = brainstem compression
    - Rare survivors beyond infancy have been described

Treatment
- No real or neonatal treatment available
- Amniocentesis
  - Therapeutic reduction amniocentesis for maternal symptoms in continuing pregnancy or prior to labor
  - Molecular testing for FGFR3 mutations
- Other pregnancy termination
  - If pregnancy progresses and diagnosis certain
    - Avoidance of fetal monitoring, cesarean section
    - No intervention for preterm labor
    - Psychological support for family, fetal loss support
  - If diagnosis unclear and infant lives, resuscitation appropriate until confirmatory tests performed
- Autopsy important for final specific diagnosis
  - X-rays even if prenatal survey performed
  - DNA analysis for FGFR3 mutations
  - Imaging/cartilage biopsy
  - International Skeletal Dysplasia Registry at Cedars Sinai Hospital in Los Angeles for various cases
- Deliver in tertiary center with expertise in fetal neonatal pathology/neonatal dysplasia

DIAGNOSTIC CHECKLIST

Consider
- Fetal skeletal survey should be performed in 2nd trimester

Image Interpretation Pearls
- Micromelia with normal ossification, curved femora, cloverleaf skull

SELECTED REFERENCES

**THANATOPHORIC DYSPLASIA**

**IMAGE GALLERY**

**Typical**

*Left:* Clinical photograph of TD type I shows marked frontal bossing with depressed nasal bridge (curved arrows) and short, downturned nasal tip. Note the heart is micrognathic, but normal in shape. 

*Right:* Clinical photograph of TD type II shows unusual skull shape (skelletal thickening) (curved arrows). The eye is very small (arrows). Note the typical "trident" hand sign.

**Typical**

*Left:* Ultrasound of the hand (arrows) shows short phalanges and ulnar deviation of the fingers, all of equal length. This configuration gives the hand a classic "indice" appearance.

*Right:* Radiograph shows the curved femur (arrows) of TD type I. Platybasia (flattening of the base of the skull) is obvious in the lambdoid suture (curved arrows) and the speculated appearance of the Baculara sign is shown (open arrows).

*Left:* Ultrasound of the abdomen shows a very small thoracic cavity (arrows) compared to the abdomen. Chest findings are similar in both TD type I & II with pulmonary hypoplasia often being cause of death. 

*Right:* Axial ultrasound shows an abnormal skull configuration with unTTonted pterional prominence (arrows) typical of a bleb shaped or "cloverleaf" skull in TD type II.
CLUBFOOT

TERMINOLOGY

Abbreviations and Synonyms
- Clubfoot (CF)
- Talipes equinovarus

Definitions
- Malformation/malposition of foot and ankle bones
  - Talipes equinovarus
  - Most common
  - Foot rotated inward (varus)
  - Foot plantar flexed (equinus)
  - Talipes varus
  - Talipes equinovarus
  - Foot rotated outward (valgus)
  - Talipes valgus
  - Flat

IMAGING FINDINGS

General Features
- Best diagnostic clue
  - Foot mediadly deviated at ankle
  - Long bones of foot lie in same plane as tibia and fibula
  - Must be a consistent finding

- Location
  - 60% bilateral
  - 40% unilateral
- Size: Mild or severe angulation

Ultrasoundographic Findings
- Normal lower extremity orientation
  - Coronal axis tibia/fibula (tib/fib) + short axis foot
  - Long tib/fib + cross section metatarsals

Clubbfoot
- Talipes varus
  - Foot turned inward
  - Coronal tib/fib + coronal foot
  - Long tib/fib + long metatarsals
  - Talipes equinovarus
    - Foot plantar flexed and short
    - Talipes varus + equina foot
  - Equinus + horse hoof
  - Talipes valgus
  - Less common
  - Long tib/fib + long metatarsals
  - Foot turned outward
- 60% bilateral
  - 75% with other anomalies at time of ultrasound
  - 15% false positive rate
  - 8% will have normal feet
  - 8% will have only unilateral clubfoot
  - 40% unilateral

DDx: Dysmorphic Foot
- Rockerbottom
- Scoliotic
- Angulations - RT
- Exostosis - RT
CLUBFOOT

Terminology
- Talipes equinovarus

Imaging Findings
- Long bones of foot lie in same plane as tibia and fibula
- 60% bilateral
- 20% unilateral
- Foot turned inward
- Foot plantar flexed and short
- 20% clubfoot missed at first ultrasound
- High false positive rates
- 30% with chromosome abnormality
- Chronic oligohydramnios important risk factor
- Association with early amniocentesis (EA)
- Rule out transient foot position

- 62% with other anomalies at time of ultrasound
- 29% false positive rate
- Normal feet
- High false negative rates
- 20% clubfoot missed at first ultrasound
- 6% found to have additional anomalies at birth
- High false positive rates
- Positional foot
- Foot is against uterine wall
- Look for extended period of time
- Follow-up when isolated finding
- Clubfoot and aneuplody
  - 30% with chromosome abnormality
  - Same for unilateral as bilateral
  - Almost all have associated anomalies
- Trisomy 18 most common
- 23% with clubfoot
- 10% with rockerbottom foot
- Associated anomalies common
  - Spinal bifida
  - 24% with clubfoot
  - Usually bilateral
- Arthrogryposis
  - Fetal akinesia deformation sequence
- Multiple joint contractures
- Intrathoracic growth restriction (UGR)
- Polyhydramnios
- Restricted in utero environment
  - Chronic oligohydramnios important risk factor
  - Uterine anomalies
  - Any restriction on gestational sac growth
- Intrinsic abnormality of muscle
- Myotonic dystrophy
- Association with early amniocentesis (EA)
  - Procedure at 11-13 wk is EA
  - 4x 1 risk for clubfoot
  - Compared with chorionic villus sampling

Imaging Recommendations
- Best imaging tool
  - Routine view of both lower extremities
  - Coronal view of tib/fib and foot
  - 3D ultrasound may be helpful

Key Facts
- Top Differential Diagnoses
  - rockerbottom foot
  - ectodactyly
  - amniotic bands

Pathology
- Epidemiology: 1:1,000 live births

Clinical Issues
- Do well with treatment
- 60% surgery
- 40% conservative
- Decision for surgery after 3 months

Diagnostic Checklist
- Look carefully at feet when associated anomalies seen
- Remember false positive diagnoses are common

- Multidisciplinary imaging advantage
- Allows for meticulous exam
- Protocol advice
  - Rule out transient foot position
  - Follow-up when isolated finding
- Role for amniocentesis
- Controversial for isolated cases
- Some "isolated" cases show additional anomalies on follow-up

DIFFERENTIAL DIAGNOSIS

Rockerbottom foot
- "Persian slipper" appearance
  - Convex foot on lateral view
  - Foot hyperextended
- May be seen with clubfoot
- Rarely isolated
  - Strong association with trisomy 18
  - 70% bilateral
- Almost always need surgery for repair

Ectodactyly
- Split hand/foot deformity
  - "Loafer-claw" deformity
- Abnormal central ray formation
  - Absent middle fingers/toes
  - Deep median cleft
  - Fusion of remaining digits
  - Isolated or with other anomalies

Amniotic bands
- Entrapment of fetal parts by disrupted amnion
- Amputations
  - Missing toes/fingers common
- Constrictions
  - Bands around limb
  - 2° lymphedema
- Clefts
  - Bizarre body wall defects
PATHOLOGY

General Features
- Genetics
  - Associated with aneuploidy in 30%
  - Trisomy 18
  - Trisomy 21
  - 47,XY/47,XX
- Biomechanics
  - Persistent embryonic positioning implicated
  - Normal foot position is rare
  - Lack of movement from any cause
  - Movement starts at 7-8 wks
  - Primarily affects middle of foot
    - Mostly involving talus and calcaneus
  - Spina bifida
  - Unsupposed muscle group action
- Epidemiology: 1:1,000 live births

Staging, Grading or Classification Criteria
- Talocalcaneal angle
  - Measured on frontal and lateral x-rays
  - Normal:
    - Frontal: 35° (or > 35° in children)
    - Lateral: 35°
  - Clubfoot:
    - Frontal < 35°
    - Lateral: Talus and calcaneus are parallel
  - Used to follow treatment
- Dimaggio score
  - 0-20 points based on 4 parameters
  - Varus in frontal plane
  - Forefoot adduction in frontal plane
  - Calcaneo-forefoot rotation around talus
  - Equines in sagittal plane
  - Grade I (mild): 1-5 points
  - Easily reducible
  - Grade II (moderate): 5-10 points
  - Reducible but partly resistant
  - Grade III (severe): 10-15 points
  - Resistant but partly reducible
  - Grade IV (very severe): 15-20 points
  - Resistant

CLINICAL ISSUES

Presentation
- Most common sign/symptoms
- Club feet or other anomalies
- Incidentally noted on routine ultrasound

Demographics
- Age
  - Advanced maternal age (AMA) at greater risk for trisomy
- AMA > 35 yrs at time of delivery

Natural History & Prognosis
- Isolated
  - Do well with treatment
- Non-isolated
  - Depends on karyotype
- Severity of associated anomalies

Treatment
- Clubfoot
  - 60% surgery
  - 40% conservative
- Physical therapy (PT)
  - Gentle manipulation
  - 30 minutes/day
  - Baby should never cry during PT
  - Progressive reduction of deformity
  - Feet reduced correctly first
  - Hindfoot corrected second
  - Equinus corrected last
  - Decision for surgery after 3 months
- Flexible splint
  - Applied between PT sessions
  - Light below-knee splint
- Surgery
  - Arches tendon lengthening
  - +/- Fusion/tenor release
  - +/- Medial tendo release
  - Bone operation
  - Usually only in fully-grown foot

DIAGNOSTIC CHECKLIST

Consider
- Diagnosis in high-risk fetuses
- Spina bifida
- Arthrogryposis
- oligohydranios

Image Interpretation Pearls
- Look carefully at feet when associated anomalies seen
- Remember false positive diagnosis are common

SELECTED REFERENCES
Typical

[Images of clubfoot ultrasound scans showing typical features]

Typical

[Images of another ultrasound scan with different features]

Typical

[Images of yet another ultrasound scan with additional details]

Clubfoot ultrasound

Images showing typical clubfoot features include:
- Enlarged calcaneus (bone) and talus (bone) on X-ray.
- Overlapping bones on X-ray, indicating deformity.
- Presence of a bony spur on the lateral side of the foot.

Clubfoot 3D ultrasound

Images showing 3D ultrasound features include:
- Detailed visualization of bone structures.
- Improved identification of clubfoot deformities.

Clavicle fracture

Images showing a clavicle fracture include:
- Visible bone fracture on X-ray.
- Presence of a displaced bone fragment.
- Pain and swelling at the fracture site.

Endotoxin therapy

Images showing endotoxin therapy include:
- Injection of endotoxin into the affected area.
- Immediate relief of symptoms.
- Progression of the healing process.
ROCKERBOTTOM FOOT

TERMINOLOGY

Abbreviations and Synonyms
- rockerbottom foot
- Congenital valgus of the foot
- Congenital vertical talus
- Congenital cubitus varus

Definitions
- Dorsal dislocation of the midfoot and hindfoot

IMAGING FINDINGS

General Features
- Best diagnostic clue
  - "Rollerblading" deformity
- Site of foot is convex
- Degree of foot is concave
- Location
  - 70% bilateral
  - 30% unilateral

Ultrasoundographic Findings
- Convex foot on lateral view
- Foot hyperextended
- Convex sole
- Valgus deformity on frontal view

DDx: Dysmorphic Foot
- Clubfoot
- Cleftfoot
- Exostodyls
- Amniotic bands

- Long axis of tibia/tibial (tib/fib) - long axis of foot
- Foot turned away from midline
- Rarely isolated when diagnosed in utero
- 30% isolated in siborial series
- Common associations
- Clubfoot
  - 1:1,000 with additional rockerbottom morphologic
  - Trisomy 18
  - Rockerbottom foot in 10%
  - Clubfoot in 25%
  - Other severe anomalies usually also present
- Spina bifida
  - Clubfoot more common (24%)
- Arthrogryposis
  - Fetal akinesia deformation sequence
  - Multiple-limb contractures
  - Polyhydramnios
  - Restricted in utero environment
  - Chronic oligohydramnios
  - Intrinsic abnormality of muscle
  - Myotonic dystrophy

Imaging Recommendations
- Best imaging tool
- Routine lower extremity evaluation
- Lateral tib/fib = lateral foot
- Coronal a/c tib/fib = short axis foot
- Protocol advice
ROCKERBOTTOM FOOT

Terminology
- Congenital convex pes valgus
- Dorsolateral dislocation of midfoot on hindfoot

Imaging Findings
- "Persian slipper" foot
- 70% bilateral
- Rarely isolated when diagnosed in utero
- Trisomy 18
- Rule out transient foot position
- Amniocentesis recommended when not isolated

DIFFERENTIAL DIAGNOSIS

Clubfoot
- Talipes equinovarus
- Medial angulation of foot
- Foot abnormally flexed
- More common than rockerbottom

Ectodactyly
- Split hand/foot deformity
- "Lobster-claw" deformity
- Absent central ray/rays
- Deep median cleft
- Fusion of remaining digits

Amniotic band syndrome
- Entrapment of fetal parts by disrupted amnion
- Amputations
- Missing fingers/toes
- Constrictions
- 2° lymphedema
- Bizarre body wall defects

PATHOLOGY

General Features
- General path comments
  - Dorsal dislocation of talocalcaneonavicular joint
  - Secondary equinus of hindfoot
  - Vertical orientation of toes
- Genetics
  - High risk of aneuploidy when non-isolated
  - Trisomy 18 most common
- Epidemiology: 1:10,000

CLINICAL ISSUES

Natural History & Prognosis
- Depends on karyotype and associated anomalies

Treatment
- Surgery almost always necessary
  - Often multiple
  - Often need further bracing

KEY FACTS

Top Differential Diagnoses
- Clubfoot

Clinical Issues
- Surgery almost always necessary

Diagnostic Checklist
- Amniocentesis in non-isolated cases
- Look carefully at feet when associated anomalies seen

DIAGNOSTIC CHECKLIST

Consider
- Amniocentesis in non-isolated cases
- Follow-up on cases which appear isolated
- Rule out transient finding
- Re-evaluate for associated anomalies

Image Interpretation Pearls
- Look carefully at feet when associated anomalies seen

SELECTED REFERENCES

IMAGE GALLERY

(Left) Sagittal T2W MR shows a rockerbottom foot in a fetus with multiple other anomalies. The tibia is the most obvious finding (arrows). In addition, this fetus had skin edema (open arrow). (Right) Lateral clinical photograph shows isolated rockerbottom foot in a child. The hindfoot is most severely affected (arrow) and the tip of the foot is curved. Almost all rockerbottom feet need surgical correction.
SANDAL GAP FOOT

Clinical photograph shows sandal gap foot and syndactyly. Notice the gap (arrows) between the first and second toes. Soft tissue syndactyly of the other toes is also seen (curved arrows).

Clinical ultrasound shows sandal gap foot (arrow) in a normal fetus. The increased space between the first and second toe was persistent and no other anomalies were observed.

TERMINOLOGY

Abbreviations and Synonyms
- Sandal gap foot (SGF)

Definitions
- Big toe angled medially
- Gap between first and second toe

IMAGING FINDINGS

General Features
- Best diagnostic clue: Increased space between first and second toe
- Location: Unilateral or bilateral

Ultrasound Findings
- Routine lower extremity views
  - Coronal view of tibia and fibula
  - Toes and metatarsals in cross section
  - Usually first toe gap in cross section view
  - Sole view
  - Parallel to border of foot
  - SGF
  - Big toe abducted
  - Other toes normally positioned
  - Most often normal fetus
  - Often familial
  - Rule out polydactyly
  - SGF and trisomy 18
  - 45% of fetuses with T21 have SGF
  - Look for other markers for T21
  - Increased nuchal fold thickness
  - Echogenic intracardiac focus
  - Echogenic bowel
  - Mild renal pelvics
  - Urogenital
  - SGF and trisomy 18 (T18)
  - Almost never an isolated finding
  - Short femur = unbalanced = SGF
  - Sandal gap + other foot anomalies common
    - Clubfoot
    - Foot is turned inward
    - Rocker-bottom foot
    - Toes splayed and upward displaced
    - Additional abnormal gaps
  - SGF and amnioncetosis
    - Isolated usually idiopathic
    - No need for amnioncetosis
    - Consider amnioncetosis only if high risk for T21 or T18
    - Obstruct anomalies or murines
    - Abnormal maternal serum quadruple screen
    - Advanced maternal age

DDx: Dysmorphic Foot
**SANDAL GAP FOOT**

**Terminology**
- Big toe rotated medially
- Gap between first and second toe

**Imaging Findings**
- Most often normal fetus
- 45% of fetuses with T21 have SGF
- Look for SGF when other markers for T21 seen
- As an isolated finding in low-risk patients, no need for amniocentesis

**Imaging Recommendations**
- Protocol advice
  - Look for SGF when other markers for T21 seen
  - As an isolated finding in low-risk patients, no need for amniocentesis

**DIFFERENTIAL DIAGNOSIS**

**Ectrodactyly**
- Split hand/foot deformity
- Lobster claw deformity
- Deficiency of middle phalanges
- Missing fingers/toes

**Syndactyly**
- Fusion of adjacent digits
- Soft tissue or bone fusion
- Isolated or part of syndrome
- Apert Syndrome
  - Broad first toe, inward hand

**Amniotic bands**
- Fraying of amniotic with entrapment of fetal parts
- Amputations
  - Loss of toes with secondary gaps
- Bizarre body wall/facial defects

**PATHOLOGY**

**General Features**
- Genetics
  - Usually normal
  - T21 (rarely isolated)
  - T18 (never isolated)
- Epidemiology
  - 45% of fetuses with T21
  - 2.5% of normal feet

**CLINICAL ISSUES**

**Presentation**
- Most common signs/symptoms
  - Routine view of lower extremities
  - In association with other anomalies or markers

**Natural History & Prognosis**
- Excellent prognosis when isolated

**Key Facts**

**Top Differential Diagnoses**
- Ectrodactyly
- Syndactyly
- Amniotic bands

**Diagnostic Checklist**
- T21 when other markers present
- Look at other family member's toes
- Examine for an extended period of time to rule out positional finding

**Treatment**
- Usually none necessary

**DIAGNOSTIC CHECKLIST**

**Consider**
- T21 when other markers present
- Look at other family member's toes
- Examine for an extended period of time to rule out positional finding

**SELECTED REFERENCES**

**IMAGE GALLERY**

(Left) Coronal ultrasound of the foot shows a persistent SGF (arrow) in a fetus with multiple other anomalies. (Right) Four-chamber view of the heart shows a large atrioventricular septal defect. Note the lack of any central cardiac structures. Other minor markers were present and the amniocentesis results were normal T1.
**RADIAL RAY MALFORMATION**

**TERMINOLOGY**

**Abbreviations and Synonyms**
- Radial ray malformation (RRM)
- Radial ray hypoplasia
- Radial ray aplasia

**Definitions**
- Spectrum of anomalies including absence or hypoplasia of:
  - Radius
  - Radial carpal bones
  - Thumbs
  - +/− Malposition or "fingerprint" of thumb (triphalangeal)

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue: Single forearm bone

**Ultrasoundographic Findings**
- Grayscale Ultrasound
  - Radius is absent or hypoplastic
  - Hypoplasia involves distal portion
  - Hand position: abnormal
  - Medial rotation

**DDX: Abnormal Hand**
- Anomalous Band Defect
- Arthrogryposis
- Hypoplastic Thumbs
- Adducted Thumbs

- Fixed on prolonged scanning
- Has been detected in first trimester
- Thumb appearance variable
- Absent
- Hypoplastic or malpositioned ("floating")
- Other anomalies/syndromes common
- Multiple anomalies increase likelihood of chromosome defect or VACTERL association
- Vertebra anomalies
- Anal atresia
- Cardiovascular anomalies
- Tracheoesophageal fistula, esophageal atresia
- Renal anomalies
- Limb anomalies (radial ray malformation)
- Trisomy type absent radial ray syndrome (17p)
  - Has thumb and radial aplasia
  - Holt-Ostertag syndrome (thumb-hand syndrome)
  - Cardiac defect and upper extremity anomalies including RRM
  - 3D
    - Useful to show hand position
    - Helpful to count digits
    - Detail on thumb
    - Triphalangeal
    - Hypoplastic
    - May show facial detail allowing specific syndromal diagnosis
    - Cornelia de Lange syndrome
### Imaging Findings
- Best diagnostic clue: Single forearm bone
- Hand position abnormal
- Thumb appearance variable
- Multiple anomalies increase likelihood of chromosome defect or VACTERL association
- Thrombocytopenia-absent radius syndrome (TAR) has normal thumbs but radial aplasia
- TAR may involve lower extremities
- Cardiac defects common in Holt-Oram
- 80% of patients with hypoplastic thumbs have other anomalies
- Fetal incidence higher due to trisomies/lethal syndromes

### Top Differential Diagnoses
- Amputation defects
- Nager syndrome

### Imaging Recommendations
- Best imaging tool: Targeted endovaginal ultrasound in first trimester if positive family history
- Measure all long bones
- Nephrogenia exist for length
- TAR may be associated with other bone anomalies
- Holt-Oram upper extremity only, asymmetric
- TAR may involve lower extremities
- Fetal echocardiogram recommended in all cases
- Cardiac defects common in Holt-Oram
- Atrial septal defect 34%
- Ventricular septal defect 25%
- VACTERL association: C = cardiac lesion
- Careful search for other structural anomalies
- 86% of patients with hypoplastic thumbs have other anomalies
- 44% either Holt-Oram or VACTERL
- Total incidence higher due to trisomies/lethal syndromes
- Monitor growth
- Fetal-uterine growth restriction
- Chromosome abnormality especially trisomy 18
- Cornelia de Lange syndrome
- Fanconi anemia
- Look for evidence of bleeding
- TAR: Thrombocytopenia predisposes to bleeding
- Fanconi anemia may also cause thrombocytopenia

### Key Facts
- **Arthrogryposis**
- **Short limbed skeletal dysplasia**
- **X-linked aque ductal stenosis**
- **13q deletion syndrome**

### Pathology
- Damage to apical ectoderm of limb bud at 6-12 weeks
- Bilateral in 50%

### Clinical Issues
- Detailed clinical evaluation of newborn infant and family members

### Diagnostic Checklist
- Syndrome identification important in ERM
- Prognosis and specific clinical complications vary for each condition

### PATHOLOGY

#### General Features
- Genetics
  - Autosomal dominant
  - Holt-Oram maps to chromosome 12q3 mutation in TBX5
  - Nager syndrome (many cases are new sporadic mutations)
  - Autosomal recessive
    - Fanconi anemia
    - TAR
    - X-linked dominant
    - Proves X-linked recessive forms exist but are extremely rare
    - Split hand/split foot syndrome
    - Critical region chromosome 10q24
    - Axenfeld dysplady
    - Trisomy 18, 13
    - Diploid/triploid mosaicism
- Embryology
  - Damage to apical ectoderm of limb bud at 6-12 weeks
  - Normal hand is fully formed by 14 weeks
  - Maternal infection
**CLINICAL ISSUES**

**Presentation**
- Most common sign/symptom
  - Should be detected on routine anatomic survey at 16-18 weeks
  - Single forelimb bone
  - Abnormal hand position
  - Absent thumb

**Demographics**
- Gender: 63% patients with hypoplastic thumbs are male

**Natural History & Prognosis**
- Depends on associated anomalies
  - TAR
  - Risk of bleeding
  - 40% liveborn die in early infancy
  - Fanconi anemia
  - Proximal bone marrow failure in childhood
- Depends on underlying cause
  - Trisomy 18: Dimal
  - Taphalangeal thumbs: If isolated, can be surgically corrected at 1-2 years
- Recurrence risk related to underlying condition
  - Trisomy: 18 overall recurrence risk given as 1%
  - Autosomal recessive conditions: 25%
  - Autosomal dominant: 50%

**Treatment**
- Genetic counseling
- Careful maternal history for drug exposure
- Offer karyotype
- Aneuploidy
- Fanconi anemia
- Chromosomes must be studied after exposure to diethylstilbestrol
- Exclude maternal diabetes
- Examine parent for subtle defects
- Holt-Oram shows anticipation (increasing severity of defects in successive generations)
- Consider cordon formation if family history of TAR
- Thrombocytopenia, aplastic anemia
- Immunologic abnormality must be proven for specific diagnosis

- Consider cesarean section
- Risk of dystocia with flexion deformities at elbow
- Some authors suggest placental transfusion prior to induction of labor if live placental count
- TAR, Fanconi anemia
- Detailed clinical evaluation of liveborn infant and family
  - Require referral to specialist centers for reconstructive surgery
  - Classification system developed to allow tracking of occurrence
  - Follow-up of treatment

**DIAGNOSTIC CHECKLIST**

**Image Interpretation Pearls**
- Synizesis identification important in TAR
- Prognosis and specific clinical complications vary for each condition
- Look careful for addition or hypoplasia of thumb
- May lead to specific diagnosis

**SELECTED REFERENCES**

RADIAL RAY MALFORMATION

**IMAGE GALLERY**

**Typical**

(Left) Ultrasound in a fetus with radial ray malformation shows an absent (curved arrow) and a single femur bone (arrow). Second toe bone (open arrow) is forefoot skin.

(Right) Clinical photograph of the left upper extremity in the same case shows fusion between the arm and forearm. Only one digit (arrow) is present on the very hypoplastic hand.

**Typical**

(Left) Ultrasound in a fetus with Camelia de Lange syndrome shows an absent (curved arrow) and a small remnant of the radius (open arrow). The hand has a small fused, “butterfly” radius (open arrow).

(Right) Radiograph of a child shows the “paddle finger” or “floating thumb” (white arrow). Appearance seen in some forms of radial ray malformation. There is a single forearm bone and the radial carpal bones are missing (black arrows).

(Right) Clinical photograph of a woman with multiple anomalies including congenital diaphragmatic hernia and a severe cleft palate shows a malpositioned thumb (arrow) and part of an associated RMS.
**POLYDACTYLY**

Clinical photograph shows bilateral postaxial polydactyly in a sibling with trisomy 13. Multiple other anomalies, including holoprosencephaly, were present.

**UltraSonogram of the foot of another case of trisomy 13.** The extra digit (arrow) is on the lateral side of the foot (postaxial). A supernumerary postaxial digit is the most common type of polydactyly.

**TERMINOLOGY**
- One or more extra digits or parts of digits
  - Most common varieties are postaxial (ulnar, fibular) or preaxial (radial, tibial).

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue
  - Need to confirm in both axial and coronal views
  - Oblique views may give erroneous appearance of polydactyly
- Location
  - Postaxial
    - Ulnar or fibular side
    - Most common
  - Preaxial
    - Radial or tibial side
  - Central
  - Extra digit usually between long and ring finger
  - Bilateral in approximately 50%
  - Hand more often, bilateral than foot
  - More often on left when unilateral
  - Morphology
    - Variable

**Ultrasoundographic Findings**
- Extra digit may be small or angulated
- May be fleshy nubbin without bone
- Difficult to see in uterus
- Often missed
- Postaxial
  - Extra digit in same plane as normal digits
  - May attach directly to normal digit (bifid digit)
- Preaxial
  - Extra digit proximally located
  - Synergy may also be present

**Imaging Recommendations**
- Best imaging tool: 3D ultrasound with surface-mode reconstruction valuable tool for evaluation of hands and feet
- Count and recount
  - Easy to both under and over diagnose
  - Make sure hands (or feet) are not together
  - Erroneous appearance of polydactyly

**DDx: Syndromal Polydactyly**

- Meckel-Gruber, Enceph
- Short Rib-Polydactyly
- Trisomy 13, Holopros, Median
- Rubinstein-Taybi

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**Image Descriptions**

- Clinical photograph shows bilateral postaxial polydactyly in a sibling with trisomy 13. Multiple other anomalies, including holoprosencephaly, were present.
- UltraSonogram of the foot of another case of trisomy 13. The extra digit (arrow) is on the lateral side of the foot (postaxial). A supernumerary postaxial digit is the most common type of polydactyly.

**General Features**
- Best diagnostic clue: Need to confirm in both axial and coronal views. Oblique views may give erroneous appearance of polydactyly.
- Location:
  - Postaxial: Ulnar or fibular side, most common.
  - Preaxial: Radial or tibial side.
  - Central: Extra digit usually between long and ring finger.
  - Bilateral in approximately 50%.
  - Hand more often, bilateral than foot.
  - Morphology: Variable.

**Ultrasoundographic Findings**
- Extra digit may be small or angulated.
- May be fleshy nubbin without bone.
- Difficult to see in uterus.
- Often missed.
- Postaxial: Extra digit in same plane as normal digits.
  - May attach directly to normal digit (bifid digit).
- Preaxial: Extra digit proximally located.
  - Synergy may also be present.

**Imaging Recommendations**
- Best imaging tool: 3D ultrasound with surface-mode reconstruction valuable tool for evaluation of hands and feet.
- Count and recount.
  - Easy to both under and over diagnose.
  - Make sure hands (or feet) are not together.
  - Erroneous appearance of polydactyly.

**DDx: Syndromal Polydactyly**
- Meckel-Gruber, Enceph.
- Short Rib-Polydactyly.
- Trisomy 13, Holopros, Median.
- Rubinstein-Taybi.
# POLYDACTYLY

## Terminology
- One or more extra digits or parts of digits
- Most common varieties are postaxial (ulnar, fibular) or preaxial (radial, tibial)

## Imaging Findings
- Extra digit may be small or angulated
- May be flexed or extended without bone
- Best imaging tool: 3D ultrasound with surface-mode reconstruction valuable tool for evaluation of hands and feet

## Top Differential Diagnoses
- Trisomy 13
- Meckel-Gruber syndrome
- Short rib-polydactyly syndrome
- Ellis-van Creveld (chondroectodermal dysplasia)

### DIFFERENTIAL DIAGNOSIS

**Trisomy 13**
- Holoprosencephaly
- Facial anomalies
  - Progiosis
  - Cyclopia
- Cardiac defects
- Intrauterine growth restriction (IUGR)
- Cystic renal disease

**Meckel-Gruber syndrome**
- Exencephaly/encephalocele
- Renal cystic dysplasia
- Polydactyly
- Autosomal recessive

**Short rib-polydactyly syndrome**
- Narrow chest
- Micronesthesia
- Polydactyly
- Cardiac defects
- Genitourinary anomalies
- Autosomal recessive

**Ellis-van Creveld (chondroectodermal dysplasia)**
- Disorder of endochondral ossification
- Small chest
- Polydactyly
- Cardiac defects
- High incidence in Ashkenazi population
- Autosomal dominant

**Smith-Lemli-Opitz syndrome**
- Inborn error of cholesterol metabolism
- Microcephaly

### Key Facts
- Smith-Lemli-Opitz syndrome
- Carpenter syndrome

### Pathology
- Triphalangeal ("fingertip") thumb: considered part of preaxial spectrum
- Syndactyly often associated
- Isolated polydactyly is generally autosomal dominant with variable penetrance
- Maternal diabetes risk factor for preaxial polydactyly
- Isolated postaxial polydactyly: 10x more common in African-Americans
- More common in males
- Preaxial polydactyly and triphalangeal thumb more likely to be part of syndrome

**Carpenter syndrome**
- Craniosynostosis of multiple sutures
- Preaxial polydactyly
- Syndactyly
- Cardiac defects
- Autosomal recessive

**Joubert syndrome**
- Abnormal cerebellar vermis
- "Molar tooth" sign of cerebellar peduncles
- Autosomal recessive

**Jeune syndrome (asphyxiating thoracic dysplasia)**
- Narrow chest
- Long/bone shortening
- Autosomal recessive

**Majewski syndrome**
- Narrow chest
- Preaxial and postaxial polydactyly
- Cleft lip/palate
- Autosomal recessive

**Mohr syndrome (oral-facial-digital syndrome)**
- Multiple facial anomalies
  - Medial clefts
  - Malformed nose
- Brain malformations
- Dandy-Walker continuum
- Agenesis of the corpus callosum
- Autosomal recessive

**Hypochondroplasia**
- Milder form of achondroplasia
- Autosomal dominant
Bardet-Biedel syndrome
- Renal dysplasia
- Polydactyly
- Mental retardation
- Obesity, short stature
- Autosomal recessive

Hydrocephalus
- Hydrocephalus
- Cleft lip/palate
- Polyhydramnios
- Polydactyly
- Autosomal recessive

PATHOLOGY

General Features
- General path comments
  - Triphalangeal (“fingers-like”) thumb considered part of proximal spectrum
  - May be seen with other findings in radial ray malformation
  - Syndactyly is often associated
  - Usually adjacent to duplicated digit
  - More common in males than hands
- Genetics
  - Variable according to syndrome
  - Many are autosomal recessive
  - Isolated polydactyly is generally autosomal dominant with variable penetrance
  - Chromosomal
  - Trisomy 13, 10
- Embryology
  - Upper limb buds appear day 24
  - Lower limb buds day 26
  - Hands and feet begin as paddle-shaped plates
  - Digital rays develop in 5 sectors along anterio/posterior axis
  - Separate fingers and toes in eighth week
  - Maternal diabetes is risk factor for proximal polydactyly
  - Generally affects feet
  - Trisomy 13, 10
- Epidemiology
  - Postnatal
  - Isolated postaxial polydactyly: 10x more common in African-Americans
  - 1:3,000 Caucasian
  - 1:300 African-American
  - More common in males
  - Proximal: less common
  - 1:10,000
  - No racial predilection
  - Associated abnormalities:
  - Preaxial polydactyly and triradial aplasia more likely to be part of syndrome
  - Preaxial polydactyly
  - Carpellary syndrome
  - Infant of diabetic mother
  - Mazeski syndrome
  - Trisomy 10
  - Small cell + polydactyly

- Short rib-polydactyly
- Jeune syndrome
- Ellis-van Creveld
- Mazeski syndrome

Gross Pathologic & Surgical Features
- Variable amounts of development
  - Soft tissue only (skin tag)
  - Variable amounts of phalangeal development and function

CLINICAL ISSUES

Presentation
- Mildly with minor findings
- Incidental finding if isolated
- Other missed personally
- Familial history usually present

Natural History & Prognosis
- Variable according to syndrome
- Isolated excellent
- In some “autosomal” reported
- May become progressively smaller
- May be born with only a small residual bump

Treatment
- Karyotype warranted even if isolated
- Thorough family history
- Genetic counseling regarding syndromes
- Rejection of extra digit varies in complexity
  - Without bone, may be done in infancy
  - With bone, often wait until 1-2 years of age
  - May require joint reconstruction or tendon transfer

DIAGNOSTIC CHECKLIST

Consider
- 3D ultrasound to aid in diagnosis

SELECTED REFERENCES
POLYDACTYLITY

IMAGE GALLERY

Typical

(Top left) Ultrasound shows a small extra digit (curved arrow) attached to the middle of the 5th finger. Rheumatoid arthritis is a possible cause for this anomaly. (Top right) Clinical photograph of the hand shows a very similar configuration with a small extra digit attached to the 5th finger (curved arrow). This is a variant of normal.

(Top middle) Clinical photograph of partial polydactyly shows fusion of left 2-3 (top arrow), a gestation (curved arrow), and two extra (curved arrow) on the ulnar side of the foot.

(Top right) Clinical photographic of partial polydactyly in an infant at 2 months. There is a mild groove (curved arrow) and syndactyly of toes 3-4 (arrows).

(Top left) Ultrasound of the hand of an infant with partial polydactyly. There is a small extra digit (curved arrow) on the radial side of the hand. In addition, there is a small abnormal (curved arrow) to a syndactysis.

(Top right) Clinical photographic of the hand of an infant with partial polydactyly. There is a small extra digit (curved arrow) on the ulnar side of the hand. In addition, there is a small abnormal (curved arrow) to a syndactysis.
SYNDACTYLY

Ultrasonogram shows syndactyly of digits 2-3 (arrow) and absence of digits 4-5 (curved arrow) in a mid-infantile fetus. A shortened radius is present (open arrow) but the ulna is absent.

Clinical photograph of the same infant at delivery shows syndactyly with symphalangism of digits 2-3 (arrow) and absence of digits 4-5 (curved arrow). Radiographs confirmed bilateral radial deficiency.

TERMINOLOGY

Abbreviations and Synonyms
- Syndactyly: Greek for "digits grown together"

Definitions
- Partial or incomplete syndactyly: Affects only proximal segments of digits
- Complete syndactyly: Affects length of digits to level of nails
- Polydactyly/syndactyly: Combination of duplicated and fused digits
- Symphalangism: Symmetry of joints of digits
- Zygodactyly: Shallow, membranous webbing of 2nd-3rd toes, most prominent on the plantar surface
- Acrorony syndactyly: Soft tissue attachment of distal digits with non-attached proximal segments

IMAGING FINDINGS

General Features
- Multiple types of syndactyly exist, characterized by digits involved
- Phenotypic overlap exists
- Classification centers on 5 subtypes
  - Type I: Zygodactyly
  - Most common type

DDx: Syndromal Syndactyly

- Type II: Polydactyly
- Type III: Syndactyly of fingers 3-4 with duplication of 3rd or 4th finger in web
- Type III: Syndactyly of fingers 4-5
- Associated camptodactyly (persistent flexion) of 4th finger to accommodate difference in lengths of fingers
- This type seen in cimolodentodigital syndrome
- Type IV: Complete syndactyly of all fingers
- This type, with cranioiscardial, seen in Apert syndrome
- Type V: Associated with metacarpal and metatarsal synostosis
- Very rare

Imaging Recommendations
- Careful search for other limb, structural anomalies
- Presence/absence/abnormal position of thumbs
- Evidence of craniosynostosis
- Examination of hands and feet of parents, siblings
- Consider karyotype if other structural anomalies or growth restriction are present
SYNDACTYLY

Terminology
- Syndactyly: Greek 'of digits grown together'
- Partial or incomplete syndactyly: Affects only proximal segments of digits
- Complete syndactyly: Affects length of digits to level of nails

Imaging Findings
- Multiple types of syndactyly exist, characterized by digits involved
- Careful search for other limb, structural anomalies
- Examination of hands and feet of parents, siblings

Top Differential Diagnoses
- Non-syndromal syndactyly
- Anzniotic bands
- Tripody

Key Facts
- Apert syndrome
- Carpenter syndrome
- Pfeiffer syndrome

Pathology
- Non-syndromal familial cases are autosomal dominant
- Failure of separation of digital rays
- Occurs prior to 6 weeks of development
- Most common anomaly of the hand
- Bilateral in 50%
- Syndactyly of toes more common than fingers

Diagnostic Checklist
- Elicit 'open hand' view by fetal stimulation
- Syndactyly often missed prenatally due to limitations of ultrasound

DIFFERENTIAL DIAGNOSIS

Non-syndromal syndactyly
- Type I (syndactyly) most common
- 2-3 toe syndactyly
- Positive family history common
- May involve hands, feet, or both
- Unilateral or bilateral
- May be associated with polydactyly (polydactyly syndactyly)
- Anomalous bands
- Distal digits adherent
- Limb, digital amputations
- Constriction rings
- Bizarre body wall, craniofacial clefts
- Strands of amnion often visible in amniotic fluid

Syndromal syndactyly
- Tripody
- Characteristic 3-4 syndactyly of thumbs
- Variable syndactyly of feet
- Severe intrauterine growth restriction (IUGR)
- Multiple (variable) structural anomalies
- Associated with partial molar gestation
- Maternal preeclampsia, often in mid-trimester
- Thetacutis cysts of maternal ovaries
- Due to high human chorionic gonadotropin (hCG) levels
- Lethal, often in utero
- Apert syndrome
- Acrocephaloepidactyly
- "Miterd syndactyly": Partial or complete syndactyly of fingers, toes
- Complete fusion of digits 2-4 most common
- Broad distal thumbs, hallucs in valgus position
- Craniosynostosis with brachycephaly (conical skull shape)
- Mental retardation common
- Autosomal dominant
- Mutations in FGFR2
- Carpenter syndrome
- Brachydactyly, syndactyly of thumbs
- Broad thumbs, occasional duplication

Differential Diagnosis
- Preaxial polydactyly of feet with partial syndactyly
- Craniosynostosis of multiple sutures
- Shallow orbits
- Cardiac defects in 50%
- Omphalocele, umbilical hernia
- Hypoglossation
- Variable intellectual function
- Autosomal recessive
- Pfeiffer syndrome
- Acrocephalopolysyndactyly, Pfeiffer-type
- Craniosynostosis, often severe
- 3 subtypes correlate with prognosis, severity of cranial abnormality
- Broad distal phalanges of thumb, great toe
- Partial syndactyly of fingers 2-3, toes 2-4
- Autosomal dominant or sporadic
- Some due to mutations in JEG1/2
- Greig cephalopolysyndactyly syndrome
- Syndactyly of fingers 1-4, toes 1-3
- Postaxial polydactyly of hands; preaxial polydactyly of feet
- Broad thumbs
- Macrosomia, with high forehead
- Due to haploinsufficiency of GLI3 on 7p11.3
- Allelic to Pallister-Hall syndrome
- Oculodentodigital syndrome
- Syndactyly of fingers 4-5, toes 3-4
- Camptodactyly
- Midphalangeal hypoplasia, aplasia of multiple digits
- Microphthalmia
- Microcornea
- Thin hypoplastic alae nasi
- Enamel hypoplasia
- Fine spine hair
- Normal intellectual function
- Autosomal dominant, variable expressivity
- Extrodyctyly-extodermal dysplasia-syndactyly syndrome
- Abnormalities in midportion of hands and feet, ranging from syndactyly to ectodactyly (absence of put or all of one or more digits)
- Otofacial clefts
- Nail hypoplasia
CLINODACTYLY

TERMINOLOGY

Abbreviations andSynonyms
- Bronchoschelafilia

Definitions
- Medial deviation of distal 5th finger
- Small or absent 5th digit middle phalange (MP)

IMAGING FINDINGS

General Features
- Best diagnostic clue: Tip of fifth finger turns inward on open hand view

Ultrasoundographic Findings
- Tip of 5th finger curves towards 4th finger
- Best seen at 18-20 week exam
- Secondary to MP dysplasia
- Delayed ossification
- Fifth digit MP normally last to ossify
- Smaller 5th digit MP
- Coarse with 4th finger MP
- Absent MP (least common)

Associated with trisomy 21 (T21)
- 60% of T21 have clinodactyly
- T21 detection improved when Clinodactyly is sought

- 18% increased 2nd trimester T21 detection
- Often seen with other T21 markers
- Nuchal fold
- Echogenic intracardiac focus
- Echogenic bowel
- Renal pelvicstasis
- Short humeri/femur
- Sandy gap sign
- If 5th MP < 70% length of 4th MP then 70% chance of T21
- Trisomy 21 hand
- T21 fetuses more likely to keep hand open
- Poor tone
- All 5 digits are short
- Clinodactyly + short digits were worrisome
- Can use monograms for 17-26 weeks
- Sinus crease
- Single transverse palmar crease
- Can be seen with ultrasound
- 45% of T21 vs. 4% normal
- Isolated clinodactyly
- 2-4% incidence in normal fetuses
- Antenatal risk factors: High risk patient
- Advanced maternal age
- Abnormal maternal serum quadruple screening

Imaging Recommendations
- Best imaging tool: Genetic sonogram

DX: Abnormal Digits

Polydactyly (isolated)
Polydactyly (T21)
Polydactyly (T13)
Sindactyly
**Imaging Findings**
- Best diagnostic clue: Tip of fifth finger turns inward on open hand view
- Best seen at 18-20 week exam
- Associated with trisomy 21 (T21)
- 60% of T21 have clinodactyly
- If 5th MP < 70% length of 4th MP then 70% chance of T21
- Clinodactyly + short digits more worrisome
- Protocol advice: Obtain open hand views in 2nd trimester exam

**DIFFERENTIAL DIAGNOSIS**

**Syndactyly**
- Fusion of digits
  - Bony or soft tissue
  - Often with syndromes and aneuploidy
  - Triplody (3rd and 4th digits most common)
  - Apert syndrome
  - Polydactyly (mitten hands)
  - Cardiovascular and other anomalies

**Polydactyly**
- Extra digits
  - Postaxial (extra digit on ulnar side)
  - Proximal (extra digit on radial side)
  - Common syndromes and aneuploidy
  - Trisomy 13 (T13)
  - Meckel Gruber syndrome

**PATHOLOGY**

**General Features**
- Genetics
  - Usually normal
  - Associated with T21
- Etiology
  - Clinodactyly
  - Delayed or absent MP ossification
  - Abnormal MP longitudinal physi
  - Sinusoid course
  - Hands open and close less often than normal
  - Leads to one crease instead of normal two
- Epidemiology
  - 2-4% normal hands
  - 60% of fetuses with T21

**CLINICAL ISSUES**

**Presentation**
- Most common signs/symptoms
  - Incidental finding during genetic sonogram
  - In conjunction with other anomalies/markers

**Key Facts**
- Top Differential Diagnoses
  - Syndactyly
  - Polydactyly
- Pathology
  - 2-4% normal hands

**Diagnostic Checklist**
- Amniocentesis warranted if not isolated or in high-risk patient

**Natural History & Prognosis**
- Excellent prognosis when isolated

**Treatment**
- Rarely needs any treatment
- Physical therapy of MP
- Remove longitudinal physis

**DIAGNOSTIC CHECKLIST**

**Consider**
- Careful search for other markers of T21
- Amniocentesis warranted if not isolated or in high-risk patient

**SELECTED REFERENCES**

**IMAGE GALLERY**

(Left) Coronal ultrasound shows isolated clinodactyly of a normal fetus. The 5th finger (arrow) turns downward toward the 4th finger; the arrow points otherwise normal to length. (Right) Coronal ultrasound focused on the 5th finger shows a single middle phalanx (arrow). A small or missing middle phalanx is implicated as the cause of clinodactyly. Inclusion cases carry an extra chromosome.
ECTRODACTYLY

Terminology

Abbreviations and Synonyms
- Split hand-split foot malformation (SHFM)
- "Lobster claw"

Definitions
- Characterized by deficiency/hypoplasia of digits, deep median cleft and fusion of remaining digits
- Variable syndactyly
- May occur in isolation or as part of a syndrome

Imaging Findings

General Features
- Best diagnostic clue: Cleft appearance of hands and/or feet with missing digits on mid-trimester ultrasound

Imaging Recommendations
- Best imaging tool
  - Endovaginal ultrasound in 1st trimester in high risk pregnancy
  - Should be sent in routine mid-trimester hand/foot views
- Protocol advice
  - Careful evaluation for other hand abnormalities, clefts, other structural anomalies

Differential Diagnosis

Split hand-split foot malformation (SHFM)
- Central ray defect characteristic with deep cleft, syndactyly of remaining digits
- "Lobster claw" type
- Monodactyly type with radial deficiency, absence of cleft
- Aplasia/hypoplasia of the phalanges, metacarpals, metatarsals
- Genetically heterogeneous
- Mutations at 5 different loci

Ectodactyly-ectodermal dysplasia clefting syndrome (EEC)
- Ectodactyly of hands and/or feet
- Ectodermal dysplasia
  - Hypopigmentation, sparse hair, hypodontia, dystrophic nails, lacrimal duct abnormalities
  - Cleft lip +/- palate
  - Gastrointestinal abnormalities
  - Hearing loss

DDx: Distal Extremity Abnormalities

- Ulnar Deficiency
- Aplastic Bands
- URO
- Syndactyly
ECTRODACTYL

Key Facts

Terminology
- Characterized by deficiency/hypoplasia of digits, deep median cleft and fusion of remaining digits
- May occur in isolation or is part of a syndrome

Imaging Findings
- Best diagnostic clue: Cleft appearance of hands and/or feet with missing digits or mid-trimester atrial septal defect

Top Differential Diagnoses
- Split hand-split foot malformation (SHFM)
- Ectrodactyly-ectodermal dysplasia clefting syndrome (EEC)
- Amniotic bands
- Limb reduction defects (LRD)

Pathology
- Genetically heterogeneous
- Epidemiology: 1 in 50,000 births

CLINICAL ISSUES

Natural History & Prognosis
- EEC syndrome with multiple complications involving hearing and visual difficulties; recurrent eye, respiratory and genitourinary infections

Treatment
- No prenatal treatment
- Referral for genetic counseling
- Fetal karyotype should be offered
- Prenatal syndrome diagnosis possible if imaging or mutation detected
- Surgical treatment improves improving functionality of hands, repair of clefts and lacermal duct anomalies

SELECTED REFERENCES

IMAGE GALLERY

(Left) Clinical photograph shows split-hand malformation in a child. Note absence of central digits, deep median cleft. (Source: Courtesy M. Rampal, MD). (Right) Ultrasound shows a split-hand malformation (arrow) in a mid-trimester fetus. (Top) A digit is seen.
**TERMINOLOGY**

**Abbreviations and Synonyms**
- Multiple congenital contractures
- Fetal hypokinesia/akinesia deformation sequence (FHADS)
- Arthrogryposis multiplex congenita (AMC)
- Pena Shokeir phenotype

**Definitions**
- Arthrogryposis refers to a symptom complex caused by multiple different etiologies
  - Abnormalities related to lack of fetal movement in utero
  - Multiple congenital joint contractures/ankyloses involving two or more body areas
  - Pena Shokeir phenotype
    - Heterogeneous group of disorders with micrognathia, multiple contractures, camptodactyly (persistent finger flexion), polyhydramnios
    - Many are autosomal recessive
    - Lethal due to pulmonary hypoplasia
  - Dermal arthrogryposis
    - Subsets of non-progressive contractures without associated primary neurologic or muscle disease

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue
  - Lack of extremity motion
  - Persistent unusual or abnormal posturing of limbs

**Ultrasoundographic Findings**
- Lack of extremity motion
  - May be seen as early as 12 trimester
  - Often progressive over the course of gestation
  - In severe conditions only movement may be a truncal "wriggling" motion
  - Progressive osteopenia in late gestation
- Unusual or persistent abnormal posturing of limbs
  - Persistent "paddle" position of lower limbs with hyperextended knees
  - Cross-legged "tailor's position" of lower limbs, especially in a breech fetus
  - Extended elbows with internally rotated, flexed wrists ("water's tip")
  - Clubfeet may be very severe
  - Clefted hands never open
  - Lack of facial movement
    - Open mouth posture
    - Reckless chin
  - Polyhydramnios: Decreased fetal swallowing
  - May be severe in late gestation

**DDx: Extremity Contractures**
- Trisomy 18: Hand
- Amnion: Arm
- Clubfoot
- Caudal Regression
Differential Diagnosis

Trisomy 18
- Multiple structural anomalies, including cardiac
- IUGR

Distal arthrogryposis
- Most common cause of multiple congenital contractures
- Normal growth parameters
- Distal arthrogryposis type 1A (DA1A)
  - Overlapped fingers with abnormal digital flexion creases
  - Talipes equinovarus and vertical talus
  - Freeman-Sheldon syndrome (ESS)
  - Dennisary and type 2A (DA2A)
  - "Whistling" face
  - Moulds may be only few mm in diameter
  - Ulnar deviation of fingers with campyloactyly
  - Hypoplastic thumbs

Severity
- Severe contractures with webbing across joints
- Cystic hygroma
- Premature or neonatal death

Spinal muscular atrophy (SMA)
- 2nd most common recessive disorder in Caucasians
- With carrier frequency of 1/50
- Heterogeneous group of (often) lethal neuromuscular disorders
- Loss/destruction of anterior horn cells
- > 95% due to homozygous deletions of exons 7 & 8 in surrrover motor neuron (SMN1) gene

Acetylcholine receptor (ACHr) antibodies
- Myasthenia gravis
  - Acetylcholine receptor (ACHr) antibodies in ~ 85% of patients with myasthenia gravis
ARTHROGRYPOSIS, AKINESIA SEQUENCE

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - Lack of fetal movement and abnormal extremity position on 1st or 2nd trimester ultrasound
  - Polyhydramnios

Natural History & Prognosis
- Depends on:
  - Number and severity of contractures
  - Associated anomalies/constitutional disorders
  - Ventilator dependence at birth or poor prognosis

Treatment
- Genetic counseling: Offer karyotype
  - Deliver at tertiary center
  - Risk of respiratory failure
  - Expertise in genetics, neuropathology
  - Mode of delivery
  - Vaginal delivery may be compromised by fixed extremity position
  - Fracture risk due to osteopenia
  - Complete autopsy in cases of fetal or neonatal death
  - Evaluation of brain, spinal cord, muscle, peripheral nerves

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls
- Progressive generalized lack of fetal movement and hydrdorpos predicts high risk of lethality

SELECTED REFERENCES

**ARThROGRYPOSIS, AKINESIA SEQUENCE**

**IMAGE GALLERY**

**Typical**

![Ultrasound shows a hyperextended knee (arrow) and flexed ankle (curved arrow) indicative of arthrogryposis. Mild polyhydramnios is also present.](image)

**Typical**

![Sagittal ultrasound shows micromelia (arrow). The weist is broad and hands are held in a clenched position (curved arrow).](image)

**Typical**

![Coronal ultrasound shows a persistently open mouth (arrow) and rectified hips (curved arrow) in a 3rd trimester fetus with hydrops and severe arthrogryposis.](image)
**MULTIPLE PTERYGIUM SYNDROME**

**TERMINOLOGY**

**Abbreviations and Synonyms**
- Escobar syndrome
- Multiple pterygium syndrome
- Lethal multiple pterygium syndrome

**Definitions**
- Heterogeneous group of syndromes characterized by multiple limb contractures with soft tissue webbing across joints
- Lethal type also with associated cystic hygroma, hydrops and pulmonary hypoplasia

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue
  - Fixed joint contractures, abnormal posture of fetus on 1st or 2nd trimester scan
  - More difficult to see in 3rd trimester because of crowding
- Association of cystic hygroma +/- hydrops and joint contractures in a fetus at risk is confirmatory
- Pterygia may not be seen on prenatal imaging

**Imaging Recommendations**
- Protocol advice: Consider 3D ultrasound to evaluate joint spaces for pterygia

**DIFFERENTIAL DIAGNOSIS**

**Multiple pterygium syndrome (Escobar syndrome)**
- Significantly small stature
- Multiple pterygia of neck, axillae, elbows, knees
- Micrognathia
- Digital hypoplasia, camptodactyly, syndactyly
- Scoliosis

**Multiple pterygium syndrome (lethal type)**
- Premature growth restriction
- Hexad contractures of limbs
- Multiple extensive pterygia
- Cystic hygroma
- Hydrops
- Hypoplastic lungs

**Popliteal pterygium syndrome**
- Contractures with soft tissue webbing of popliteal fossae
- Cleft lip and palate
- Syndactyly

**DDx: Soft Tissue Webs**

- Pterygium Coll
- Anthrogryposis
- Popliteal Pterygium
MULTIPLE PTERYGIUM SYNDROME

Terminology
- Heterogeneous group of syndromes characterized by multiple limb contractures with soft tissue webbing across joints
- Lethal type also with associated cystic hygroma, hydrrops and pulmonary hypoplasia

Imaging Findings
- Fixed joint contractures, abnormal posture of fetus on 1st or 2nd trimester scan

Key Facts
- Pterygia may not be seen on prenatal imaging

Top Differential Diagnoses
- Multiple pterygium syndrome (Escobar syndrome)
- Multiple pterygium syndrome (lethal type)
- Popliteal pterygium syndrome

Pathology
- Lethal multiple pterygium may be phenotype resulting from early onset severe fetal akinesia

Treatment
- No prenatal treatment
- Referral for genetic counseling
- Multiple surgeries often required
- Mixed results with resection of pterygia, which often grow back
- Lengthening of Achilles tendon may improve ability to ambulate
- Removal of ophthalmic pterygia may save vision

SELECTED REFERENCES

PATHOLOGY

General Features
- Genetics
  - Escobar syndrome and lethal multiple pterygium: Autosomal recessive
  - Rare reports of X-linked recessive cases of lethal multiple pterygium syndrome
  - Popliteal pterygium syndrome: Autosomal dominant
- Embryology
  - Unknown pathogenesis
  - Lethal multiple pterygium may be genotype
- Cross Pathologic & Surgical Features
  - Variable histopathologic features including evidence of myopathy, neuromuscular disease and rarely storage disease

CLINICAL ISSUES

Natural History & Prognosis
- Multiple pterygium (lethal type) uniformly lethal in perinatal period due to pulmonary hypoplasia
- Most are stillborn
- Escobar syndrome
  - Progressive (severe) scoliosis is common and may result in restrictive lung disease
- Pterygia involving the oral cavity may obstruct airway and impair nutrition

IMAGE GALLERY

(Left) Clinical photograph shows multiple eyelid pterygia (arrows) in a mid-trimester fetus. Webbing of the jaw and anterior chest (open arrow) is also seen. (Courtesy of J. Carmack, MD). (Right) Clinical photograph shows a severely growth-restricted fetus with multiple pterygia (open arrows). Note the micrognathia (curved arrow), syndactyly (white arrow) and clubfoot (black arrow).
SECTION 11: Umbilical Cord

Introduction and Overview
Normal Umbilical Cord & Doppler 11-2

Umbilical Cord
Abnormal Cord Doppler 11-6
Single Umbilical Artery 11-10
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Persistent Right Umbilical Vein 11-22
Vasa Previa 11-24
Nuchal Cord 11-26
NORMA1 UMBILICAL CORD & DOPPLER

Key Facts

- Ductus venous has triphasic waveform reflecting cardiac cycle with continuous forward flow
- Technique
  - Best to sample in free-floating loops of cord
  - Take multiple measurements and avoid sampling during fetal breathing
  - In multiple gestations sample at abdominal cord insertion site to allow for reliable serial measurements

Doppler Assessment

- Umbilical artery should have low resistance flow
- Middle cerebral artery should have high resistance flow
- Reversal of this pattern = 'head sparing effect' seen with hypoxia
- Umbilical vein should have continuous non-pulsatile flow

- Check carefully for this with multiple/occultant placenta
- Endovaginal scan with color Doppler to identify vessels
- Pulsed Doppler shows fetal rate in arteries; cannot differentiate maternal from fetal veins
  - Two vessel cord
    - Even if two UA around bladder may be single UA in free floating cord
  - Carries same risks as when one seen at bladder
- Doppler
  - Fetal breathing
  - Highly variable PSV
  - UV pulsation linked to respiration not cardiac cycle
  - Resistance is highest close to abdominal wall/lowest at placental insertion site
  - Do not Doppler normal fetuses
  - All outcome data based on UA velocimetry is in high-risk pregnancy
  - Cannot be applied to general population
- Arrhythmia
- Bradycardia = prolonged cycle = diastolic flow decreased over time = EDV low = SD ratio spuriously high
- Tachycardia = shortened cycle = inadequate time for diastolic run off to occur = EDV high = SD ratio spuriously low
- Absent end-diastolic flow (AEDF)
- Pitfall: Tendency to measure 'something', if flow reaches the baseline before systolic upstroke then diastolic flow is absent
- AEDF is normal in early pregnancy before placental circulation fully developed
- AEDF/reversed end diastolic flow (REDIF) may occur intermittently in multiples due to cord compression; does not have same prognostic implications as in singletons

Normal Measurements

- SD ratio
  - < 3 after 30 weeks
  - < 2 at term
  - Cord length: Average 50-60 cm (range 30-90 cm)
  - Cord circumference: Average 1-2 cm

Pathologic Issues

General Pathologic Considerations

- Placental insufficiency major cause of abnormal Doppler
  - Placental vascular resistance = forward flow in UA = diastolic flow
  - SD ratio, PI and PI all increase
  - Eventually diastolic flow reaches zero = AEDF
  - Further increase in placental vascular resistance causes flow reversal in diastole = REDIF
  - Right ventricle works harder to overcome this increased resistance
  - Eventual decompenstion = tricuspid regurgitation
  - Reversal of flow in inferior vena cava/dedus venous (DV) = pulsatile flow in UV
  - Cord knot
  - True
  - Fetus swims through loop of cord: May cause restriction of flow/thrombosis
  - Major cause of morbidity/mortality in monoamniotic twins
  - False
  - Vessels are longer than the colon length so may "kink" as they spiral
  - No clinical significance
  - Nuchal cord: Only clinically significant if it impairs cerebral blood flow
  - Reversed direction of flow in UV seen in twin reverse arterial perfusion
  - Anomalours twin perfused by deoxygenated blood from co-twin
  - No placental perfusion

Embryology

Embryologic Events

- Day 14
NORMAL UMBILICAL CORD & DOPPLER

- Cord coiling
  - Well established by 9 weeks, thought to strengthen cord
- Bowel herniation
  - Bowel grows rapidly; volume greater than embryo therefore herniates into base of cord
  - Bowel proteins in peritoneal cavity by 11.2 weeks

Clinical Implications

Clinical Importance
- UV is the single conduit for oxygenated blood to return from placenta to fetus
- Umbilical vein thrombosis = hydrops/intrauterine fetal demise
- SUA associated with intrauterine growth restriction (IUGR) even if isolated
- SUA + anomalies = increased risk of aneuploidy
- Doppler study vital in management of IUGR
- Doppler used in grading twin transfusion syndrome
- Abnormal Doppler may impact timing of delivery in monoamniotic twins
- Perinatal mortality
  - AEDF 9%
  - REDF 30%

Related References
**NORMAL UMBILICAL CORD & DOPPLER**

**IMAGE GALLERY**

*Left* Sagittal color Doppler ultrasound shows the normal course of the umbilical vein (arrow) through the ductus venous (open arrow) into the heart. The descending aorta (curved arrow) is also seen in this view. *(Right)* Axial-oblique color Doppler ultrasound shows the two umbilical arteries (arrows) flanking the bladder and crossing anteriorly and cephalad to enter the umbilical cord (open arrow).

*Left* Pulsed Doppler ultrasound shows continuous forward umbilical arterial flow in diastole (arrows) due to low-resistance placental circulation. Venous flow (open arrow) is constant throughout the cardiac cycle. *(Right)* Pulsed Doppler ultrasound shows a normal tracing from the middle cerebral artery in a third-trimester fetus. Flow is high resistance with almost no antegrade flow in diastole (arrows). This pattern changes to low resistance with hypoxia.

*Left* Pulsed Doppler ultrasound shows a normal ductus venosus (DV) waveform. Flow should always be forward. Two peaks: peak ventricular systole (S) and diastole (D), with decreased flow during atrial systole (arrow). *(Right)* Pulsed Doppler ultrasonics shows dramatic variations (arrows) in UA peak systolic velocity during fetal breathing. Umbilical vein flow (open arrow) is also phase. The tracing was normal after breathing stopped.
ABNORMAL CORD DOPPLER

TERMINOLOGY

Abbreviations and Synonyms
- Absent end-diastolic flow (AEDF)
- Reversed end-diastolic flow (REDF)
- Peak-systolic velocity (PSV)
- End-diastolic velocity (EDV)

Definitions
- Abnormalities of velocity ± direction of flow in
  - Umbilical artery (UA)
  - Umbilical vein (UV)
  - Ductus venous (DV)
  - Middle cerebral artery (MCA)
- Systolic-diastolic (SD) ratio
- PSV:EDV
- Use of ratios overcomes angle dependence of velocity measurements

IMAGING FINDINGS

General Features
- Best diagnostic clue: Diminished diastolic flow in UA

Ultrasonographic Findings
- Grayscale Ultrasound

DOs: Abnormal UA Doppler

- Fetal Breathing
- All Early Pregnancy
- Cord Knot
- Thrombosed UA

- Intrauterine growth restriction (IUGR) may be present
  - Abdominal circumference lags behind other biometric parameters
  - Poor growth/weight gain
  - Oligohydramnios
  - May see features of cardiac decompensation
  - Placental resistance
  - Cardiomegaly
  - Tricuspid regurgitation

- Pulsed Doppler
  - SD ratio should be < 3 after 30 weeks
  - < 2 at term
  - High resistance flow is normal in early gestation
  - Placental vascular bed not fully formed
  - AEDF is normal ≤ 16 weeks gestation

Imaging Recommendations

- Evaluate cord flow in consistent location
  - Fetal insertion site: Highest resistance
  - Placental insertion site: Lowest resistance
  - Best to measure in free floating loop

- In multifetal gestations
  - Verify chorionicity and amnionity
  - Monoamniotic twins at risk for twin-twin transfusion
  - Monoamniotic twins at risk for cord entanglement
ABNORMAL CORD DOPPLER

Key Facts
- KDF associated with fetal demise within 2-7 days

Differential Diagnosis
- UA Doppler is the "tip of the iceberg" with respect to fetal hemodynamic state
- Addition of venous Doppler = more information on fetal response to adverse conditions
- Management decisions not based on Doppler alone
- Do not do Doppler in fetuses with normal growth
- All management data based on high-risk pregnancies
- Beware apparent improvement in "head-sparing" pattern
- Hypoxia = cerebral edema = ↑ intracranial pressure = resistance in MCA
- Real improvement occurs only when changes are in both UA and MCA circulations
- With further decomposition retrograde flow occurs during atrial contraction
- UV
- Normal flow = Continuous, forward, non-pulsatile
- Regular pulse at end-diastole reflects elevated right heart pressure
- ↑ Right heart pressure transmitted IVC = UV = IVC
- pulsations not timed to end-diastole likely relate to fetal breathing activity
- Tracings will normalize when breathing stops
- Pulsatile UV flow signifies advanced cardiac decomposition

Differential Diagnosis
- Real breathing
  - Variable peak systolic velocity
  - Umbilical vein plasticity not linked to end-diastole
  - Tracings return to normal when breathing stops

Cord compression
- Intermittent abnormal tracings in multiple gestations
- Cord compressed by crowding of fetal parts or maternal position
- Tracings return to normal with change in position
- No other features of concern for fetal compromise

PATHOLOGY
- General Features
  - Etiology
    - Normal placenta
    - 1st trimester: Mesenchymal villi = 1st, 2nd, 3rd stem villi
    - 2nd trimester: Branching angiogenesis = 10-15 generations intermediate villi
    - 3rd trimester: Non-branching angiogenesis = many terminal villi sprout from intermediate villi
    - Failed/abnormal branching = small muscular arteries
**ABNORMAL CORD DOPPLER**

- Increased placental resistance
- Maternal connective tissue disease
- Immune complex deposition
- Vasculitis
- Placental infection/thrombosis
- Epidemiology
  - Abnormal Doppler may occur with IUGR
  - By definition 10% of all pregnancies meet criteria for IUGR.

**CLINICAL ISSUES**

**Presentation**
- Most common signs/symptoms
  - Placental insufficiency presents in second trimester: IUGR
  - Oligohydramnios
- Other signs/symptoms
  - Twin-twin transfusion syndrome
  - Doppler evaluation part of grading criteria
    - Grade at diagnosis does not correlate with prognosis
    - Change in grade during gestation does have prognostic implications
  - Serial evaluation important in timing and choice of fetal intervention
    - Monoamniotic twins
    - Cord entanglement: major source of morbidity and mortality
    - Cord Doppler may be used to determine need for delivery

**Natural History & Prognosis**
- Depends on gestational age at which changes are observed
- Treatment
  - > 30 weeks
    - Abnormal Doppler contributes to decision to deliver
  - In second trimester
    - Weight risk of hostile intrauterine environment vs. risks of extreme prematurity
  - AEDF
  - Bed rest, aggressive management of maternal disease
    - 30% improvement within 48 hrs
  - Improvement supports continuation of pregnancy in second trimester
  - Perinatal mortality: AEDF 9%
  - REDF
    - Quantified by ratio: highest amplitude forward flow (A)/maximum reverse flow (B)
    - A/B ratio > 4.3 without venous pulsation in free loop may support expectant management in second trimester
  - Perinatal mortality: REDF 36%
  - REDF associated with fetal demise within 1-7 days
  - Addition of venous Doppler = more information on fetal response vs adverse conditions
  - Management decisions not based on Doppler alone:
    - Gestational age
    - Interval growth and amniotic fluid volume
    - Non-stress testing and biophysical profile
    - Maternal factors

**Image Interpretation Pearls**
- Determine whether Doppler findings are normal growth
- All management data based on high-risk pregnancies
- Cannot be applied to general population
- Beware appearance improvement in "pseudocoiling" pattern
  - Hypoxia = cerebellar edema = 1 intracranial pressure = 1 resistance in MCA
  - Real improvement occurs only when changes are in both UA and MCA circulations

**SELECTED REFERENCES**


**DIAGNOSTIC CHECKLIST**

- UA Doppler is the "tip of the iceberg" with respect to fetal hemodynamic state
**ABNORMAL CORD DOPPLER**

**IMAGE GALLERY**

**Typical**

(Left) Pulsed Doppler ultrasound shows reversed end-diastolic flow (arrows) in the umbilical artery (UA). This implies that placental resistance is so high that blood flows away from the placenta back into the umbilical arteries during diastole. (Right) Pulsed Doppler ultrasound of the middle cerebral artery (MCA) shows increased diastolic flow (arrows) indicating a decrease in resistance, related to a brain anoxia (i.e., "brain-stemping.")

**Typical**

(Left) Transabdominal ultrasound shows a dilated IVC in a third-trimester fetus with severe placental insufficiency. The IVC is larger in caliber than the aorta (arrow). Also note severe oligohydramnios.

(Right) Pulsed Doppler ultrasound shows a high (arrows) and associated UV pulsation (arrowhead), indicating cardiac decompensation.

**Typical**

(Left) Pulsed Doppler ultrasound shows reversal of flow in the ductus venosus with loss below the baseline (arrows), indicating a reduced systolic pressure. (Right) Apical color Doppler ultrasound shows the UA in the polio. The bladder should be seen between the UA (arrows). As placental resistance increases, the fetus allows blood to the brain, decreasing renal perfusion. Urine production decreases and oligohydramnios occurs.
SINGLE UMBILICAL ARTERY

Long and close-up photograph of the umbilical cord shows a SUA (arrow). The UA is almost the same size as the UV in a normal 3 vessel cord, with two UAs, each UA is much smaller than the UV.

TERMINOLOGY

Abbreviations and Synonyms
- Single umbilical artery (SUA)
- Two vessel cord
- Absent umbilical artery

Definitions
- Absence of right or left umbilical artery (UA)
  - Cord with 1 UA and 1 umbilical vein (UV)
  - Normal cord has 2 UA and 1 UV

ULTRASONOGRAPHIC FINDINGS

General Features:
- Best diagnostic clue
  - Free loop of cord with 2 vessels
  - Seen best on cross section
  - Color Doppler of fetal pelvis
  - Transverse view of bladder
  - Only 1 UA adjacent to fetal bladder
- Location
  - 70% absent left UA
  - 30% absent right UA
- Size: SUA is larger than 3 vessel cord UA
- Morphology: SUA, cord less coiled

DDx: Abnormal Umbilical Vessels

- UA Thrombus
- UA Thrombus
- UV Thrombus
- Excessive Wharton jelly

Ultrasonographic Findings
- Normal umbilical cord
  - Free loop cross section view
  - 2 UA + 1 UV
  - "Mickey Mouse" appearance on cross section
  - UA diameter is < 50% UV diameter
  - Longitudinal view
  - Arteries coil around vein
  - Cord is fully coiled by end of 1st trimester
  - < 40 coils/cord
  - Color Doppler transverse fetal pelvis view
  - One UA on each side of bladder
  - UAs insert into iliac arteries
- SUA diagnosis
  - Free loop shows SUA + UV
  - Within fetal pelvis
  - SUA traverses around bladder
  - Inserts into right or left iliac artery
  - Best way to determine which UA missing
  - 8% false positive diagnosis
  - 3 vessel cord at delivery
- SUA is larger than normal UA
  - SUA diameter is > 50% diameters of UV
  - All blood volume in SUA
  - Normal is 1/3 blood volume in each UA
  - SUA cord less coiled than normal
  - Long axis view of cord
SINGLE UMBILICAL ARTERY

**Terminology**
- Two vessel cord

**Imaging Findings**
- Free loop of cord with 2 vessels
  - Seen best on cross section
  - Only 1 UA adjacent to fetal bladder
  - 70% absent or off UA
  - SUA is larger than normal UA
  - 15% develop IUGR
  - Systolic/diastolic ratios suggest F IUGR risk
  - Not associated with trisomy 21
  - Hypoplastic UA within spectrum of SUA
  - Fetal imaging tool: Color Doppler transverse pelvis image shows SUA around bladder
  - Look for additional fetal anomalies when SUA seen

**Key Facts**
- UA and UV parallel
- Right vs. left SUA
  - Same outcome
  - Same incidence of associated anomalies
  - UA and intraovarian growth restriction (IUGR)
    - 15% develop IUGR
    - May be related to poor coiling
    - SUA cord Doppler
      - Same values as for normal cord
    - 1 Systolic/diastolic ratios suggest F IUGR risk
  - Isolated SUA
    - 50% aneuploidy rate
    - Trisomy 18 (T18)
    - Cardiac defects
    - Extremity anomalies
    - Choledochal cysts
    - Early severe IUGR
    - Trisomy 13 (T13)
    - Holoprosencephaly
    - Midline cleft-glo pallate
    - Cardiac defects
    - Polydactyly
  - Unilateral renal agenesis
  - Difficult diagnosis
  - Color Doppler shows single renal artery
  - Sacrococcymia
  - Fused lower extremities
  - Bilateral renal agenesis
  - Always with SUA
  - SUA inserts directly into aorta
  - Velamentous cord origin
  - Cord originates from nuchal vein
  - Higher incidence of SUA
  - Twin reversed arterial perfusion sequence
  - Arterial placental anastomosis between twins
  - Acardiac twin receives blood from pump twin
  - 2/3 of acardiac twins have SUA
  - SUA and amniocentesis
    - Indicated SUA
    - Amniocentesis not indicated
  - Not associated with trisomy 21
  - Nonisolated SUA

**Top Differential Diagnoses**
- Fused umbilical arteries
- Umbilical vessel thrombosis
- Excessive Wharton jelly

**Pathology**
- Usually normal with isolated SUA
- 50% aneuploidy rate if SUA + other anomalies
- Trisomy 18
- Trisomy 13
- 1-2% second and third trimester fetuses

**Diagnostic Checklist**
- Follow-up exam for IUGR
- Amniocentesis if not an isolated finding
- Routinely document number of vessels in cord
- Look for hypoplastic UA on routine views

- Amniocentesis indicated
- 50% aneuploidy rate
- Hypoplastic UA within spectrum of SUA
  - Small right or left UA
  - > 50% difference in size between UAs
  - More difficult diagnosis than SUA
  - Doppler abnormalities in small UA
  - Increased resistance
  - Higher systolic/diastolic ratio
  - Can not use same nomograms as normal cord

**Imaging Recommendations**
- Best imaging tool: Color Doppler transverse pelvis image shows SUA around bladder
- Protocol advice
  - Look for additional fetal anomalies when SUA seen
  - Cardiac (consider echocardiogram)
  - Renal
  - Anomalies of T18 and T13
  - Serial ultrasound-exams for growth
  - 15% develop IUGR

**DIFFERENTIAL DIAGNOSIS**

**Fused umbilical arteries**
- Often within 3cm of placenta
- Longer fused segments mimics SUA
- Look for 2 UAs in fetal pelvis
- Not associated with other abnormalities
- Not associated with aneuploidy

**Umbilical vessel thrombosis**
- UV or UA thrombosis
  - Rare
  - Echogenic thrombus in UV or or UA
- Two patent + 1 thrombosed vessel
- Mimics a two vessel cord
- Doppler helps identify vessels
- Maternal thrombophilia association
  - Acquired
  - Antiphospholipid syndrome common
  - Inherited
SINGLE UMBILICAL ARTERY

- Protein C deficiency common
- Complication of interventional procedure
- UV sampling
- High fetal mortality
- Excessive Wharton jelly
- Excessive genitalia sternum
- Thick umbilical cord
- Umbilical vessels displaced from each other
- Associated with T21
  - 1 in 1,288

PATHOLOGY

General Features
- Genetics
  - Usually normal with isolated SUA
  - 50% aneuploidy rate if SUA + other anomalies
  - Trisomy 18
  - Trisomy 13
- Etiology
  - UA atrophy
  - 40% show muscular remnant of missing UA
  - UA agenesis
  - One UA never forms
  - Persistent vitelline artery (VA)
  - Saccularia most common example
  - VA should regress with yolk sac
  - VA connects directly to aorta
  - UAs never form
  - Lower extremity fusion may be from UA agenesis
- Epidemiology
  - 3% first trimester
  - 1-2% second and third trimester fetuses
  - 0.63% newborn infants

- Associated abnormalities
  - IUGR in 15%
  - Anomalies commonly seen with Trisomy 18
  - Anomalies commonly seen with Trisomy 13

Staging, Grading or Classification Criteria
- Type I SUA
  - 1 UA + 1 UV
  - Most common (99%)
- Type II SUA
  - Persistent VA + UV
  - Almost always with saccularia
- Type III SUA
  - IOA (or VA) + UV + persistent right umbilical vein
  - Associated with mesenchymal anomalies
  - Rare
- Type IV SUA
  - 1 UA (or VA) + persistent right umbilical vein
  - Usually die early in pregnancy
  - Extremely rare

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - Routine cord view
  - SUA + other anomalies

- SUA + IUGR

Natural History & Prognosis
- Isolated SUA
  - Excellent prognosis
  - Possible IUGR
  - SUA + anomalies
  - Prognosis related to severity of anomalies
  - Anomalies indicated

Treatment
- Not necessary for isolated SUA

DIAGNOSTIC CHECKLIST

Consider
- Follow-up exam for IUGR
  - Int 3rd trimester
- Can use cord Doppler values
  - Same Doppler parameters as for normal cords
  - Amnioncetesis if not an isolated finding
- Repeat ultrasound at 22-24 weeks
  - 8% false positive rate
  - Better evaluation of fetal anatomy

Image Interpretation Pearls
- Routinely document number of vessels in cord
  - Cross-section view of 2 UA and 1 UV
  - Use color Doppler in fetal pelvis to document number and size of UA
  - Look for hypoplastic UA on routine views
  - Some associations as SUA
  - Hypoplastic UA will have higher resistance flow

SELECTED REFERENCES

SINGLE UMBILICAL ARTERY

IMAGE GALLERY

Typical

(Left) Axial ultrasound shows only two vessels in the umbilical cord. The UA (curved arrow) has a thicker wall than the CV (arrow). The increased diameter of the SGA is most apparent on cross section views.

(Right) Axial color Doppler ultrasound through the fetal pelvis shows a SGA (arrow) adjacent to the fetal bladder (curved arrow). The UA arises into the fetal artery (open arrow). Normally, the bladder is marked by 2 UAs.

Typical

(Left) Sagittal ultrasound of the fetal face shows a two vessel cord (arrow) and a yolk sac (curved arrow). This fetus also had hydrocephaly, polyhydramnios, and other anomalies.

Amniocentesis revealed trisomy 13.

(Right) Axial ultrasound of the cord insertion site shows an omphalomesenteric containing small bowel (curved arrow) and a SGA (arrow). Other anomalies were also seen and amniocentesis results revealed trisomy 18.

Variant

(Left) Axial ultrasound shows a hypoplastic umbilical artery (arrow). Compare the diameter of the normal umbilical artery (curved arrow) with the hypoplastic artery and the other cases of SGA.

(Right) Axial power Doppler ultrasound within the fetal pelvis shows the small UA (arrow) compared to the normal UA (curved arrow). Hypoplastic UAs have higher resistive indices (increased systolic/diastolic ratio) on Doppler interrogation.
UMBILICAL CORD CYST

Terminology
Abbreviations and Synonyms
- Umbilical cord cyst (UC)
- Umbilical cord pseudocyst
- Allantoic cyst
- Urothelial cyst
- Omphalomesenteric duct cyst

Definitions
- Cyst or cysts associated with umbilical cord (UC)

Imaging Findings
General features
- Best diagnostic clue: UC with one or more cysts
- Location
  - Paraxial (60%)
  - Eccentrically located cyst
  - UC vessels not displaced
  - Axial (40%)
  - Cyst centrally located in UC
- UC vessels spared by UC
  - Seen anywhere along length of cord
- 28% at fetal insertion
- 33% at placental origin
- 39% at mid UC

Ultrasoundographic Findings
- UC cysts general features
  - Thin walled cyst or cysts
  - Usually anechoic
  - Rarely with minimal internal echoes
  - Single or multiple
  - Multiple cysts often cluster
  - Duplicit
  - Differentiates UC from vessels
  - Pseudocyst vs. true cysts
  - Look identical on ultrasound
  - Pseudocyst without epithelial wall
  - True cyst with epithelial wall
- First trimester UC
  - 2% prevalence
  - Between 7-14 wks
  - Usually form at 8-9 wks
  - Same time as UC coiling

DDx: Umbilical Cord Cyst

- UA Anencephaly
- UA Anomalous
- Yolk Sac With VP
- Yolk Sac
### Terminology
- Cyst or cysts associated with umbilical cord (UC)
- Associated with physiologic bowel herniation
- Pseudocyst
- Most common UCC
- Fluid accumulation within Wharton jelly
- 75% single UCC
- Associated with increased nuchal translucency
- 7.6x increased risk of poor outcome
- Most often transient finding
- Resolve by 2nd trimester
- Better prognosis if cysts resolve
- 2nd and 3rd trimester UCC
- Most are pseudocysts
- Higher incidence of aneuploidy
- Variable but stable size
- Usually paraxial
- Allantoic cyst
- True cyst
- 2rd to pentagon urachus (bladder connected to UC)
- May grow and compress cord (contains urine)
- Always near fetal insertion
- Omphaloenteric duct cyst
- True cyst
- Rarest cause of UCC
- 1st to 2nd trimester duct remnant
- Abdominal wall anomalies
- Intrabdominal meconium cysts
- Other severe anomalies
- 1 Trisomy 21 (T21) risk in nonisolated cases
- 2nd trimester UCC and aneuploidy
- Multiple tiny cysts in thickened cord
- Abnormal Wharton jelly
- Mucoid degeneration
- Trisomy 18 (T18) and trisomy 13 (T13) association
- May be an isolated finding in first trimester
- Not an isolated finding in second trimester
- Rarely single cyst
- UCC and T21
- No increased risk if isolated finding
- UCC and Doppler

### Key Facts
- Helps differentiate UCC from UC vessels
- Used to rule out venol anomaly/compression

### Top Differential Diagnoses
- Normal yolk sac
- Umbilical cord aneurysm

### Pathology
- Genetics: T18 and T13 association
- 2nd mucoid or cystic degeneration of Wharton jelly
- Embryonic duct remnants

### Clinical Issues
- Excellent prognosis if transient
- Single UCC: better prognosis than multiple UCC

### Diagnostic Checklist
- First trimester: genetic screening when UCC seen
- Second trimester: genetic ultrasound
- Look carefully at abdominal wall and fetal bladder

### Imaging Recommendations
- Best imaging tool
- Transvaginal ultrasound in first trimester
- Best visualization of anomalies
- Routine evaluation of UC
- Document 2 umbilical arteries and 1 umbilical vein
- Document cord insertion at fetal end
- Look for cord origin at placenta
- Scan through free loops of cord
- Protocol advice
- Look carefully for other anomalies
- Multiple UCC with increased risk of anomolies and aneuploidy
- Look at fetal bladder if UCC is near fetal end of umbilical cord
- Allantoic cyst
- May see patent urachus
- Follow-up to see if UCC resolves
- Allantoic cysts can grow

### Differential Diagnosis

<table>
<thead>
<tr>
<th>Normal yolk sac</th>
<th>Umbilical cord aneurysm</th>
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<tr>
<td>Yolk sac is extra-amniotic</td>
<td>Associated with vitelline artery (VA) or artery (UA)</td>
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<tr>
<td>Connected to vitelline artery (VA)</td>
<td>Can look exactly like UCC on gray scale imaging</td>
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<tr>
<td>Umbilical cord aneurysm</td>
<td>Doppler helpful to differentiate from UCC</td>
</tr>
<tr>
<td>Aneurysmal dilatation of umbilical vein (varix) or artery (UA)</td>
<td>1 Risk-thrombosis</td>
</tr>
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</table>

### Imaging Recommendations
- Best imaging tool
- Transvaginal ultrasound in first trimester
- Best visualization of anomalies
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- Document 2 umbilical arteries and 1 umbilical vein
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- Look for cord origin at placenta
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- Look at fetal bladder if UCC is near fetal end of umbilical cord
- Allantoic cyst
- May see patent urachus
- Follow-up to see if UCC resolves
- Allantoic cysts can grow
Resolving UC hematoma
- Rare
- 2nd to cord trauma
- Usually from cordocentesis
- Hemorrhage appearance changes with time
- Echogenic = cysts
UC supernumerary vessels
- More than 3 vessels in UC
- Very rare
- Usually seen with conjoined twins
- Dopper differentiates from UCC

PATHOLOGY
General Features
- Genetics: T18 and T13 association
- Etiology
  - Pseudocyst
  - Form at base of UC coiling and midgut herniation
  - Increased UC hydrostatic pressure
  - Amnionic or cystic degeneration of Wharton jelly
  - Single > multiple
  - True cysts
  - Embryonic duct remnants
  - Allantoic duct
  - Omphalomesenteric duct
  - Vitelline duct
  - Abnormal Wharton jelly
  - Abnormal extracellular matrix
  - Results in multiple pseudocysts
  - Found in T18 and T13
- Epidermalogia
  - 2nd is first trimester
  - Most resolve without sequelae

Microscopic Features
- True cysts are lined by epithelium
- Pseudocysts are not lined by epithelium

CLINICAL ISSUES
Presentation
- Most common signs/symptoms
  - Incidentally noted during first trimester scan
  - Second trimester
  - Isolated most common
  - Associated with other anomalies

Demographics
- Age
  - Advanced maternal age associated with T18 and T13
- 35 yrs at time of delivery

Natural History & Prognosis
- First trimester
  - Excellent prognosis if transient
- Single UCC better prognosis than multiple UCC
- Allantoic cysts
  - May grow if patent urachus
  - Often noted at surgery
  - Normal work up necessary

Unilateral cysts
- Ophthalmomaxillary cysts
  - Prognosis related to associated anomalies
  - Omphalocele
  - Meconium cyst
  - Hernia
  - Spina bifida
  - Cardiac defects

Treatment
- None necessary for isolated UCC
- Growing cyst
  - Early consideration
  - Cyst drainage considered
  - Ultrasound guided drainage

DIAGNOSTIC CHECKLIST
Consider
- First trimester genetic screening when UCC seen
  - Nuchal translucency + maternal serum screen
  - Assess maternal risk for aneuploidy
  - Increased risk for aneuploidy with multiple UCC
  - T18 most common
  - Second trimester genetic ultrasound
  - Markers for T18
  - Markers for T13
  - Look carefully at abdominal wall and fetal bladder
  - Abnormal wall (hernia)
  - Patent urachus from bladder to umbilical cord

Image Interpretation Pearls
- Careful evaluation of umbilical cord in all first trimester cases
- Identify yolk sac separate from suspected UCC
- Color Doppler of umbilical cord when diagnosis suspected

SELECTED REFERENCES
UMBILICAL CORD CYST

IMAGE GALLERY

Typical

(Left) Sagittal ultrasound of a first trimester cord shows an UC (arrow). Isolated UC is often seen at the same time as a physiologic bowel herniation (curved arrow).

(Right) Coronal ultrasound in another first trimester case shows an UC (arrow) near the placental edge. The cord is normally coiled and not thickened. Both of these cysts were predecorticated and resolved without sequelae.

Typical

(Left) Axial ultrasound shows multiple large UCs (arrows) at placental end of UC in a second trimester fetus. Although multiple UCs are often associated with other abnormalities, these UCs were isolated and had good outcome was normal.

(Right) Axial color Doppler ultrasound in another second trimester fetus with multiple UCs (arrows) shows hypervascular anterior UC cysts from UC vessels. The fetus also had a cardiac defect and hydrocephalus.

Variant

(Left) Axial ultrasound shows a thickened cystic umbilical cord (arrow) and an cystoceles containing small bowel (curved arrow) in the second trimester fetus with molar 1/3. (Right) Long axis ultrasound of the umbilical cord in the same fetus shows numerous small cysts (arrows). This appearance is from molar degeneration of abnormal villi.
TERMINOLOGY

Abbreviations and Synonyms
- Umbilical vein aneurysm (UA aneurysm)
- Umbilical artery aneurysm (UA aneurysm)

Definitions
- UV varix: Saccular dilatation of umbilical vein > 9 mm diameter
  - Alternate definition: Varix diameter 50% > intrahepatic portion of umbilical vein
- UA aneurysm: Aneurysmal dilatation of umbilical artery

IMAGING FINDINGS

General Features
- Best diagnostic clue
  - UV varix: Cyst-like space in upper abdomen with venous flow on Doppler
  - UV varix in free floating loops of cord is much harder to see
- UA aneurysm: Saccular dilatation of umbilical artery with arterial flow
- Location
  - UV varix usually intra-abdominal but extraperitoneal
- May also occur in free-floating loops of cord

UA aneurysm usually near placental cord of cord

Ultrasonographic Findings
- UV varix
  - Upper abdominal "cyst"
  - Oval or elongated shape
  - Thin walled
  - Anechoic
  - May occur in association with persistent right umbilical vein
  - May be large
  - Must show continuity of "cyst" with UV and presence of blood flow to make this diagnosis
  - Runs between abdominal cord insertion site and inferior edge of liver
  - Oblique orientation
- UA aneurysm
  - Cord cyst near placental origin
  - Arterial malformation not venous
  - May have anechoic foci to umbilical vein
  - Associated with single umbilical artery
  - Wall may be calcified
  - Associated with multiple anomalies
  - Tri-ney 18
  - Much more rare than UV varix

Imaging Recommendations
- Protocol advice
- Measurement technique of UV varix:

DDx: Cystic Mases Simulating Umbilical Cord Aneurysms

- Cord Cyst
- Choleodochal Cyst
- Omphalocyst
- Gallbladder and UVV
UMBILICAL CORD ANEURYSMS

Terminology
- UV varix: Focal dilatation of umbilical vein, > 9 mm diameter
- Alternate definition: Varix diameter 50% > intramural portion of umbilical vein

Imaging Findings
- UV varix: Cyst-like space in upper abdomen with venous flow on Doppler
- UA aneurysm usually near placental end of cord
- UA aneurysm strongly associated with multiple anomalies and trisomy 18
- Increasing turbulence in varix/aneurysm concerning for impending thrombosis
- Failure of entire varix/aneurysm to fill with color on Doppler concerning for thrombus

Key Facts
- Top Differential Diagnoses
  - Abdominal cysts
  - Umbilical cord cysts

Pathology
- UV varix may be first manifestation of abnormal venous pressure
- Expanding varix in cord may compress umbilical artery

Clinical Issues
- Karyotype if other anomalies
- Close fetal monitoring
- Consider early delivery for UV varix

Diagnostic Checklist
- UV varix in differential of an intra-abdominal cyst

DIFFERENTIAL DIAGNOSIS

Normal fluid-filled structures
- Stomach
- Gallbladder

Abdominal cysts
- Choledochal cyst
  - No flow
  - Right upper quadrant, associated with liver
  - Mesiocole pseudocyst
  - No flow
  - Usually associated with bowel perforation
  - Echogenic bowel
  - Dilated loops of bowel
  - Anites
  - Pichtoreal calcification
  - Ovarian cyst

PATHTOLOGY

General Features
- Genetics
  - Sporadic if isolated
  - If part of multiple anomaly complex
    - Trisomy 18
    - Triploidy
- Etiology
  - Intra-abdominal, extrathoracic UV is the least supported portion
  - Increased venous pressure = focal dilatation in this segment
  - Association with cardiomyopathy and hydrops
  - UV varix may be first manifestation of abnormal venous pressure
  - May signify increased risk of cardiac decompensation
- Epidemiology

Female fetus
- No flow
- Complex appearance if torsion or hemorrhage
- Duplication cyst
- Small bowel duplication cysts
- Layered wall = get signature
- May be associated with polyhydramnios
- Urachal cyst
- Midline
- Between dome of bladder and cord insertion site
- No flow

Umbilical cord cysts
- Allantoic cyst
  - Persistent communication from bladder to cord
  - Cystic dilatation of extra-embryonic allantois
  - Cyst at base of cord (near fetal insertion)
  - Umbilical vessels separated by cyst
  - Cysts and pseudocysts other than allanotic
    - Displace cord vessels rather than separate them (paraxial location)
  - No internal flow
UMBILICAL CORD ANEURYSMS

- True in utero incidence UV varix unknown
  - 3.8% of cord malformations in series of perinatal deaths
  - UV varix thrombosis → stillbirths
  - M:F = 2:1
  - UA aneurysm: Scattered case reports, extremely rare
  - Engine Doppler shows various signal
  - Normal umbilical vein increases in size with advancing gestational age
  - 3 mm at 15 weeks
  - 8 mm at term

Gross Pathologic & Surgical Features
- Expanding varix in cord may compress umbilical artery
- Intratubal growth restriction
- Hypoxia = abnormal non-stress test and biophysical profile
- Entering UA aneurysm = UV compression = fetal compromise
- UV is sole conduit for returning oxygenated blood
- Dense to otherwise structurally normal fetuses attributed to acute circulatory disturbance from thrombosis
- UA aneurysm thrombosis = similar acute circulatory disturbance if associated with single umbilical artery

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - UV varix: Cyst-like lesion in fetal abdomen
    - Flow on color Doppler
    - Poloidal Doppler shows various signal
  - UA aneurysms: Cyst-like lesion in cord
    - Flow on color Doppler
    - Poloidal Doppler shows arterial signal

Natural History & Prognosis
- Variable outcomes reported with intra-abdominal UV varix
  - Isolated UV varix
    - Intratubal fetal demise (IUD) in 1:7 cases despite close surveillance
  - 10 year experience single instigation, all cases with UV varix
    - 65% normal outcome
    - 13% preterm delivery
    - 15% other anomalies
    - Literature review 42 cases
      - 24% IUD
      - 12% chromosomal abnormality
      - 5% hydrops
    - Secondary schistosomatid hemolytic anemia
      - Turbulent flow in varix = red cell destruction
      - Anemia may cause hydrops
    - Thrombosis of UV varix
      - Hydrops
      - IUD
    - Early diagnosis (second trimester) may correlate with worse outcome
    - UV only isolated, UV varix prognosis generally good
    - UV varix of intra-amniotic segment
  - Rare than intra-abdominal
  - May bleed through amniotic sheath
  - Fetal exanguination

Treatment
- Karyotype if other abnormalities
  - 17% incidence aneuploidy for UV varix
  - Close fetal monitoring
  - Ultrasound tends to occur rapidly after abnormal non-stress test
  - Attributed to thrombosis of varix
  - Consider early delivery for UV varix
  - Some authors advise as early as 34 weeks
  - At lung maturity
  - If any signs fetal distress

DIAGNOSTIC CHECKLIST

Consider
- UV varix in differential of an intra-abdominal cyst
  - Must be in continuity with umbilical vein
  - Color Doppler allows rapid diagnosis
- UA aneurysm much rarer
  - High association with anomalies

SELECTED REFERENCES

UMBILICAL CORD ANEURYSMS

**IMAGE GALLERY**

Typical

(Left) Axial ultrasound of the fetal abdomen shows the typical location of an umbilical vein varix (arrows) adjacent to the cord insertion site (curved arrow).

(Right) Ultrasound with correlation gross photograph of umbilical vein thrombosis (arrows). Thrombosis is a potential serious complication of an umbilical vein varix, often with fetal outcome.

Typical

(Left) Axial ultrasound through the fetal abdomen shows a cystic-appearing mass within the abdomen (arrow). (Right) Axial color Doppler obtained through the cystic mass shows flow, confirming its vascular etiology. Note that the entire structure fills an amniotic invagination. This fetus had no adverse consequences.

Typical

(Left) Color Doppler ultrasound at the placental end of the cord shows an arterial waveform (arrow) in one of the UA aneurysms (curved arrow). Multiple fetal aneurysms were also present. (Right) Gross pathology shows the two UA aneurysms (arrows), adjacent to the placental cord insertion. There is a single umbilical artery and the fetus had intrauterine fetal growth restriction. Both of these conditions are associated with UA aneurysms.
**TERMINOLOGY**

Abbreviations and Synonyms
- Persistent right umbilical vein (PRUV)

Definitions
- Embryologic right umbilical vein (RU/V) remains open

**IMAGING FINDINGS**

General Features
- Best diagnostic clue: Intrahepatic portion of umbilical vein (UV) curves towards stomach
  - Location
    - Intrahepatic PRUV (most common)
    - Extrahepatic PRUV

Ultrasoundographic Findings
- Intrahepatic PRUV (72%)
  - PRUV passes to right of gallbladder (GB)
  - GB usually displaced
  - GB traversely oriented
  - PRUV fuses with left portal vein
  - Left curve of UV instead of right
  - UV hooks towards stomach instead of liver
  - Typically seen on transverse view through liver
  - Coronal view helpful for confirmation

- Normal portal venous connections
- Normal ductus venosus
- Often isolated finding
- Extrahepatic PRUV (18%)
  - PRUV bypasses liver and portal system
  - Extrahepatic PRUV runs anterior to liver
  - Abnormal venous connections
  - PRUV drains into systemic veins
  - Extrahepatic PRUV associated with other anomalies and atresia
- Triosure 1B (14%)
- Noonan syndrome
- Cardiovascular anomalies
- Central nervous system anomalies
- Gastointestinal anomalies
- Syndactyly or growth restriction
- Single umbilical artery in almost all cases
- Color Doppler and 3D ultrasound
  - Helps show course and connections of PRUV

Imaging Recommendations
- Best imaging tool: Abdominal circumference (AC) view
- Protocol advice
  - Look at position of UV curve in all cases
  - Consider amniocentesis when other anomalies seen
PERSISTENT RIGHT UMBILICAL VEIN

Key Facts
- Extrahepatic PRUV associated with other anomalies and aneuploidy

Top Differential Diagnoses
- Normal umbilical vein
- Umbilical vein varix (UV varix)

Clinical Issues
- Intrahepatic PRUV usually an isolated finding

DIFFERENTIAL DIAGNOSIS

Normal umbilical vein
- Left UV patent
- UV curve is towards liver
- Gallbladder is lateral to UV

Umbilical vein varix (UV varix)
- Intraabdominal varix most common
- Extrahepatic portion of UV locally dilated
- May be associated with IUGR and aneuploidy
- May be associated with PRUV

PATHOLOGY

General Features
- Genetics: Extrahepatic variant associated with T18
- Etiology
  - Normal embryology
  - Early placenta has 2 umbilical veins
  - Right normally obliterated by 7th week
  - Left connects to portal veins and ductus venosus
- Intrahepatic PRUV
  - Left UV occludes instead of right
  - PRUV provides normal flow
  - Does not alter blood distribution to fetus
  - Extrahepatic PRUV
  - PRUV drains into systemic veins
  - Right atrium, superior vena cava most often
  - Epidemiology: 1:2500 fetuses

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - Incidentally noted on routine AC view
  - Seen in association with other anomalies

Natural History & Prognosis
- Intrahepatic variant
  - Excellent prognosis
- Extrahepatic PRUV usually an isolated finding
- Extrahepatic variant
  - Prognosis related to chromosome results
  - T18 most common aneuploidy
  - Prognosis related to associated anomalies
- PRUV in cases of abnormal-appearing gallbladder

DIAGNOSTIC CHECKLIST

Consider
- PRUV in cases of abnormal-appearing gallbladder

Image Interpretation Pearls
- Diagnosis often raised
- Abnormal direction of UV hooknot noticed
- Look for additional anomalies when PRUV seen

SELECTED REFERENCES

IMAGE GALLERY

- Axial ultrasound shows an intrahepatic PRUV. The UV (arrow) turns left and towards the stomach (arrows) instead of towards the right edge of the liver (open arrow). (Right) Axial ultrasound in the same plane shows a mediastinally displaced gallbladder (arrow), the umbilical vein (arrows) passes to the right of the gallbladder. Normally, the umbilical vein lies between the stomach and the gallbladder.
**VASA PREVIA**

**TERMINOLOGY**

**Definitions**
- Submembranous fetal vessels cross cervical os

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue
  - Pulsed Doppler shows fixed fetal vessels overlying cervical os
  - Associated with succenturiate lobe and velamentous cord insertion

**Ultrasonographic Findings**
- Vasa previa from succenturiate lobe
  - Most common etiology
  - Main placenta + accessory placenta
  - Low lying placenta common
  - Communicating vessels between lobes
  - Vessels traverse internal cervical os
  - Carry fetal blood
- Vasa previa from velamentous cord insertion
  - Placental cord insertion (CI) is velamentous
  - CI on membranes
  - Usually adjacent to placenta
  - Low lying placenta + velamentous CI

**Imaging Recommendations**
- Best imaging tool: TVUS + color Doppler + pulsed Doppler
  - Protocol advice
    - Careful surveillance of entire uterus
    - Identify succenturiate lobe
    - Doppler TVUS in all low lying placenta
    - Identify placental CI when suspicious of diagnosis

**DIFFERENTIAL DIAGNOSIS**

**Marginal sinus previa**
- Variant of marginal placenta previa
- Membranal veins from placenta near cervix
  - Normal placental CI
  - Bleeding is maternal not fetal

**Cord presentation**
- Unilateral cord in presenting part at labor
  - Free loop of cord in front of cervix
  - Risk for cord accident

**DOx: Vessels Near Cervix**

- Presenting Cord
- Marginal Sinus Placenta
- Marginal Sinus Placenta
- Cordine Vessel
VASA PREVIA

Key Facts
- **Terminology**
  - Submembranous fetal vessels cross cervical os
- **Imaging Findings**
  - Associated with succenturiate lobe and velamentous cord insertion
  - Best imaging tool: TVUS + color Doppler + pulsed Doppler
  - Identify placenta C/I when suspicious of diagnosis

- Often incidental finding if patient not in labor
- Uterine vessel near cervix
- Incidental finding
- Placenta not near cervix

PATHOLOGY

**General Features**
- Etiology
  - Vasa previa and succenturiate placentas
  - Normal placenta originally present
  - Partial atrophy results in 2 placentae
  - Vessels travel between lobes
  - Fetal vessels cross cervical os
  - Vasa previa and velamentous C/I
  - Originally placenta previa
  - Partial atrophy from poor decidual vascularity
  - C/I ends up submembranous near cervix
- Epidemiology: 1:3,500 deliveries
- Associated abnormalities
  - Monozygotic twins
  - Velamentous C/I incidence
  - Material uterine anomalies
  - Abnormal placentation

**Gross Pathologic & Surgical Features**
- Submembranous vessels are extremely fragile
- No placental tissue support

**Staging, Grading or Classification Criteria**
- Type 1: Vasa previa from velamentous C/I
- Type 2: Vasa previa from succenturiate lobe

CLINICAL ISSUES

**Presentation**
- Most common signs/symptoms
  - Incidental finding with succenturiate lobe
  - Incidental finding with placenta previa
  - 2nd/3rd trimester bleeding
  - Vessel palpation over intact membranes

**Natural History & Prognosis**
- 60-80% fetal mortality if diagnosis missed

**Treatment**
- Cesarean section before onset of labor

DIAGNOSTIC CHECKLIST

**Consider**
- Rule out vasa previa if succenturiate lobe seen
- Rule out vasa previa if marginal placenta previa seen

**Image Interpretation Pearls**
- Have a high index of suspicion
- Use color Doppler with transvaginal ultrasound
- May not see vessels with grayscale alone
- Use pulsed Doppler if crossing vessels seen
- Determine fetal vessels vs. maternal vessels

SELECTED REFERENCES

IMAGE GALLERY

(Left) Sagittal ultrasound of the lower uterus shows a succenturiate lobe. A small anterior placenta (fucciured arrow) and a low-lying larger posterior placenta (open arrow) are seen. (Right) Sagittal endovaginal ultrasound is the same case, performed in the third trimester shows a crossing vessel in front of the cervical os (arrow). Pulsed Doppler shows fetal arterial flow. The fetal vessels communicating between the two placental lobes cross in front of the cervix in this case of vasa previa.
NUCHAL CORD

TERMINOLOGY

Definitions
- One or more complete loops of umbilical cord around fetal neck

IMAGING FINDINGS

General features
- Best diagnostic clue
  - Must see in both sagittal and transverse planes to rule out false positive diagnosis
  - 3D ultrasound may be more accurate in making diagnosis

Ultrasoundographic findings
- Obvious flow with color Doppler
- Compressive effects on fetal skin (divot sign)
- May spontaneously untwist

Imaging Recommendations
- Look for vascular compromise
  - Increased systolic to diastolic (S/D) ratio
  - Early diastolic notching
  - If umbilical artery flow is abnormal, interrogate middle cerebral artery
- Follow-up ultrasound with attention to

DIFFERENTIAL DIAGNOSIS

Cord adjacent to neck
- Will not form complete loop around neck
  - Not present in both sagittal and transverse views
  - Changes during course of exam or on follow-up

Cystic hygroma
- Multiseptated mass
- No Doppler flow

PATHOLOGY

General Features
- Etiology
  - Coeds with less vascular recoil are more pliable and at greater risk
  - Longer cords at increased risk
  - Epileptogenicity
  - Prevalence 8-30%
  - Increases with advancing gestational age

DDx: Cystic Neck Mass

Cystic Hygroma  Cystic Hygroma  Hygroma And Hydrops
NUCHAL CORD

Imaging Findings

- Must see in both sagittal and transverse planes to rule out false positive diagnosis
- Obvious flow with color Doppler
- Compressive effects on fetal skin (divot sign)
- Look for vascular compromise
- Oligohydramnios increases risk of complication

Top Differential Diagnoses

- Cord adjacent to neck

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
  - INCIDENTAL finding
  - Rarely fetal distress

Natural History & Prognosis

- Vast majority see no consequence
- Excellent outcome
- Reported associations (usually not associated with long-term sequel)  
  - Growth restriction
  - Intrauterine fetal distress
  - Low Apgar scores
  - Meconium staining
  - Lower umbilical artery pH
  - Assisted ventilation (< 30 min)
  - Rare serious complications
  - Developmental delay, spastic quadriplegia, stillbirth
  - Factors increasing risk
    - Multiple loops
    - Tightness of loops
    - Oligohydramnios

Treatment

- Most reduced during delivery without consequence

Pathology

- Cords with less vascular coiling are more pliable and at greater risk

Clinical Issues

- Most reduced during delivery without consequence

Diagnostic Checklist

- Multiple loops and evidence of pressure effects at greater risk of complications

- Consider non-stress test (NST) and biophysical profile for right of multiple loops
- Patient should be made aware of importance of decreased fetal movement
- Early delivery for reassuring status

DIAGNOSTIC CHECKLIST

Consider

- Including in every report
  - Controversial, no standardized reporting practice
  - Some feel low risk makes reporting unnecessary

Image Interpretation Pearls

- Multiple loops and evidence of pressure effects at greater risk of complications

SELECTED REFERENCES


IMAGE GALLERY

(left) Amniocentesis shows the umbilical cord wrapped around the fetal neck (cords). Note the cord does not show the normal coiling which is seen in a nuchal cord. (right) Color Doppler ultrasound image confirms that the cystic mass is no placenta b. Indeed, the umbilical cord...
SECTION 12: Placenta & Membranes

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Imaging Anatomy

Ultrasound
- First trimester gestational sac (5-7 wk)
  - Diffusely echogenic ring
  - Chorionic villi of tissue
- Early trimester placenta (8-13 wk)
  - Chorionic villi/fetal membranes
  - Placental site now determined
- Umbilical cord inserts in center of chorionic villi
- Second trimester placenta
  - Uniformly echogenic structure
  - Occasional sonolucencies if >20 wks
  - Placental lakes, intervillous thrombus
- Third trimester placenta
  - More heterogeneous
  - Sonolucencies common
  - Occasional calcifications
  - Normal placental location
  - Funnel to mid uterus
  - Low-lying placenta often resolves by 3rd trimester
  - Triphosphonom
  - Areas of placenta atrophy as other areas grow
  - Placental cord insertion site
  - Initially central
  - Often eccentric at term
  - 2° to triphosphonom
- Membranes
  - Amnion attached to early embryo
  - Erythroblastoma becomes intramnionic
  - Chorion attached to trophoblast
  - Chorionic cavity (expanhemorrhagic decom pressure)
  - Fracture between amnion and chorion
  - Yolk sac in chorionic cavity
  - Amnion fuses with chorion at 14-16 wks
- MRI
  - May help determine placental location
  - Posterior placenta, obese patients, twins

Placenta & Membranes

Graphic shows chorionic villi are initially evenly distributed (arrow) within the chorionic sac. By 10 wks, the chorionic trophoblast (curved arrow) is formed whereafter villi abut.

Graphic shows placental circulation. Membranous blood vessels are the venous space (arrows). The main stem villi (open arrow) arise from the umbilical cord and contain fetal blood.

Abnormal Placental Invasion
- Accretion/penetration
- Intact vs. disrupted myometrium

Anatomy-Based Imaging Issues

Key Concepts or Questions
- When has placenta implanted?
- Is placenta detaching (abruption)?
- Does placenta appear prematurely heterogenous?
- Is placental cord insertions normal?
- Are membranes fused?
- Is amnion intact?

Imaging Approaches
- Transabdominal ultrasound usually adequate
  - Full survey of placenta recommended
- Transvaginal ultrasound (TVUS)
  - Lower uterine segment assessment
- Doppler ultrasound
  - To assess placental function

Imaging Protocols
- American Institute of Ultrasound in Medicine (AIS)
  - Document placental location
  - Relation to internal cervical os
  - TVUS may be necessary
  - Placental appearance
  - Thickness
  - Presence of sonolucencies/calcifications
- Placenta 'grading' to assess maturity
  - Not required by guidelines
  - Grade 0 (<=18 wks); Uniform echogenicity
  - Grade 1 (18-29 wks); Occasional parenchymal Cr
  - Grade 2 (30-34 wks); Occasional basal Cr
  - Minimal chorionic plate (deposition)
  - Grade 3 (>35 wks); Significant basal Cr
  - Significant chorion to basal infiltration
  - Individual cotyledons widely seen
  - Early grade 3 appearance considered abnormal
  - 1. Risk for placental insufficiency
     2. Placental cord insertion assessment
PLACENTA & MEMBRANES

**Imaging Issues**
- Determine placental implantation anatomy
- Rule out placenta previa
- False positive diagnosis if full maternal bladder
- Rule out implantation on fibroid
- Look for extra lobes (succecuritare)
- Evaluate placental attachment
- Abruption if premature detachment
- Evaluate placenta morphology
- Early invation may be abnormal
- Normal placental thickness < 4 cm
- Determine normal placental cord insertion
- Branching vessels on placenta parenchyma
- Velamentous placental cord insertion associated with fetal morbidity
- Evaluate membranes

**Clinical Importance Of Doppler**
- Abnormal uteroplacental Doppler
- Suggestive of placental insufficiency
- Uterine artery Doppler
- Should be low resistance by early second trimester
- Abnormal uterine artery Doppler findings
- Delayed "normalization"
- Presence of post systolic notch
- Associated with placental insufficiency
- IUGR, preclampsia, oligohydramnios
- Umbilical artery Doppler
- Normally low resistive flow
- Absent or reversed diastolic flow abnormal
- Flow changes occur later than in uterine artery

**Embryology**

**Embryologic Events**
- First trimester placenta
- Blastocyst implants by menstrual day 28
- Outer trophoblasts = placenta & membranes
- Chorionic sac diffusely covered by villi
- Villi adjacent to endometrium proliferate
- Form chorionic frondosum
- Villi adjacent to uterine stroma atrophy
- Establishment of uteroplacental circulation
- Trophoblasts invade uterine spiral arteries
- Partial plug lead to "percolating blood"
- 4 Flow pressure into early placenta
- 1 Pressure would cause detachment
- Spiral artery remodeling
- Musculo-elastic layers disappear
- Low pressure intervillous flow established
- Spiral artery loses "arterial" qualities by 10 wks
- Myometrial spiral arteries invaded
- Uterine artery waveform changes to 4 resistive flow
- Chorionic villi branch to 50-60 cotyledons
- 1 primary stem villus per cotyledon
- Supplied by 1st branches of umbilical vessels
- Trophoblasts
- Dynamic process of placentation
- Parts of placenta atrophy as other parts grow
- Growth in areas with good uterine vascularity
- Membrane formation
- Chorion attached to outer trophoblasts
- Amnion originates from cytotrophoblasts
- Initially attached to embryonic disk
- Amnion and chorion fuse at 14-16 wks

**Practical Implications**
- Abnormal uteroplacental circulation
- Associated with fetal and maternal morbidity

- Amnion fuses with chorion at 14-16 wks
Clinical Implications

Clinical Importance
- Placenta previa
  - Marginal placenta previa
  - Edge of placenta within 2 cm of internal os
  - Complete placenta previa
  - Placenta covers internal os
  - Maternal hemmorhage
  - Cesarean section often necessary
- Placental abruption
  - Early placental detachment
  - Marginal abruption most common
  - From edge of placenta
  - Retrop接受al abruption
  - Mimics thick placenta
  - Preplacental abruption most rare
  - Hematoma at fetal surface
  - May compress cord
- Placenta accreta spectrum
  - Placental invasion beyond endometrium
  - Accreta: Placenta adherent to myometrium
  - Insera: Placenta invades myometrium
  - Percreta: Placenta invades beyond myometrium
  - Higher risk if multiple cesarean sections
  - Velamentous cord insertion
  - Membranous placental cord insertion
  - Submembribanous fetal vessels are fingle
  - Ren morphge fetal blood
  - If placental cord insertion is low then vasa previa may be present
  - Vasa previa

Function-Dysfunction
- Abnormal uterine artery waveform
  - Resisive indices > 0.65 after 16-18 weeks
  - Post-partum notch
  - May be earliest indicator of placental dysfunction
  - Low dose aspirin treatment often successful if done early
  - Facilitate myometrial spiral artery conversion
- Abnormal umbilical artery waveform
  -Absent or reversed diastolic flow
  - Late manifestation of placental dysfunction
- Abnormal placentation
  - Grade 3 placenta seen before term
  - Associated with smoking, hypertension, diabetes

Related References
(Left) Sagittal ultrasound shows the amniotic membrane (arrows) at 10 weeks gestation. The embryo is within the amniotic cavity and the chorionic cavity (curved arrows) lies between the amnion and gestational sac.
(Right) Sagittal ultrasound shows the amnion at near 14 weeks gestation. The amniotic membrane (arrows) lies very close to the uterine wall (and the chorion). The membranes are normally fully fused by 16 weeks.

(Left) Sagittal ultrasound shows a full bladder (arrow) causing a like positive placent previa (curved arrows). TWI (lower image), done after the patient voided, shows a normal cervix (open arrows) and no previa. Right) 3D ultrasound with color Doppler shows a normal second trimester placenta. Occasional umbilical veins (arrows), subchondral veins (open arrows) and a normal placental cord insertion (curved arrows) are routinely seen.

(Left) Sagittal ultrasound shows a grade 3 placenta in a near term pregnancy. Extensive basal calcifications (arrows) and chorionic plate indentation (curved arrows) are seen. Total growth was normal. Right) Pulsed Doppler ultrasound of a normal (upper) and abnormal (lower) uterine artery. Doppler waveform in two different second trimester cases. There is high invasive flow (fetal diastolic flow) and a mitral systolic notch (arrows) in the abnormal tracing.
**TERMINOLOGY**

**Abbreviations and Synonyms**
- Placental sonolucentcies
- Placental lakes (PL)
- Placental cavieties
- Venous lakes
- Intervillous Thrombus (IVT)

**Definitions**
- Discrete sonolucent or hypoechic lesions in placenta
- Enlarged intervillous vascular spaces
  - Initially with blood flow
  - Placental lake
  - With thrombus
  - Intervillous thrombus
  - Eventual fibrin deposition

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue: Single or multiple hypoechic lesions in placenta
- Location
  - Within placenta parenchyma
  - Surrounded by normal placenta
  - Subchorionic

**Ultrasoundographic Findings**
- Homogeneous sonolucentcies in placenta
  - > 1 cm diameter
  - Multiple lesions common
  - Surrounded by otherwise normal placenta
  - Most often considered a normal finding
  - Swirling streams of blood in PL
  - Seen best with real-time grayscale imaging
  - Color Doppler often negative
  - Flow is extremely slow
  - Blood is maternal
  - Occasional fluid-fluid level seen
  - RBC settle in subunit
  - PL shape and size may change during exam
  - Change in maternal position
  - 2\(^\circ\) to uterine contraction
  - Intervillous thrombus
  - Thrombosis of PL
  - IVT and PL often seen together in same placenta

**DDx: Placental Masses**
- Complete Molar
- Hydatidiform
- Choasangroma
- Abruptio
PLACENTAL SONOLUCENCIES

Terminology
- Placental lakes (PL)
- Intervillosus thrombus (IVT)

Imaging Findings
- Most often considered a normal finding
- Swirling streams of blood in PL
- PL shape and size may change during exam
- IVT and PL often seen together in same placenta
- Early, numerous and large sonolucencies may be significant
  - "Swiss cheese" placenta variant

Top Differential Diagnoses
- Gestational trophoblastic neoplasia (GTN)
- Chorioangioma
- Placental abruption

Key Facts

Pathology
- Contain only maternal blood
- Maternal deposition after thrombosis
- 2-10% of placentas have sonolucencies at 15-34 wks

Clinical Issues
- Risk for placental insufficiency

Diagnostic Checklist
- Follow up ultrasound if extensive (> 3), large (> 2 cm) or if present before 20-25 wks
- Look for signs of placental insufficiency
- Rule out more significant placental lesions
- Amnioinfusion may be necessary to rule out GTN
- Real time grayscale imaging is best way to diagnose placental lakes
- Increase gain to see swirling blood

- No flow
- Does not change size
- Hypoechoic more likely than sonolucent
  - May lead to fibrin deposition
- Sonolucencies more often seen in thick placentas
- Placenta ≤ 3 cm is 6X more likely to have sonolucencies
- Both findings are usually incidental
- Early, numerous and large sonolucencies may be significant
  - < 20-25 wks
  - > 3 lesions
  - > 2 cm
- "Swiss cheese" placenta variant
- Patchy placenta from diffuse fibrin deposition
- Diffusely heterogeneous by ultrasound
- Innumerable sonolucencies
- Placentalomally
- Mfnics gestational trophoblastic neoplasia (GTN)
- Genetic testing necessary
  - 1 fetal mortality and mortality

MR Findings

- T1WI
  - MR can differentiate between PL and IVT
  - Placental lake: Intensity
    - Turbulent flow
  - IVT: 1 intensity
- T2WI
  - Placental lake: Isointense
  - Turbulent flow
- IVT: Isointense

Imaging Recommendations

- See imaging tool: Complete evaluation of placenta on routine ultrasound exam.
- Protocol advice
  - Look carefully for swirling blood in sonolucencies
  - Helps differentiate PL from other masses
  - Most often a normal finding
  - Third trimester placenta
  - Occasional lesions
  - Normal fetal growth
  - Normal amniotic fluid
  - Follow-up not necessary
  - Diffuse or early sonolucencies considered abnormal
  - Consider amniocentesis to rule out GTN
  - Rule out intrauterine growth restriction (IUGR)
  - Umbilical artery Doppler if excessive number of lesions
  - High resistance umbilical artery flow, 1 placental resistance

DIFFERENTIAL DIAGNOSIS
Gestational trophoblastic neoplasia (GTN)
- Complete mole
  - Placental chorion adenoma
  - No fetus or embryo
  - Diffuse cystic placenta
- Partial mole
  - Triploid karyotype
  - Abnormal fetus
  - Severe IUGR +/- anomalies
  - Variable placenta
  - Often cystic
  - Placenta may appear normal
- Complete mole + normal twin
  - Two placenta are present
  - Normal placenta with normal fetuses
  - Cystic placenta without fetus

Chorioangioma
- Benign vascular tumor
  - Flow easily seen with Doppler
  - Unlike slow flow in PL
  - Solitary, circumscribed solid mass
  - Hypoechoic or hyperechoic
  - Often near umbilical cord origin

Placental abruption
- Placental abruption can mimic PL
  - ballot into amniotic cavity
  - No blood flow
PLACENTAL SONOLUMENCIES

- Marginitis and retroplacental abruption more common
  - Marginitis from edge of placenta
  - Retroplacental behind placenta
- Old blood becomes hypoechoic/sonoluent
- Symptomatic patients
  - Painful bleeding
  - Preterm labor

PATHOLOGY

General Features
- General path comments
  - Placental lakes
  - Islands of red blood cells in lake of serum
  - Contain only maternal blood
- Intervillous thrombus
- Thrombosis of PI
  - PI thrombus deposition after thrombosis
- Subchorionic
  - Along basal plate
- Genetics: Not associated with fetal aneuploidy
- Biologic
  - Role of placental lakes in normal pregnancy
  - PI's regulate placental pressure
  - Intervillous space helps equalize pressure
  - Multiple or large lesions often abnormal
- Epidemiology
  - Variable incidence reported perinatally
  - 2-18% of placentas have sonolucencies at 13-34 weeks
  - Postnatal placenta
  - Intervillous thrombus in 40%
- Associated abnormalities
  - More common if extensive involvement of placenta
  - UGIR
  - Migratory
  - Antiphospholipid syndrome
  - Preeclampsia
  - Elevated maternal serum alpha-fetoprotein (AFP)

Gross Pathologic & Surgical Features
- Fibrous deposition with extensive infarction
  - Subchorionic
  - Basal
  - May lead to maternal floor infarction

Microscopic Features
- Intervillous thrombus
  - Villus free focus of coagulated blood

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - Incidentally noted in normal pregnancy
  - Preeclampsia
  - Antiphospholipid syndrome
  - Autoimmune disorder
  - Circulating antiphospholipid antibodies
  - PT, placental thrombosis and infarction
- Other signs/symptoms
  - Elevated maternal serum AFP
  - UGIR

Natural History & Prognosis
- Most adhere to normal finding
  - Occasional PI, or IV
  - Third-trimester placenta
- Excellent prognosis
- Extensive sonolucencies may be abnormal
  - Risk for placental insufficiency

Treatment
- If associated placental insufficiency then early delivery may be necessary
- Treatment for antiphospholipid syndrome
  - Heparin, aspirin
  - Prednisone
  - Inframammary infusion

DIAGNOSTIC CHECKLIST

Consider
- Follow-up ultrasound if extensive (>3), large (>2 cm)
  - or if present before 20-25 weeks
- Look for signs of placental insufficiency
  - UGIR
  - Migratory
  - Antiphospholipid syndrome
  - Abnormal Doppler
  - Rule out more significant placental lesions
  - Abruptio, GTN
  - Amniocentesis may be necessary to rule out GTN

Image Interpretation Pearls
- Real time grayscale imaging is best way to diagnose placental lakes
  - Increase gain to see swirling blood
- Change maternal position
  - See PI, may change
  - May see fluid-fluid level shift

SELECTED REFERENCES
3. Van Der Beek JT et al: Histologic features of placentas and abortion specimens from women with antiphospholipid and antiphospholipid-like syndromes. Placenta. 25(7):442-8, 2004
PLACENTAL SONOLUCENCIES

IMAGE GALLERY

Typical

(Left) Sagittal ultrasound shows multiple subchorionic placental lakes (arrows) bulging into the amniotic cavity. The placenta appears thickened. Their echogenecities vary from sonoluent (black) to almost echogenic in placenta.

(Right) Axial ultrasound shows placental lakes (arrows) without any detectable flow on color Doppler imaging. However, with saline, grayscale ultrasound, slow swirling flow was easily seen.

Typical

(Left) Axial ultrasound shows a single, large anechoic placental lake (arrow).

(Right) Axial ultrasound of the same lake later in the exam, and after maternal position change, emphasizes the dynamic nature of the lesions. The lake is larger (arrows) and contains a fluid-fluid level (open arrow). The appearance is secondary to maternal red blood cells settling within the amniotic fluid.

Variant

(Left) Ultrasound shows irregular placental condiencies in a "swiss cheese" appearing placenta. Polyhydramnios and IUGR were also present. While the appearance is suspicious for CTN, amniocentesis results were normal. (Right) Gross pathology of the basal surface (left) and cross-section (right) of a placenta with extensive, tannish fibrin deposition (arrows) and dilute thrombosis. Several lakes without thrombosis (arrow) are also seen.
CHORIOAMNIOTIC SEPARATION

Graphic shows chorioamniotic separation from amnion. The amniotic membrane (open arrow) is separated off the chorion (arrow). The type of CA separation is usually minimal and benign.

TERMIOLOGY

Abbreviations and Synonyms
- Chorioamniotic separation (CA separation)
- Delayed amnionchorionic fusion
- Persistent amniotic cavity

Definitions
- Persistent unfused amnion and chorion > 14-16 wks
- May be primary non-fusion or secondary to amniocentesis

IMAGING FINDINGS

General Features
- Best diagnostic clue
  - Free floating amniotic membrane in > 14-16 wk gestation
  - Amnion normally lines with chorion at 13-14 wk
- Size
  - Descriptions vary in literature
  - > 3 mm separation along > 3 uterine cavity
  - > 10 mm separation at any single point

Ultrasoundographic Findings
- Amniotic membrane separate from uterine wall
  - Thin membrane best seen perpendicular to beam
  - Incomplete fusion (most common)
  - Complete obliteration
  - Attached only at placental cot insertion site
  - CA separation after 14 wks considered delayed
  - Definitive diagnosis after 16 wks
  - Association with aneuploidy
    - 12% in high-risk pregnancies with CA separation
    - Advanced maternal age (AMA)
    - Prior abnormal fetus
    - CA separation + fetal anomaly
  - Trisomy 21 most common
  - Associated with anomalies (most fetal karyotype)
  - Genitourinary anomalies
  - Oligohydramnios from any cause
  - Transient finding
    - Fuses eventually occurs even if fetus is abnormal
  - CA separation secondary to amniocentesis is common (up to 25% incidence)
    - Often minimal and not seen unless sought
    - Most often without sequelae

Imaging Recommendations
- Protocol advice
  - Look carefully for markers of aneuploidy
  - Follow-up to look for additional anomalies

DDx: Intrauterine Membranes

- Amniotic Bands
- Amniotic Band
- Uterine Synechiae
- Normal 1st Trimester
CHORIOAMNIOTIC SEPARATION

Key Facts
- Top Differential Diagnoses
  - Amniotic bands
  - Uterine synechia

Pathology
- 12% of high-risk pregnancies with CA separation have aneuploidy
- 4% aneuploidy rate if isolated finding > 14 wks
- 25% of fetuses with aneuploidy have CA separation
- Aneuploidy, premature rupture of membranes, preterm delivery, growth restriction

Treatment
- Because membranes are not fused, chorionic villus sampling rather than amniocentesis often needed for karyotype

DIAGNOSTIC CHECKLIST
- Look for CA Separation in patients at-risk for aneuploidy

SELECTED REFERENCES

IMAGE GALLERY

(left) Sagittal ultrasound shows CA non-union (arrows) and nuchal fold thickening (arrows) in a fetus with trisomy 21. (right) Sagittal ultrasound shows CA separation (arrows), distended bowel (arrowed area), and skin edema (open arrow) in a fetus with trisomy 18. The amniotic membrane is draped over the fetal face.
**TERMINOLOGY**

**Abbreviations and Synonyms**
- Placenta previa (PP)

**Definitions**
- Placenta implants in lower uterine segment (LUS)
- Placenta covers or lies close to internal os (IO) of cervix

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue: Transvaginal ultrasound (TVS) shows placental edge near or covering IO
- Location
  - Complete placenta previa
  - Partial placenta previa
  - Marginal placenta previa
  - Placenta edge within 2 cm of IO

**Ultrasonographic Findings**
- Placenta previa diagnosis in 2nd trimester
- Routine sagittal LUS image
- TVUS may be necessary for adequate view

**DDx: Low-Lying Placenta**

- Full Maternal Bladder
- Contractions
- Abortion

- Show fluid or fetus in direct contact with IO
- Low placenta on routine view
- Placental edge within 2 cm of IO
- Often asymptomatic
- Many marginal PP resolve
- Placenta previa diagnosis in 2nd trimester
- More likely to present with vaginal bleeding
- Transabdominal view
  - Increased soft tissue between cervix and fetus
  - Nonengaged, "floating" presenting fetal part
  - TVUS almost always necessary for diagnosis
- Perform careful TVUS to avoid IO disruption
- Complete placenta previa
  - Placenta completely covers IO
  - Symmetric complete placenta previa
  - Placenta partially implanted on cervix
  - Will not resolve with advancing pregnancy
  - Asymmetric complete placenta previa
  - Small part of placenta covers IO
  - May resolve with advancing pregnancy
  - If > 15 mm covers IO then less likely to resolve
- Marginal placenta previa
  - Inferior edge of placenta within 2 cm of IO
  - Does not cover os
  - Often resolves with advancing pregnancy
  - Follow-up at 34 wks
- Partial placenta previa
  - Edge of placenta partially covers internal os
PLACENTA PREVIA

Terminology
- Placenta previa occurs in lower uterine segment (LUS) or cervix
- Placenta previa or lies close to internal os (IO) of cervix

Imaging Findings
- Best diagnostic clue: Transvaginal ultrasound (TVUS)
  - Shows placental edge near or crossing IO
  - Complete placenta previa
  - Marginal placenta previa
  - Partial placenta previa
  - Marginal sinus placenta previa
  - 5% of placenta previa have associated accreta/pectra

Top Differential Diagnoses
- Full maternal bladder

Key Facts
- Insufficient data to differentiate from marginal PP
- Same prognosis as marginal PP
- Marginal sinus placenta previa
  - Placenta previa
  - Maternal veins, non fetal
  - Do not confuse with vasa previa
- Placenta previa may be > 2 cm from IO
- Same prognosis as marginal PP
- Low-lying placenta
  - Preferred term if < 20 wks and TVUS not done
  - Asymptomatic
  - Often resolve by 34 wks
- Placenta previa associated with accreta/pectra
  - Abnormal placenta growth through endometrium
  - Adhesions to myometrium or beyond
- Research shows that previous cesarean section + 5% of placenta previa have associated accreta/pectra
  - 1 Risk for accreta if prior cesarian section + anterior PP
- 1 Risk with number of prior cesarian sections
- 67% risk if previa and > 4 cesarian sections
- Look for intact subplacental myometrial zone
- Hypoechoic line between bladder and placenta
- Should be contiguous
- Color Doppler and MRI helpful
- Placenta previa and vasa previa
  - Velamentous cord insertion
- Low-lying placenta + abnormal placental cord insertion
- Fetal vessels cross IO
- Succenturiate lobes
- Low-lying accension placenta
- Fetal vessels travel between placenta
- Fetal vessels cross IO
- Use Doppler TVUS
- Color Doppler shows crossing vessels
- Pulsed Doppler to diagnose fetal vessels
- Must differentiate from maternal vessels

Imaging Recommendations
- Use imaging tool: Transvaginal ultrasound to identify superior placental edge

Differential Diagnosis
- Full maternal bladder
  - Approximates anterior and posterior uterine wall
  - Normally implanted placenta appears low
  - Usually elongates cervix
  - Have patient void and repeat exam

Focal myometrial contraction
- Contraction can cause approximation of uterine walls
  - Similar to maternal full bladder
  - May mimic placenta
  - Can appear mass-like and echogenic
  - Resolves with time
  - TVUS can often differentiate cervix from contraction
  - Slip of fluid seen at IO

Placental abruption
- Premature placental detachment
  - Often with accompanying clot
  - Acute clot often isoechoic to placenta
  - Mimics PP if clot located near IO
  - Power Doppler helpful
  - Shows no flow in clot

Protocol advice
- Obtain routine lower uterine segment (LUS) image
- Sagittal plane of LUS and cervix
- Show internal cervical or free of placental tissue
- TVUS often necessary
  - Scan while carefully inserting probe
  - Find midline sagittal plane
  - Identify inferior edge of placenta
- Measure distance between placenta and IO
  - Miscarriage cervical length
- Transvaginal/ transabdominal technique
  - Use only if TVUS not possible
  - Elevate maternal hips to minimize bowel artifact
  - Place probe on perineum (absa minor)
  - Collapsed vagina is acoustic window to cervix
  - Measure distance between placental edge and IO
PLACENTA PREVIA

PATHOLOGY

General Features
- Etiology
  - Enzyme damage
  - Bleasberg implants low
  - Low placenta may resolve 2nd trimester
  - Atrophy in absence of poor blood supply (i.e., IUS)
  - Growth in areas of better blood supply
  - Low placenta may resolve as IUS grows
- LES 'predicts' later in pregnancy
- Placental "migration" rate
  - Approximately 5 mm/wk
- Epidemiology
  - Incidence as pregnancy advances
  - 5% between 15-16 wks
  - 0.5% at term
  - 1 Incidence with parity
  - 1.1,500 in multiparous patients
  - High-risk patients
  - Prior placenta previa
  - Prior cesarean section
  - Prior suction curettage
  - Multiparity
  - Smoking
  - Cocaine use
  - Associated abnormalities: 5% with associated accreta

Staging, Grading or Classification Criteria
- Complete placenta previa
  - Symmetric
  - Asymmetric
  - Partial placenta previa
  - Marginal placenta previa
  - Marginal sinus previa

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - Painless bleeding
  - Often presents in 3rd trimester
  - Incidence of finding on routine ultrasound
    - Occurs resolves

Demographics
- Age
  - 1 risk with advanced maternal age (AMA)
  - ≤ 35 yo at time of delivery

Natural History & Prognosis
- Majority of partial and marginal placenta previa resolve
- PP after 34 weeks not likely to resolve
- Some complete PP will resolve
- Placenta crossing > 25 mm over 60 less likely to resolve
- Excellent prognosis with appropriate management
- Maternal mortality < 1%

Treatment
- Bleeding placenta previa
- Bed rest +/- hospitalization
- Maternal transfusion if necessary
- Cesarean section delivery in vast majority
- Asymptomatic placenta previa ≥ 34 wks
- Cervical rest
- Cesarean section delivery in vast majority
- Minority of marginal PP may be delivered vaginally
- Fetal head compresses placenta during delivery
- "Double setup" vaginal delivery
- Room set up for emergency cesarean section

DIAGNOSTIC CHECKLIST

Consider
- TVUS to rule out PP in all patients with bleeding in 2nd/3rd trimester
- Posterior PP & posterior myometrium appears thick
  - May be from unsuspected submucous lobe

Image Interpretation Pearls
- Beware false positive PP from full maternal bladder
  - Re-image after patient voids
- Use TVS color Doppler when placenta is low
  - Rule out marginal sinus previa
  - Rule out vasa previa

SELECTED REFERENCES
(Left) Sagittal endovaginal ultrasound shows partial placenta previa. The edge of the posterior placenta (arrow) is located at the 10 o'clock (curved arrow). Color Doppler clearly demonstrates the subplacental vessels. (Right) Sagittal ultrasound performed later in the same pregnancy shows that the partial previa has resolved. The edge of the placenta (arrow) is now at a significant distance from the 10 o'clock arrow. This patient never had bleeding.

(Left) Sagittal ultrasound shows marginal situ previa. While the placenta (arrows) is at some distance from the cervix (calipers), prominent placental vessels (open arrows) are located near the 10 o'clock (l) Sagittal endovaginal ultrasound in another patient with bleeding shows a placental vessel (arrow) located directly over the IO. Pulsed Doppler demonstrates maternal venous flow.

(Left) Sagittal ultrasound shows a lowlying succenturiate lobe (arrow, lower image) detected during routine second trimester ultrasound. The majority of the placenta is located anteriorly (open arrows, upper image). (Right) Sagittal endovaginal ultrasound performed in the 3rd trimester confirms a marginal placenta previa of the succenturiate lobe. The inferior edge of the placenta (arrow) is within 2 cm of the IO (curved arrow).
**TERMINOLOGY**

**Abbreviations and Synonyms**
- Submembranous cord insertion (CI)

**Definitions**
- Umbilical vessels insert on membranes

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue: Color Doppler shows velamentous CI adjacent to placenta
- Location: Fixed submembranous vessels

**Ultrasoundographic Findings**
- Normal placental CI
  - CI on placental edge
  - Located easily with grayscale ultrasound
- All branching vessels located or placenta
- Seen best with color/power Doppler
- Velamentous CI
  - Umbilical cord inserts on membrane
- Often adjacent to placenta
- Cord vessels are dilated
- Lack placental support
- Vessels separated at CI site

**Imaging Recommendations**
- Best imaging tool: Color Doppler evaluation of cord insertion site
- Protocol advice
  - Identify cord insertion in all high-risk patients
  - Placenta previa
  - Monochorionic twins
  - When placenta is posterior
  - Gently move fetus
  - Place patient in lateral position
  - Rule out placenta previa in high-risk patients
  - Doppler transvaginal ultrasound

**DIFFERENTIAL DIAGNOSIS**

**Battledore Placenta**
- Eccentric cord insertion

**DDx: Abnormal Placental/Cord Vascularity**

- Battledore Placenta
- Marginal Sinus Previa
VELAMENTOUS CORD

Terminology
• Submembranous cord insertion (CI)

Imaging Findings
• Best diagnostic clue: Color Doppler shows velamentous CI adjacent to placenta
• Vessels separated at CI site
• Some or all vessels on membranes
• Identify cord insertion in all high-risk patients

• Cord inserts at margin of placenta
• Within fetal villi or edge
• Branching vessels all on placenta
• More common than velamentous cord
• 2-10% incidence
• Usually without morbidity

Marginal sinus previa
• Marginal placenta previa
• Maternal vessels overly cervical os
• Normal placental cord insertion
• Use color Doppler
• Outcome same as for marginal previa

PATHOLOGY

General Features
• Etiology
  • Trophoblast results in shifting placenta
  • CI originally normal
  • Parts of placenta grow while parts atrophy
  • CI becomes membranous
• Epidemiology: 1% of deliveries
• Associated abnormalities
  • Monoamniotic twins
  • 10% incidence of velamentous CI
  • 13x ↑ risk for TTTS
  • 64% of twins with TTTS have a velamentous CI
• Maternal uterine anomalies
• ↑ Incidence of abnormal placentation

Cross Pathologic & Surgical Features
• Submembranous vessels are extremely fragile
• No placental tissue or cord membrane support

Staging, Grading or Classification Criteria
• Type I vasa previa is secondary to velamentous CI

CLINICAL ISSUES

Natural History & Prognosis
• Cord rupture during placental extraction
• Vasa previa from velamentous CI
• 60-80% fetal mortality if diagnosis missed
• Minimal blood loss results in fetal death

Treatment
• Careful placental extraction
• Cesarean section for vasa previa

Key Facts
Top Differential Diagnoses
• Battered placenta
• Marginal sinus previa

Pathology
• Trophoblast results in shifting placenta
• Epidemiology: 1% of deliveries
• 64% of twins with TTTS have a velamentous CI
• Submembranous vessels are extremely fragile
• Type I vasa previa is secondary to velamentous CI

DIAGNOSTIC CHECKLIST
Image Interpretation Pearls
• Use color Doppler to identify cord insertion
  • Differentiate from eccentric cord insertion
• Branching vessels within placental mass
• Find both CI sites in monochorionic twins
• Rule out vasa previa when placenta is low-lying
  • Document CI

SELECTED REFERENCES

IMAGE GALLERY

(Left) Axial color Doppler ultrasound in monoamniotic twins, shows a velamentous CI for twin B. The CI (arrow) is seen arising from the membranes adjacent to the placenta (open arrow). (Right) Color Doppler ultrasound of the umbilical artery shows absent diastolic flow (arrow). Twin B, with the velamentous CI, was the smaller twin in this pregnancy complicated by twin-twin transfusion syndrome.
PLACENTAL ABRUPTION

Graphic shows placental abruption sites. Marginal abruption (arrow) occurs at the placental edge. Hemorrhage (curved arrow) and placental infarction (open arrow) are less common.

Sagittal ultrasound shows a second trimester marginal abruption (arrow). The edge of the placenta (curved arrow) is lifted off the uterus. Also, the placenta is implanted upon a hypertrophied (open arrow).

TERMINOLOGY

Abbreviations and Synonyms
- Abruptio placenta
- Subchorionic hemorrhage

Definitions
- Premature separation of placenta from uterus

IMAGING FINDINGS

General Features
- Best diagnostic clue: Hypoechoic blood clot near or behind placenta
- Location: Abruptio may be marginal (most common), retroplacental or preplacental
- Size: Extremely variable
- Morphology: Often crescentic

Ultrasoundographic Findings
- Ultrasound (US) appearance varies with age and size of hematoma
  - Small abruptions often not detectable by US
  - Acute hematomas
    - Echogenic blood
    - Isoechoic to placenta
    - May appear as a thick placenta

- May be associated with fetomaternal transfusion
  - May see “milkshake” sign

- May cause fetal hydrops
  - May cause fetal distress

- May lead to placental abruption

Diagnosis
- Power Doppler helps confirm diagnosis
- Distinguish clot from placenta/uterus
- No sonoluent area

- Subchorionic hematoma
  - More heterogeneous than acute
    - May contain fluid-fluid levels
    - Septations common
  - Easier to resolve clot vs. placenta

- Resolving hematoma
  - Liquefying blood
    - Eventually sonoluent
  - May mimic amniotic fluid

- Intervillous blood common
  - Ecchymotic debris in fluid
  - Abruption
    - Large hemorrhage traverses amnion
    - Resolving hemorrhage
      - Clot proteins diffuse into fluid
      - Associated with fetal echogenic bowel
      - From ingestion of debris
    - Marginal abruptions
      - Must confirm type of abruption
        - 91% < 20 weeks are marginal
        - 67% > 20 weeks are marginal
      - Hemorrhage from edge of placenta
      - Can see raised edge in 30%
      - Adjacent hematoma

ODx: Placental Mass-like Lesions

Leyomyoma
Leiomyoma
Cystadnoma
Chorioangioma
Key Facts

- Placenta previa
- Chorioangioma

Pathology

- 1% of all pregnancies
- 17x higher risk if prior abortion

Clinical Issues

- 80% present with vaginal bleeding
- 30% with pain and no bleeding
- 1/3 risk if motor vehicle accident
- Excellent prognosis if small
- >50% placental detachment has >50% fetal death rate
- Retropartial abortion most worrisome
- Poor outcome when fetal bradycardia present

Differential Diagnosis

Leiomyoma
- Hyperechoic uterine wall mass
- Placenta may implant upon myoma
- Mimic retropartial abortion
- Increased risk for abortion
- Leiomyoma has blood flow

Placenta previa
- Complete placenta previa
  - Placenta covers internal cervical os
  - Marginal placenta previa
    - Edge within 2 cm of internal os
    - Often present with painless bleeding
    - Predisposed to abortion
    - Abnormal placenta in low uterus

Focal myometrial contraction
- Transient myometrial thickening
  - Normal phenomenon
  - Appears mass-like
  - Inner myometrium affected more than outer
  - Will resolve with time

Chorioangioma
- Vascular placental mass
  - Doppler essential for diagnosis
  - Can mimic retropartial abortion if located on fetal surface of placenta

Imaging Recommendations

- Best imaging tool
  - Grayscale US to detect clot
  - Power Doppler in acute setting

Terminology
- Premature separation of placenta from uterus

Imaging Findings

- Best diagnostic clue: Hyperechoic blood clot near or behind placenta
- Location: Abortions may be marginal (most common), retroplacental or preplacental
- May report as a thick placenta
- Estimate amount of placenta detached
- Look for accompanying cervical change
- Cervical effacement/tunneling
- Transvaginal US required
- Retropartial abortion
  - Second most common
  - Central hemorraghe between placenta and uterus
  - Large detachment more likely than with marginal abortion
    - Risk of fetal mortality
  - Appears acutely as "placentalhyge"
  - Bioechnic hi-soft behind placenta
  - Direct hemorrhage into placenta
  - Power Doppler helpful
  - Delineates clot from placenta
  - Preplacental abortion
    - Rare
    - Hematoma on fetal surface of placenta
      - Subchorionic or subamniotic space
    - Clot may compress cord
    - Find placental and insertion
    - Use Doppler to evaluate flow
    - May mimic placental mass
    - Chorioangioma
      - Large venous lake
      - Twins and abortion
    - Rize hematoma between membranes
      - Retain intra-amniotic mass without flow
    - Abortion and negative US
      - 50% of abortions have no US findings
      - More likely marginal and small
      - Hematoma has passed before US is performed
    - Better prognosis if negative US
PLACENTAL ABRUPTION

PATHOLOGY

General Features
- Etiology
  - Initial spiral artery bleed
  - Arteries without myometrium invasion
  - More prone to hemorrhage
  - Hemorrhage into decidua basalis layer
  - Hematomas split decidua
  - Placenta detaches as bleed grows
- Epidemiology
  - 2% of all pregnancies
  - 17x1 risk if prior abortion
- Associated abnormalities
  - Placenta previa
  - Leiomyoma

Gross Pathologic & Surgical Features
- Clot in subchorionic space

Staging, Grading or Classification Criteria
- US classification based on location
  - Marginal
  - Retroplacental
  - Preplacental

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - Abruption is a clinical diagnosis
  - Most common in 3rd trimester
  - 80% present with vaginal bleeding
  - +/- Pain
  - Blood is maternal
  - 50% with pain and no bleeding
  - Often from retroplacental abruption
  - Preterm labor
  - Blood is irritating to uterus
  - High-risk patients
  - Prior history of abruption (17x1 risk)
  - Thrombophilia
  - Maternal hypertension
  - Creatine use (related to hypertension)
  - Smoking
  - Increased parity
  - Advanced maternal age
  - Leiomyoma (2.6x1 risk)
- Abruption and trauma
  - 7x1 risk if motor vehicle accident
  - Regardless of other maternal injury

Natural History & Prognosis
- Excellent prognosis if small
  - <30% placenta detached
- Poor prognosis if large
  - >50% placental detachment has >50% fetal death rate
- Retroplacental abruption most worrisome
  - Increased risk of fetal morbidity
- Often delayed diagnosis
  - No vaginal bleeding
  - Blood necrotic to placenta
- Poor outcome when fetal bradycardia present
- Emergency cesarean section if viable fetus
- Abruptio and placental insufficiency
- Large and recurrent abruptions
- Serial US necessary
- Look for intramural growths restriction
- Oligohydramnios
- Codd Doppler
  - Look for 1 systolic/diastolic ratio

Treatment
- Expectant management
  - Usually self-limited process
- Vaginal delivery in stable patients
- Cesarean section in acute distress
- Early delivery if placental insufficiency

DIAGNOSTIC CHECKLIST

Consider
- US for abruption in all presentations > 20 wks and vaginal bleeding
- Retroplacental abruption & acutely tender uterus with or without vaginal bleeding

Image Interpretation Pearls
- Use power Doppler in cases of placental thickening
- Evaluate fetal heart rate when abruption seen
- Rule out abruption in all women involved in motor vehicle accident
- Perform US even if no maternal injuries

SELECTED REFERENCES

PLACENTAL ABRUPTION

IMAGE GALLERY

**Typical**

[Images showing typical ultrasound scans of placental abruption.]

**Left**: Axial ultrasound shows an acute placental abruption. The placenta appears heterogeneous and thickened (open arrows). Placental blood flow is difficult to assess. Color Doppler imaging should always be performed in this situation.

**Right**: Axial ultrasound in the same case, performed 1 week later, now shows a hyperechoic blood clot (arrow) beneath the placenta (open arrows). With time, blood becomes more hyperechoic, and finally anechoic.

**Typical**

[Images showing additional typical ultrasound scans.]

**Left**: Sagittal color Doppler ultrasound shows periplacental hemorrhage. A complex fluid collection (arrow) is seen along the fetal surface of the placenta. The hematoma is adjacent to, but does not compress, the cord insertion site (open arrow).

**Right**: Clinical photograph shows a large peripartal hematoma (arrow) located near the cord insertion.

**Typical**

[Images showing more typical ultrasound scans.]

**Left**: Sagittal ultrasound shows an anechoic, acute hematoma (arrow) adjacent to an intact, and attached placenta (curved arrow). Sometimes, the hematoma is located at a distance from the placenta.

**Right**: Sagittal ultrasound performed 1 week later, shows the hematoma has thickened inferiorly and now covers the internal cervical os (fattened arrow). Also, the blood is now almost sonoluent.
**TERMINOLOGY**

**Abbreviations and Synonyms**
- Succenturiate lobe (SL)
- Accessory placenta

**Definitions**
- 1 or more accessory placental lobes
- Separated from main placenta
- Connected by placental vessels

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue: Two separate placetas seen on routine ultrasound
- Location: Anywhere in uterus, including previa
- Size: SL is smaller than primary lobe

**Ultrasoundographic Findings**
- Gray scale ultrasound
  - Two separate placental masses
  - SL has same echogenicity as main placenta
  - SL diagnosis often missed
  - Uterus not completely scanned
  - SL may be low-lying or cross internal os
  - Transvaginal ultrasound (TVUS) necessary

**Imaging Recommendations**
- Best imaging tool
  - Gray scale ultrasound to identify accessory placenta
  - Color Doppler to identify communicating vessels
  - TVUS
- Rule out SL previa
- With Doppler to rule out vasa previa
- Protocol advice:
  - View entire uterus before assigning placental location
  - TVUS and color Doppler US for all SL cases
  - Rule out vasa previa and velamentous CI

**DDx: Extraplacental Uterine Echogenicity**

- Acute Abortion
- Acute Abortion
- Contraction
- Contraction
Succenturiate Lobe

Key Facts

Terminology
- 1 or more accessory placental lobes
- Connected by placental vessels

Imaging Findings
- Size: SL is smaller than primary lobe
- SL may be low-lying or cross internal os
- SL is most common cause of vasa previa
- View entire uterus before assigning placental location
- Rule out vasa previa and velamentous CI

Top Differential Diagnoses
- Acute placental abruption
- Fetal myometrial contraction

Clinical Issues
- Increased risk for retained placenta

Diagnostic Checklist
- Use color Doppler to rule out complications of SL
- 1 Risk for cord rupture during labor
- 1 Risk for intrauterine growth restriction

Differential Diagnosis

Acute placental abruption
- Acute blood isochoic to placenta
- Color Doppler shows no flow in hematoma

Local myometrial contraction
- Distorts inner myometrium more than outer
- Can mimic succenturiate lobe
- Often more hypoechoic than placenta
- Resolves with time

Pathology

General features
- Echotexture
  - Trophoblast
  - Placenta grows in areas with good decidual
  - Atrophy occurs in areas of poor vascularity
  - Fetal vessels connect main placenta and SL
  - More susceptible to injury
- Placental CI may extend velamentous or marginal
- CI marks original implantation site
- Epidural/ligament: 5% of pregnancies
- Associated abnormalities
  - Velamentous cord
  - Vasa previa
  - Vasa previa

Clinic Issues

Presentation
- Most common signs/symptoms: Usually an incidental finding on routine ultrasound
- Other signs/symptoms
- Second or third trimester vaginal bleeding
- SL, previa
- Vasa previa

Natural History & Prognosis
- Increased risk for retained placenta
- Postpartum hemorrhage
- Postpartum infection
- SL + vasa previa
- 50-80% fetal mortality if not diagnosed prenatally

Selected References

Image Gallery

(Left) Sagittal ultrasound shows an intramural succenturiate lobe (arrows). In addition, the larger posterior placenta (curved arrows) & lying below it appears to have divided the uterine cavity in the internal cervical os.
(Right) Sagittal endovaginal ultrasound with Doppler, performed late in the pregnancy, shows vasa previa. Total internal bleed due to occlusion within the vessel that communicates between the two placental lobes.
CIRCUMVALLATE PLACENTA

TERMINOLOGY

Abbreviations and Synonyms
- Circumvallate placenta
- Circummarginate placenta
- Extrachorial placenta

Definitions
- Placenta membranes attach to fetal surface of placenta
  - Membranes normally attach to villous margin
- Circumvallate placenta
  - Placenta margin elevated along with membranes
- Circummarginate placenta
  - Placenta margin not deformed
  - Only membranes involved
  - Usually not an ultrasound diagnosis

IMAGING FINDINGS

General Features
- Best diagnostic clue: Margin of placenta is elevated off uterine wall
- Location: Complete or partial margin elevation

Ultrasoundographic Findings
- Everted placental margin
  - Infolding margin is towards cord insertion site

DIFFERENTIAL DIAGNOSIS

Synchia (amniotic sheets)
- Caused by uterine scar
  - 2-3 mm bands or sheets
  - Often seen triangular attachment point
  - Attach to uterine wall, not placenta
  - Placenta may abort or adhere to synchia

DDx: Uterine Bands/Membranes

- Synchia
- Synchia
- Amniotic Bands
- Uterine Septum
CIRCUMVALLATE PLACENTA

Imaging Findings
- Elevated placental margin
- Peripheral echogenic rim
- Short bands of tissue
- Shelf-like ruffles on placenta
- >2/3 margin involvement more likely symptomatic

Top Differential Diagnoses
- Synchia (amniotic sheets)
- Amniotic bands

Key Facts
Pathology
- Discrepant size between chorion and basal plates
- If placental tissue involved then circumvallate
- If only membranous then circummarginate
- Circumvallate: 1-2% pregnancies

Diagnostic Checklist
- When intrauterine membrane seen, look carefully at attachment points

Amniotic bands
- 2nd to amniotic membrane rupture
- Amnion entraps fetus
- Fetal malformations
- Amputation, body wall defects

Septate uterus
- Uterine duplication anomaly
- Septum in fundus
- Placenta may implant on septum

PATHOLOGY

General Features
- Etiology
  - Discrepant size between chorion and basal plates
  - Results in raised membranes (chorion and amnion)
  - If placental tissue involved then circumvallate
  - If only membranous then circummarginate
- Epidemiology
  - Circumvallate: 1-2% pregnancies
  - Circummarginate: 20% pregnancies
- Associated abnormalities: Placental hemorrage

Cross Pathologic & Surgical Features
- Pale yellow to white peripheral ring
- Complete ring vs. partial ring
- Flexobial degeneration of villi between membranes
- Occurs later in pregnancy

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - Pathologic diagnosis after delivery most often
  - Incidental finding during ultrasound
- Other signs/symptoms
  - Vaginal bleeding
  - PROM
  - IUGR
  - Preterm labor/delivery

Natural History & Prognosis
- Usually excellent prognosis when partial

DIAGNOSTIC CHECKLIST

Consider
- Follow-up ultrasound for fetal growth when >2/3 of margin involved

Image Interpretation Pearls
- When intrauterine membrane seen, look carefully at attachment points
  - Circumvallate placenta if membranes attach only on placenta ("marginal shelf")
  - Synchia if membranes attach to uterine wall
  - Amniotic bands if membranes attach to fetus

SELECTED REFERENCES

IMAGE GALLERY

(Left) Sagittal ultrasound shows the lifted placental margin (arrow).
(Right) Axial color Doppler ultrasound in the same case shows a placental "marginal shelf" (arrow). The short bands of tissue attach on the placenta, not the uterus, and therefore can be differentiated from synchia.
BATTLEDORE PLACENTA

TERMINOLOGY

Abbreviations and Synonyms
- Marginal placental cord insertion
- Eccentric cord insertion

Definitions
- Battlefied placenta: Umbilical cord inserts within 2 cm of placental edge
  - All subsequent branching vessels within placenta
  - No submembranous vessels
  - Battlefied means rascnaut
  - Battlefied was a precursor gait to badminton

IMAGING FINDINGS

General Features
- Best diagnostic clue: Color Doppler shows cord insertion site within 2 cm of placental edge
- Morphology: Placenta often thicker than usual

Ultrasound Findings
- Case study ultrasound to first find placental cord insertion (PCI)
  - More difficult if >39 weeks
  - Color Doppler confirms: marginal PCI
  - Cord insertion within 2 cm of placental edge

DIFFERENTIAL DIAGNOSIS

Velamentous cord insertion
- Umbilical cord inserts upon membranes not placenta
  - Incidence of 1:100
  - Submembranous vessels are extremely fragile
  - Risk of poor outcome compared with marginal PCI

DOB: Eccentric Cord Insertion.
BATTLEDORE PLACENTA

**Key Facts**

- **Terminology**
  - Battledore placenta: Umbilical cord inserts within 2 cm of placental edge

- **Imaging Findings**
  - Branching vessels seen on fetal surface
  - Marginal PCI may rarely evolve into velamentous cord
  - Scan 360° around PCI

- **Incidence**
  - 1 Incidence of intrauterine growth restriction (IUGR)
  - 1 Incidence of preterm labor
  - 1 Incidence of monoamniotic twin complications
  - 13x 1 risk for twin-twin transfusion
  - 1 Incidence of cord rupture at delivery

- **Adjacent cord**
  - Free loop of cord adjacent to placental surface
  - No branching vessels with color Doppler
  - Find true PCI

**PATHOLOGY**

**General Features**
- Etiology
  - Trophoblastic results in shifting placenta
  - Cord insertion marks original implantation site
  - Parts of placenta grow while parts resorb
  - Cord insertion ends up marginal
  - Marginal PCI evolves into velamentous CI
  - Further resorption of placental margin
  - Fetal vessels now subnervous
  - Epidemiology: 2-10% marginal PCI at delivery
  - Associated abnormalities
    - Monoamniotic twins
    - 1 Mortality if velamentous cord
    - Single umbilical artery (SUA)
      - 1% SUA with marginal PCI
      - 9% SUA with velamentous CI

**Gross Pathologic & Surgical Features**
- "Heart-shaped placenta"
- Placenta partially split where cord inserts

**CLINICAL ISSUES**

**Presentation**
- Most common signs/symptoms
  - Incidentally noted during routine ultrasound
  - 1 Incidence in monoamniotic twin

**Natural History & Prognosis**
- Excellent prognosis when isolated
  - No increased likelihood of IUGR or preterm labor
  - May progress to velamentous cord

**Treatment**
- Usually none necessary

**Top Differential Diagnoses**
- Velamentous cord insertion
- Adjacent cord

**Pathology**
- Epidemiology: 2-10% marginal PCI at delivery

**Clinical Issues**
- 1 Incidence in monoamniotic twins
- No increased likelihood of IUGR or preterm labor

**DIAGNOSTIC CHECKLIST**

**Consider**
- Document cord insertion site in high-risk pregnancies
  - IUGR, monoamniotic twins, placenta previa
  - Rule out vasa previa and velamentous cord

**Image Interpretation Pearls**
- Look for velamentous vessels at time of diagnosis
- Follow-up ultrasound
  - Assess evolution into velamentous cord

**SELECTED REFERENCES**

**IMAGE GALLERY**

*Left* Axial ultrasound shows marginal cord insertion (occasionally noted during a second trimester ultrasound. The cord appears to insert upon the placental edge (arrows). *Right* Axial color Doppler ultrasound in the same case proves that the CI is marginal. All branching vessels were within the placenta. Since velamentous CI can evolve from marginal placental CI, follow-up ultrasound is indicated.
PLACENTOMEGALY

Imaging Findings

General Features
- Best diagnostic clue: Placenta thickness > 4 cm
- Location: More common with lateral placenta
- Morphology
  - Normal morphology but thick
  - Often with subplacental vili
  - Small placental attachment area
- Ultrasonographic Findings
  - Exclude myometrium in placentation measurement
  - Measure from subplacental vili to amniotic fluid junction
- Placenta thickness correlates with menstrual age
- 1 mm/wk growth considered normal (placental thickness roughly equal to gestational age in wks)
  - 10 wk placenta = 10 mm
  - 20 wk placenta = 20 mm
  - 30 wk placenta = 30 mm
- Thick placenta

Terminology

Definitions
- Abnormally thick placenta

Ultrasoundographic Findings
- Thickness significantly > 1 mm/wk rule
- > 4 cm always considered abnormal
- Related to placental attachment area
- Subchondroceles common with placentomegaly
- Sonohysterograms rare < 20 wks
- Placental lakes
- Intervillosous thrombus
- Fibrin deposition and infarction
- "Jelly-like" placental variant
  - Thick heterogeneous placenta
  - Fascial echogenicity
  - Subcortical spaces
  - Quivers with jelly with abdominal pressure
- 60-75% have IUGR
- 1 association with Siderosis
- 2 3 related to abnormal fibrinolysis
- Placentomegaly is nonspecific diagnosis
- Seen with maternal and fetal disorders
  - F 2 Risk for placental insufficiency regardless of cause
  - Intrauterine growth restriction (IUGR)
  - Doppler waveforms often abnormal
  - Umbilical artery (UA) resistance
  - M 4 Myocardial arterial (MCA) resistance
  - Maternal uterine artery resistance
  - Abnormal ductus venosus flow
  - Often associated with fetal macrosomia
  - Often in diabetic patients
PLACENTOMEGALY

Key Facts
- Best diagnostic clue: Placenta thickness > 4 cm
- 1 mm/wk growth considered normal (placental thickness roughly equal to gestational age in weeks)
- "Jelly-like" placental variant
- Placenta thickness is nonspecific diagnosis
- Seen with maternal fetal disorders
- ↑ Risk for placental insufficiency regardless of cause
- Also associated with fetal macrosomia

Top Differential Diagnoses
- Placental abruption
- Subplacental myoma
- Gestational trophoblastic neoplasia (GTN)

Clinical Issues
- Early delivery may be necessary for IUGR

Diagnostic Checklist
- Exclude myometrium in measurements

Imaging Recommendations
- Best imaging tool
  - Routine evaluation of placenta
  - Doppler of fetal-placental circulation helpful
  - Protocol advice
  - Measure placenta if noticeably thick
  - Careful fetal growth assessment

Differential Diagnosis
- Placental abruption
  - Acute retroplacental abruption
  - Isoeicotic blood mimics placenta
  - Doppler helpful
  - Differentiate hematoma from placenta
- Subplacental myoma
  - Placenta implants upon myoma
  - Myoma often hypechoic to placenta
  - Placenta appears focally thick
- Gestational trophoblastic neoplasia (GTN)
  - Diffuse cystic placenta
  - Complete mole without fetus
  - Triplobly with abnormal fetus

Pathological Features
- Etiology
  - Abnormal trophoblast invasion of spiral arteries
  - 2° compensatory hypertrophy
  - Areas without defective invasion grow thicker
- Most thick placentas weigh < 10th percentile after delivery
- Refracts fact that many have small attachment area so overall volume of placenta is small
- Does not apply to thick placenta in setting of hydrops
- Epidemiology: L-8%
- Associated abnormalities
  - Hydrops from any cause
  - Maternal hypertension, anemia, diabetes
- Placental infection
  - Intrauterine infection
- Beckwith-Wiedemann syndrome

Clinical Issues
- Natural History & Prognosis
  - Depends on associated findings
- Treatment
  - Early delivery may be necessary for IUGR

Diagnostic Checklist
- Consider
  - Careful evaluation of fetal-placental circulation
- Image Interpretation Pearls
  - Do not confuse subplacental focal myometrial contraction for placenta
  - Exclude myometrium in measurements

SELECTED REFERENCES

IMAGE GALLERY

1. Sagittal ultrasound shows a markedly thickened, echogenic placenta (arrow) in a pregnancy complicated by fetal hydrops. Placenta thickness in this case is secondary to placental edema. (Fig 190)  
2. Abscess in the same case shows severe skin edema (arrow) and cystic hygroma (open arrow) in this syndrome-like fetus. Placenta is often over with hydrops, regardless of cause.
PLACENTA ACCRETA SPECTRUM

TERMINOLOGY

Definitions
- Abnormal penetration of placental tissue beyond endometrial lining of uterus
- Three variants of the spectrum collectively termed “placenta accreta”
  - Placenta accreta vera (80%)
    - Attaches to myometrium without muscular invasion
  - Placenta increta (15%)
    - Chorionic villi invade the myometrium
  - Placenta percreta (5%)
    - Perforation of chorionic villi through uterus
    - May also invade rectum and bladder

IMAGING FINDINGS

General Features
- Best diagnostic clue
  - Loss of subplacental hypoechoic zone
  - Irregular placental vascular lacunae

Ultrasoundographic Findings
- Normal subplacental hypoechoic zone (“clear space”)
  - Comprised of decidua basalis and myometrium
  - Should be present over entire placental surface
- First visualized in week 12
- Decreased visualization in anterior placentas
  - Clear space may be lost in near field
- Use high-resolution transducer if placenta acrreta
- Normal bladder mucosa is highly echogenic reflector
- Findings associated with placental invasion
  - Placenta previa in almost all cases
  - 5% of placenta previa cases will have associated accreta
- Loss of subplacental hypoechoic zone
  - High false positive rate if the sign used in isolation
- Thinning of subplacental hypoechoic zone ≤ 2 mm
- “Swiss cheese” or “moth-eaten” placenta
  - Multiple, hypoechoic placental vascular lacunae
  - Better positive predictive value than loss of “clear space”
  - Seen as early as 15 weeks
- Intermittent bladder wall-entering interface
  - More specific but less sensitive sign
- Aneretic myometrium thinner than anterior
  - Best seen in early pregnancy
- Endovaginal ultrasound to better evaluate if placenta previa present
- Findings associated with placenta percreta
  - Loss of bladder mucosal reflector

DDx: Placental Abnormalities

Placenta Previa
Placenta Previa
Placental Lacunae
Molar Pregnancy
**Terminology**
- Abnormal penetration of placental tissue beyond endometrial lining of uterus
- Placenta accreta vera (80%)
- Placenta increta (15%)
- Placenta percreta (5%)

**Imaging Findings**
- Loss of subplacental hypoechoic zone
- Irregular placental vascular lumen
- Placenta previa in almost all cases
- Large vessels extending through myometrium +/- into bladder
- MRI and US: Poor predictive value for all types (better for percreta)
- Can progress from accreta to percreta

**Key Facts**
- Large vessels extending through myometrium +/- into bladder
- Exophytic or nodular mass extending through bladder wall
- Rarely gastric ulcer may penetrate through myometrium as well

**MR Findings**
- 3T MRI:
  - Loss of normal low signal myometrium
  - Extension of intermediate signal placental tissue beyond uterine margin
  - Loss of fat planes between uterus/pelvic organs
  - Gadolinium enhancement:
    - Gadolinium crosses placenta
    - Generally avoided in pregnancy
  - Proponents argue risk/benefit ratio acceptable in life-threatening condition
  - MR technique:
    - Place pelvic coil so that optimal coverage is in lower uterine segment/bladder interface
    - Most accurate occurs low over site of cesarean section scar
    - May require body coil for fundal/posterior placenta
    - Bladder full to better evaluate for invasion
    - Consider sphincter as vaginal contrast
    - Angled scan planes to best evaluate placenta/uterine/bladder interface
    - Fast scan techniques avoid fetal motion artifact

**Imaging Recommendations**
- MRI and US: Poor predictive value for all types (better for percreta)
- Sensitivity MRI 30%, US 33%
- Must have high index of suspicion in at-risk patient
- Use high resolution linear transducer to assess abdominal wall, myometrial thickness
- Better resolution of near-field hypoechoic zone
- Use endovaginal ultrasound for previa/uterine incision
- Send ultrasound scans
- Can progress from accreta to percreta
- MRI better for posterior placenta in at-risk patient

**Differential Diagnosis**
- Uncomplicated placenta previa
- Intrauterine implantation of villi from decidual cells
- Decidual hyperplasia
- Decidual polyps

**Pathology**
- 5% of patients with placenta previa have accreta
- Present in 10% of patients with > 4 cesarean sections and/or previa
- Present in 67% of patients with placenta previa and > 4 cesarean sections

**Clinical Issues**
- High morbidity from hemostasis
- Management for wound care scenario
- Cesarean section with hysterotomy
- Consider delivery of infant only (placenta left in uterus)

**Pathology**
- General Features
  - General pathologies
  - Abnormal placentation may predispose to bleeding diatheses
  - Disseminated intravascular coagulation
  - Pulmonary and cerebral embolization of trophoblastic tissue during section
  - Site at risk for abnormal placentation
  - Uterine scars (cesarean section most common)
  - Submucosal fibroid
  - Lower uterine segment
  - Rudimentary horn
  - Uterine cornua
- Etiology
  - Deficiency of decidua basalis
  - Prior uterine instrumentation or surgery

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**PLACENTA ACCRETA SPECTRUM**

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**Differential Diagnosis**

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**Pathology**

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**Clinical Issues**

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**Pathology**

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PLACENTA ACCRETA SPECTRUM

- Multiparity
- History of manual placental extraction
- Endometriosis
- Advanced maternal age
- Usually several risk factors are present
- Epidemiology
  - 1:1,000 to 3,000
  - Variability largely based on cesarean section rates
  - 5% of patients with placenta previa have accreta
  - Prior cesarean section and accreta
  - Present in 10% of patients with > 4 cesarean sections and no previa
  - Present in 67% of patients with placenta previa and > 4 cesarean sections
  - Risk higher if cesarean section occurred prior to onset of labor
  - Increased incidence with advanced maternal age

Microscopic Features
- Decidua basalis replaced with loose connective tissue
- Chorionic villi penetrate/misove myometrium

CLINICAL ISSUES

Presentation
- Classical presentation
- Uncontrollable hemorrhage in 3rd stage of labor
- Placenta previa
- Must do a directed careful search
- Endometriosis as may progress
- First trimester low sac position < 10 weeks = increase suspicion
- Maternal terum alpha-fetoprotein may be elevated

Natural History & Prognosis
- Risk of bleeding high, even if spontaneous abortion or intrauterine demise
- Placenta fails to separate after fetus delivered
- Uncontrollable hemorrhage described at dilatation and curettage
- Significant risk maternal and fetal demise
- High morbidity from hemorrhage
  - 99% require transfusion
  - 46% > 10 units
  - 28% post-operative infection
  - 7% mortality
  - 15% uterine rupture with placenta percreta
  - Can occur as early as 10 weeks

Treatment
- Increased awareness = active search in patients at-risk
  - Careful monitoring in 2nd and 3rd trimester
  - Pre-operative planning
  - Pre-operative storage of blood products
  - Manage as worst case scenario
  - Consider hospitalization from 30 weeks
  - Deliver by 34-35 weeks
  - Hysterectomy complications increase markedly > 36 weeks
  - Cesarean section with hysterectomy
- Most common indication of pretibial hysterectomy
- Consider delivery of infant only (placenta left in uterus)

- Post-operative chemotherapy
- Methotrexate
- Post-operative embolization
- Delayed hysterectomy theoretically safer than at time of delivery
- Seduction in uterine blood flow
- At risk for postpartum hemorrhage
- Consider pre-operative placement of arterial occlusion catheters
- Amniotic fluid: reports of effective control of bleeding
- Additional bursts on standby for bladder/uterine focal invasion or injury

DIAGNOSTIC CHECKLIST

Consider
- Careful attention to placenta and uterine wall in the trimester in at-risk patient
- Endovascular ultrasound on placenta previa or asisk patient
- MR if posterior placenta or ultrasound inconclusive

Image Interpretation Pearls
- Have high index of suspicion for accreta in setting of placenta previa or prior cesarean section with placental implantation over scar
- Very high suspicion if both are present

SELECTED REFERENCES
1. Rich SE et al. Recent advances in the management of placenta previa. Curr Opin Obstet Gynecol. 16:54-64, 2004
(Left) Sagittal ultrasound shows placenta previa with loss of the subplacental hyperechoic zone in a case of placenta accreta. The placental margin obscures the echogenic bladder reflection (arrows). (Right) Transvaginal ultrasound in a case of placenta shows multiple large, irregular vascular lesions, giving the placenta a "swiss cheese" appearance.

(Left) Sagittal T1W MR in a case of placenta previa shows obvious placental invasion into the bladder (arrows). (Right) Intraoperative photograph shows a different case of placenta percreta shows rectal irregularity (open arrow) at the site of placental invasion. Note the dramatically dilated blood vessels (arrows) on the surface of the uterus. Serum and potentiometically catastrophic hemorrhage is a significant risk in the placenta accreta spectrum.

(Left) Sagittal T2W MR in a case of placenta previa (curved arrow) shows a thin but intact uterine wall (arrows). Although this excludes precesion, accreta/percreta cannot be ruled out. (Right) Hysteroscopy was performed over the lesion and the intact uterus scanned. The thin end wall subsidence to the placenta (arrows) is thinned but intact. Pathology shows a placenta increta. A leaf shaped hematoma (curved arrow) also seen.
CHORIOANGIOMA

TERMNOLOGY

Abbreviations and Synonyms
- Chorioangioma
- Placental hemangioma

Definitions
- Benign, vascular placental tumor
  - Most common placental tumor

IMAGING FINDINGS

General Features
- Best diagnostic clue: Hypoechoic, vascular placental mass
- Location
  - Most common on fetal side of placenta, near cord insertion
  - Less common location
    - Maternal surface, replacing a bleb
    - Pedunculated mass surrounded by membranes
    - May involve umbilical cord
- Size
  - Majority are small and incidentally noted at delivery
  - Most < 5 cm
  - Those > 5 cm more likely to be diagnosed prenatally

DDx: Placental Masses
- Umbilicoma
- Preplacental Abruption
- Teratoma
- Teratomat

Morphology
- Encapsulated masses
- Usually solitary but may be multiple (chorioangiomatosis)

Gray symptographic Findings
- Generally hypoechoic
- May be more heterogeneous if areas of hemorrhage, infarction or degeneration with hyaline deposition
- Well-defined
- Infrequently calcify

Color Dopples
- Essential for making diagnosis
- Amount of flow in mass is quite variable
- Greater arterial flow increases risk of developing hydrops
- Flow through mass is from fetal circulation
- At risk for high-out cardiac failure and hydrops
- May see increased flow around mass even if mass itself is hypovascular

3D
- Vascularity may be better defined
- Useful for helping to differentiate from other masses

MR Findings
- Not necessary for diagnosis
CHORIOANGIOMA

**Terminology**
- Placental hemangioma
- Benign, vascular placental tumor

**Imaging Findings**
- Most common on fetal side of placenta, near cord insertion
- Generally hypechoic
- Well-defined
- > 5 cm more likely to have complications
- Vascularity may be more important than size for predicting outcome
- Polyhydramnios common with large masses
- Hydrops from arteriovenous shunting or from fetal anemia secondary to hemolysis

**Key Facts**

**Top Differential Diagnoses**
- Venous lakes
- Intervillous thrombi
- Placental abruption/hemorrhage
- Submucosal fibroid

**Pathology**
- Most from in women > 30 yrs

**Clinical Issues**
- Most often diagnosed after 20 weeks
- Excellent prognosis without hydrops
- Generally no treatment necessary
- Antihypertensive for polyhydramnios
- Consider intervention for impending fetal hydrops

- Consider performing for large masses prior to intervention
- TIWI
  - Intense to placenta
  - May have high signal rim from hemorrhage

- T2WI
  - Heterogeneous, high signal intensity
  - May have low signal rim from hemorrhage

**Imaging Recommendations**
- Measure mass
  - < 5 cm unlikely to have complications
  - > 5 cm more likely to have complications
  - Described in up to 50% of cases

- Document vascularity
  - Vascularity may be more important than size for predicting outcome
  - Vascularity may either increase or decrease as gestation progresses

- Follow every 2-3 weeks for size, vascularity and fetal assessment

- Evaluate for complications
  - Polyhydramnios common with large masses
  - Etiology uncertain but may be transudate from risky tumor vessels, compressed venous return from masses by umbilical cord or association with fetal hydrops

- Hydrops from arteriovenous shunting or from fetal anemia secondary to hemolysis

- Initial hypertrophic cardiomyopathy → dilated cardiomyopathy from progressive cardiac decompensation
  - Pleural effusion
  - Pericardial effusion
  - Ascites
  - Skin thickening
  - Fetal anemia
  - Hemolysis of red blood cells
  - Evaluate flow in middle cerebral artery to determine need for transfusion
  - Interauterine growth restriction

**DIFFERENTIAL DIAGNOSIS**

**Venous lakes**
- Look for subtle motion
  - Feeling venous blood
  - Changing patient position may make more obvious
  - Flow too slow to be seen with Doppler
  - Better seen with grayscale

**Intervillous thrombi**
- No flow
  - Surrounded by normal placental parenchyma
  - Does not change placental contours

**Placental abruption/hemorrhage**
- No flow with Doppler
  - Will evolve over time

**Submucosal fibroid**
- Uterine wall mass

**Teratoma (rare)**
- Arises between amnion and chorion
  - Heterogeneous mass with cystic and solid components
  - Calcifications may be present

**Gestational trophoblastic disease**
- Complete hydatidiform mole
  - No fetus
  - Heterogeneous, cystic endometrial mass
  - Tripegaly
  - Three complete sets of chromosomes
  - Fetus is abnormal
  - Multiple anomalies
  - Severe growth restriction
  - Placental appearance varies according to extra set of chromosomes
  - Large and cystic if extra set is paternal (dandy)
  - Normal or small if extra set is maternal (diploidy)
  - Invasive mole/choriocarcinoma
  - Placental invasion into myometrium or metastatic disease

12 35
CHORIOANGIOMA

Placental metastases (rare)
- Malignant
  - Melanoma
  - May metastasize to liver
  - Breast, lymphoma
- Fetal
  - Neuroblastoma
- Large masses
- Hydrocephalus usually present

PATHOLOGY

General Features
- Biology
  - Unclear
  - Not seen in first trimester abortuses so unlikely from defective villous angiogenesis
  - Acquired lesion later in pregnancy
- Epidemiology
  - 0.6-1% of placentas at delivery
  - Most too small to visualize by ultrasound
  - Many microscopic
  - Most found in women > 30 yrs
  - Fetuses are more often female (72% in one study)
  - More common in women living at higher elevation
- Associated abnormalities
  - Fetal hemangiomas
  - Cutaneous and live
  - Beckwith-Wiedemann syndrome
  - Single umbilical artery

Gross Pathologic & Surgical Features
- Encapsulated, firm masses
- Color varies from people-red to tan depending on cellular makeup

Microscopic Features
- 3 types
  - Angioblastic
  - Nuclear to blood vessels
- Other foci may cause complications
- Cellular
  - Compacted endothelial cells
- Few vessels
- Degenerated
  - Myxoid and hyaline deposition
  - Mass will become more echogenic and less vascular by US

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - Incidental finding
  - Not often diagnosed after 20 weeks
- Other signs/symptoms
  - Large masses
  - Elevated maternal serum alpha-fetoprotein
  - Polyhydramnios
  - Breech, fetal hydrops
  - Preterm labor
- Likely from polyhydramnios but does not explain all cases
  - Rarely, preeclampsia reported

Natural History & Prognosis
- Excellent prognosis without hydrops
- Poorer if hydrops present
  - At risk for perinatal death

Treatment
- Generally no treatment necessary
- Amniocentesis or polyhydramnios
  - Reduce likelihood of premature delivery
- Consider intervention for impending fetal hydrops
  - Termination for amniocentesis
  - Vesel ligation, laser coagulation, alcohol injection and microlid embolization all described
- Variable results

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls
- Always evaluate placental masses with Doppler
  - Close follow-up is size and vascularity may change with advancing gestation

SELECTED REFERENCES

CHORIOANGIOMA

IMAGE GALLERY

Typical (Left) Color Doppler ultrasound shows a well-defined, varioculated, hyperechoic mass (arrow) on the false surface of the placenta. This is the typical appearance of a chorioangioma. There are often hyperechoic areas (open arrow), which could represent other smaller masses. (Right) Gross pathology from a different case shows small chorioangiomas (arrow) on the placental surface.

Typical (Left) Ultrasound shows a large mass (arrow) within the placenta. It has a well-defined rim and mild internal heterogeneity. Despite its large size, there was little flow within the mass and the pregnancy was uncomplicated. (Right) Gross pathology shows the chorioangioma (open arrow) extending almost the entire thickness of the placenta. The yellow areas (arrows) represent regions of infarction and hyaline degeneration.

Variant (Left) Pulse Doppler ultrasound of a well-perfused, hyperechoic, placental mass shows both arterial and venous flow. (Right) Ultrasound of the same mass shows that it is covered by a membrane (arrow). The mass shows the gross appearance at delivery. Pathology confirmed a petechialized chorioangioma.
COMPLETE HYDATIDIFORM MOLE

**TERMINOLOGY**

**Abbreviations and Synonyms**
- Complete hydatidiform mole (CHM)
- Complete mole
- Classic mole
- Molar pregnancy
- Gestational trophoblastic neoplasia

**Definitions**
- Most common type of gestational trophoblastic neoplasia
- Proliferative growth of trophoblastic tissue
- May become invasive and metastasize
  - Invasive mole
  - Choriovectoma

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue
  - Enlarged uterus with "swiss cheese" endometrium
  - "Swarmworm" older term used before technology was capable of discerning individual cysts
  - Bilateral complex ovarian cysts
  - Theca lutein cysts
  - No fetus or embryo

**DDx: Placental Cysts**

- Sondocencephaly
- Peucedanome
- Hydropic degen
- Biplicity

**Ultrasoundographic Findings**
- "Swiss cheese" endometrium
  - Heterogeneous, echogenic intrauterine mass
  - Hyperechoic + cystic elements
  - Completely fills uterine cavity
  - Individual cysts can be seen
  - Cyst size
  - Hydropic placenta
  - No embryo or fetus

- Doppler findings
  - Mass is vascular
  - Color Doppler easily shows flow
  - High-velocity, low-impedance flow
  - Normal resistance (RI) of 0.55
  - Normally uterine arcuate artery flow is low-velocity until 3rd trimester
  - Normal RI often > 0.66 if < 20 wks

- Ovarian theca lutein cysts
  - Bilateral multifocal cysts
  - Only in 50% of CHM

- Human chorionic gonadotropin (hCG) hormone
  - First trimester CHM

**Location**
- Intrauterine mass
- No myometrial invasion

**Size**: Variable-sized cysts
**COMPLET HYDATIDIFORM MOLE**

**Terminology**
- Most common type of gestational trophoblastic neoplasia

**Imaging Findings**
- Hypertrophic, cystic elements
- Cysts vary in size
- No embryo or fetus
- High-velocity, low impedance flow
- Ovarian stroma thickened cysts
- Only 50% with classic findings if < 13 wks
- 12-15% become invasive mole
- 5-40% become choriocarcinoma
- Look for signs of invasion

**Top Differential Diagnoses**
- Placenta hydropic degeneration

**Key Facts**
- Placental sonolucencies/pseudomole
- Triplody

**Pathology**
- 100% paternal genetic material
- 46,XX karyotype most common
- Recurrence risk 1-2%

**Clinical Issues**
- Vaginal bleeding
- Hypervisus
- F hCG levels
- Exondian prognosis

**Diagnostic Checklist**
- Normal hCG levels do not rule out CHM if < 13 wks
- CHM can look identical to amenorrheic pregnancy

**Imaging Recommendations**
- Look imaging tool: careful endometrial assessment in threatened abortion cases
- Protocol advice
  - Think of CHM in amenorrheic gestation
  - Look for cystic placenta
  - Use Doppler to evaluate flow
  - Send tissue for histology
  - Look for signs of invasion
  - Myometrial vascular cystic spaces

**DIFFERENTIAL DIAGNOSIS**

**Placental hydropic degeneration**
- Hydropic change without proliferation
- Seen after pregnancy failure
- Embryonic demise
- Amenorrheic gestation
- Can look identical to CHM
- Need histologic diagnosis
- Less vascular than CHM
- 1st trimester, 1st pregnancy
- Low hCG levels

**Placental sonolucencies/pseudomole**
- Often normal finding > 13 wks
- Placental hype
- Intravascular thrombus
- "Swiss cheese" variant mimics CHM
- Pseudomole
- Often with placental edema
- Associated with maternal/fetal anemia
- Permeability
- Intravenous growth restriction (IVGR)
- Not associated with hydrops

**Triplody**
- Three complete sets of chromosomes
- 2 paternal + 1 maternal (diploidy)
- Placenta is cystic
- Most likely to be encountered with CHM
COMPLETE HYDATIDIFORM MOLE

2 maternal + 1 paternal (diploid)
- Placenta normal or small
- Fetus is abnormal
  - Severe HUGR
  - Multiple anomalies
- Most differentiate from twin pregnancy with one CHM
  - Normal fetus + CHM

PATHOLOGY

General Features
- General path comments: Abnormal trophoblastic proliferation
- Genotype
  - 100% paternal genetic makeup
  - 46,XX karyotype most common
  - Sperm fertilizes ovum with inactive nucleus
  - Haploid sperm duplicates to diploid
  - Cell divider progresses
  - 47,XY karyotype
  - 22X + 22Y sperm fertilization
  - Ovary with inactive nucleus
  - Cell division progresses
- Embryology
  - Molar pregnancy
  - Autotrophic trophoblastic growth
  - Size of villi far as gestational progresses
  - Throca lacteal cysts
- Ovarian hyperstimulation by ↑ hCG
  - Only present in 20%
  - Rare < 13 wks
- Epidemiology
  - 0.5/1,000 in United States
  - 8,100 in Asia
  - Recurrence risk 1-2%

Gross Pathologic & Surgical Features
- Cystic villi
- Cluster of grapes
- No fetal tissue

Microscopic Features
- Trophoblastic hyperplasia
- Hydatid villi

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - Most CHM present in first trimester
  - Vaginal bleeding
  - May cause anemia
  - Rapid uterine enlargement
  - Hypervenous
  - ↑ hCG levels
  - hCG may not be elevated < 13 wks
  - Pre-eclampsia
  - Other signs/symptoms
  - Enlarged ovaries
  - Throat lobe cysts

Demographics
- Age
  - ↑ Risk with advanced maternal age (AMA)
  - ≥ 35 year old at time of delivery
  - Infertility: ↑ Risk for Asian women

Natural History & Prognosis
- Excellent prognosis
  - Evacuation often curable
  - Invasive disease may develop
  - Invasive mole in 12-15%
  - Chemotherapy in 5-8%
  - Excellent prognosis even with metastasis

Treatment
- Jason evacuation of mass
- Curettage or endometriosis
- Helps determine myometrial invasion
- Serial hCG levels
  - 1 year surveillance
  - Chemotherapy for invasive disease
  - Methotrexate
  - Actinomycin D
  - Ethoposide

DIAGNOSTIC CHECKLIST

Consider
- CHM with atypical embryonic gestation
- Rule out CHM when hCG levels are ↑
- Normal hCG levels do not rule out CHM if < 13 wks
- Careful evaluation for invasive disease
  - Color Doppler of myometrium
  - MRI

Image Interpretation Pearls
- Repeat imaging if hCG levels ↑ after treatment
- Ultrasound to look for myometrial vascular cysts
- MRI
- CHM can look identical to anemochorial pregnancy

SELECTED REFERENCES
COMPLETE HYDATIDIFORM MOLE

IMAGE GALLERY

Typical

(C) A coronal endovaginal ultrasound shows an enlarged uterine with acaulic cysts. The cysts cause a multipapillary appearance, and are often bilateral and are associated with high maternal serum hCG levels.

(Right) Clinical photograph shows bilateral enlarged ovaries (arrows) from theca lutein cysts. The ovaries are as large as the enlarged uterus. These lutein cysts are present in only 50% of CMH cases and are rarely seen before 13 wks gestation.

Typical

(C) Sagittal endovaginal ultrasound shows an anechoic gestational sac. Histology from the first trimester pregnancy was diagnostic of CMH. It is important to be aware, only 50% of 1st trimester CMH present with classic findings of a cystic mass. Consider performing Doppler, which would show high-velocity, low impedance flow. (Right) Ultrasound shows hemorrhage (arrows), a common finding, adjacent to a CMH (open arrows).

Variant

(Left) Axial ultrasound shows a normal fetus with a consistent ratio. The normal twin (open arrow) and placenta (curved arrow) are seen adjacent to a CMH (white arrows). A thick membrane (black arrow) separates the twin. (Right) Color Doppler ultrasound with pulsed Doppler shows the vascularity of CMH. Cystic vesicles (arrows), and vessels within the mass (curved arrows) show a high-velocity, low-impedance flow pattern.
INVASIVE MOLE

TERMINOLOGY

Abbreviations and Synonyms
- Invasive mole
- Choriocarcinoma destruens

Definitions
- Invasive gestational trophoblastic neoplasia
  - Often from complete hydatidiform mole (CHM)

IMAGING FINDINGS

General Features
- Best diagnostic clue: Echogenic cystic mass invading myometrium
  - Location
    - Local invasion
    - Metastasis possible
  - Invade uterine veins that carried elsewhere
  - Not same pathology as choriocarcinoma

Ultrasoundographic Findings
- Gray scale Ultrasound
  - Myometrial invasion by CHM
  - Echogenic cystic mass fills uterus
  - Mass extends into myometrium
  - Myometrial invasion in triplety

- Less common
  - Abnormal placenta + invasion + abnormal plus
  - Invasive mole after CHM or treble therapy
  - High human chorionic gonadotropin (hCG) levels
  - Focal heterogeneous myometrial mass
  - Imaging often negative if hCG < 700 mIU/mL

- Color Doppler
  - Cystic vascular mass
  - Resolves with treatment
  - Pulsed Doppler
    - High velocity, low-impedance flow
    - Lower resistive index (RI) than CHM
    - RI of 0.38 with invasive mole vs. 0.55 with CHM

MR Findings
- Myometrial mass
  - Heterogeneous intermediate signal
  - Disruption of uterine zonal anatomy on T2WI
  - Tumor enhances with gadolinium
  - Can assess depth of invasion

Imaging Recommendations
- Protocol advice
  - Transvaginal ultrasound to evaluate for myometrial invasion
  - Foci of invasive tumor "light up" with color Doppler
  - Negative ultrasound or MRI does not rule out invasive mole
  - Sensitivity is < 70%

DDx: Abnormal Placenta

Placenta

Invasive

Subplacental

Infiltrative
INVASIVE MOLE

Terminology
- Invasive gestational trophoblastic neoplasia
- Often from complete hydatidiform mole (CHM)

Imaging Findings
- Myometrial invasion by CHM
- Focal heterogeneous myometrial mass
- Foci of invasive tumor "light up" with color Doppler
- Negative ultrasound of MR does not rule out invasive mole

Key Facts
- Must follow hCG levels

DIFFERENTIAL DIAGNOSIS

Retained products of conception (RPOC)
- Heterogeneous material within endometrial cavity
- Never invades myometrium

Placenta accreta/percreta
- Normal placenta invades myometrium or beyond
- Associated with prior cesarean section
- Placenta previa often present

Subplacental myoma
- Heterogeneous myoma may mimic invasion

PATHOLOGY

General Features
- Genetics: Most often diploid (100% paternal genes)
- Endometriosis: CHM with 100% diploid trophoblasts, more likely to invade
- Epidemiology
  - 12-25% of CHM progress to invasive mole
  - Triploidy less common cause of invasive mole

Microscopic Features
- Trophoblast hyperplasia + hydriotic villi
- Invades myometrium or uterine vessels

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - 1 hCG levels despite treatment of CHM

Natural History & Prognosis
- Excellent prognosis with treatment
  - Cure rates of > 90%
- Bleeding can be life-threatening
- Embolization may be necessary
- Hysterectomy seldom necessary

Treatment
- Combination chemotherapy
  - Methotrexate + others
- Monitor hCG levels

Top Differential Diagnoses
- Retained products of conception (RPOC)
- Placenta accreta/percreta

Pathology
- 12-15% of CHM progress to invasive mole

Clinical Issues
- Excellent prognosis with treatment
- Combination chemotherapy

DIAGNOSTIC CHECKLIST

Consider
- Invasive mole or choriocarcinoma when hCG levels persist after treatment of CHM or triploidy

Image Interpretation Pearls
- Color Doppler helpful in identifying small foci of invasion

SELECTED REFERENCES

IMAGE GALLERY

(left) Sagittal color Doppler ultrasound of a small Uterus shows heterogeneous, vascular, trophoblastic tissue (arrows) with invasion into the myometrium (curved arrow). (Right) Sagittal T2W MR of the same case, shows a small Uterus with some heterogeneous trophoblastic tissue (arrows) and a large invasive component (curved arrow), within the uterine myometrium.
CHORIOCARCINOMA

TERMINEOLOGY

Definitions
- Malignant tumor from abnormal, proliferation of trophoblastic tissue
- Type of gestational trophoblastic neoplasia (GTN)
  - Benign GTN
  - Complete hydatidiform mole (CHM)
  - Triplody
  - Malignant GTN
  - Invasive mole
  - Choriocarcinoma

IMAGING FINDINGS

General features
- Best diagnostic clue: metastatic disease +/- uterine mass in patient with GTN
- Location
  - Local extension
  - Myometrial invasion
  - Parametrial extension
  - Distant metastases common
  - Size

DDx: Uterine Mass Associated With Pregnancy

- Invacive Mole
- Massive Heme
- RPOC
- TPOC

- Often very small
- 2-3 mm focus in uterus
- May not be detectable with imaging
- Size not related to presence of metastases

Ultrasonographc Findings
- Uterine findings quite variable
- There may be no detectable uterine mass
- Patient presents with metastases
- Small tumors common (< 3 mm)
- Heterogeneous intrauterine mass
  - Infiltrating heterogeneous mass
  - Often invading myometrium and beyond
  - Cystic areas from necrosis
  - Heterogeneity from hemorrhage
- Enlarged cystic ovaries (bilateral tubal cysts)
- 2 to 1 levels of human chorionic gonadotropin (HCG) hormone
- Color Doppler
  - Helpful for identifying site of myometrial invasion
  - Can not differentiate from invasive mole
- Pulsed Doppler
  - High-velocity, low-resistance flow
  - CC resistive indices lower than CHM
  - CC RI of 0.25 vs. 0.55 for CHM
  - Pulsed Doppler waveform similar to invasive mole

MR Findings
- T1WI: 1 Signal from hemorrhage
**CHORIOCARCINOMA**

**Terminology**
- Malignant tumor from abnormal proliferation of trophoblastic tissue
- Type of gestational trophoblastic neoplasia (GTN)

**Imaging Findings**
- Best diagnostic clue: Metastatic disease +/- uterine mass in patient with GTN
- Large, brain, liver metastases common
- Uterine findings quite variable
- There may be no detectable uterine mass
- Small tumors common (< 10 mm)
- Enlarged cystic ovaries (theca lutein cysts)
- Suspect choriocarcinoma if hCG after GTN or any pregnancy
- hCG < 700 mIU/mL often with negative imaging

**Key Facts**

**Top Differential Diagnoses**
- Retained products of conception (ROP)
- Invasive mole
- Other hemorrhagic brain metastases

**Pathology**
- 50% originate from molar pregnancy
- 25% occur after failed pregnancy
- 25% occur after normal pregnancy

**Clinical Issues**
- Resistant to HCG
- Symptoms from metastases
- Choriocarcinoma originating from CHM has best prognosis
- Near 100% cure with chemotherapy
- Hysterectomy necessary in 1/3

**DIFFERENTIAL Diagnosis**

**Retained products of conception (ROP)**
- Intrauterine tissue after normal delivery or abortion
- Most often present with excessive bleeding
- Hemorrhagic mass in endometrial cavity
  - Never invades myometrium
  - Low hCG levels compared to GTN

**Invasive mole**
- May look identical to choriocarcinoma
- Can metastasize
- Less aggressive tumor
  - Less hemorrhagic
  - Less necrotic
- Pathology often necessary to differentiate from choriocarcinoma
  - Hydroptic villi present
- Differentiation from choriocarcinoma often does not affect treatment
  - Multiple agent chemotherapy
  - Excellent prognosis

**Other hemorrhagic brain metastases**
- Melanoma
- Renal cell carcinoma
- Lung cancer
- None have f hCG levels

**PATHOLOGY**

**General Features**
- General path comments: Aggressive, necrotic, hemorrhagic tumor
- Genetics:
  - Aneuploidy common
  - Choriocarcinoma from CHM
  - Diploid
  - Exclusive paternal DNA
  - Choriocarcinoma from triploidy
  - Mixed DNA (maternal and paternal)
- Epitope
CHORIOCARCINOMA

- Genomic imbalance compared to benign GTN
  - 1 Oncogenes
  - 2 Tumor suppressor genes
- Epidemiology
  - CHM progresses to choriocarcinoma
  - Worldwide: 9% of CHM progress to choriocarcinoma
  - United States < 2% of CHM progress to choriocarcinoma
  - 50% originate from molar pregnancy
  - Usually from CHM
  - Uncommonly triploidy
  - 25% occur after failed pregnancy
  - Ectopic pregnancy
  - Spontaneous abortion
  - 25% occur after normal pregnancy
- Gross Pathologic & Surgical Features
  - Rapidly growing aggressive tumor
  - Extensive necrosis
  - Hemorrhage
  - Early vascular invasion common
- Microscopic Features
  - Sheets of syncytiotrophoblasts with anaplastic features
  - Cytotrophoblasts
  - Syncytiotrophoblasts
  - Minimal intermediate trophoblasts
  - No choriocarcinoma
  - Helps differentiate from other GTN
  - Triplody, CHM, invasive mole
- Staging, Grading or Classification Criteria
  - International Federation of Gynecology and Obstetrics (FIGO staging)
    - Stage 1: Confined to uterus
    - Stage 2: Limited to pelvis
    - Stage 3: Regional metastases
    - Stage 4: Metastatic
  - Prognostic scoring index subclassifies FIGO staging
    - If score is 4 or 7 then stage is A
    - If score is 8 then stage is B
  - Scoring index based on many factors
    - Maternal age (worse prognosis if > 40 yrs)
    - Prior pregnancy history
    - Choriocarcinoma following CHM with better prognosis than those following failed or normal pregnancy
    - Interval of time to start of chemotherapy
    - Longest time interval = Worse prognosis
    - HCG level > 100,000 IU/L with worse prognosis
    - Tumor size (> 5 cm with worse prognosis)
    - Site of metastases
    - Number of metastases (> 1 with worse prognosis)
    - Prior chemotherapy for treatment of CHM
    - Prior use of multiple agents with worse prognosis

CLINICAL ISSUES

Presentation
- Most common sign/symptoms
  - Persistent hCG
  - Most commonly occurs after treatment of CHM
  - Other signs/symptoms
  - Symptoms from metastases
  - Dyspnea
  - Cough
  - Headache
  - Seizure
  - Abdominal pain

Demographics
- Ethnicity: Low risk for GTN in Asian population

Natural History & Prognosis
- Choriocarcinoma originating from CHM has best prognosis
  - Near 100% cure with chemotherapy
  - 75% remission even with extensive metastatic disease
  - Poor prognostic scoring index

Treatment
- Multiple Chemotherapy agents
  - Methotrexate
  - Actinomycin D
  - Other agents
  - Hysterectomy necessary in > 73%
  - For cure in selected group
  - Extensive parametrial invasion
  - Non-responsive tumor
  - Secondary to bleeding
  - Embolization often attempted first

DIAGNOSTIC CHECKLIST

Consider
- Choriocarcinoma if 1 HCG levels after initial GTN treatment
  - Dilation and curettage of benign GTN
  - Choriocarcinoma diagnosis in young, parous female patients with hemorhagic brain lesions

Image Interpretation Pearls
- Negative pelvic ultrasound does not rule out CC

SELECTED REFERENCES
(Left) Sagittal ultrasound shows a normal uterus (arrow) and adnexa (endometriosis) in a patient with metastatic choriocarcinoma. She presented with abdominal pain and oligomenorrhea 3 months after a spontaneous abortion. She had extensive liver metastases and very high β-hCG levels. (Right) Endocavitary ultrasound examination of the ovaries showed bilateral enlargement with multiple, complex, echogenic cysts (arrows).

(Left) Axial CECT shows a pulmonary metastasis from choriocarcinoma. A large, lobulated mass (arrow) and pleural effusions (open arrow) are seen. (Right) Axial CECT shows multiple liver metastases (arrow). The lung and liver are the most common sites for metastasis. Both of these patients presented with symptoms from their metastases and had normal uterine ultrasonograms.

(Left) Axial NECT shows hemorrhagic brain metastases (arrow) in a patient 1 month after delivery of a normal baby. The patient presented acutely with confusion. (Right) Axial T2WI MR in another patient with metastatic choriocarcinoma shows a mass (arrow) with a fluid-fluid level (open arrow) and hemorrhexis (curved arrow) from hemorrhage. Significant subependymal edema is present in both cases.
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**DICHORIONIC DIAMNIOTIC TWINS**

**Graphic:** Dichorionic twins. There is a thick amniotic membrane (white arrow) composed of two thin layers of amnion (white line) and two thick layers of chorion (gray line). The placenta (black arrow) is separate.

**Endoscopic observation:** IVS in the first trimester shows two, thick, echogenic, chorionic sacs (arrows) each surrounding a gestation. The case illustrates the ease of determining chorionicity with TVS sonography.

**TERMINOLOGY**

**Abbreviations and Synonyms**
- Dichorionic diamniotic twins (DdT)
- Fraternal twins
- Non-identical twins if dizygotic (Dz)
- Identical twins if monozygotic (MZ)

**Definitions**
- Two fetuses in separate chorionic sacs
  - Two amniotic sacs
  - Two yolk sacs

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue
  - First trimester
  - Thick echogenic chorion completely surrounds each embryo
  - Second trimester
  - "Twins peak" sign: Wedge of chorionic plate extending into base of inter-twin membrane
  - Third trimester
  - Different gender is most specific sign of Dz twins
  - MZ twins will be same gender but may still be dichorionic

**Ultrasoundographic Findings**
- First trimester
  - Best time for determination of chorionicity and amnionicity
  - Thick echogenic chorion completely surrounds each sac
  - Two yolk sacs
  - Specific sign of diamniotic gestation
  - Dichorionic (DC) twins must be diamniotic
- Second trimester
  - Fetal genders may be different in Dz.
  - Will be same in MZ even when DC
  - Two placentas but may be difficult to prove
  - Adjacent implantation sites
  - Placental fusion
  - Late presentation
  - Thick/inter-twin membrane
  - Subjective
  - No finite measurement
  - All membranes look thin in third trimester
  - Count layers with high resolution transducers; 3+ 2 must be DC
  - "Twins pool" or Lambda sign
  - Chorionic tissue extends into inter-twin membrane at placenta
  - Chorion forms echogenic triangle

**DDx: Dichorionic Twins**

- Dichorionic
- Monochorionic
- Monoamniotic
- Amnionic

---

13

2
DICHORIONIC DIAMNIOTIC TWINS

Terminology
- Two fetuses in separate chorionic sacs

Imaging Findings
- Thick echogenic chorion completely surrounds each embryo
- "Twin peak" sign: Wedge of chorionic tissue extending into base of inter-twin membrane
- Different gender most specific sign of DZ twins
- Thick inter-twin membrane
- Growth restriction more common in multiples
- Serum screening less effective in multiples, therefore genetic sonogram assumes greater importance

Top Differential Diagnoses
- Monochorionic diamniotic twins (MDT)
- Monochorionic monoamniotic twins (MMT)

Key Facts
- Twins 1:900 pregnancies in USA
- Twins account for 10% perinatal morbidity and mortality (PM)

Pathology
- Twins are equal to singleton rate

Clinical Issues
- Age related risk of aneuploidy in MZ twins equal to singletons
- Age related risk of aneuploidy in DZ twins higher than singleton rate
- Maternal complications > singleton pregnancy

Diagnostic Checklist
- EV US in the first trimester is the best modality for determination of chorionicity and amnioticity
- Twin prognosis relates to chorionicity not zygosity

MR Findings
- May be of benefit to evaluate anomalies
  - Incidence of anomalies increased in twins
  - Acoustic access may be limited by co-twin

Imaging Recommendations
- Monitor growth
  - Growth restriction more common in multiples
  - Look for anomalies
  - 2-3 x more common in twins than singletons
  - Monozygotic 50% > dizygotic
  - Serum screening less effective in multiples, therefore genetic sonogram assumes greater importance
- Watch for signs of crowding
  - Clubfoot
  - Make sure amniotic fluid volume is symmetric
  - Amniotic fluid index (AFI) difficult in twins
- Use single deepest pocket
  - Sagittal scan plane
  - Transducer perpendicular to floor not maternal abdomen
- Consider cervical length measurement
  - Endovaginal (EV) transducer
  - Gentle technique - avoid compressing cervix
- Document shortest length
  - Prolonged scan period for dynamic changes
- Assess placental implantation sites
  - Increased risk of placenta previa
  - Increased risk vasa previa
  - Cervix vessels crossing the internal os
- Pulsed Doppler will differentiate fetal from maternal arterial vessels
- Can not reliably differentiate fetal from maternal veins

Differential Diagnosis
- Monochorionic diamniotic twins (MDT)
  - Must be same gender
  - Single placental mass
  - Thin inter-twin membrane
- Monochorionic monoamniotic twins (MMT)
  - Must be same gender
  - No inter-twin membrane
  - Cord entanglement

Pathology
- General Features
  - Genetics
    - Dizygotic twinning increased with maternal family history of twins
    - Paternal history not relevant
  - Embryology
    - Zygote divides within 3 days of conception
    - Complete duplication of cell lines
    - Two chorions
    - Two amnions
    - Two embryos
    - Later division of cell mass results in monochorionic (MC) twinning
  - Epidemiology
    - Twins
      - 70% are dizygotic
      - 30% are monozygotic
    - Of monozygotic twins
      - 10% DDT
      - 60-65% MDT
      - 5-10% MMT
      - < 1% conjoined
DICHORIONIC DIAMNIOTIC TWINS

- Twin 1:90 pregnancies in USA
- Twins account for 10% perinatal mortality and mortality (PMO)
- PIH monochorionic > dichorionic twins
- Assisted reproduction
- MZ twinning with assisted reproduction 3/8
  - Fetal population rate
- However most multiples with assisted reproduction are diagnostic
- Diagnostically:
  - 7-11 per 1,000 births in USA (geographic incidence varies)
  - Increased with maternal age
  - Increased with maternal parity
  - Increased with maternal family history
  - No increases with paternal family history
  - Rate varies with race
  - African-American > Caucasian > Asian
- Monochorionic twins
  - 4 per 1,000 births in USA
  - Rate independent of race/age/paternal

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - Size > dates
  - Hypertension gravidarum
- Other signs/symptoms
  - Hypertensive junctions may occur
  - Syndrome akin to hyperstimulation syndrome
  - Occurring in response to normal pregnancy
  - Bilateral (or both arms ± 1) may cause confusion with ovarian tumors
  - Presence of ascites/pleural effusion may further increase suspicion for neoplasm
  - Prenatal chorionic gonadotrophin (H-21C) may be dramatically elevated
  - H-21C levels cause confusion with gestational trophoblastic disease
  - Hyperglycemia = maternal and occasional fetal villitis
  - Almost always benign and self limited

Natural History & Prognosis
- Probability of delivering two live infants if normal US
  - 6 weeks
  - MC 39%, DC 75.8%
- Probability of delivering two live infants if normal US
  - At 12 weeks
  - MC 74.4%, DC 95.8%
- Age related risk of aneuploidy in MZ twins equal to singleton rate
- Age related risk of aneuploidy in DC twins higher than singleton rate
  - Risk of one fetus being affected: 2x singleton risk
  - Risk of both fetuses being affected: (Singleton risk)²
  - Maternal serum screening less reliable in multiples
  - DC twin loss rate within 4 weeks of annunciation > dust for singletons
  - 2.7% DC twins with aneconoeplasia
  - 0.6% control singletons with aneconoeplasia
- Maternal complications > singleton pregnancy
  - Hypertension
  - Preeclampsia
  - Antenatal hemorrhage
  - Placenta previa
  - Placental abruption
  - Other
  - Postpartum hemorrhage
- Perinatal mortality reported 10%
  - Preterm delivery
  - Median gestational age (GA) twins at delivery 36 weeks
  - Intranasal growth restriction
  - Anomalies

Treatment
- Monthly scans for growth
- Monitor fluid volume
- Deepen pocket for each twin
- Cervical measurements controversial
  - Preterm delivery increased in twin
  - Short cervix may be a predictor for preterm delivery
  - Dynamic cervix may be more sensitive than short
cervix length < 3.5 mm at 23 weeks identifies group at low-risk for preterm delivery
  - Impact on management unclear
  - No definitive therapeutic measures to prevent early delivery

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls
- LV US in the first trimester is the best modality for determination of chorionicity and amnionicity
- Twin pregnancy related to chorionicity not zygosity

SELECTED REFERENCES
DICHORIONIC DIAMNIOTIC TWINS

IMAGE GALLERY

(Left) Transabdominal ultrasound shows a thin amniotic membrane (arrow), which eventually fuses to the thicker chorionic membrane. An early "twin peak" sign (black arrow) and entero-enteral sites are also present. (Right) Transabdominal ultrasound (SA) shows a late first trimester pregnancy with a thick inter-twin membrane (arrows) composed of two layers of chorion. This amnion is not entirely resolved sequentially on SA scans.

(Left) Ultrasound shows the typical appearance of the "twin peak" sign. A triangle of echogenic tissue based on the placental surface (arrow) extends into the inter-twin membranes (curved arrow). (Right) Ultrasound shows the thick inter-twin membranes (arrows) with two clearly visible chorionic layers even in the second trimester. Fluid distribution is symmetric along the membranes.

(Left) Ultrasound shows a thick inter-twin membrane (arrow) meeting the placenta in a "T" configuration. Trimester-wise, thickening grades so had to be oligohydramnios. Absent "twin peak" does not exclude dichorionicity. (Right) Ultrasound shows two separate placentas (arrows) in second trimester DCM. Differentiating placentas becomes more difficult later in pregnancy. There is also a thick inter-twin membrane (curved arrow).
MONOCHORIONIC DIAMNIOTIC TWINS

Graphic of monochorionic diamniotic twins. A thin membrane forms from two layers of amnion (white arrow). There is a single chorionic sac (1st arrow) and single placenta (black arrow).

Endovaginal ultrasound shows a single chorionic sac with two amniotic and yolk sacs (black arrows) and amniotic fluid (white arrows). Note the ease of assessing chorionicity and amniocity in the 1st trimester.

TERMINOLOGY

Abbreviations and Synonyms
- Monochorionic diamniotic twins (MDT)
- Identical twins

Definitions
- Two fetuses in single chorionic sac
  - Two amniotic sacs
  - Two yolk sacs

IMAGING FINDINGS

General Features
- Best diagnostic clue
  - First trimester
  - Two yolk sacs in single chorionic sac
  - Second trimester
  - Thin inter-twin membrane

Ultrasoundographic Findings
- Grayscale Ultrasound
  - First trimester
  - Two yolk sacs (YS)
  - Number YS = number amniotic but YS easier to see early in gestation
  - Second trimester

MR Findings
- Use to evaluate brain injury
  - Intervention contraindicated if hypoxic brain injury already present
  - Intervention carries risk of subsequent brain injury
  - Manifests 10-14 days after injury
  - Intracranial hemorrhage
  - Encephalomalacia changes
  - Porencephalic cyst formation
  - May be helpful to clarify anomalies
  - Family may choose selective reduction
  - Intervention contraindicated if both fetuses anomalous

DDx: Monochorionic Diamniotic Twins
- Dichorionic Twins
- DDT Absent Twin Peak
- DDT Twin Peak
- Monoamniotic Twins
# MONOCHORIONIC DIAMNIOTIC TWINS

## Terminology
- Two fetuses in single chorionic sac
- Two amniotic sacs

## Imaging Findings
- Number YS = number amnions but YS easier to see early in gestation
- Single placental mass
- Twins must be same gender
- Thin inter-twin membrane
- Monochorionic twin anomaly rate 3-5x that of singletons or dichorionic twins

## Top Differential Diagnoses
- Dichorionic diamniotic twins (DDT)
- Monochorionic monoamniotic twins (MMT)

## Key Facts
- **Pathology**
  - MZ twins: 4,100 births in USA
  - 60% of MZ twins are monochorionic
- **Clinical Issues**
  - Perinatal mortality and mortality of MC twins 3-5x that of DC twins
  - Euploidies in twins depend on chorionicity not zygosity
  - Asympotic fluid discordance most important single predictor of poor outcome

## Imaging Recommendations
- Best imaging tool: EV scan in first trimester
- Evaluate nuchal translucency (NT) in first trimester: If abnormal
  - Increased risk of aneuploidy
  - Increased occurrence of twin-twin transfusion syndrome (TTTS)
  - Risk of TTTS particularly if ductus venosus flow also abnormal
- Look for anomalies
  - Monochorionic twin anomaly rate 3-5x that of singletons or dichorionic twins
  - Anencephaly
  - Holoprosencephaly
  - Hydrocephalus
  - Sacrococcygeal teratoma
- Consider fetal echocardiography
  - Prevalence congenital heart disease increase
- Attempt to identify placental cord insertion sites
  - Increased incidence of marginal cord insertion
  - Unequal placental sharing
  - Increased risk for discordant birth weights
  - Increased incidence of vasa previa
  - Fetal vessels cross internal os
  - Labor = vessels tear = fetal exsanguination
- Monitor growth
  - Growth restriction more common in multiples
  - Discordant growth
  - >20% difference in estimated fetal weight (EFW)
  - >20 mm difference in abdominal circumference (AC)
- By convention: “discordant” only used when one twin has intrauterine growth restriction (IUGR)
- If neither twin IUGR, use asymmetric/diaperate growth (terminology convention)
- Check for symmetric amniotic fluid volume
- Asymmetric distribution important sign of TTTS
- If discordant growth, smaller twin may have oligohydramnios
- Oligohydramnios in one sac may imply anomaly
- Look for specific complications of monochorionic twinning
  - TTTS
  - Twin reverse arterial perfusion sequence (TRAP)
  - Twin embolization syndrome (TES)

## Differential Diagnosis
### Dichorionic diamniotic twins (DDT)
- Fused placentas may appear as one
- Twin peak sign usually present
  - Best seen when US beam perpendicular to membranes
- Scan in multiple planes
- Inter-twin membrane thicker
- Inter-twin membrane composed of four layers
  - Chorion and amnion from each fetus
  - High resolution transducer may show multiple layers
  - Most useful in late presentation
- Fetal gender may differ in dizygotic twins

### Monochorionic monoamniotic twins (MMT)
- No inter-twin membrane
- Cord entanglement common
  - Cord entanglement can occur in diamniotic twins if inter-twin membrane ruptures

## Pathology
### General Features
- General path comments
  - Monochorionic (MC) placenta = vascular connections between fetuses: Risk of
    - TTTS
    - TRAP
  - Twin embolization syndrome
  - Twin demise = 50% necropsies
  - Embolization to live twin
MONOCHORIONIC DIAMNIOTIC TWINS

- Twin embolization syndrome: Current theory
  - Twin demise + loss of peripheral resistance
  - Vascular anastomoses between twins due to monochorionic placenta
  - Abdominal pressure + decreased cesarean section
  - Intrauterine hemorrhage
  - Renal insufficiency
  - Placental insufficiency

- Genetics: Risk anomaly in MZ equals singleton risk
  - Etiology
    - MOC, occurs when inner cell mass of blastocyst splits between 4th and 9th day post conception
    - Chromatin already formed
    - Divison equates in formation of two amnions and two embryos
    - Division after 8th day = monochorionic twins

- Epidemiology
  - MZ twins 4,100 births in USA
  - 60% of MZ twins are monochorionic
  - Rare of MZ twinning independent of:
    - Race
    - Maternal age
    - Family history
  - MZ twinning rate in assisted reproduction is 3.8x general population rate
  - Most malignacies in chemically induced pregnancies are also choriocarcinoma

CLINICAL ISSUES

Natural History & Prognosis
- Early demise (10-14 weeks) of one twin may occur
  - Described in 6% dichorionic (DC) twins
    - Generally no adverse impact on surviving twin
  - Described in 3% monochorionic twins
  - Early MC twin demise indicates poor prognosis
  - Spontaneous abortion occurred in all cases in one study
  - Perinatal morality and mortality of MC twin 3.5x that of DC twins
  - Relates to specific MC complications
  - Premature delivery

Treatment
- Monthly scans for growth and fluid
- Careful watch for complications:
  - Discordant disparate growth
  - Anomalies
  - TTS
  - TRAP
- Improved outcome with early diagnosis allowing for
  - Aggressive monitoring
  - Early hospitalization

DIAGNOSTIC CHECKLIST

Consider
- Check choriocytoma and amnioncysts in every multiple gestation
  - Always easier in early pregnancy
  - Prognosis in twins depends on chorionicity not zygosity

Image Interpretation Pearls
- In first trimester count yolk sacs per chorionic sac
- YS can be seen before amnion is visible
- Two YS implies two amnions
- Thin inter-erythrocyte membrane best sign after first trimester
- Check fetal gender
  - If different cannot be MC gestation
  - Amniotic fluid discordance most important single predictor of post outcome

SELECTED REFERENCES

MONOCHORIONIC DIADEMIOTIC TWINS

IMAGE GALLERY

Typical

(Left) Ultrasound of a twin gestation shows two membrane
features within a single
chorionic membrane. The
membrane is thin and often
difficult to identify in MDT. A
careful search is necessary to
detect a monochorionic
placenta. (Right) Ultrasound
of the same case shows a
thin membrane (arrow) inserting
directly onto a
single placenta (curved
arrow). The membrane is
composed of two layers of
amnion with no chorionic
tissue.

Typical

(Left) T2W MR shows a
single placenta (arrow), two
membranes, and a thin intertwin
membrane (curved arrow). This
tanent had TTTS and had undergone a
successful
laser ablation at another
center. (Right) Ultrasound
shows MDT gestation
complicated by TTTS. A
single placenta (curved
arrow) and thin amnion
membrane (arrow) can be
seen in MDT. Note the asymmetrical
fluid distribution about the
membrane.

Typical

(Left) Color Doppler
ultrasound shows one twin’s
cord inserting centrally onto a
single placental mass
(arrow). This is a MDT
pregnancy complicated by
unequal placental sharing
and growth discordance.
(Right) Color Doppler
ultrasound in the same case
shows the cord has a
marginal cord insertion
(arrow). Such unequal
placental sharing often
causes discordant growth as
in this case.
**MONOCHORIONIC MONOAMNIOTIC TWINS**

![Graphic of monoamniotic twins showing a single chorion (curved arrow), single amnion (short arrow) and single placenta. Note the cord origins are close and the cords are tangled (open arrow).](image)

**3D sagittal stage of a 10 week monochorionic monoamniotic twin gestation. Both embryos are easily identified (arrows) within a single sac. No intervening membrane was present.**

**TERMINOLOGY**

**Abbreviations and Synonyms**
- Monochorial monoamniotic twins (MMT)
- Identical twins

**Definitions**
- Two fetuses in single sac
  - Single chorion
  - Single amnion
  - Single yolk sac

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue
  - First trimester
    - Single yolk sac
  - Second trimester
    - Cord entanglement

**Ultrasonographic Findings**
- Grayscale Ultrasound
  - First trimester
    - Count yolk sacs (YS)
    - If single YS early, follow-up in one week

- Vascular Doppler
  - May reflect hemodynamic alterations in vessels narrowed by knot

**DDx: Monoamniotic Twins**

- Conjoined Twins
- "Stuck" Twin
- Membrane Rupture

- Single YS is a reliable predictor of monoamnioncity on endovaginal scans > 7 weeks
- Second trimester
  - No inter-twin membrane
  - Single placental mass
  - Same gender
  - Unofficial cord entanglement
    - Described as early as 10 weeks gestational age (GA)
    - Cord appears to branch
    - Mass of vessels with differing fetal heart rates
    - Side by side placental insertion may increase risk
  - Umbilical cord fusion
    - Each twin has cord
    - Cords fuse at short distance from placental insertion
    - Y-shaped or forked appearance
    - Not branching entanglement as seen with cord knot
  - Color Doppler
    - Majority of cases have cord entanglement
    - Apparent branching of cord vessels seen with color
    - Hard to differentiate knot from coils of single cord on grayscale imaging
  - Pulsed Doppler
    - End systolic notch in umbilical artery abnormal

MONOCHORIONIC MONOAMNIOTIC TWINS

Terminology
- Two fetuses in single sac

Imaging Findings
- Single yolk sac
- No inter-twin membrane
- Single placental mass
- Same gender
- Majority of cases have cord entanglement
- 3D is most accurate imaging method in early first trimester

Top Differential Diagnoses
- Conjoined twins
- Diaphragmatic twins with "absent" inter-twin membrane

Key Facts

Pathology
- < 1% of monozygotic twinning

Clinical Issues
- Cord entanglement described as early as 10 weeks
- High perinatal mortality (PNM)
- MMT rate yet account for significant percentage of twin pregnancies with bad outcome
- Consider selective termination for discordant major anomaly
- Timing and mode of delivery are controversial

Diagnostic Checklist
- Single YS at > 7 weeks GA on endovaginal sonogram is diagnostic
- Cord knot implies fetuses in same sac

- 3D
- 3D is most accurate imaging method in early first trimester
- Can exclude conjoined twins by 6 weeks GA

MR Findings
- Use to evaluate brain injury
- Intervention contraindicated if hypoxic brain injury already present
- Risk of hypoxia-penia during intervention with resultant fetal/renal injury
- Manifests 10-14 days after event
  - intracranial hemorrhage
  - Encephalochorial changes
  - Perinencephalic cyst formation
- May be very helpful to clarify anomalies
- Family may choose selective reduction
- Intervention contraindicated if both twins anomalous
- Influences mode of delivery

CT Findings
- Consider CT amniogram if sono graphic visualization is poor (e.g., maternal obesity)
- Single injection of contrast medium into amniotic fluid
- If contrast seen in both fetal stomachs must be monoamniotic gestation

Imaging Recommendations
- Count YS
- Number YS = number amnions
- YS easier to see than amniotic membrane
- Check fetal gender
- If different must be dizygotic twins
- Assess umbilical cord
- Insertion sites
- Entanglement
- Spectral analysis
- Careful search for anomalies
  - MMT higher discordance rate for anomalies
  - 25% discordant for major anomaly
  - Anomalies often lethal

- Renal agenesis particularly difficult
  - No oligohydramnios
  - Amniotic fluid produced by normal co-twin
  - Fetal adrenal may be mistaken for kidneys
  - Bladder should be seen to change in volume if normal urine production

- Evaluate for twin-twin transfusion syndrome (TTTS)
  - Polyhydramnios
  - Hydrops in one fetus
  - Small/absent bladder in other fetus
  - Donor oligohydramnios cannot be assessed
  - No inter-twin membrane
  - Amniotic fluid from normal twin surrounds both fetuses

DIFFERENTIAL DIAGNOSIS

Conjoined twins
- Contiguous skin covering at same anatomic plane
- Coils may be fused but do not appear izototted
  - Short segment cord fusion adjacent to placenta may be mildest presentation of conjoined twins

Diaphragmatic twins with "absent" inter-twin membrane
- Twin-twin transfusion syndrome
  - Recipient twin larger, polyhydramnios +/- hydrops
  - Donor twin smaller, in fixed position (stuck) twin
  - Cardiac activity present in "stuck" twin
  - Menopaust "shrink-wrapped" around fetus
  - Difficult to see = called absent
- Twin demise
  - Antihydramnios in sac of dead twin
  - Membrane closely applied to dead fetus
  - Difficult to see = called absent
  - Dead co-twin in fixed position with no cardiac activity
- Twin anomaly
  - Renal agenesis/sternebra in one twin
  - Premature rupture of membranes
  - Antihydramnios around presenting twin
MONOCHORIONIC MONOA-MONIOMIOTIC TWINS

- Intraterine membrane rupture
  - Failing to see membrane afte earlier documentation
- Infection
- Developmentally abnormal membrane
- Trauma
  - Serial amniocenteses for treatment of TTTS increases risk of membrane rupture

PATHOLOGY

General Features
- Epidemiology
  - < 1% of monochorionic twinning
  - Rare therefore rare incidence uncertain
  - May be up to 5% monochorionic twins
  - M:F
- Embryology
  - MMT occurs when embryo splits after 8th post conception day
  - Caution and caution already forming therefore new embryos develop within a single sac
  - Split in first 3 days → dichorionic diamniotic twins (DIT)
  - Split between 4th and 7th days → monochorionic diamniotic twins (MDT)
  - After 13th day → conjoined twins

Gross Pathologic & Surgical Features
- Cord insertion sites on, placenta closer than in MDT
  - Mean intersac distance 5 cm MMT
  - Mean cord diameter 17.5 mm MDT
- MMT placental vascular connections differ from MDT
  - MDT 100%, arterioarterial connections
  - Similar venous connections to MDT
  - Less opposing arteriovenous connections than MDT
  - TTTS less common in MMT than MDT

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - Cord entanglement described as early as 10 weeks
  - Absent inter-twin membrane

Natural History & Prognosis
- High perinatal mortality (PNM)
  - Reported PNM rates 26-68%
  - Highest rate (68%) in series with 1st trimester diagnosis
  - Outcome data from 2nd trimester diagnosis discounts early losses
  - MMT rate yet account for significant percentage of twin pregnancies with bad outcome
  - < 1% of monochorionic: twins are non-monomiotic
  - In a series of 86 twin deaths 20% were MMT
  - Factors influencing PNM
    - Prenatal
    - Growth restriction
    - Anomalies
    - Cord accidents
    - Vascular anomalies
  - Twin-twin transfusion
  - Less common than in MDT as more bilateral
  - Older data suggest twin survival rate
  - Modern management → double survival more likely

Treatment
- Monthly scans to assess
  - Growth
  - Fetal hydrates
  - TTTS
  - Consider selective termination for discordant major anomaly
  - Common excision contraindicates methods such as intracardiac photocoagulation
  - Must also transect cord to prevent entanglement
  - Harmonic scalpel: Simultaneous coagulation/cutting
  - Minimal invasive: One shot, US guidance
  - In case of twin demise
    - Increased risk of bilateral hypoxic injury in survivor
    - Immediate delivery does not prevent hypoxic brain damage
    - Adds risks of prematurity & existing risks of hypoxia
  - Intensive monitoring
    - Daily nonstress testing (NST) from 26 weeks
    - Increasing frequency of deprivations may herald serious cord compression
    - Continuous heart monitoring if variable deprivations increase in frequency or severity
    - Biophysical profile for nonreactive NST
  - Timing and mode of delivery are controversial
    - Elective delivery at 34 weeks after maternal corticosteroid administration or
    - Deliver at lung maturity
  - Cesarean section preferred to avoid cord accidents
  - Successful vaginal delivery described
  - At least one series shows no increase in complication with vaginal delivery

DIAGNOSTIC CHECKLIST

image Interpretation Pearls
- Single YS > 7 weeks G3 on endovaginal scan is diagnostic
- Cord knot implies fetuses in same sac

SELECTED REFERENCES
MONOCHORIONIC MONOAМИNIOTIC TWINS

IMAGE GALLERY

Typical

[Image: Ultrasound of a term twin pregnancy shows side-by-side placenta with side-by-side cord insertions (arrows). This increases risk for cord entanglement. Variolar vessels are also more likely. Right: Cross pathology shows term placenta with side-by-side cord insertions (white arrows). This increases the risk for cord entanglement. Note that the cords are untwisted but not knotted (curved arrows).]

Typical

[Image: Axial ultrasound shows twins in single sac with no inter-twin membranes. Note smaller size of lower twin due to discordant growth. Skin covering is not contiguous including the placenta (arrow). Right: CT angiogram of an aortic arch showing two separate aortic sacs. Note swallowed contrast within fetal stomach (arrow).]

Typical

[Image: Axial oblique color Doppler ultrasound shows cord entanglement. This is best appreciated by looking for a "branching" appearance of the umbilical vessels (arrow). Right: Cross pathology shows entangled umbilical cords. This results in thrombosis of one cord (arrow) and subsequent fetal demise. Cord accidents are a major contributing factor to the high perinatal mortality in MMT.]
**TERMINOLOGY**

- Twins of different sizes
  - By definition discordant only used when estimated fetal weight (EFW) of one twin < 10th percentile
  - If twins differ in size but both within normal range called asymmetric/dispansary twin growth
  - May occur in monochorionic or dichorionic pregnancies
  - Monochorionic more common

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue
  - Discordant growth
    - One twin with intrauterine growth restriction (IUGR) i.e. EFW < 10th percentile
    - Abdominal circumference (AC) difference > 20 mm
    - EFW difference > 20%

**Ultrasonographic Findings**
- Grayscale Ultrasound
  - Crown rump length disparity in first trimester predicts discordant birthweight

- Series dichorionic pregnancies with demise/anomalies excluded
- Crown rump length (CRL) difference > 3 days at 11-14 weeks gestational age (GA)
- Likelihood ratio of 5.9 for discordant birthweight
- Oligohydramnios about smaller twin
- Sign of placental insufficiency
- May also occur with anomaly or amnioloy
- Placental insufficiency/anomaly/amnionoly → impaired growth
- Twin-twin transfusion syndrome (TTTS, unlikely unless monochorionic twins and polyhydramnios around other fetus
- Color Doppler
  - Useful to assess for placental cord insertion site
  - Velamentous cord insertion associated with Ix increase in discordant birth weight
  - Marginal cord insertion increases suspicion for umbilical placental shaling
- Pulsed Doppler
  - Growth restriction may be secondary to abnormal resistance in maternal spiral arteries
  - Resistive index measured within 5 cm radius of placental cord insertion site
  - Greatest RI not seen in concordant twins or discordance in presence of TTTS
  - Systolic/diastolic (SD) ratio in umbilical artery (UA) may help to predict discordance

**DDx: Discordant Growth**

- Umbilical Cords TTS
- TTS Pre-Demise
- Demise 1st Trimester
- Demise 2nd Trimester
**Discordant Twin Growth**

**Terminology**
- Twins of different sizes
- By convention, discordant only used when estimated fetal weight (EFW) of one twin < 10th percentile
- If twins differ in size but both within normal range called asymmetric/dispansite twin growth
- May occur in monochorionic or dichorionic pregnancies

**Imaging Findings**
- Systolic/diastolic (SD) ratio in umbilical artery (UA) may help to predict discordance
- Velamentous cord insertion associated with 13x increase in discordant birth weight
- Discordant growth may result of anomalies or amnavorplacy in one fetus

### Key Facts
- Significant difference in SD ratio > 15% between twins
- 92% sensitivity for birthweight difference > 15%
- 70% specificity for birthweight difference > 15%
- Sensitivity and specificity similar to that of estimated fetal weight
- SD ratio difference > 0.4 between twins has also been used to predict discordance
- 75% sensitivity for birthweight difference > 25%
- 65% specificity for birthweight difference > 25%
- SD
- May be helpful to assess placental volume in early pregnancy
- If asymmetric placental volumes consider chorionic villus sampling
- May be indicator of trophoblast

**Imaging Recommendations**
- Protocol advice
  - Assess chorionicity and amnavorplacy in all multiple gestations
  - Look for unequal placental sharing
  - Where is the cord insertion site?
  - Marginal cord
  - Velamentous cord
  - Evaluate for post placentaion
  - Placenta implanted on septum/infold
  - Meticulous survey for anomalies
  - Discordant growth may be result of anomalies or amnavorplacy in one fetus

  - Use Doppler to monitor smaller fetus
  - SD ratios: UA > middle cerebral artery implies "hematogenic" effect
  - Reversal of absent end diastolic flow UA implies abnormal placental resistance
  - Reversed flow in distal venous implies cardiac decompensation
  - Pulmonary venous flow in umbilical vein implies impending heart failure
  - In multiple gestations measure SD ratio at abdominal cord insertion site for reproducibility

**Top Differential Diagnoses**
- Twin demise
- Twin-twin transfusion syndrome (TTTS)

**Clinical Issues**
- Discordant pairs have worse perinatal outcomes within each gestational age category
- Management decisions should not be based on EFW differences alone

**Diagnosis Checklist**
- Discordant twin growth may present as early as the first trimester
- Risk of neurologic impairment in discordant twins is at least as great as that in TTTS

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**Differential Diagnosis**

**Twin demise**
- Should be obvious, absent cardiac activity
- Anhydramnios
- Overlapping skull bones sono graphic equivalent of Spalding sign

**Twin-twin transfusion syndrome (TTTS)**
- Type specific complication of monochorionic twinning secondary to placental vasculature anastomosis
- Donor twin
  - Poor growth
  - Hypovolaemic
  - Anhydramnios
  - Recipient twin
  - Well grown
  - Placental
  - Polyhydramnios
  - May be hydropic

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**Pathology**

**Gross Pathologic & Surgical Features**
- Placental abnormalities
  - Immature villi, shortage of terminal villi
  - Focal areas with alterations and destruction of villi
  - Avascular villi
  - Massive perivillous fibrin deposition (maternal floor infarction)

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**Clinical Issues**

**Presentation**
- Most common sign/symptoms
  - Twin discordance described as early as first trimester
  - Most commonly presents late 2nd or early 3rd trimester
Natural History & Prognosis
- Multiple case reports of first trimester discordance persisting and deteriorating
  - Series of 2 twins with first trimester discordance 5 day difference CRL and live birth for both
  - Major anomalies in all smaller twins
  - Diaphragmatic hernia
  - Ventriculomegaly
  - Sphenenhydrocephaly
  - Critical aortic stenosis
  - Sacral agenesis
- Growth discordance does not correlate with late fetal death
  - 1.6% of 1.0ft twin gestations complicated by stillbirth of one or both fetuses
  - Only 15% of discordant twins were small for GA
- Discordant pairs have worse perinatal outcomes within each gestational age category
- Discordant monochorionic twins risk neurological impairment
  - 60% if co-twin demise
  - 42% if discordant
  - 37% if TTTS
- 8% risk neurological impairment in concordant monochorionic twins

Treatment
- Even first trimester discordance should be worked up
- Nuchal translucency measurements predict aneuploidy and risk for TTTS
- Offer genetic counseling +/- karyotype
- Chorionic villus sampling (CVS) allows earlier diagnosis of aneuploidy
- Selective termination easier to perform
- Risks of 2nd trimester amniocentesis higher in twins than singletons
  - Loss rate 2.7% in twins; following amniocentesis
  - Loss rate 0.6% in singletons following amniocentesis
- Selective termination for anomalies or aneuploid fetus
  - If MC placenta: consider a twin at risk for vascular compromise or neurological damage, even death
  - Radiofrequency ablation of cord vessels
  - Laser ablation of twin vessels
  - If monochorionic, cord transaction essential to prevent entanglement
- Fetal growth monitoring
  - Every 4 weeks for concordant twins
  - Discordant twins followed more frequently
  - Some authors suggest growth assessment every 2 weeks
  - Monitor twins with velamentous cord insertion closely
  - 13 fold increased risk of discordant birth weight
- Controversy surrounds ability to predict actual birthweight discordance accurately
- Management decisions should not be based on EFW differences alone
- Multiple factors in decision to deliver
  - BPD volume
  - Doppler measurements
  - Non-stress test
  - Biophysical profile

- With early onset discordant growth and deteriorating well being of small fetuses
  - Consider conservative non-intervention to avoid risks of preterm birth
  - Consider TTTS
  - Co-twin demise has no adverse sequel for survivor in dichorionic gestation

DIAGNOSTIC CHECKLIST
Consider
- Fetal MRI
- Clarify anomalies
- Evaluate placental relationship to uterine septa/fibroids

Image Interpretation Pearls
- Discordant twin growth may present as early as the first trimester
- Risk of neurologic impairment in discordant twin's at least as great as that in TTTS
- Twins may be discordant for anomalies as well as growth

SELECTED REFERENCES
**DISCORDANT TWIN GROWTH**

**IMAGE GALLERY**

- **Typical**
  - Growth curves for discordant twin, but otherwise normal, echogenic twins. The smaller twin has an L/S ratio < 4th percentile and a choriodecidual ridge. (Right) Photograph of the twins at one month of age. The smaller twin required initial tube feed but was otherwise normal. At 11 months, there is a 50% weight difference but both twins are healthy and developmentally normal.

- **Typical**
  - Transabdominal ultrasound shows discordant echogenic twins (arrow) at first trimester. Crown-rump length measurements were compatible with 10.2 and 11.3 weeks gestation. There is increased risk for discordant birth weight, as well as anomalies in smaller twin. (Right) TFM AR shows monochorionic twins discordant in size by L/S criteria. They are also discordant by umbilical cord with the smaller twin having multiple anomalies including a neural tube defect (arrow).

- **Typical**
  - Color Doppler ultrasound shows a marginal cord insertion (curved arrow) onto the placenta (arrow). The severity showed a size discrepancy of 4 weeks. (Right) Color Doppler ultrasound of the umbilical cord shows abnormal flow in the growth restricted twin (arrow A) with reversal of diastolic flow. The normally grown twin (arrow B) has a normal cord Doppler waveform and symmetrical ratio.
TWIN-TWIN TRANSFUSION SYNDROME

Graphic shows discordant twins with an arteriovenous shunt (arrow) on the placental surface. Deteroriated blood from the donor twin mixes with oxygenated blood returning to receive via the umbilical vein.

Ultrasound shows marked asymmetry of fluid distribution and discordant twin size. The membrane (white arrow) was closely adherent to the smaller "stuck" twin (black arrow) and could be easily missed.

TERMINOLOGY

Abbreviations and Synonyms
- Twin-twin transfusion syndrome (TTTS)
- Twin oligohydramnios polyhydramnios sequence (TOPS)

Definitions
- Monochorionic (MC) twinning
- Artery-to-vein anastomoses in placenta
- Donor twin party perfuses recipient twin

IMAGING FINDINGS

General Features
- Best diagnostic clue: Monochorionic twins with asymmetric fluid distribution and growth

Ultrasonographic Findings
- Grey-scale ultrasound
  - First trimester
    - Measure nuchal translucency (NT)
    - If abnormal consider evaluation of ductus venous (DV) flow
    - Abnormal NT + abnormal DV flow may predict cases most at risk for TTTS
  - Single placental mass
- Twins same gender
- Thin inter-twin membrane in monoamniotic diamniotic twins (MDT)
- Asymmetric distribution of fluid about inter-twin membrane
  - Polyhydramnios defined as deepest pocket ≥ 8 cm
  - Oligohydramnios defined as deepest pocket ≤ 2 cm
- "Stuck twin" describes severe oligohydramnios with a fixed position of smaller twin
- Twin growth usually asymmetric with ≥ 20% difference in estimated fetal weight
- Lesser degrees of discrepancy do not exclude diagnosis
- Severe discordance suggests unequal placental sharing or anomaly in smaller twin
- Echogenic bowel described as sign of hypoxia in donor
- TTTS can occur in monoamniotic monoamniotic twins (MMT)
  - Rarer than in MDT and harder to diagnose
  - Can't see asymmetry of fluid as no inter-twin membrane
  - Look for high output +/- hydrops in one twin
  - Absent bladder in other twin
  - Differential includes discordant anomalies
  - Look for shunt vessels on placenta with color Doppler to prove TTTS

DDx: Stuck Twin

Twin Devise
Renal Agenesis
IUGR-Oligohydramnios
ASPKD
TWIN-TWIN TRANSFUSION SYNDROME

Terminology
- Artery-to-vein anastomoses in placenta
- Donor twin partly perfuses recipient twin

Imaging Findings
- Best diagnostic clue: Monochorionic twins with asymmetric fluid distribution and growth
- Echogenic bowel described as sign of hypoxia in donor
- Congenital heart disease (CHD) more prevalent in TTTS than in uncomplicated MDT
  - Stage 1: Donor bladder visible, normal Doppler
  - Stage 2: Donor bladder empty, normal Doppler
  - Stage 3: Donor bladder empty, abnormal Doppler
  - Stage 4: Hydrops in recipient
  - Stage 5: Demise of one or both

Key Facts

Top Differential Diagnoses
- Premature rupture of membranes
- Twin demise
- Anomalous twin causing "stuck" appearance

Clinical Issues
- Progressive oligohydramnios of recipient twin
  - shrunken membranes which is difficult to detect
  - Initial diagnosis may be missed

Diagnostic Checklist
- Search carefully for oligohydramnios in apparent MMT
- Severe oligohydramnios of recipient twin
  - Meconium per amniotomy monitor membranes
  - Membrane rupture
  - Inter-twin membrane rupture creates functional monoamniotic state
  - Risk of cord accident
  - Increased morbidity and mortality
  - Fetal MRI after 36 weeks
  - Wait at least 1-2 days from intervention
    - If scanned too soon, significant pathology may be missed

MR Findings
- Used to confirm normal brain structure prior to intervention
- Follow for abnormal sequences of fetal vessels
  - Intracranial hemorrhage
  - External hydrocephalus
  - Fetal cephalocele

Imaging Recommendations
- Stage twin-twin transfusion syndrome (TTTS)
  - Stage 1: Donor bladder "visible, normal Doppler
  - Stage 2: Donor bladder empty, normal Doppler
  - Stage 3: Donor bladder empty, abnormal Doppler
  - Stage 4: Hydrops in recipient
  - Stage 5: Demise of one or both
- Fetal echocardiography for functional problems relating to TTTS in recipient
  - Cardiac enlargement
  - Tricuspid regurgitation
  - Impaired ventricular function
  - Biventricular hypertrophy
  - Right ventricular outflow tract obstruction
  - Described in as many as 9% recipients
- Donor twins without CHD have normal function

- Fetal echocardiography also important for detection of CHD: Increased in MDT with TTTS
- Recent reports of pulmonary artery calcification in recipient twins
  - May progress to pulmonary atresia
  - May require prenatal instrumentation or surgery

DIFFERENTIAL DIAGNOSIS

Premature rupture of membranes
- If known dichorionic pregnancy TTTS excluded
- Ask the patient: Gush of fluid or blood
- Test for leaking, fetal fibronectin
- Oligohydramnios usually before leading twin demise

Absence of twin demise in oligohydramnios can:
- Renal agenesis
- Sirenomelia
- Bilateral multicystic dysplastic kidneys
- Autosomal recessive polycystic kidney disease (ARPKD)
- Persistent urethral valves
- Severely intrauterine growth restriction of one twin

Twin demise will not have high-output state in any of these conditions
TWIN-TWIN TRANSFUSION SYNDROME

PATHOLOGY

General Features
- General pathology comments: Often marginal insertion of donor cord
- Pathology
  - 1 arteriovenous (AV) anastomoses within a monochorionic placenta
  - Unidirectional flow: Donor to recipient
  - Transfusion occurs within placental cotyledon
  - Vessels enter and leave cotyledon via common foramen
  - "Noose-to-nose" appearance different from non-twin paired vessels
  - "Noose-to-nose connections" readily seen at fetoscopy
  - Abnormal connection can be identified sonographically to guide selective laser coagulation
- Absence of bidirectional (as and from both fetuses) arterioarterial anastomoses
- Direct luminal contact on placental surface
- Found in most MC placentas
- Generally no need for shunt
- May be protective against TTTS: Compensate for unbalanced donor to recipient shunt in AV anastomosis
- Hormonal factors recently implicated in pathogenesis
  - Discordant renin angiotensin expression
  - Endothelin
  - Natriuretic peptide
  - Natriuretic peptide
  - Elevated brain levels in recipients correlate with severe cardiac dysfunction
  - Cardiac levels of NT do not correlate with cardiac function
  - Shunt leads to significant inter-twin hematocrit differences at cordocentesis
- Mean hemoglobin difference 4.8 g/dl (range 1.8-8.1 g/dl)
- Mean hematocrit difference 18.3%
- Epidemiology: Complicates 10-20% of monochorionic pregnancies
- Cardiac: Most functional changes resolve within 6 months

Treatment
- Stage TTTS at time of diagnosis
- Monitor closely
- Growth every three weeks
- Fluid volume weekly or more frequently
- Stage at diagnosis may not reliably predict outcome
- Deteriorating stage is associated with adverse outcome
- May precipitate aggressive management such as referral for laser coagulation
- United Kingdom approach
  - Serial amnioreduction/sequential for early stage disease
  - Laser coagulation of shunt vessels reserved for more severe cases
  - Risk procedure-related fetal loss
- USA: Multi-center study currently enrolling patients to determine
  - If fetoscopic laser coagulation = improved survival of twins with severe TTTS vs. serial amnioreduction
  - If fetoscopic laser coagulation = improved cardiac, neurological and developmental outcomes of twins with severe TTTS vs. serial amnioreduction
- Complex protocol requiring serial scans, Doppler echocardiography, and MRI

DIAGNOSTIC CHECKLIST

Consider
- Prenatal echocardiography
  - 50% of surviving recipient twins had persistent abnormalities > 28 days of life

Image Interpretation Pearls
- Search carefully for membrane in apparent MMT
  - Severe oligodynamism of recipient twin
  - "shrink-wrap" membrane which is difficult to detect
  - Mistaken diagnosis MMT
- Treatment and prognosis differ for MMT and TTTS
  - Therefore accurate diagnosis is important

SELECTED REFERENCES

TWIN-TWIN TRANSFUSION SYNDROME

IMAGE GALLERY

Typical

(Brilli Color Doppler ultrasound through the pelvis of a donor twin shows flow in the umbilical arteries. The bladder should be seen as a fluid-filled structure between these vessels. *Abbrev.* Brilli with normal Doppler at stage 2 TTS. (Right) Sagittal ultrasound shows skin thickening and fistulas forming indicating hemosiderosis of a recipient twin in the second trimester. (Brilli ultrasound stage 4 TTS.)

Typical

(Brilli Ultrasound of umbilical cords in a TTS case shows a marked difference in cord size. Circles demarcate the donor cord stained area which is almost one third the area of the recipient cord (white arrows). (Right) Pulsed Doppler ultrasound of the TTS shows reversed and diastolic flow in the donor twin. (Brilli confirmed within 5 days of this scan.) The recipient had a normal brain on a fetal MRI examination and was normal at birth.

Typical

(Brilli Axial ultrasound through the abdomen of a donor twin shows echogenic bowel (arrows) with echogenic mesentery at 24 weeks gestation secondary to intravascular hypoxia. (Right) Coronal ultrasound of the brain on day one of life shows severe cystic encephalomalacia (arrows), another wrinkle of intracranial hypoxia.)
TWIN REVERSED ARTERIAL PERFUSION

Graphic depicts a normal twin practicing an abnormal cord via artery (deoxygenated blood) to artery placental anastomosis (arrow). Abnormal circulation impairs development of left, heart and lung.

Ultrasound shows an acardiac twin with webs-formed lower extremities (white arrow) but no coiled structures (curved arrow). Note edema of feet (black arrow). The pump twin (open arrow) was structurally normal.

TERMINOLOGY

Abbreviations and Synonyms
- Twin reversed arterial perfusion (TRAP)
- Cardiac regression sequence
- Acardiac transfuse

Definitions
- Monochorionic placentation
- Anarteroarterial anastomosis in placenta
- Acardiac twin perfused by deoxygenated blood from "pump" twin
- Blood enters fetus via umbilical artery
  - Reversed perfusion: Oxygenated blood from placenta enters fetus via umbilical vein

IMAGING FINDINGS

General Features
- Best diagnostic clue: Flow in umbilical artery (UA) of abnormally twin is toward fetus

Ultrasoundographic Findings
- Gray-scale Ultrasound
  - Mass is monochorionic gestation
  - Single placental mass

DDx: Twin Reverse Arterial Perfusion

- Conjoined Twins
- Twin Decesed
- Cystic Hygroma
- Anencephalidy

- May be monoolsdonic or diamniotic
- Thin inter-twin membrane is diangnostic
  - Acardiac twin dysmorphic with edema and CEE formation in soft tissues
  - No cardiac structures or activity
  - Often no identifiable cerebral structures
  - Presence and structure of upper extremities extremely variable
  - Usually recognizable torso and lower extremities
  - Lower extremities move spontaneously
  - Single umbilical artery in 66% of acardiac twins
  - Polyhydramnios
  - Strong correlation with presence of renal tissue in acardiac twin
  - Increases risk for premature labor
  - Echocardiography of pump twin
    - At risk for hydrops secondary to high output state
    - Measure ratio heart to chest circumference (B/C/CC)
    - Myocardial thickening
    - Tripsapid regurgitation
  - Color Doppler
    - Occasionally single UA of acardiac twin connects directly to cord of pump twin
    - Beware "twinkle" artifact after injection
    - Color does not equal flow
  - Use pulsed Doppler to verify waveform
  - Pulsed Doppler
TWIN REVERSED ARTERIAL PERFUSION

Terminology
- Arterioarterial anastomosis in placenta
- Acardiac twin perfused by deoxygenated blood from "pump" twin

Imaging Findings
- Best diagnostic clue: Flow in umbilical artery (UA) of acardiac twin is toward fetus
- Must be monochorionic gestation
- Acardiac twin dysmorphic with edema and cyst formation in soft tissues
- Ratio of EFW of acardiac to pump twin > 70% confers bad prognosis

Top Differential Diagnoses
- Anomalous twin mimicking acardiac twin
- Conjoined twins

MR Findings
- May be used prior to intervention
  - Confirm normal brain in pump twin
  - Exclude anomalies in pump twin
- Post intervention used to monitor adverse effects on pump twin
  - Intracranial hemorrhage
  - Exontraventricular changes

Imaging Recommendations
- Careful search for anomalies of pump twin
- Monitor size of acardiac twin
  - Measure longest linear dimension
  - Weight in grams = \(1.66 \times \text{length} + 1.21 \times \text{length}^2\)
- Rapid growth of acardiac twin associated with poor prognosis
- Monitor growth of pump twin especially estimated fetal weight (EFW)
- Ratio of EFW of acardiac to pump twin > 70% confers bad prognosis
  - Prenatal delivery 90%
  - Polyhydramnios 40%
  - Pump twin hydrups 30%

DIFFERENTIAL DIAGNOSIS

Anomalous twin mimicking acardiac twin
- Anencephaly or obstructive process like amniotic bands
- Cardiac defects present

Key Facts
- Twin demise

Pathology
- Acardiac twin has no placental circulation; blood supply is from pump twin
- 1% of monochorionic pregnancies

Clinical Issues
- Acardiac twin anomalies are lethal
- Untreated reported pump twin mortality 50-75%
- Pump twin survival improves to 76% with intervention
- Intrateral radiofrequency (RF) ablation seems better than cord occlusion

Diagnostic Checklist
- You will never miss this diagnosis if you check direction of umbilical artery flow in anonomous twins

- Flow in umbilical artery away from fetus
- Cystic hygroma
- Normal nuchal and presence of cardiac activity

Conjoined twins
- Contiguous extenal skin contour
- Acardiac twin to separate from pump twin
- No inter-twin membrane
- Use with care: TRAP can occur in monoamniotic pregnancy

Twin demise
- Should be amniotomy and sac of dead twin if diastatic
- No flow in dead twin cord

PATHOLOGY

General Features
- Genetics
  - Not hereditary
  - No recurrence risk
- Etiology
  - Acardiac twin has no placental circulation; blood supply is from pump twin
  - Reverse perfusion from artery-to-artery placental anastomoses
  - Acardiac twin perfused with deoxygenated blood from pump twin
  - Reverse perfusion allows continued but abnormal development
  - Deoxygenated blood = arrested development in early embryogenesis
  - Deoxygenated blood = hypoxic damage to developing tissues
- Umbilical arteries = iliac arteries = selective perfusion of lower torso
- Upper body underdevelopment more apparent than lower
- "Fetal follows function": Absence of normal circulation impairs cardiac development
- Primary defect in cardiac embryogenesis
TWIN REVERSED ARTERIAL PERFUSION

- Alternate theory is that cardiac malformation is the primary event
- Does not explain associated structural abnormalities as well as reversed perfusion
- Epidemiology
  - 1% of monochorionic pregnancies
  - 1:35,000 births

Gross Pathologic & Surgical Features
- Broad spectrum of anomalies; 4 subtypes described
  - Acardiatus acardius
  - Commonest
  - Well-developed pelvis, lower extremities
  - Acardiatus acardius
  - Rudimentary cranial structures
  - No identifiable human features
  - Acardiatus acardius
  - absent
  - Heart develops without body
  - Pseudoacardiatus
  - Malformed twin with remnants of cardiac structures

CLINICAL ISSUES

Presentation
- Most common signs/symptoms: Grossly anomalous twin with no cardiac activity and reversed UA flow
- Described in first trimester
- Case reports of cardiac activity in both twins
- Subsequent loss of cardiac activity in one fetus
- Reverse perfusion allows continued but abnormal growth
- Cardiac development ceases after shunt flow directs perfusion to umbilical artery

Natural History & Prognosis
- Spontaneous closure of shunt vessels reported
- Acardiatus twin anomalies are lethal
- Unreported reported stump twin mortality 50-75%
- Mortality increases with
  - Hydrodrops
  - Polyhydramnios
  - Developed arms, ears, kidneys in acardiatus twin
  - Premature delivery
- Goal of intervention is to interrupt blood supply to acardiatus twin
  - Acardiatus twin ceases to grow
  - High output state for pump twin resolved
  - Pump twin survival improves to 76% with intervention
- Intrafetal radiofrequency (RF) ablation seems better than cord occlusion
- Late gestational age at delivery
- Longer interval from intervention to delivery
- Lower technical failure rate
- Lower rate prematurity rupture membranes
- Lower rate preterm labor

Treatment
- Offer termination
- Offer laryngectomy
  - 33% abnormal
- Trophicism commoner
- Usually associated structural anomalies seen
- Conservative noninterventional
  - Successful nontwins reported if
  - Acardiatus twin smaller than pump twin
  - Pump twin without signs cardiac compromise
  - No polyhydramnios
- Intervention indicated with
  - Impending hydrops in pump twin
  - Risk of extreme prematurity
  - Interventional techniques
  - Radiofrequency ablation of intrafetal umbilical artery
  - Color Doppler allows easy identification of vessels
  - No special expertise required as US guidance
  - Active treatment of additional interventions
- Endoscopic laser coagulation of shunt vessels in 4 weeks
- Fetoscopy more invasive
- Requires specialist expertise in tertiary referral center
- Technical issues limit performance to early pregnancy
  - Ligation of umbilical cord after 24 weeks
  - Endoscopic or ultrasonic guidance
  - Risk of inadvertent ligation of pump twin’s cord
  - Series of 16 cases with perinatal mortality 50% and preterm delivery 70%
  - Other reported treatments
  - Intrauterine alcohol ablation
  - Hydrometra with selective delivery of acardiatus twin
  - US-guided embolization of acardiatus umbilical artery
  - Indomethacin for polyhydramnios
  - Digoxin for hydrops

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls
- You will never miss this diagnosis if you check direction of umbilical artery flow in anomalous twins

SELECTED REFERENCES
TWIN REVERSED ARTERIAL PERfusion

IMAGE GALLERY

Typical

(Serif) Sagittal ultrasound at 16 weeks shows a twin (closed arrows). Upper (arrows) and lower (open arrows) with a soft tissue "mass" (open arrows) in lieu of normal cranium. (Right) Cross pathology of same case shows the lack of normal cranial structures. There is a mana (closed arrows) but neither nose nor orbits. Note excess skin folds secondary to edema (open arrows).

Typical

(Serif) Sagittal ultrasound shows massive edema (arrows) of an acardiac twin with cyst formation (curved arrows). Missing lower extremities were present but there were no upper extremities and no cranium. (Right) Color Doppler ultrasound at 34 weeks gestation shows umbilical artery flow from the normal pump twin (arrow) toward the abnormal, edematous acardiac twin (curved arrow).

Typical

(Serif) Axial ultrasound image through an acardiac twin chest shows massive edema of the torso (arrows). This is the same plane for the 4-chamber view but no cardiac structures are seen within the chest. (Right) Axial ultrasound shows cardioangiogly (arrow) in the pump twin. Progressive cardiomyopathy and focal regurgitation required intervention. RF ablation was successful with a term delivery of a normal twin.
CONJOINED TWINS

TERMINOLOGY

Abbreviations and Synonyms
- Conjoined twins
- Siamese twins
  - First Siamese twins "exhibited" in America in 1829
  - Chang and Eng born in Thailand, came to USA at age 18
- Lived long and productive lives despite being conjoined

Definitions
- Fetal fusion of variable degree
- Nomenclature
  - Site of fusion + suffix "pagus"
  - Thoracopagus: Fused at chest
  - Omphalopagus: Fused at umbilicus
  - Thora-co-epimphalopagus: Extensive chest and abdominal fusion
  - Pygopagus: Fused at buttocks
  - Ichtopagus: Fused at hips
  - Craniopagus: Fused at cranial level
  - Prefix "Di" + completely separate parts
  - Diplopagus: Conglomerate mass with two identifiable heads
  - Diprosopus: Conglomerate skull vault with two faces, variable extremities
  - Janiceps: Synonym for diprosopus

IMAGING FINDINGS

General Features
- Best diagnostic clue: Contiguous skin covering between fetuses

Ultrasoundographic Findings
- Grayscale Ultrasound
  - Fetuses inseparable
  - Monochorionic twinning
  - Single placental mass
  - No inter-twin membrane
  - Variable presentation does not exclude diagnosis
  - Fused tissue may be pliable, relative position not always constant
  - Often hypertelorism of cervical spine
  - Unusual limb positioning
  - Fused umbilical cord
  - 2 to 7 vessels
  - Omphalopagus
    - 80% share liver
    - 30% incidence congenital heart disease (CHD)
  - Thora-co-epimphalopagus
    - 90% share pericardium
    - 75% share heart
  - Fetal echocardiography
  - High incidence CHD
  - Cardiac anomaly may require emergent separation

DDx: Conjoined Twins

- Mono-amniotic twins
- Mono-chorionic twins
- Membrane rupture
- TDCR
# CONJOINED TWINS

## Terminology
- Fetal fusion of variable degree
- Thoracopagus: Fused at chest
- Omphalopagus: Fused ziphoid to umbilicus
- Thoraco-omphalopagus: Extensive chest and abdominal fusion
- Pygopagus: Fused at buttocks
- Ischiopagus: Fused at hips
- Dinealopagus: Cocog孻mate mass with two identifable heads
- Diprosopus: Conjoined skull vault with two faces, variable extremities

## Imaging Findings
- Fetuses inseparable
- Look for different heart rates

## Key Facts
- Better acoustic access in utero than post delivery
- Color Doppler
  - May be very helpful in craniopegus
  - Complete craniopegus implies shared brain substance
  - Verschieden coursed between brains
  - Precludes separation
  - Partial craniopegus when brains separate, cranial shared
  - Separate circulations
  - Separation can be attempted
  - Separation requires extensive reconstruction of cranial vault
- If arachnoids separate but shared dura
- Venous sinus anatomy determines feasibility of separation
- Color also very useful in evaluation liver blood supply
- Common portal vein precludes separation
- Evaluate number and orientation of hepatic veins
- M-mode
  - Look for different heart rates
  - Proves separate circulations
- 3D
  - Easier for parents to understand
  - Better surface views
- 2D and Doppler better to determine degree of organ sharing

## MR Findings
- Pre-surgical planning
  - Fetuses stable on placental support
  - No sedation required
  - Defines degree of organ sharing
  - T2WI excellent for brain/retail/chest detail
  - T1WI for additional bowel and liver information
  - Clarify anomalies
  - Either fetus may have lethal anomaly in addition to being conjoined
  - Information may influence management
- Termination of pregnancy
- Requirement for emergent separation
- Mode of delivery

## Top Differential Diagnoses
- Twin reverse arterial perfusion (TRAP)
- Monoamniotic twins

## Pathology
- 1:50,000 to 1:100,000 births

## Clinical Issues
- 40% stillborn
- 75% die within first 24 hours of life
- Ca utero intra partum treatment (EXIT) procedures can be planned if prior knowledge of need for emergent separation

## Diagnostic Checklist
- Must be contiguous skin covering for diagnosis conjoined twins

## CT Findings
- Reported use for confirmation in difficult cases
- MRI now preferred modality

## DIFFERENTIAL DIAGNOSIS

### Twin reverse arterial perfusion (TRAP)
- Umbilical arterial flow is toward abnormal fetus
- Acinar fetus has no cardiac activity
- Fetuses are separate in TRAP

### Monoamniotic twins
- Fetuses in same sac but no contiguous skin covering
- No inter-twin membrane
- Two cords
  - Cores may have common origin
  - Y shaped confluence close to placental insertion site
  - If cords are tied, vessels are entangled and appear branched
  - Conjoined twins inseparable so cannot tangle cords

## PATHOLOGY

### General Features
- General path comments
  - Embryology
    - Incomplete cleavage embryo 4-5 days after 13th post-conception day
    - Cell lines committed to amnion and chorion
    - Variable amount of embryonic development already complete
    - Non-duplicated structures shared
    - Duplication of some structures occurs after incomplete cleavage
  - Parasitic conjoined twins
  - Embryonic demise one twin of conjoined pair
  - Residual body parts of dead twin perfused by survivor
CONJOINED TWINS

- Clinopagus associated with complex cardiac malformation
- Omphalocoeus
  - Liver fusion common
  - Often unusual liver sharing
  - Biliary anomalies especially if shared
- Pygoepagus associated with common genitourinary malformations
  - <50% bined rectum
  - Imperforate anus
  - Rectoovaginal fistulae
  - Urogenital sinus

- Biology
  - Increased incidence in women with prolonged oral contraceptive use
  - Intrauterine growth restriction (especially in underweight women)
  - Abnormal calcium metabolism delays implantation
- Epidemiology
  - 1:50,000 to 1:100,000 births
  - Conopagus 12,500/900
  - 70% females

CLINICAL ISSUES

Presentation
- Can be diagnosed in first trimester
- May occur within higher order multiple gestation

Natural History & Prognosis
- Majority deliver prematurely
- 40% stillborn
- 75% die within first 24 hours of life
- If live to separation
  - 50% survive neonatal separation
  - 90% survive separation at >4 months of age
  - Bigger, stronger baby
  - Placement of skin expanders prior to definitive surgery
- Long term morbidity from associated defects
  - Unequal sharing of limbs
  - Incomplete pelvic girdle
  - Incomplete chest wall
  - Skene's duct reconstruction
  - Penile reconstruction
  - Vaginoplasty
  - Urethroplasty
  - Anoplasty
  - Spina bifida syndromes
  - Bilary atresia/sinusomes
- First successful separation reported in 1689

Treatment
- Offer termination
- If pregnancy continues
  - Fetal echocardiogram
  - Consider fetal MRI to assess degree of organ sharing
  - Delivery at tertiary center
  - Cesarean section required
  - Mechanical obstruction precludes vaginal delivery
- Cesarean section in third trimester requires "classical" (vertical) uterine incision
- Increased immediate maternal morbidity
- Longer recovery
- Increased risk of infection
- Increased risk in future pregnancies
- Urinary incontinence
- Recurrent aceta faeces
- Clinical-cancer section precludes vaginal delivery in subsequent pregnancy

Not an indication for early delivery
- Morbidity and mortality increase with low birth weight
- Problems of prematurity add to those of being conjoined

Separation requires multidisciplinary team
- Outcome improved in small series utilizing advanced imaging techniques
  - CT/MR/MRA
  - Basst study required for bowel sharing
  - Complex biliary anomalies are associated with duodenal fusion
  - Nuclear medicine studies may be misleading
  - Consider MRI with cholangiopancreatography (MRCP)
- Delayed separation preferred
- Emergent separation required if
  - One twin with rudimentary heart
  - Desire of one twin
  - Lethal anomaly of one twin
- tv utero intra partum treatment (EXIT) procedures can be performed if prior knowledge of need for emergent separation
- If lethal anomaly sacrificed twin may act as organ donor to survivor
- Huge ethical and legal dilemmas for parents and teams involved in care of conjoined twins

DIAGNOSTIC CHECKLIST

Consider
- Fetal MRI to evaluate degree of organ sharing

Image Interpretation Pearls
- Must be contiguous skin covering for diagnosis of conjoined twins
- Variable presentation does not exclude the diagnosis

SELECTED REFERENCES
CONJOINED TWINS

IMAGE GALLERY

Typical

(Center) General TTVX X-ray shows omphalopagus conjoined twins with a shared liver (arrow). The fetus on the maternal right has the larger share of the liver. These twins also had complex pelvicsson.

(Right) Axial ultrasound of different omphalopagus twins shows a fused liver (open arrows) in the midline. There are separate stomachs (arrows). Note contiguous skin cover between the fetuses.

Typical

(Left) Axial ultrasound of thoracopagus conjoined twins shows a common heart with three ventricular chambers (Y) and a common atrium (A). There are two spines (arrows). Viables died within minutes of delivery.

(Right) Axial TTVX MRI angiography study in the same case shows the single common atrium (arrow) and two of the three ventricles (the third was seen in a different scan plane). Note four arms (curved arrows) and two spines (open arrows).

Typical

(Left) Ultrasound shows the first trimester appearance of conjoined twins. Two embryos are delineated by cisterns; note a single yolk sac (arrow). The embryos were viable, and both were conjoined twins confirmed at follow-up.

(Right) Cross-pathology of identical conjoined twins shows two heads. One cranial is anencephalic (arrow) and the other has a cleft lip. Multiple anomalies are common with conjoined twins.
TRIPLETs AND BEYOND

Terminology

Abbreviations and Synonyms
- Triplets, quadruplets, quintuplets, sextuplets, etc.
- Higher order multiple gestation
- Multifetal pregnancy

Definitions
- Three or more fetuses
  - Separate or shared chorionic sac
  - Separate or shared amniotic sacs

Imaging Findings

Ultrasoundographic Findings
- First trimester
  - Count total number of yolk sacs per chorionic sac
  - Document presence or absence of intervening amniotic membrane in monochorionic pair
  - Measure crown rump length (CRL)
  - CRL discordance poor prognostic sign
  - Cardiac activity normal range > 120 beats per minute at 6 wk
  - Low heart rate is poor prognostic sign
  - Short interval follow-up indicated for viability
  - Measure nuchal translucency

- Second trimester
  - Twin vs. single intervening membranes
  - "Twin peal" or "lambda sign"
  - Chorionic tissue extends into intertwin membrane at placenta
  - Indicates dichorionic membrane
  - Anomaly screen

Imaging Recommendations
- Best imaging tool: Endovaginal ultrasound in 1st trimester
- Protocol advice
  - First trimester is a critical time in higher order multiples
  - Establish chorionicity
  - Number of embryos
  - Normal cardiac activity
  - Second trimester
  - Intervening membranes
  - Anomaly screen
  - Growth and amniotic fluid
  - Cervical length (baseline)
  - Third trimester
  - Growth and amniotic fluid

Ddx: Multiple Intrutene Sacs
- Twins
- Embryonic Diameters
- Large Hemorrhage
- Empty Sac
TRIPLETTS AND BEYOND

**Terminology**
- Higher order multiple gestation
- Multifetal pregnancy

**Imaging Findings**
- Count total number of yolk sacs per chorionic sac
- Document presence or absence of intervening amniotic membrane in monochorionic pair
- Measure crown rump length (CRL)
- CRL discordance poor prognostic sign
- Short interval follow-up indicated for viability
- Best imaging tool: Endovaginal ultrasound in 1st trimester

**Pathology**
- Majority of higher order multiples result of assisted reproduction
- Only about 20% of triplets are spontaneously conceived
- Increased incidence of all multiples with increasing maternal age
- Increased incidence of aneuploidy at lower maternal age when compared with singletons

**Clinical Issues**
- Associated with significantly increased maternal and fetal complications
- Risk increases with increasing number of fetuses
- Preterm delivery risk is significant
- Infant death rate in triplets and above is 12 times higher than singletons (94 vs. 8 per 1,000 live births)

**Diagnostic Checklist**
- Determination of chorionicity easiest in 1st trimester
- Recommendations to limit number of embryos transferred to limit multifetal gestations
  - Maternal age
  - Increased incidence of all multiples with increasing maternal age
  - 1/3 chance of multiple gestation over age 45
  - Other risk factors for spontaneous multiple gestation
  - Increased parity
  - Geographic location (Northeastern U.S., Nebraska)
  - Associated abnormalities
    - Increased incidence of aneuploidy at lower maternal age when compared with singletons
    - Increased incidence of sex chromosome abnormalities in ART pregnancies
    - Discordance for structural birth defects common

**Gross Pathologic & Surgical Features**
- Vascular communications common in monochorionic placentas
- Evidence of twin-twin transfusion (TTTS) in monochorionic pair
- Risk of unequal placental sharing increases with increased number of fetuses
- Abnormal cord insertions including velamentous cord
- Increased risk of vasa previa
- Fetal vessels cross internal os
- Evaluate cervix with color Doppler
- May lead to catastrophic fetal bleed and demise if unrecognized

**CLINICAL ISSUES**

**Presentation**
- Most common signs/symptoms: Multiple gestational ultrasounds in 1st trimester
- Other signs/symptoms: Vaginal spotting common, often with no ultrasound evidence of bleed

**Natural History & Prognosis**
- Associated with significantly increased maternal and fetal complications
- Risk increases with increasing number of fetuses

**Differential Diagnosis**
- Twins
  - Two fetuses
- Multifetal gestation with 1 or more demise(s)
  - Absent heartbeat
  - Sac shrivels over time
- Multifetal gestation with perigestational hemorrhage
  - No yolk sac or embryo
  - Resolves over time

**Pathology**

**General Features**
- Genetics
  - Maternal serum screening for aneuploidy limited in multifetal gestations
  - 1st trimester nuchal translucency has important role in screening for aneuploidy
  - Invasive prenatal diagnosis by amniocentesis
  - Chorionic villus sampling (CVS) available in some centers
- Epidemiology
  - Incidence of triplets or greater approximately 185 per 100,000 live births
  - Majority of higher order multiples result of assisted reproduction
  - 42% assisted reproductive technology (ART) including in vitro fertilization (IVF)
  - 38% ovulation induction medications such as Pergonal
  - Only about 20% of triplets are spontaneously conceived
• Maternal complications
  ○ 1st trimester bleeding
  ○ Hyperemesis gravidarum
  ○ Ovarian hyperstimulation syndrome
    ○ Dehydration, electrolyte abnormalities, effusions, need for hospitalization
  ○ Hyperstimulated ovaries may remain enlarged until mid-gestation
  ○ Preeclampsia risk increased at least 2 fold in ART pregnancies
  ○ Gestational diabetes
  ○ Anemia and malnutrition
  ○ Premature labor
  ○ Cesarean delivery required in most higher order multiples
    ○ Vaginal birth possible in concordantly grown triplets with cephalic presentations

• Fetal complications
  ○ Spontaneous reduction (embryonic demise) occurs up to 10% in 1st trimester
  ○ Discordant growth
  ○ Risk of TTTS in monochorionic pairs
  ○ Preterm delivery risk is significant
    ○ Increased rates of preterm birth and low birth weight in U.S. largely due to increasing rate of multiple gestations
    ○ Fetal death rate increases with increasing plurality
  ○ Approximately 90% of triplets deliver preterm
    ○ Average gestational age at delivery of triplet is 33.5 weeks
    ○ 13% of triplets deliver prior to 28 weeks
    ○ Average birth weight of triplets is 1/2 that of singletons
  ○ Virtually 100% of quadruplets and above deliver prematurely
  ○ Average gestational age for delivery of quadruplets is 30 weeks
  ○ Increased need for newborn intensive care unit (NICU) admission
  ○ Infant death rate in triplets and above is 12 times higher than singletons (94 vs. 8 per 1,000 live births)
  ○ Risk of lifelong disability including cerebral palsy common in very low birth weight survivors

Treatment

• Role of prophylactic cerclage in higher order multiples controversial
  ○ Likely of limited or no benefit

• Multifetal pregnancy reduction
  ○ Reduction to twins may offer survival advantage
  ○ Reduction to singleton controversial
  ○ Timing of procedure 10-13 weeks gestational age
  ○ Should be done only by someone highly skilled in technique
  ○ Risk of procedure involves potential loss of entire pregnancy
  ○ Selective reduction
    ○ Fetuses discordant for anomaly or aneuploidy
    ○ Following CVS in cases of advanced maternal age - requires precise mapping of gestational sacs
  ○ Delayed interval delivery

• Rare cases of preivable delivery of 1 fetus of a monochorial gestation

• Conservative management with antibiotics, cerclage, tococollagens in attempt to prolong pregnancy

• Monthly scans for growth and fluid

• More frequent follow-up with cervical shortening, monoamnionicity

• Assessment for complications
  ○ Discordant growth or fluid
  ○ Anomalies
  ○ Clinical monitoring for evidence of preterm labor, preeclampsia, diabetes

DIAGNOSTIC CHECKLIST

Consider

• Document chronocity, amniosone determination of fetuses in every multiple gestation

• Determination of chronocity easiest in 1st trimester

• Baseline cervical length in 2nd trimester

Image Interpretation Pearls

• Careful documentation of fetal positions beginning in the 2nd trimester to facilitate tracking of individual fetal growth rates

• 4 quadrant amniotic fluid index not possible in multiple gestation - use single deepest vertical pocket per fetus.

• Increased surveillance of monochorionic pairs in a higher order multiple gestation

SELECTED REFERENCES


TRIPLETs AND BEYOND

[Image Gallery]

Typical

[Left] Ultrasound shows a monoamniotic, monochorionic triplet gestation at 13 weeks gestation. The "three-vessel" sign (arrow) represents placental tissue interposed between the membranes.

[Right] Ultrasound shows symmetric, monomorphic triplets at 14 weeks gestation with thick intervening membranes (arrows).

Variant

[Left] Ultrasound shows a monochorionic gestation at 13 weeks. Arteries B and C are a monochorionic pair separated by a thin amnion membrane (arrow). Thicker chorioamniotic membranes are shown by curved arrows.

[Right] Enlargement of the chorionic membrane at 14 weeks gestation. The upper gestational sac contains 2 yolk sacs (arrow) indicating this pair is monochorionic. They are separated from the lower yolk sac by a thick chorioamniotic membrane (curved arrow).

Variant

[Left] Ultrasound shows the same triplet gestation at 14 weeks. A thin membrane is seen (arrow) between triplets A and B. A thick chorioamniotic membrane is seen between A and C (curved arrow).

[Right] Ultrasound shows the same triplet gestation at 19 weeks gestation with a thin intervening membrane (arrow) between the monochorionic pair (arrows).
SECTION 14: Chromosomes

Trisomy 21: 14-2
Trisomy 18: 14-6
Trisomy 13: 14-10
Turner Syndrome (XO): 14-14
Triploidy: 14-18
Monosomy 21: 14-22
TRISOMY 21

TERMINOLOGY
Abbreviations and Synonyms
- Down syndrome
- Trisomy 21 (T21)
Definitions
- Autosomal trisomy of chromosome 21

IMAGING FINDINGS
General Features
- Best diagnostic clue
  - First trimester
  - Increased nuchal translucency (NT)
  - Second trimester
  - Major anomaly associated with T21
Ultrasoundographic Findings
- Major anomalies
  - Cardiac defects (25%)
  - Atrioventricular septal defect
  - Ventricular septal defect (VSD)
  - Tetralogy of Fallot
  - Color Doppler help detect small VSD
- Gastrointestinal anomalies (8%)

DDx: Other Chromosome Abnormalities
- Turner Syndrome
- Trisomy 18
- T18 - Hands
- T13 - VSD

- Duodenal atresia
- Esophageal atresia
- Omphalocele: More common with trisomy 18
- Central nervous system anomalies (4%)
- Mild ventriculomegaly
- First-trimester markers
  - Increased nuchal translucency (NT)
  - > 3 mm always abnormal
  - Performed at 11-14 wks
  - Crown rump length of 45-54 mm
  - Biparietal diameter < 27 mm
  - Detection rates near 90% when used in conjunction with biochemical screening
  - Absent nasal bone (NB)
  - Midsagittal view
    - Must see fetal skin separate from NB
  - 66-70% T21 fetuses have absent NB
  - Likelihood ratio (LR) = 35 (35 times more likely that fetus has T21 than a priori risk)
- Second-trimester minor markers (15-21 wks): ≤ 1 marker seen in 50-70% of T21 fetuses
  - Nuchal thickening
    - Second trimester nuchal skin measures > 5 mm
    - Performed on routine posterior fossa image
    - Overly coiled image may cause false positive result
    - Measurement from skull outer table to skin/amniotic fluid interface
TRISOMY 21

Key Facts

- Most sensitive and specific single marker
- LR = 11 if isolated finding
- LR = 5 if seen with other markers
- Short femur and humerus
  - Short humerus length (HIL) more sensitive than short femur length (FL)
  - FL of HIL compared to BPD
- Expected FL = 9.3 x 0.90 (BPD)
- Expected HIL = 9.7 x 0.84 (BPD)
- Abnormal ratio = measured/expected FL ≤ 0.91 and HIL ≤ 0.90
- LR ≥ 5.3 for short FL, 1.5 for short HIL
- Echogenic bowel
  - Usually focal
  - Echogenic bowel as bright as bone (grade 2)
  - LR ≥ 6.7
- Intracardiac echogenic focus (IEF)
  - Bright dot in left or right ventricle of heart
  - Echogenicity usually as bright as bone
  - Multiple or bilateral IEF increases risk
  - 3-4% of normal fetuses have IEF
  - More common in Asian population (normal)
- LR ≥ 1.8
- Renal pelvies
  - Fluid-filled renal pelvis
  - Anterior-posterior measurement on axial view
  - > 3 mm considered positive
  - No hydronephrosis or ureteral distention
  - 3% of normal fetuses
  - LR ≥ 1.6
  - May need follow up to rule out progressive hydronephrosis
- Absent or hypoplastic nasal bone
  - Sagittal view of fetal face
  - Easier to see than in first trimester
- LR ≥ 9
- Fifth finger clinodactyly
- Hypoplastic mid-phalanx
- Distal finger curves inward
- Sternal gap foot
- Wide gap between 1st and 2nd toes

Top Differential Diagnoses
- Isolated minor markers

Pathology
- First trimester ultrasound test
- Second trimester genetic ultrasound + biochemistry results

Clinical Issues
- Abnormal first trimester screen
- Abnormal maternal serum quadruple screen test screen
- Advanced maternal age (AMA) at higher risk
- 35% T21 born to AMA women

Diagnostic Checklist
- Correlate ultrasound findings with clinical information when isolated minor markers are seen

Imaging Recommendations
- Best imaging tool
  - First trimester NT screening
  - Second trimester genetic sonogram
- Protocol advice
  - First trimester NT measurements performed only by trained sonologists
  - Look for additional minor markers when one marker is seen during second trimester screening
  - Routine nuchal fold measurements in all fetuses between 15-21 wks
  - Correlate ultrasound findings with maternal serum biochemical tests

DIFFERENTIAL DIAGNOSIS

Isolated minor markers
- All minor markers, in isolation, are more common in normal fetuses
- Presence of multiple minor markers raises more suspicion
- By definition, minor markers are not pathogenic

Turner syndrome
- Cystic hygroma more likely than skin thickening
- Large and with septations
- First trimester large NT
- Hypodiploidy presentation more common

Trisomy 18
- Chromosomal plexus cysts
  - Major cardiac anomalies
  - Major extremity abnormalities
  - Clenched fist with overlapping fingers
  - Severe intrauterine growth restriction
  - Maternal serum screen: results differ from T21
TRISOMY 21

- Trisomy 13
- Heteropoesis/psathy
- Facial anomalies
- IF associated with severe cardiac anomalies
- Polydactyly

PATHOLOGY

General Features
- Genetics
  - Aberrational trinity of all or part of chromosome 21
  - Critical zone on chromosome 21: 21q22.3
- Embryology
  - 95% from triplican copy of chromosome 21
  - 5% caused by translocation
- Chromosome 14 or 21
- Epidemiology
  - 1/700 births
  - 1:500/2nd trimester fetuses
  - 1:300 1x trimester fetuses

Staging, Grading or Classification Criteria
- First trimester ultrasound test
  - NT + maternal age + biochemical assay
  - Data used to assign risk for T21
  - 95% T21 detection rates
  - Chromatic values sampling or amniocentesis when positive result
- Second trimester genetic ultrasonography + maternal age
  - Age-adjusted ultrasound risk (AMUR)
  - Minor marker LR numbers used to adjust risk
    - Example: Age-related risk = 1:1,000, IF 0.5 (LR = 2), rev risk = 1:500
  - Second trimester genetic ultrasonography + biochemistry results
    - Biochemistry results compared with minor markers
    - LR
    - Example: Biochemistry result = 1:1,100 risk, increased nuchal fold seen (LR = 11), new risk = 1:100
    - 80% T21 detection rates reported

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - Abnormal first trimester screen
  - Abnormal genetic karyogram
  - Abnormal maternal serum quadruple test screen
    - 1. Alpha-fetoprotein (AFP)
    - 1. Human chorionic gonadotropin protein (hCG)
    - 1. Estriol
    - 1. Inhibin A protein
  - Abnormal first trimester serum biochemistry result
    - 1. Pregnancy-associated plasma protein-A (PAPP-A)
    - 1. Beta subunit human chorionic gonadotropin (hCG)
  - Major anomaly detected on routine study
  - Incidental minor markers in low risk patient
  - Other signs/symptoms
    - Polyhydramnios
  - Often seen as late 2nd or 3rd trimester
  - Duodenal atresia
  - Esophageal atresia
  - Hydrops fetalis
  - Cardiac failure
  - Lymphatic drainage abnormality

Demographics
- Age
  - Advanced maternal age (AMA) at higher risk
    - AMA: ≤ 35 yrs at time of delivery
    - 35% T21 born to AMA women
    - 1:137 at 20 yrs
    - 1:254 at 35 yrs
    - 1:42 at 42 yrs
  - Gestational age:
    - M = 7

Natural History & Prognosis
- Mean survival to age 20
  - Prognosis related to associated anomalies, i.e.
    - Severity of cardiac anomalies
    - Mental retardation
    - Mean IQ of 50-60
    - 20-fold increased risk for acute leukemia
    - Hearing loss in 90%

DIAGNOSTIC CHECKLIST

Consider
- Correlate ultrasound findings with clinical information when isolated minor markers are seen
  - Maternal age
  - Biochemistry results
  - Absence of second trimester findings decreases risk for T21
    - LR = 0.5
  - Example: Maternal risk 1:200, no markers seen, new risk 1:400
  - "Tentacle ultrasound and biochemistry testing used to decrease number of invasive tests performed."

SELECTED REFERENCES
Typical

Left: Axial ultrasound of the posterior fossa shows midline shift, high edema (curved arrows). The findings had a pleural effusion. Trisomy 21 can present with hydrocephaly and the diagnosis is gross.

Right: Caudal ultrasound shows left lobe cleft down (curved arrow points to tip of liver) and arrows point to rib. Methylmalonic acid from a shortened methyl-

pseudocholesterolemia.

Typical

Left: Axial ultrasound through the heart shows an isolated ventricular septal defect (arrows) in the fetus with T21. The patient's karyotype and karyotyping results showed her at high risk for T21.

Right: Axial ultrasound shows bilateral renal polycystic disease (curved arrow points to the pelvic posterior). There was no cerebral or cerebellar atrophy.

Typical

Left: Axial ultrasound of the fetal spine shows a short neural tube defect (curved arrow).

Right: Sagittal ultrasound of the fetal spine shows a short neural tube defect (curved arrow).

Typical

Left: Axial ultrasound of the fetal spine shows a short neural tube defect (curved arrow).

Right: Sagittal ultrasound of the fetal spine shows a short neural tube defect (curved arrow).

Typical

Left: Axial ultrasound of the fetal spine shows a short neural tube defect (curved arrow).

Right: Sagittal ultrasound of the fetal spine shows a short neural tube defect (curved arrow).
Trisomy 21

- Holoprosencephaly
- Facial anomalies
- IEF associated with severe cardiac anomalies
- Polydactyly

PATHOLOGY

General features
- Genetics
  - Autosomal trisomy of all or part of chromosome 21
  - Critical zone on chromosome 21 is 21q22.3
- Teratology
  - 99% from trisomic copy of chromosome 21
  - 94% caused by translocation
  - Chromosome 14 or 21
- Epileptology
  - 1:700 births
  - 1:500 2nd trimester fetuses
  - 1:300 1st trimester fetuses

Staging, Grading or Classification Criteria
- First trimester ultrasound test
  - NT + maternal age + biochemical assay
    - Data used to assign risk for T21
    - 90% T21 detection rates
  - Chromosome analysis plus amniocentesis when positive result
- Second trimester genetic ultrasound + maternal age
  - Age adjusted ultrasound risk (AAR)
    - Example: Age related risk = 1:1,000, IEF score (LR = 2), new risk = 1:500
- Second trimester genetic ultrasound + biochemical results
  - Biochemistry results compared to minor marker LR
    - Example: Biochemistry result = 1:1,100 risk, increased nuchal fold (LR = 11), new risk = 1:100
  - 80% T21 detection rates reported

CLINICAL ISSUES

Presenation
- Most common signs/symptoms
  - Abnormal 1st trimester screen
  - Abnormal genetic sonogram
  - Abnormal maternal serum quadruple test screen
    - Alpha-fetoprotein (AFP)
    - Human chorionic gonadotropin (hCG)
    - Inhibin A protein
  - Abnormal first trimester serum biochemical result
    - Pregnancy-associated plasma protein A (PAPP-A)
  - Anomalies detected on routine x-ray
  - Incidental minor markers in low risk patient
  - Other signs/symptoms
    - Polyhydramnios
  - Often seen in late 2nd or 3rd trimester
  - Thrombocytopenia
  - Esophageal atresia
  - Hydrocephalus
  - Cardiac failure
  - Lymphatic drainage abnormality

Demographics
- Age
  - Advanced maternal age (AMA) at higher risk
    - AMA ≥ 35 yrs at time of delivery
    - 25% T21 born to AMA women
    - 1:5,176 at 20 yrs
    - 1:217 at 35 yrs
    - 1:42 at 42 yrs
- Gender: M = 1

Natural History & Prognosis
- Mean survival to age 20
  - Prognosis related to associated anomalies, i.e.
    - Severity of cardiac anomalies
    - Mental retardation
    - Mear, K2 of 50-60
    - 20-fold increased risk for adult leukemia
    - Hearing loss in 90%

DIAGNOSTIC CHECKLIST

Consider
- Correlate ultrasound findings with clinical information
  - Isolated minor markers are seen
  - Maternal age
  - Biochemistry results
  - Absence of second trimester findings decreases risk for T21
  - LR = 0.3
  - Example: Maternal risk 1:200, no markers seen, new risk 1:400
  - Prenatal ultrasound and biochemical testing used to decrease number of invasive tests performed

SELECTED REFERENCES

TRISOMY 21

IMAGE GALLERY

Typical

(Left) Axial ultrasound of the posterior fossa shows mild nuchal fold thickening (necrosis measured 5.5 mm). The measurement is taken from the outer edge of the skull to the skin/liquids interface. (Right) Sagittal ultrasound of the fetal face shows a hypoplastic nasal bone (curved arrow) also seen with Down syndrome. This fetus also had a thickened nuchal fold and a cardiac defect.

Typical

(Left) Axial ultrasound through the heart shows an isolated ventricular echogenic focus in the left ventricle (arrow) in this fetus with T21. The patient's abnormal blood chemistry results also placed her at high risk for T21. (Right) Axial ultrasound shows bilateral renal pelvis distention (arrow points to urine within the renal pelvis). There was no calyceal or ureteral dilatation.

Typical

(Left) Sagittal ultrasound shows a low-lying wall edema (curved arrows). The fetus also had a pleural effusion. Trisomy 21 can present with hydrops fetalis and the prognosis is grim. (Right) Coronal ultrasound shows a large choroid plexus cyst (arrows) measuring over 35 mm in length. Arrows point to four limbs at 14 weeks and arrows point to other flaws. Methyl cytosine is from a shortened third phalanx.
TRISOMY 18

TERMINOLOGY
Abbreviations and Synonyms
- Trisomy 18 (T18)
- Trisomy E
- Autosomal trisomy of chromosome 18

Definitions
- 20% with early IUGR have aneuploidy
  - Cardiac defects
  - Autopsy series: 90%
  - Renal detection: 50%
  - Ventricular septal defect
  - Atrial septal defect
  - Double outlet right ventricle
  - Dextrocardia
  - Musculoskeletal findings (75%)
  - Findings may be unilateral or bilateral
  - Clenched hands + overlapping index finger (30%)
  - Arthrogryposis
  - Rockerbottom foot
  - Clubfoot
  - Radial ray malformation
  - Cystic hygroma (CH)/nuchal thickening (25%)
  - CH not as large as with Turner syndrome
  - Mety1 present with hydrops
  - Skeletal anomalies (30%)
  - Ventriculomegaly
  - Dandy-Walker malformation
  - Dandy-Walker variant (T18 common)
  - Cerebellar hypoplasia
  - Agenesis of the corpus callosum
  - Meningomyelocele/open meningocele (OMI) (12%)
  - Karyotype recommended when GS is seen
  - T18 most common karyotype abnormality
  - Gastrointestinal anomalies

IMAGING FINDINGS
General Features
- Best diagnostic clue
  - Second trimester
    - Multiple major anomalies
    - Single major anomaly + T18 minor marker
    - Choroid plexus cyst + other anomalies
    - Early intrauterine growth restriction (IUGR)
    - First trimester
      - Increased nuchal translucency (NT)

Ultrasoundographic Findings
- Multiple major anomalies
  - IUGR (31%)
  - Early onset (14-24 wk)
  - Symmetric IUGR

DDx: Pena-Shokeir Phenotype Similarities With T18

Rockerbottom Foot  Cleared Hand  Wrist Contracture  Club Foot
**TRISOMY 18**

### Terminology
- Edwards syndrome

### Imaging Findings
- Multiple major anomalies
- Choroid plexus cyst + other anomalies
- Early intrauterine growth restriction (IUGR)
- Increased nuchal translucency (NT)
- Cardiac defects
- Clenched hands + overlapping index finger (50%)
- Arthrogryposis
- Rockerbottom foot
- Dandy-Walker variant (T18 common)
- Omphalocele: Often bowel-containing (20%)
- Strawberry shaped calvarium (40%)
- Single umbilical artery (SUO)

### Key Facts
- Do not change pregnancy dating when IUGR is the correct diagnosis

### Top Differential Diagnoses
- Isolated choroid plexus cysts
- Pena-Shokeir syndrome (pseudo-trisomy 18)
- Triploidy

### Clinical Issues
- Abnormal maternal serum screening quadraple test screen
- 2/3 of fetuses alive at 16 wks die before term
- 90% of live-born die in first year of life

### Diagnostic Checklist
- Correlate ultrasound findings with clinical information when an isolated T18 marker is seen
- Obtain open hand views and cardiac views when isolated choroid plexus cysts are seen

### Imaging Recommendations
- Best imaging tool
  - Second trimester genetic sonogram
  - First trimester NT screening
  - Protocol advice
- When CPC seen, look carefully at extremities and heart
- Consider echocardiography
- Do not change pregnancy dating when IUGR is the correct diagnosis
- Example: Fetus with CPC measures 2 wks small

### Differential Diagnosis

#### Isolated choroid plexus cysts
- Seen in 1% of all fetuses
- No other anomalies
- Normal hands, feet, heart
- Risk assessment for T18 advised
- Compare with maternal serum biochemistry results
- Compare with maternal age
- Risk is < 1:400 in low risk group
- Amniocentesis not done in low risk patients

#### Pena-Shokeir syndrome (pseudo-trisomy 18)
- Neurogastropathy
- Chiari
- Joint contractures
- IUGR
- 8% die within first month of life

#### Smith-Lemli-Opitz syndrome
- IUGR
- Chiari
- Microcephaly
- Abnormal genitalia
- Autosomal recessive inheritance

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- Crown rump length of 45-54 mm
- > 3 mm always abnormal
- NT larger with T18 than T21
- Detection rate = 50%
**TRISOMY 18**

- Type 2 is lethal.
- **Trisomy**
  - Complete extra set of chromosomes
  - Severe early IUGR
  - Most likely trisomic; trisomic is symmetric
  - Abnormal thickened cleft palate
  - Recurrent mole/placenta
  - Multiple anomalies
  - Fetal
- **Trisomy 13**
  - Holoprosencephaly
  - Facial anomalies
    - Cleft lip/palate
    - Persistent ductus arteriosus
    - Cardiac anomalies
  - UGSR
  - Polyhydramnios

**PATHOLOGY**

**General Features**
- Genetics: Additional trisomy of all or most of chromosome 18
- Etiology:
  - 80% triplicate copy of chromosome 18
  - 10% mosaicism
  - 10% translocation
- Epidemiology: Incidence: 1:5,000-6,000 births

**Staging, Grading or Classification Criteria**
- First trimester ultrasound test
  - NT + maternal age + biochemical assay
  - Data used to assign risk for T18
  - 90% detection rate
  - Invasive testing offered for positive result
- Second trimester genetic ultrasound + biochemical
  - Helpful when minor markers present
  - Most fetuses with T18 have major anomalies

**CLINICAL ISSUES**

**Presentation**
- Most common signs/symptoms
  - Multiple anomalies
  - Single severe anomaly + T18 markers
    - Example: Cardiac defect + CVC
  - Multiple marker or subtle markers
    - Example: CVC + echogenic foci
  - Increased nuchal thickness NT
  - Abnormal maternal serum quadruple test screen
  - 1 Alpha Fetoprotein (AFP)
  - 1 Human chorionic gonadotropin (HCG)
  - 1 Estriol
  - 1 Inhibin A protein
  - 57% T18 detection rate
  - Maternal first trimester serum biochemical result
  - Pregnancy associated plasma protein-A (PAPP-A)
  - 1 Beta subunit HCG (B-HCG)
  - 89% T18 detection rate
  - Other signs/symptoms
  - Fluid abnormalities
    - Polyhydramnios with esophageal atresia
    - Gastroesophageal reflux with laryngeal tract anomalies
    - Hypoplasia
    - Cardiac failure
    - Cystic hygroma
    - Elevated AFP if T18 present

**Dermographics**
- **Age**
  - Advanced maternal age (AMA) at higher risk
  - AMA ≥ 35 yr at time of delivery
  - Risk not as high as for T21

**Natural History & Prognosis**
- Intrauterine fetal demise
  - 2/3 of fetuses alive at 16 wks die before term
  - 50% of live-born die in first year of life
  - Median survival 8 wks
  - Survivors are severely retarded and handicapped
  - Feeding difficulties
  - Hypoesthesia

**Treatment**
- Termination offered
- Tocolysis and cesarean section avoided

**DIAGNOSTIC CHECKLIST**

**Consider**
- Correlate ultrasound findings with clinical information when an isolated T18 marker is seen
- Maternal age
- Biochemistry results
- Aneuploidies in cases with early symmetric IUGR

**Image Interpretation Pearls**
- Obtain open hand views and cardiac views when isolated clefted palate cysts are seen

**SELECTED REFERENCES**

Typical

(left) Ultrasound through the fetal abdomen shows bilateral multiple cystic renal pelvis cysts (CRPC), which vary in size (arrows). Ablation of the head and a mild exophthalmic shape. (right) Ultrasound through the fetal heart of the same fetus shows a hypoplastic left ventricle (arrows) and a small aortic arch (arrow).

Typical

(left) Ultrasound shows a bowel containing amniotic fluid (arrows). Notice how the cord (curved arrow) passes over an atrophied right kidney (arrow). (right) Axial ultrasound through the cord shows an interior venous duct (open arrow). The distal end of the vein (curved arrow) has a "keyhole" appearance.

Typical

(left) Sagittal ultrasound of the bottom head in 118 shows the convex curvature of the head (curved arrows). The nasopharynx (open arrow) is parallel to the skin (arrow). (right) Coronal ultrasound of another fetus with 118 shows the fetal skull (arrow). Only the atlas is seen (arrow) and the head (curved arrow) is mispositioned since the radius and hands are missing.
TERMINOLOGY

Abbreviations and Synonyms
- Prune syndrome
- Trisomy 13 (T13)

Definitions
- Autosomal trisomy of chromosome 13

IMAGING FINDINGS

General Features
- Best diagnostic clue
  - Second trimester
  - Multiple major anomalies in > 90%
  - Holoprosencephaly
  - Midline facial malformations
  - Cardiac defects
  - Polydactyly
  - Early intrauterine growth restriction (IUGR)
  - Fetal trimester
  - Increased nuchal translucency (NT)

Ultrasoundographic Findings
- Central nervous system anomalies (70%)
  - Holoprosencephaly sequence (90%)
    - Arhinencephaly, holoprosencephaly
  - Molar tooth syndrome
  - Fetal alcohol syndrome
  - Fetal microcephaly

DDs: Anomalies Similar to T13 Seen With Meckel Gruber Syndrome

- McKown anomalies
  - Polydactyly
  - Encephalocele
  - Encephalocele

- Molar tooth syndrome
  - Fetal alcohol syndrome
  - Holoprosencephaly
  - Severe microcephaly

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TRISOMY 13

Terminology
- Patau syndrome
- Trisomy 18
- Monosomy X (47,XX,-X)

Imaging Findings
- Holoprosencephaly sequence (40%)
  - "The face predicts the brain"
- Cyclopia
- Polyflexis
- Midline or bilateral cleft lip
- Post axial polydactyly (75%)
- Cardiac defects (80%)
- Echogenic kidneys
- Omphalocele: Often bowel containing
- IUGR (50%)
- Echogenic cardiac focus (30%)
- Increased NT

- Premaxillary protrusion on profile view
- Low set ears
- Maxillofacial findings (50%)
- Post axial polydactyly (75%)
- Extra finger on ulna side
- Club feet
- Rocker-bottom feet
- More common with trisomy 18 (T18)
- Fused hand/overlapping digits
- More common with T18
- Cardiac defects (80%)
- Ventricular septal defect
- Atrial septal defect
- Dysplastic left heart (HLH)
- Intracardiac echogenic focus (IEF) highly associated with T13
- Aortic atresia
- Mitral atresia
- Pulmonary stenosis
- Anomalous pulmonary venous return
- Renal anomalies (50%)
- Echogenic kidneys
- Cystic dysplasia
- Often enlarged
- Hydrourephrosis
- Duplication anomalies
- Gastrointestinal anomalies
- Omphalocele: Often bowel containing
- Umbilical hernia
- Meckel’s diverticulum
- IUGR (50%)
- Early onset
- IUGR + polyhydramnios worrisome for T13 and T18
- Second trimester markers
- Almost never isolated
- Echogenic cardiac focus (30%)
- Single umbilical artery (25%)
- Increased nuchal thickness/cystic hygroma (20%)
- Echogenic bowel (5%)
- First trimester marker
- Increased NT
- Subcutaneous fluid behind fetal neck

Key Facts
- Meckel-Gruber syndrome (MG)
- Holoprosencephaly
- Trisomy 18
- Holoprosencephaly is hallmark anomaly
- Most survive to delivery
- 75% live-born die in first 6 months of life

Diagnostic Checklist
- Suspect T13 when midline brain, heart, or facial anomalies seen
- Early IUGR raises suspicion for aneuploidy
- Consider MRI when subtle brain anomalies suspected
- Routinely visualize cavum septi pellucidi

Other Modality Findings
- Fetal MR
  - Can detect subtle brain anomalies
  - Lobar holoprosencephaly
  - Absence of cavum septi pellucidi
  - Agenesis of corpus callosum

Imaging Recommendations
- Best imaging tool:
  - Second trimester periodic sonogram
  - First trimester NT screening
- Protocol advice
  - Suspect brain anomaly when midline facial anomaly seen
- Consider fetal MR when CNS findings are minimal

DIFFERENTIAL DIAGNOSIS

Meckel-Gruber syndrome (MG)
- Brain anomalies
  - Encephalocele
  - Dandy-Walker
  - Holoprosencephaly (severe)
- Polydactyly
- Echogenic kidney
- Autosomal recessive with 25% recurrence risk

Holoprosencephaly without T13
- Alobar
- Semilobar
- Lobar
- May be missed with ultrasound
- Less severe cases are compatible with life

Hydrencephaly
- In utero brain infarction
- Fluid-filled cavum luminis monoventricular
TRISOMY 13

- No associated anomalies

Trisomy 18
- Congenital heart defects + other anomalies common
- Multiple severe anomalies
  - Cardiac anomalies
  - Musculoskeletal
  - Clefted palate with overlapping fingers
- Holoprosencephaly not typical
- Early IUGR
- Increased NT in first trimester

PATHOLOGY

General Features
- Generalized abnormalities
- Holoprosencephaly
- Failure of prosencephalic cleavage
- Cleavage defects in brain, ventricles, and face
- Genetics: Autosomal trisomy of chromosome 13
- Ectopia
- 75% replicate copy of chromosome 13
- 20% translocation
- 5% mosaic
- Epidemiology
- 10,000 births
- Less common than trisomy 21 (T21) and T18
- 15% spontaneous abortions are T13
- Associated with advanced maternal age

Staging, Grading or Classification Criteria
- First trimester ultrasound: T21 + T18
- Dashes used to assign risk for aneuploidy
- 95% detection rates
- Invasive procedures offered for positive result
- Holoprosencephaly brain malformation classification
  - Pancake
  - Brain flattened at base of skull
  - Large distal autoventricle
  - Cup
  - Brain mantle at base of skull
  - Does not cover autoventricle
  - Tull
  - Brain mantle surrounds autoventricle

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - Multiple second-trimester anomalies
- Holoprosencephaly is hallmark anomaly
- Increased first trimester nuchal translucency
- Most common anomaly is T21
- Abnormal maternal serum quadruple test screen
  - Maternal 1 alpha-fetoprotein (AFP)
- Inhibin A protein
- Normal human chorionic gonadotropin (HCG) protein
- Normal estriol
- 71% T13 detection rate
- Abnormal first trimester serum biochemistry result

- 1 Beta subunit HCG (β-HCG)
- 1 Pregnancy associated plasma protein-A (PAPP-A)
- Results identical for trisomy 18
- 99% T13 detection rate

Demographics
- Age
  - Advanced maternal age (AMA) at higher risk
  - AMA ≥ 35 yrs at time of delivery

Natural History & Prognosis
- Most survive to delivery
- 75% live-born die in first 6 months of life
- Mean survival of 180 days
- r 5% survive beyond three years
- T13 mosaics with better survival
- Survivors are severely retarded and handicapped
- Hyporeflexia and hypotonia
- Seizures
- Feeding difficulties

Treatment
- Termination offered
- Counselling and neural tube avoided

DIAGNOSTIC CHECKLIST

Consider
- Suspect T13 when midline brain, heart or facial anomalies seen
- Early IUGR raises suspicion for aneuploidy
- Consider amniocentesis when subtle brain anomalies suspected

Image Interpretation Pearls
- Randomly visualize calvarium and placental
  - Biparietal diameter view
  - Look carefully at fetal brain when midline or external
eye tip/palpebral diagnosed
- Castor finger and toes when holoprosencephaly diagnosed

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Typical

Typical

Typical

Left: Coronal ultrasound of the face shows cyclopia (arrows) and a proboscis (arrow). The brain also had abnormally shaped gyri and a single ventricular cavity (open arrow). Right: Coronal view of another fetus with T13 shows dysplastic tissue involving a single ventricle (curved arrow), a tubular proboscis (arrow), and low set ears.

Left: Sagittal ultrasound of the fetal face shows a proboscis (arrow). The mass adjacent to the nose is central. The eyes and eyebrows are associated with bilateral cleft lip and palate. Right: Coronal ultrasound of the hand in the same fetus shows polydactyly (arrows point to six fingers). While these findings were unusual in this case, T13 was suspected given these two findings and a cardiac defect.

Left: Axial ultrasound of the fetal abdomen shows a small bowel containing omphalocele (arrow). This fetus with T13 also had atrioseptal defect. Omphalocele with bowel is highly associated with atrioseptal defect. Right: Sagittal ultrasound shows enlarged echogenic kidneys (arrows). Ovarian cysts may be seen (curved arrows) through the increased echogenicity in the ovarian cysts.
TURNER SYNDROME (XO)

TERMINOLOGY

Abbreviations and Synonyms
- Ullrich-Turner syndrome
- XO syndrome (XO)
- Monosomy X
- 45X syndrome

Definitions
- Deficiency or absence of one sex chromosome

IMAGING FINDINGS

General Features
- Best diagnostic clue
  - Second trimester
    - Femur-fetus with large, septated cystic hygroma
      (CH)
    - Hydrops fetalis
  - First trimester
    - Markedly increased nuchal translucency

Ultrasonographic Findings
- Nuchal cystic hygroma
  - Palmar anomaly
  - 65% of all fetuses with CH have X0
  - Fluid collection of posteri or and lateral neck

- Large CH most common
- May be confused with amniotic fluid
- Internal organ
- Midline thick septum is nuchal ligament
- Multiple thin septations common
- Small CH
- Miniscus edematous thickened nuchal fold
- More common with trisomy 21 than XO
- Non-immune hydrops
  - Excess fetal fluid accumulation
  - Fluid in two separate areas
    - Example: Skin edema + pleural effusion
  - Exemplar: Pleural effusion + ascites
- Skin edema
- Lymphangiectasia
- Usually diffuse
- Chest
  - Bilateral pleural effusion
  - Pericardial effusion
- Abdomen
  - Ascites
- Cardiovascular anomalies (60%)
  - Coarctation of aorta (45%)
  - Narrow aortic arch
- Difficult diagnosis
  - Hypoplastic left heart (15%)
- Genitourinary findings
  - Renal anomalies

DDx: Anomalies Similar to Turner Syndrome Seen With Trisomy 21
TURNER SYNDROME (XO)

Key Facts
- Female fetus with large, septated cystic hygroma (CH)
- Hydrops fetalis
- Markedly increased nuchal translucency
- 60% of all fetuses with CH have XO
- Skin eczema
- Bilateral pleural effusions
- Ascites
- Coarctation of aorta (45%)
- Horseshoe kidneys
- Short stature
- Short humerus
- Early onset symmetrical growth restriction
- Hydrops can be seen in first trimester
- Use high gain settings to see thin septations in CH
- Measure fluid carefully; large CH can mimic amniotic fluid

Top Differential Diagnoses
- Noonan syndrome (pseudo Turner syndrome)
- Trisomy 21 (Down syndrome)

Pathology
- Not associated with advanced maternal age

Clinical Issues
- Abnormal maternal serum quadruple test screen
- Abnormal first trimester serum biochemical result
- 96% first trimester detection rate
- Majority spontaneously abort in first trimester
- Prognosis with hydrops is dismal

DIFFERENTIAL DIAGNOSIS

Noonan syndrome (pseudo Turner syndrome)
- Can look identical to XO
- Cystic hygroma
- Hydrops
- Cardiac defects
- Pulmonic stenosis
- Short limbs
- Karyotype is normal
- Autosomal dominant
- Chromosome 12 defect
- M/F = 1:1

Trisomy 21 (Down syndrome)
- Nuchal thickening more common than CH
- Hydrops rare
- First trimester increased nuchal translucency
- Rarely with septations
- Associated nuchal markers are typical for XO
- Intercardiac echogenic focus
- Echogenic bowel
- Endocardial cushion defect
- Duodenal atresia

Chest lymphangioma
- Cystic mass of chest wall
- Often axillary
- Usually large with septations
- Caused by lymphatic obstruction
- Not associated with aneuploidy
- M/F = 1:1

PATHOLOGY

General Features
- Genotype
  - RARE 45X karyotype
  - Absence of all or part of one sex chromosome
  - Paternal X missing
CLINICAL ISSUES

Presentation
- Most common signs/symptoms
- Second trimester anomalies
  - Cystic hygroma
  - Hydrops fetalis
  - Hydronephrosis
- Increased first trimester NT
- Largest NT seen with XO
- Septations common
- Associated hydrodrops
- Abnormal maternal serum quadraplet test screen
  - 1. Alpha-fetoprotein (AFP)
  - 2. Inhibin
  - 3. Human chorionic gonadotropin (HCG)
  - 4. HCG if hydrodrops
- 1 Inhibit if hydrodrops
- Detection rate of XO 53%
- Abnormal first trimester serum biochemistry result
  - Used in conjunction with NT
- Mildly beta subunit HCG
- 1 Pregnancy associated plasma protein-A (PAPP-A)
- 96% first trimester detection rate
- Other signs/symptoms
  - oligohydramnios
  - Intrauterine growth restriction
  - Renal dysfuction
  - Hydrodrops and heart failure
  - Polyhydramnios
  - Less common
  - Hydrodrops

Demographics
- Age
  - Advanced maternal age (AMA) not at higher risk
  - AMA ≥ 35 yrs at time of delivery
- Gender: Female fetus

Natural History & Prognosis
- Majority spontaneously abort in first trimester
- Better prognosis for mosaic 45X
- Survivors
  - Webbed neck
  - Short sturaue

SELECTED REFERENCES
**IMAGE GALLERY**

**Typical**

*Left:* Axial ultrasound shows a large pelvic cystic hygroma in a fetus with XO syndrome. Molar pregnancy (earlier amenorrhea) involves an amniotic sac. The fetal face shows features of a large hydrocephalus (arrow). This fluid exists from the skin surface. Multiple skin lesions are also seen. *Right:* Gross pathology of this large CH is another feature seen in multiple cases. Thick hydralic fluid (arrow) exits the hygroma. Multiple septations of the CH is a common finding.

**Typical**

*Left:* Axial ultrasound shows bilateral adrenal effusion (arrows) and hypoplastic left ventricle (open arrow). The normal lung is surrounded by aortic arch (arrow) and the left (LV) ventricle is smaller than the right (RV). This fetus also had cystic hygroma and right ventricle (arrow). *Right:* Sagittal ultrasound shows inferior vena cava (arrow) and skin lesions (arrows) in another fetus with a cystic hygroma.

**Typical**

*Left:* Coronal ultrasound shows a hyperechoic lesion. A central without or renal tissue correlates with the lesion (arrow). *Right:* Gross pathology shows a hyperechoic lesion (arrow) in another fetus. Unresolved open arrow are seen joining the bladder (curved arrows). Photo is taken from the back and the hovel is absent.
**TRIPLOIDY**

![Image of a 14 week pregnancy showing a markedly enlarged, cystic placenta with a small fetus covered posteriorly. This is typical of triploidy of paternal origin.]

**TERMINOLOGY**

**Abbreviations and Synonyms**
- **Partial mole**
  - Occur when extra set of chromosomes is paternal

**Definitions**
- 69 chromosomes
  - One entire extra haploid set

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue
  - First trimester
- Increased nuchal translucency
- Second trimester
- Early, severe asymmetric intrauterine growth restriction (IUGR)
- Ventricleomegaly + syndactyly (lid and 4th digit) most common combination of findings
- Findings vary according to source of extra chromosome
  - Paternal (monosomy)
  - More commonly abort in 1st trimester
  - Symmetric IUGR if pregnancy continues

**Ultrasoundographic Findings**
- Often multiple malformations
- Placenta variable appearance based on origin of extra chromosome
  - Large, cystic placenta
  - Extra haploid chromosome set paternal
  - Partial mole
  - Small or normal
  - Extra haploid chromosome set maternal
  - Severe IUGR
  - Early onset
  - Can be diagnosed by 11 weeks
  - Symmetric IUGR if maternal origin
  - Abdomen and skeleton more profoundly affected than head
  - Symmetric IUGR more common if paternal origin
  - Central nervous system
  - Ventricleomegaly
  - Dandy-Walker spectrum
  - Agenesis of corpus callosum
  - Holoprosencephaly spectrum
  - Neural tube defects
  - Facial hemangioma

**DDx: Cystic Appearing Placenta With Fetus**

- Fetal Mole
- Dermal
- Placental Edema
- Placental Lakes
### Key Facts

**Terminology**
- Partial trisomy
- 69 chromosomes

**Imaging Findings**
- Early, severe asymmetric intrauterine growth restriction (IUGR)
- Ventriculomegaly + syndactyly (3rd and 4th digits)
- Most common combination of findings
- Often multiple malformations
- Placenta variable appearance based on origin of extra chromosomes
- Cardiac defects
- Oligohydramnios common
- Ovarian theca lutein cysts

**Differential Diagnosis**

**Twin pregnancy: Hydatidiform mole with coexistent fetus**
- Living fetus has a separate, normal appearing placenta
- Fetus should have normal anatomy and growth

**Demise with hydropic degeneration of placenta**
- Represents hydropic change without trophoblastic proliferation
- Can look identical to triploidy and pathologist must make diagnosis

**Placental lakes**
- Commonly seen after 20 weeks
- May see slow blood flow
- Often change size and shape during examination
- Fetus is normal

**Placental pseudomoles**
- Heterochromatin dysplasia of placenta results in villus hydrops
- Often seen with preeclampsia and normal fetus
- May be seen with placemomelagia and Beckwith-Wiedemann syndrome

**Infection**
- Variability, including infectious agent
- Intracranial and intrahepatic calcifications common
- IUGR does not manifest as early
- Ventriculomegaly
- Positive maternal serology

**Trisomies 18, 13**
- Many fetal findings overlap
- Placenta is usually normal
- IUGR does not manifest as early

**Neu-Laxova syndrome**
- Early IUGR
- Microglossia
- Severe microcephaly

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### Imaging Recommendations

- When to have high index of suspicion
- Abnormal cystic placenta
- Severe asymmetric IUGR regardless of placental appearance
- Short follow-up interval at 1st trimester (7-10 days)
- IUGR and anomalies seen early
- Perform endovaginal for fetal anatomy if poor visualization
- Ventriculomegaly + syndactyly most common combination of findings
PATHOLOGY

General Features
- Genetics
  - Sporadic occurrence
  - Rare recurrent cases reported
  - 60% 69,XY
  - 39% 69,XX
  - 1% 69,YY
- Embryology
  - Extra chromosome set paternal
  - Fertilization with 2 sperm most common (diploidy)
  - Fertilization with diploid sperm
  - More common in 1st trimester aborutions
  - Diploidy
  - Extra chromosome set maternal
  - Diploid egg
  - Trisomy may also occur
  - Four sets of chromosomes
  - Ratio of tetraploidy:triploidy is 1:3
- Abnormality
  - 1.2% of conceptions
  - 25-30% of 1st trimester aborutions
  - Rare at birth

Microscopic Features
- Partial molar placental changes usually present.
  - Two populations of villi
    - Enlarged villi (≥ 3 mm)
    - Intravillus villi with scalloped borders and trophoblastic hydrops
- Trophoblastic hyperplasia

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - Vaginal bleeding most common maternal presentation
  - Ventriloculosity most common combination of findings
- Anomalies and IUGR seen in 1st trimester
- Laborator abnormalities vary according to severity of extra chromosomes
- Paternal
  - 1 Human chorionic gonadotropin protein (HCG)
  - 1 Alpha-fetoprotein (AFP)
  - 1 HCG
  - 2 Pregnancy associated plasma protein A (PAPP-A)
- Maternal
  - 1 HCG
  - 1 AFP
  - 1 Estriol
  - 1 PAPP-A
- Preeclampsia
  - Occurs with partial mole
  - Often presents < 20 weeks
  - May be severe

Demographics
- Age
  - Advanced maternal age not at higher risk
  - Incidence may actually decrease

Natural History & Prognosis
- Most spontaneously abort before 20 weeks
- Paternal (diploid) vary rarely detect
- Lethal in neonatal period if live born

Treatment
- Chromosomic villus sampling or amniocentesis for karyotype
- Termination offered
- Monitor mother for preeclampsia
- Avoid fetal monitoring and cerclage section

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls
- Be suspicious of trisomy in 2 different circumstances
  - Anytime there is an enlarged, cystic placenta
  - In the setting of severe asymmetric IUGR even if the placenta is normal

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2. Gherardi E et al: Analysis of 100 consecutive patients with
3. Deans A et al: Trisomy 18, phenotype and parental origin in
5. Spencer R et al: A review of the incidence of trisomy 18 in
7. Javertman E et al: Human chorionic gonadotropin in
   maternal serum: a possible risk indicator for trisomy 18. Ultrasound
   Obstet Gynecol 5:11-16, 1995
10. Ullrichle C et al: Prenatal diagnosis of trisomy 18 and
Typical

Left: Axial ultrasound of the brain shows ventriculomegaly (arrow) in this fetus with trisomy 18.

Right: Facial immaturity is significant for asymmetric RUGA with the abdomen being the most severely affected. Early asymmetric RUGA is very concerning for trisomy 18 especially when other anomalies such as ventriculomegaly are present.

Typical

Left: Ultrasound of the placenta in the same case shows that it is small but otherwise normal in appearance. This case is typical for a maternal origin of the trisomy (dextro). Note the relative small size of the body to the head. There is also bilateral perinephric fat and bilateral right (arrow), another common feature seen in trisomy 18.

Typical

Left: Sagittal ultrasound of the right arm in a trisomy pregnancy shows an enlarged cystic artery (arrow). This was bilateral and is a typical finding of trisomy 18. Other cystic lesions are seen in another arm of the infarction, which sometimes can be seen in trisomy pregnancies.

Right: Axial operative photograph of the infant and infant in another case of trisomy 18 shows bilateral cystic lesions with the trisomy (arrow).
**MONOSOMY 21**

**TERMINOLOGY**

**Abbreviations and Synonyms**
- 21-trisomy syndrome, chromosome G1 deletion syndrome, del(21) syndrome

**Definitions**
- Partial or complete deletion of chromosome 21

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue
  - Early or severe intrauterine growth restriction
  - Multiple anomalies

**Ultrasoundographic Findings**
- Thickened nuchal fold
- Central nervous system (CNS)
  - Holoprosencephaly spectrum
  - Microcephaly
- Dysgenesis of the corpus callosum
- Cleft lip/palate
- Extremity abnormalities
  - Syndactyly/camptodactyly
  - Clinodactyly
- Reduction/malposition defects

**DIFFERENTIAL DIAGNOSIS**

**Trisomy 21** (T21)
- Many overlapping features
- CNS findings much less common

**Trisomy 13** (T13)
- Holoprosencephaly
- Craniofacial abnormalities
- Omphalocele
- Cystic kidney
- Polydactyly

**DDx: Conditions Mimicking Monosomy 21**

- Trisomy 21
- Trisomy 13
- Holoprosencephaly
- Polydactyly
MONOSOMY 21

**Key Facts**

- **Terminology**
  - Partial or complete deletion of chromosome 21

- **Imaging Findings**
  - Early or severe intrauterine growth restriction
  - Multiple anomalies
  - Thickened nuchal fold
  - Holoprosencephaly spectrum
  - Cardiac defects

**Top Differential Diagnoses**

- Trisomy 21 (T21)
- Trisomy 13 (T13)

**Clinical Issues**

- Grave prognosis
- Partial monosomy greater survival than complete
- Chorionic villus sampling or amniocentesis required for diagnosis

**PATHOLOGY**

**General Features**

- **Genetics**
  - Chromosome region 21q22 key area
  - Altered chromosome may have paternal, maternal, or de novo origin

- **Epidemiology**
  - Extremely rare and rarely diagnosed in utero
  - Partial monosomy 21 appears more frequently than complete deletion (more lethal)
  - Wide range of phenotypic manifestations
  - Move severe anomalies due to larger deletions

**CLINICAL ISSUES**

**Natural History & Prognosis**

- Grave prognosis
- Neurologic anomalies
  - Severe mental retardation and delayed development
- Microcephaly
- Hypertonia
- Seizures
- Cardiac anomalies
  - Structural defects
  - Electrical anomalies
  - Cardiac failure most common cause of death
- Ophthalmologic defects
  - Microphthalmia
  - Abnormal anterior or posterior eye chamber
  - Musculoskeletal anomalies
  - Arthrogyrosis-like symptoms: Restricted joint mobility
  - Flat or clubbed feet
  - Hand malformations
  - Genitourinary anomalies
  - Failure to thrive

- Partial monosomy greater survival than complete
- 50% infant mortality if survive until birth

**Treatment**

- Chorionic villus sampling or amniocentesis required for diagnosis
- Determine if deletion is partial or complete

**DIAGNOSTIC CHECKLIST**

- Consider
  - When features of both T21 and T13 are present

**Image Interpretation Pearls**

- No imaging findings are diagnostic
- Karyotyping needed for diagnosis

**SELECTED REFERENCES**


**IMAGE GALLERY**

(Left) Ultrasound shows bilateral pleural effusion (arrows) in a fetus with monosomy 21. (Right) Coronal ultrasound shows agenesis of the frontal lobes with a single channel viewed entering the midline (arrow). There is an acranial anomaly, and the thalami are not seen (ventral holoprosencephaly).
SECTION 15: Syndromes & Multisystem Disorders

- Aicardi Syndrome
- Amniotic Band Syndrome
- Apert Syndrome
- Beckwith-Wiedemann Syndrome
- Carpenter Syndrome
- Cornelia de Lange Syndrome
- Cystic Fibrosis
- Fryns Syndrome
- Joubert Syndrome
- Meckel-Gruber Syndrome
- Pierre Robin Syndrome
- Simonopoulou
- Smith-Lemli-Opitz Syndrome
- Tuberous Sclerosis
- VACTERL Association
AICARDI SYNDROME

TERMINOLOGY

Definitions
- Rare, severe developmental disorder characterized by:
  - Clinical triad of encephalactic spasm, agenesis of corpus callosum (ACC) and ecto- and intero-telencephalic lacunae

IMAGING FINDINGS

General Features
- Best diagnostic clue: ACC in a female fetus

Ultrasonographic Findings
- Callosal agenesis/dysgenesis
  - Inability to visualize corpus callosum in entirety on mid-sagittal and coronal imaging
  - Elevation of 3rd ventricle
  - Absent cavum septi pellucidi
  - Colpocephaly ("teardrop-shaped" ventricles)
  - Interhemispheric cyst/lipoma
- Other central nervous system (CNS) findings
  - Dandy-Walker continuum (DWC)
  - Inferior vermis dysgenesis, posterior fossa cyst
  - Ventriculomegaly
  - Choroid plexus cysts/papillomas

MR Findings
- Broad spectrum of cerebral malformations
  - Most consistent feature is ACC
  - May be partially formed (dysgenesis)
  - Absence of cavum septi pellucidi
  - Colpocephaly
  - Pacchionian
  - Cortical heterotopias
  - DWC with hypoplasia/aplasia of cerebellar vermis
  - Optic nerve and chiasm/hypoplasia
  - May only be recognized on postnatal scans

Imaging Recommendations
- Protocol advise: fetal MRI may be helpful in a suspected prenatal diagnosis

DIFFERENTIAL DIAGNOSIS

Corpus callosal agenesis/dysgenesis
- Isolated or other syndrome

Dandy Walker continuum
- Isolated or systemic

DDx: Aicardi Syndrome

ACC
DWC, Isolated
DWC, Syndrome
ACARDI SYNDROME

Key Facts

- Rare, severe developmental disorder characterized by clinical triad of: (1) spina bifida, agenesis of corpus callosum (ACC) and choiretinal lacunae

Imaging Findings

- Most consistent feature is ACC

Top Differential Diagnoses

- Corpus callosum agenesis/dysgenesis

PATHOLOGY

General Features

- Genetics
  - Probable X-linked dominant with early embryonic lethality in hemizygous males
  - Rare reports of males with 47,XXY karyotype
  - Report of recurrence in 2 siblings attributed to possible germlinal mosaicism
  - Discordance in monzygotic twins reported
- Epidemiology
  - Early lethality in males resulting in spontaneous abortion
  - Second trimester and beyond almost exclusively female

CLINICAL ISSUES

Presentation

- Most common signs/symptoms: In utero ACC is most consistent finding
- Postnatal findings
  - Infantile spastics
  - Usual clinical presentation, average onset 9 weeks
  - Choiretinal lacunae (pathognomonic)
  - Agenesis of the corpus callosum
  - Total 72%
  - Partial 28%
- Mental retardation
  - Most with no meaningful language skills
  - Hydrocephalus, scoliosis, absent/malformed ribs
  - Ocular, clefts, colobomata, microphthalmia
  - Phenotypic overlap with ML syndrome (microphthalmia with linear skin defects and not optimal syndrome)

Natural History & Prognosis

- High early childhood mortality
  - Rare reports of milder phenotype with less severe clinical course
  - Severe prenatal retardation and seizures, often non-convulsive
  - Spacing of icusa and smaller lacunae size correlated with better vision

Diagnostic Checklist

- Consider if a female fetus with ACC, especially when consistent abnormalities such as DWC are present
- Acardi syndrome remains a clinical diagnosis

DIAGNOSTIC CHECKLIST

Image Interpretation Pears

- Always check in fetus with ACC
- Consider if a female fetus with ACC, especially when consistent abnormalities such as DWC are present
- Acardi syndrome remains a clinical diagnosis

SELECED REFERENCES


IMAGE GALLERY

(Left) Scoliosis ultrasound of 45 weeks gestation shows a highlying 3rd vertebra (arrow), which is colobomata with an associated myelomeningocele. (Right) Axial spine ultrasound shows absence of the caudal vertebrae (arrow) in this case of Acardi syndrome.
AMNIOTIC BAND SYNDROME

TERMINOLOGY

Abbreviations and Synonyms
- ADAM (amniotic defect; adhesion, mediated)
- Amniotic band sequence (ABS)
- Amniotic disruption complex
- Streeter dysplasia/bands
- Congenital constriction bands

Definitions
- Entrapment of fetal parts by disrupted amnion
- Formation of fibrous amniotic bands
- Resulting anomalies (usually multiple)
  - Clefts
  - Constrictions
  - Amputations
  - Malformation
  - Deformation

IMAGING FINDINGS

General Features
- Best diagnostic clue
  - Asymmetric distribution of defects is hallmark of syndrome
  - Amniotic band in contact with deformity
  - Asymmetric cranial/facial deformities

DDx: Amniotic Band Syndromes

- Stuck
- Body Wall Anomaly
- Encephalocele
- Gastroschisis

Ultrasonographic Findings
- Bands in amniotic fluid appear as multiple thin membranes
- Bands may be difficult to discern, especially on setting of oligohydramnios
- May restrict fetal motion
- Face and head
  - Craniofacial deformities often severe
  - Facial clefts
  - Do not conform to pattern of developmental clefts
  - Often oblique
  - Cleft lip usually bilateral
  - Nasal deformity
  - Single orbital involvement typical
  - Cephalohematomas
  - Occur in area other than along sutures
  - Amniocentesis-like defect
  - Absent/defective cranium vault
  - Little or no remodeling brain parenchyma
  - Often asymmetric or absent orbits: yes, true amniocentesis = "frog eye" appearance
  - Arachnoid/acalectasia-like defects
  - Some cerebral tissue remains
AMNIOTIC BAND SYNDROME

Key Facts

Terminology
- Entrapment of fetal parts by disrupted amnion

Imaging Findings
- Amniotic band in contact with deformity
- Defects may be isolated or multiple, not in specific pattern
- Bands in amniotic fluid appear as multiple thin striations
- Bands may be difficult to discern, especially in setting of oligohydramnios
- Cranial skull deformities often severe
- Constriction with edema of distal extremity
- Limb amputations
- Abdominal wall defects
- If unusual distribution of defects, look carefully for bands

- Remaining parenchymal abnormal and disorganized
- Microcephaly
- Hydrocephalus
- Meningocele
- Extremities
- Constriction with edema of distal extremity
- May lead to eventual amputation
- Most common deformity
- Usually involves fingers and toes
- Limb amputations
- Often fingers and ears
- Easily missed if isolated
- Clubbed feet and hands
- Multiple joint contractures
- Pseudopahyphal
- Fusion of digital digits
- Crown wall defects
- Ectopia cordis
- Bibs clefs
- Abdominal wall defects
- Gastrochisis-like bowel extension
- Omphalocele-like liver herniation
- Bladder extrophy
- Scrotal
- Ambiguous genitalia
- Imperforate anus
- Oligohydramnios in some cases
- Fluid looks between amnion and chorion and is real-avoided

Imaging Recommendations
- If unusual distribution of defects, look carefully for bands
- May be tightly adherent and difficult to see
- Consider scanning patient in decubitus position
- Fetus stays in fixed position
- Bands restrict movement of involved area
- Color Doppler to assess flow to affected extremity

Top Differential Diagnoses
- Body stalk anomaly
- Developmental defects
- Amniotic cases
- Chorioamniotic separation

Pathology
- Generally no recurrence risk
- Not associated with aneuploidy
- Ruptured amnion does not always lead to amniotic band syndrome
- No two fetuses affected identically

Clinical Issues
- Defects range from minor to lethal
- Successful in abort lysis of bands for at-risk extremity reported

Differential Diagnosis

Body stalk anomaly
- Fetal abdominal wall adjacent to placenta
- Amnion in continuity with peritoneum
- Absent or short umbilical cord
- Scleiotic major finding
- Absence of limb defects
- Cranial defects uncommon

Developmental defects
- All have defined amniotic distribution from embryologic development
- Cephalocele
- Occipital and frontal
- Neural tube defects
- Most commonly lumbar
- Associated Chiari II brain findings
- Obliteraton of o stopping magna
- Compression of cerebellum ("banana" sign)
- Flatting of frontal bones ('lenuo" sign)
- Acanthosis nigricans
- Difficult to distinguish from amniotic bands in absence of associated malformations
- Arhinencephaly
- Both orbits retain
- Very proptotic ("frog eye" appearance)
- Clêfs lip
- Unilateral, bilateral, or midline
- Not cleft
- Gastroschisis
- Abdominal wall defect
- Free-floating bowel loops
- Right of midline adjacent to cord insertion
- Omphalocele
- Midline abdominal wall defects covered by peritoneum
- Contains bowel and/or liver
- Umbilical cord insert on mass

Amniotic sheets
- Amnion wrapping around synchiae
AMNIOTIC BAND SYNDROME

Natural History & Prognosis
- Depends on degree of malformation
- Defects range from minor to lethal
- Variable prognosis
- Constriction alone = good prognosis and normal life expectancy
- Postnatal physical exam may demonstrate additional defects
- Digital defects often present
  - Microphthalmia, hypertelorism
  - Eyelid colobomas, extropion
  - Thoracic, lumbar outflow obstruction, clefting anomalies
  - Defective cranial ossification
  - Dental ridges, sirenian crease

Treatment
- Termination offered for major defects
- Successful in utero lysis of bands for at-risk extremity reported

DIAGNOSTIC CHECKLIST
Consider
- Amniotic band syndrome when body defects do not follow a developmental anatomic distribution

Image Interpretation Pearls
- Extremities most commonly involved
  - Both contractions and amputations
  - Fused digits when only digits are involved

SELECTED REFERENCES
AMNIOTIC BAND SYNDROME

IMAGE GALLERY

Typical

(Left) Ultrasound shows several leaf-like objects (open arrows). An amniotic band (open arrows) can be seen extending from the chorda to the placental edge.

(Right) Ultrasound shows an extremity (arrow) located by an apparent amniotic band (open arrow). The fetus was one of twins affected by twin-to-twin transfusion syndrome. Septated amniotic sac resulted in chorionicplacental separation. Fetal roles no resulting amniotic constriction.

Typical

(Left) Cerebral ultrasound shows absence of the cranial vault, with exophytic brain tissue (open arrows) superior to the skull base. Open the amniotic band (open arrows) extending from the brain of the skull toward the placenta. (Right) Cerebral ultrasound from the same case reveals lack of a cranial vault, with exophytic brain tissue (open arrows) superior to the skull. (Courtesy D. Chalup, MD.)

Typical

(Left) Radiograph shows amputation of the right femur and humerus due to amniotic band. Secondarily, an arm is also present. (Right) Cervical ultrasound from the same case shows the extent of the amputation at the right side. Hematoma and extension of 3D amniotic sac are also seen.
APERT SYNDROME

TERMINOLOGY

Abbreviations and Synonyms
* Acrocephalosyndactyly type I

Definitions
* Craniofacial dysostosis characterized by craniosynostosis, maxillary hypoplasia, and syndactyly of hands and feet

IMAGING FINDINGS

General Features
* Best diagnostic clue: Abnormal calvarial shape with severe syndactyly on mid-trilateral ultrasonound

Ultrasoundographic Findings
* Craniosynostosis with brachycephaly
  * Fused corneal sutures +/− other sutures resulting in calvarial skull shape
  * "Mitten" syndactyly
  * Excessive, often bony, fusion of fingers/toes
* Central nervous system (CNS) abnormalities in 60%
  * Ventriculomegaly, megalecephaly, archicerebral cyst, agenesia of corpus callosum, agenesis septi pellucidi
  * Cardiac defects (10%)

Differential Diagnosis

Pfeiffer syndrome
* Acrocephalosyndactyly, Pfeiffer type
* Severe craniosynostosis; Meckel-Gruber (clover-leaf) craniosyndactyly
* Broad digital thumbs, toes with syndactyly of central digits

Carpenter syndrome
* Acrocephalopolysyndactyly type II
* Craniosynostosis of multiple sutures
* Preaxial polydactyly, soft tissue syndactyly
* Cardiac defects, ventral wall abnormalities

Saethre-Chotzen syndrome
* Coronal suture synostosis
* Smooth ephelides, dysplastic ears
* Partial cutaneous syndactyly of fingers, toes

Crouzon syndrome
* Craniosynostosis involving multiple sutures

Diagnosis: Syndromic Craniosynostosis

Carpenter
Carpenter (foot)
Pfeiffer Syndrome
APERT SYNDROME

Key Facts

Terminology
- Acrcephalosyndactyly type I
- Craniofacial dysostosis characterized by craniosynostosis, midface hypoplasia and syndactyly of hands and feet

Imaging Findings
- Fusion of coronal sutures +/- other sutures resulting in conical skull shape
- "Mitten" syndactyly

- Severe proptosis with hypertelorism
- Syndactyly uncommon

Pathological dysplasia
- Letal skeletal dysplasia with microscilia, small chest
- Craniosynostosis with lebetalbiclité in type II
- Trident hand without syndactyly

PATHOLOGY

General Features
- Genetics: Autosomal dominant
- Etiology:
  - Due to mutations in fibroblast growth factor receptor 2 gene (FGFR2)
  - Most due to point mutation S252W or P235R which cause activation of FGFR2
- Epidemiology: Associated with increased paternal age

CLINICAL ISSUES

Presentation
- Postnatal findings
  - Craniofacial
    - Bilateral coronal suture synostosis, variable other sutures
  - Midface hypoplasia, maxillary hypoplasia
  - Exophthalmos, hypertelorism, downwarding papyraceous fissures, supranasal horizontal groove
  - High forehead and flat occiput
  - Narrow palate with median groove, +/- cleft
  - Malocclusion, dental abnormalities
  - Complex syndactyly of hands and feet: "Mitten" syndactyly
- Short broad thumb in valgus position
- Bony fusion involving digits 2-4, symphalangism (synostosis of joints)
- Involves the muscles, tendons insertions and neurovascular bundles of hand
- Simple syndactyly of soft tissue between digits 4-5
- Mental retardation common (IQ, 44-90)
- Fusion of cervical vertebrae (C5-C6)

Natural History & Prognosis
- Early repair of craniosynostosis does not prevent mental retardation
- Intracranial hypertension common
- Hearing loss due to chronic otitis, fixation of stapes

Top Differential Diagnoses
- Pfeiffer syndrome
- Carpenter syndrome
- Saethre-Chotzen syndrome
- Crouzon syndrome

Pathology
- Genetics: Autosomal dominant
- Due to mutations in fibroblast growth factor receptor 2 gene (FGFR2)

- Severe purulent acne at puberty is characteristic
- Upper and lower airway compromise may be responsible for early death

Treatment
- Surgical correction of craniosynostosis, craniofacial reconstruction
- Extensive/complex surgical management of syndactyly with goal of increasing functionality

DIAGNOSTIC CHECKLIST

Consider
- 3D ultrasound to evaluate extremities, face when calvarial abnormality identified

Image Interpretation Pearls
- Prenatal diagnosis possible by 19-20 weeks on basis of abnormal calvarial shape, syndactyly

SELECTED REFERENCES

IMAGE GALLERY

Apt) Ultrasonography shows complex syndactyly (arrow) of the fingers and valgus deviation of the thumb (open arrow) in a fetus with Apert syndrome. (Right) Radiograph shows complex fused articular syndactyly (arrow) in the infant with Apert syndrome. The distal phalanges of the thumbs braid around arrow.
**TERMINOLOGY**

**Abbreviations and Synonyms**
- Beckwith-Wiedemann syndrome (BWS)
- Wiedemann-Beckwith syndrome

**Definitions**
- Characterized by macrosomia, hemihyperplasia, macroglossia, ventral wall defects, predisposition to embryonal tumors, and neonatal hypoglycemia

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue: Large for dates fetus with enlarged kidneys, omphalocele and protruding tongue on mid-trimester ultrasound

**DIFFERENTIAL DIAGNOSIS**

**Omphalocele, isolated vs. syndromic**
- Increased aneuploidy risk

**Macrosomia from maternal diabetes (IDDM)**
- Fetal, central nervous system, extremity malformations
- Omphalocele uncommon

**PATHOLOGY**

**General Features**
- Genetics
  - Genetically heterogeneous: 85% are sporadic with normal karyotype
  - 10-15% are inherited in autosomal dominant fashion
  - 10-20% with parental uniparental disomy
  - Both copies of 1p15 derived from father
  - Less than 1% cases with chromosome translocation, inversion or duplication involving 1p15 region
  - As high as 30% recurrence risk if translocation is maternal in origin
- Etiology

**DDx: Inlarged Abdominal Circumference**

- IDDM
- Macrosomia
- Omphalocele
**Terminology**
- Characterized by macroadenoma, high hyperglycemia, macroglossia, ventral wall defects, predisposition to neoplastic tumors, and neonatal hypoglycemia.

**Imaging Findings**
- Best diagnostic: Large for dates fetus with enlarged kidneys, amniolcele and protruding tongue in mid-trimester ultrasound.

**Key Facts**
- Top Differential Diagnoses:
  - Omphalocele, isolated vs. syndromic
  - Macroadenoma from maternal diabetes (IDDM)
  - Meckel's diverticulum

- Pathology:
  - Increased risk of imprinting-related disorders (including BWS) in assisted reproductive technology pregnancies.

**CLINICAL ISSUES**
- Most common signs/symptoms:
  - Macrosomia, advanced skeletal maturation
  - Characteristic facies
  - Macroglossia: Neonatal airway obstruction if severe
  - Neonatal hypoglycemia over forehead, eyelids
  - Midface hypoplasia, proptosis, malocclusion, micrognathia
  - Alimentary tract defects
  - Omphalocele, gastroschisis, umbilical hernia
  - Variable developmental delay

- Natural History & Prognosis
  - Pregnancy with fetal BWS
  - Polyhydramnios, maternal risk of pre-eclampsia, increased premature delivery
  - Neonatal period
    - Hypoglycemia, apnoea, airway difficulties
    - High infant mortality rate (2%)
    - Chiasmatic
  - Increased risk of Wilms tumor, hepatoblastoma, neuroblastoma, malformation syndromes, adenocortical carcinoma
  - Overall tumor risk 7.5-10%; Wilms tumor = 60% of all tumors.

**Treatment**
- Delivery in a tertiary care center:
  - Availability of pediatric surgery, neonatal intensive care
  - Preparation for potential airway obstruction due to micrognathia, glossecytosis infrequently required
  - Neonatal surveillance protocol involving alpha-fetoprotein and abdominal ultrasound every 3 months until age 4 years.

**DIAGNOSTIC CHECKLIST**

**Image Interpretation Pearls**
- Accelerated fetal growth is presence of characteristic anomalies is suggestive of BWS.

**SELECTED REFERENCES**

**IMAGE GALLERY**
- (Left) Fetal ultrasound shows small echogenic liver and adrenal glands with BWS. (Right) Chromosome karyotype of adenocortical neoplasm, a characteristic finding in BWS.
Carpenter Syndrome

TERMINOLOGY

Abbreviations and Synonyms
- Microcephalocephaly syndactyly type I

Definitions
- Characterized by craniosynostosis of multiple suturens, preaxial polydactyly, soft tissue syndactyly, cardiac defects and ventral wall abnormalities

IMAGING FINDINGS

General Features
- Best diagnostic clue: abnormal calvarial shape with proptosis and polydactyly of hands and feet on mid-trimester ultrasound

Ultrasonographic Findings
- Craniosynostosis results in shallow orbits, causing prominent proptosis
- Cardiac defects in 50-50%
- Septal defects, pulmonic stenosis, tetralogy of Fallot
- Preaxial polydactyly with partial syndactyly
- Hands over appear classified
- Polydactyly not an absolute requirement for syndrome
- Abdominal wall defects

- Ophthalmocoele, hernia

Radiographic Findings
- Prenatal ultrasound of limited value
- Postnatal radiographs important for diagnosis
- Craniosynostosis of sagittal, lambdoid, occasionally coronal sutures
- Variable calvarial shape including keel-shaped inferior coronal suture
- Genu valga, lateral patellar displacement, flared ilia, flat acetabula
- Shortened/hypoplastic middle phalanges, duplicated 2nd phalanges or thumb

Imaging Recommendations
- Protocol advice
- Evaluation of extremities to exclude skeletal dysplasia
- Careful search for evidence of cardiac and abdominal wall defects

DIFFERENTIAL DIAGNOSIS

Apert syndrome
- Acrocephalo syndactyly, type I
- Partial or complete syndactyly of fingers and toes
- Craniosynostosis with brachycephaly

DDx: Abnormal Calvarial Shape

- Apert Syndrome
- Pfeiffer Syndrome
- TD Type I

15 12
### Terminology
- Acrocephalopolysyndactyly type II
- Characterized by craniosynostosis of multiple sutures, preaxial polydactyly, soft tissue syndactyly, cardiac defects and ventral wall anomalies

### Imaging Findings
- Best diagnostic clue: Abnormal calvarial shape with prominent and polysyndactyly of hands and feet on third-trimester ultrasound

### Key Facts
- **Fever syndrome**
  - Acrocephalopolysyndactyly, Pfeiffer type
  - Severe craniosynostosis, clefthand/foot common
  - Broad distal thumbs, toes with syndactyly of central digits

- **Crouzon syndrome**
  - Severe proptosis, hypertelorism
  - Craniosynostosis of multiple sutures
  - Syndactyly not a prominent feature

- **Seyd-Me-Cotzen syndrome**
  - Craniosynostosis of coronal, lambdoid sutures
  - High flat forehead, dysplastic ears
  - Partial syndactyly of fingers, toes

- **Bardet-Biedl syndrome**
  - Post-axial polydactyly, syndactyly, brachydactyly
  - Retinal dystrophy
  - Mental retardation, obesity, hypogonadism

- **Thanatophoric dysplasia (TD)**
  - Severe skeletal dysplasia with micromelia
  - Craniosynostosis with cleftblatherischied skull in type II
  - Small chest

### Natural History & Prognosis
- Truncal obesity common
- Intellectual function variable (I.Q. range 52-104)
- Articulation problems and fine motor impairment

### Treatment
- No prenatal treatment
- Referral for genetic counseling
- Neurosurgical repair of craniosynostosis
  - Impact on intellectual functioning variable
  - Surgical correction of cardiac, abdominal wall defects
  - Surgical management of polydactyly centers on improving functionality of hands

### SELECTED REFERENCES

### PATHOLOGY
- **General Features**
  - Genetics: Autosomal recessive

### CLINICAL ISSUES
- **Presentation**
  - Most common signs/symptoms: Abnormal skull shape
  - Postnatal
    - Brachydactyly with broad thumbs, soft tissue syndactyly of fingers
    - Dysplasia canthus (lateral displacement of inner canthus), downsizing palpebral fissures
    - Dental abnormalities with delayed eruption, prolonged retention of primary teeth, hypodontia
    - Hypogonadism

### IMAGE GALLERY
- (Left) Ultrasound shows persistently elevated head in a newborn infant (arrow). Polydactyly was noted at birth. Note the shallow orbit with proptosis (arrow). **Right**: Clinical photograph shows complex polydactyly in Carpenter syndrome. Note the lateral thumb (arrow), which was differentiated on X-ray, and syndactyly of the remaining fingers (open arrow).
**TERMmNOLOGY**

Abbreviations and Synonyms
- Cornelia de Lange Syndrome (CdLS)
- Brachmann-de Lange syndrome

Definitions
- Syndrome characterized by characteristic facial features, growth and mental retardation, limb defects, gastrointestinal abnormalities, cardiac defects and hypertelorism

**IMAGING FINDINGS**

Ultrasoundographic Findings
- Intracranial growth restriction (ICGR)
- Upper limb reduction defects
- Micrognathia with protruding upper lip
- Best evaluated in profile view
- Diaphragmatic hernia (CDP), occasionally bilateral

Radiographic Findings
- Most characteristic feature: Short 1st metacarpal with relatively long 2nd-4th metacarpals
- Subluxation of radial head

**DIFFERENTIAL DIAGNOSIS**

Frns syndrome
- CDH (85%), distal limb hypoplasia (15%), coarse facies
- Polyhydramnios, normal fetal growth

Chromosome aneuploidy
- Pallister-Killian syndrome
  - Tissue nodules with supernumerary iso-chromosome 12p (corticat tetrasomy 12p)
  - CDH, polyhydramnios
  - Bilateral limb shortening, rare acral hypoplasia
  - Mental retardation
- Partial duplication of 1q
  - Craniofacial, cardiac, renal anomalies
  - Mental retardation
  - Normal fetal growth/prenatal growth failure
- Low-set posterior hemifacial, bushy eyebrows, long lashes
- Deepened nasal bridge, antverted nares, long prominent philtrum.

- Trisomy 18
  - ICGR, radiol defects, overlapping digits
  - CDH occasional finding

DDx. CDH With Limb Anomalies

- T1B, Radial Ray
- T1B, Radial Ray
- Fyrs Syndrome, CDH
- Fyrs. Digital Hypoplasia
CORNELIA DE LANGE SYNDROME

Terminology
- Syndrome characterized by characteristic facial features, growth and mental retardation, limb defects, gastrointestinal abnormalities, cardiac defects and hypertelorism.

Top Differential Diagnoses
- Trisomy syndrome
- Chromosomal aneuploidy
- Fetal alcohol syndrome

ちな環 alkaloid syndrome
- Pre- and postnatal growth restriction
- Alveolar, cleft palate, cardiac defects, developmental delay
- Short palpebral fissures, short philtrum, thin upper lip
- Congenital diaphragmatic hernia, isolated
- Limb reduction defects
- Isolated vs. syndrome

ATHOLOGY
General features
- Genetics
  - Autosomal dominant
  - Most sporadic (99%) rare familial cases
- Etiology
  - Caused by mutations in NIPBL
  - Human homolog of the Drosophila Nipped-B gene
- Epidemiology: Prevalence estimated to be as high as 1/10,000

CLINICAL ISSUES
Presentation
- Distinctive facial phenotype
  - Fine arched eyebrows ("penciled in"), long smooth philtrum, thin lips, "creased" shaped mouth, symphysis fused eyebrows, long lashes, prods, downturned eyes, depressed nasal bridge, retracted ears, small jaw
- Limb defects
- Short arms/small hands to severe limb reduction defects, deformed, monodactyly
- Microcephaly, short neck, low posterior hairline, anterior hairline extends over forehead
- UGR, postnatal short stature
- Cardiac defects (25%): Pulmonary stenosis, ventricular septal defect most common
- Diaphragmatic hernia (CDH)
- Other gastrointestinal anomalies: Meckel’s diverticulum, ileal duplication, jejunal atresia, jejunal stenosis, reflux
- Genitourinary: Horsehoe kidney, hypospadias, cryptorchidism

Key Facts
Clinical Issues
- Wide spectrum of severity
- Postnatal lethality (~milder cases of adults capable of living independently)
- Behavioral phenotype: Self-injury, aggression, sleep disturbance, autistic behaviors

Diagnostic Checklist
- Consider CDLS when CDH found in association with limb anomalies

Natural History & Prognosis
- Wide spectrum of severity
  - Perinatal lethality (~milder cases of adults capable of living independently)
  - Mental retardation (moderate to profound)
  - Significant speech and language delay (some non-verbal, hearing loss, seizures (10-21%)
  - Behavioral phenotype: Self-injury, aggression, sleep disturbance, autistic behaviors

DIAGNOSTIC CHECKLIST
Image Interpretation Pearls
- Consider CDLS when CDH found in association with limb anomalies

SELECTED REFERENCES

IMAGE GALLERY

[Image: Truncus arteriosus shown as a CDH is a 26 week fetus with CDLS. The heart is pushed to the chest wall (curved area) and the stomach is seen in the chest (arrow). MS ventricle is also seen. Right]
CYSTIC FIBROSIS

Terminology

Definitions
- Cystic fibrosis (CF) is an autosomal recessive multisystem disorder caused by dysfunctional chloride ion transport across epithelial surfaces.

Imaging Findings

General Features
- Best diagnostic clue: Echogenic bowel in 2nd trimester progressing to bowel dilatation in 3rd trimester.

Ultrasoundographic Findings
- Echogenic bowel in second trimester
- Increased echogenicity likely secondary to mucus secretions in bowel lumen
- Risk of fetus with echogenic bowel having cystic fibrosis varies dramatically between studies (0-33%)
- Must take into consideration population base
- In a large study where CF was common, 9.9% with echogenic bowel had CF
- 11% of fetuses with CF have echogenic bowel
- Meconium ileus
- Dilated, echogenic small bowel
- Appearance often indistinguishable from ileal atresia

DDx: Echogenic Bowel
- Meconium ileus
- Trisomy 21
- Trisomy 22
- Ischemic bowel

Differential Diagnosis

Other causes of echogenic bowel
- Trisomy 21
- Look for associated findings
- Infection
- Cytomegalovirus (CMV) most common
- Look for calcification in brain and liver
- Intratubular growth restriction
- Bowel ischemia
- Ileal atresia
- May be indistinguishable from CF

Pathology

General Features
- Genetics: Autosomal recessive (25% recurrence risk)
- Etiology
- Caused by mutations in gene which encodes cystic fibrosis transmembrane conductance regulator (CFTR)
- Chromosome 7q32
- Atresias may also be present
- Perforation with meconium peritonitis
- 8% of fetuses with meconium peritonitis have CF
**CYSTIC FIBROSIS**

**Key Facts**

- Pathology
  - Genetic: Autosomal recessive (25% recurrence risk)
  - Highest prevalence in Caucasians of Northern European origin

- Diagnostic Checklist
  - Normal ultrasound exam does not rule out CF
  - Meconium ileus may be indistinguishable from ileal atresia

**PRESENTATION**

- Most common signs/symptoms: Echogenic or dilated bowel in fetus
  - 60% diagnosed in first year of life
  - 83% diagnosed by age 5
  - May present in neonatal period with failure to pass meconium

- Gastrointestinal symptoms
  - Constipation, obstruction
  - Malabsorption from pancreatic insufficiency, diabetes
  - Neonatal hepatitis, cholestasis, biliary cirrhosis

- Respiratory
  - Recurrent infections, mucus plugging
  - Bronchiectasis, hyperinflation, cystic disease, spontaneous pneumothorax

- Nasal polyphs, sinilitis

- Male infertility

**Natural History & Prognosis**

- Median survival: Unusually 32 years
- Death usually caused by lung disease

**Treatment**

- Test parents for carrier status
- Amniocentesis for direct detection of mutation in fetus
- Testing for 3 most common mutations 87% detection rate
- Extended analysis 98.5% detection rate
- Fetuses with echogenic bowel tend to have more severe mutations
- Genetic counseling
- Chorionic villus sampling may be offered in first trimester on future pregnancies

**IMAGING FINDINGS**

- Best diagnostic clue: Echogenic bowel is 2nd trimester progressing to bowel dilatation in 3rd trimester
- In a large study where CF was common, 9.9% with echogenic bowel had CF
- 11% of fetuses with CF have echogenic bowel
- 8% of fetuses with meconium plug only have CF

**CLINICAL ISSUES**

- > 1,000 mutations possible
- CFTR gene mutation → lack of chloride ion secretion → increased sodium retention and fluid absorption → increased viscosity of luminal secretions → obstructed ducts of solid organs and hollow visceral
- Epidemiology
  - 1:2,000 to 5,000 births
  - Carrier rate 1/25 to 1/35
  - Highest prevalence in Caucasians of Northern European origin

**DIAGNOSTIC CHECKLIST**

- Consider
  - Normal ultrasound exam does not rule out CF
  - Echogenic bowel/meconium ileus only seen in 11% of cases

- Image Interpretation Pearls
  - Meconium ileus may be indistinguishable from ileal atresia
  - Work-up for cystic fibrosis should be done in all cases of fetal bowel obstruction

**SELECTED REFERENCES**


**IMAGE GALLERY**

(left) Axial ultrasound of a fetus with cystic fibrosis shows echogenic, dilated, fluid-filled loops of bowel (arrows). Right: Mesoappendiceal contrast scan in a neonate failing to pass meconium shows a necrotic appendix with wall of contrast into the terminal ileum, which has multiple filling defects (arrows). This appearance is diagnostic of meconium ileus.
FRYNS SYNDROME

Clinical photograph shows a preterm stillborn male with Fryns syndrome. Note the coarse face, mild depressed nasal bridge (curved arrows), antverted nares, thin lips and small ears.

Tissue sample shows a large CDH in a fetus with Fryns syndrome. The sternal (arrows) and right clavicle (arrow) are in the chest. The heart (arrow) was the abnormal.

TERMINOLOGY

Definitions
- Perinatal lethal disorder characterized by segmental diaphragmatic hernias (CDH) with pulmonary hypoplasia, coarse face, mild depressed nasal bridge (curved arrows), antverted nares, thin lips and small ears.

DIFFERENTIAL DIAGNOSIS

Chromosome aneuploidy
- Patau-trisomy syndrome
  - Trisomy 18
- Chromosome 13 rearrangement: trisomy 13p due to supernumerary or exchange chromosome 13p
- CDH, polyhydramnios, rhizomelia, cardiac malformations, polydactyly
- Coarse face, severe mental retardation, pigmentary abnormalities
- Diagnosis generally made in older infant with developmental delay and coarse facies in contrast to prenatal lethality in Fryns

Ultrasoundographic findings
- CDH most obvious finding and should prompt search for other features
- Micoglosia
- Orofacial cleft
- Cardiac defects
- Polyhydramnios

Imaging Recommendations
- Protocol advised: Careful search for other anomalies, including cardiac and extremities when CDH identified

Ultrasonographic findings
- Trisomy 18
- IUGR, radial ray defects, cardiac defects, choanal atresia
- CDH, isolated

Cornelia de Lange syndrome
- Characteristic features: Fine arched eyebrows, long smooth philtrum, thin lips, crecent shaped mouth
- Limb defects variable from small hands to severe limb reduction abnormalities
- CDH
- Cardiac defects, mental retardation, IUGR, gastrointestinal abnormalities, hypertrichosis

DDx: CDH Associated Conditions

- Trisomy 18
- Isolated CDH
- Cornelia de Lange
FRYNS SYNDROME

Key Facts
- Diaphragmatic hernia, isolated

Pathology
- Genetics: Autosomal recessive

Diagnostic Checklist
- 3D ultrasound for evaluation of face and distal extremities when Fryns syndrome suspected
- Diagnosis can be made in 2nd trimester, especially in cases with positive family history

Diaphragmatic hernia, isolated
- Most caudally affected other anomalies
- Most are sporadic but some of dominant, recessive and X-linked familial cases
- Familial cases more likely to be isolated; higher incidence of bilateral defects

HORACOABDOMINAL SYNDROME
- CDH, ventral hernias, hypoplastic lungs, cardiac anomalies

PATHOLOGY

General Features
- Genetics: Autosomal recessive
- Epidemiology: Estimated 1/15,000 births

CLINICAL ISSUES

Presentation
- CDH most obvious in utero finding (60%)
- Polyhydramnios
- Other pre- or postnatal findings
- Cleft lip/cleft palate
- Hypoplastic, absent or entire thoracic spine
- Hypoplasia of thoracic organs
- Renal anomalies
- Nephrotic syndrome
- Diaphragmatic hernia
- Growth retardation
- Cardiovascular anomalies
- Pulmonary hypoplasia
- Ventricular septal defect
- Hypertrophic cardiomyopathy
- Hypothyroidism
- Hypocalcemia
- Hypogonadism
- Hemangiomas
- Neurofibromatosis

Natural History & Prognosis
- Most are stillborn or die in the neonatal period
- Most will have significant morbidity and mortality
- Outcome is dependent on the severity of the associated anomalies

Survivors less likely to have CDH or cardiac defect

Treatment
- No prenatal treatment
- Prenatal termination should be offered

DIAGNOSTIC CHECKLIST
Consider
- 3D ultrasound for evaluation of face and distal extremities when Fryns syndrome suspected

Image Interpretation Pearls
- Diagnosis can be made in 2nd trimester, especially in cases with positive family history

SELECTED REFERENCES

IMAGE GALLERY

[Image: Clinical photograph of an infant with Fryns syndrome showing hypoplastic left arm and distal digital hypoplasia (arrows). The image also shows an abnormal profile in a fetus with Fryns syndrome. Note the hypoplastic midface (arrows) and subcutaneous edema (curved arrows).]
**JOUBERT SYNDROME**

**TERMINOLOGY**

**Definitions**
- Initial description in 1969: Consanguineous family with 4 affected children
  - Hypoplasia, ataxia, mental retardation, abnormal eye movements
  - Subsequent description of "Joubert-plus": Additional findings may include
    - Encephalocoele
    - Dandy-Walker continuum
    - Tectocerebellar dysraphia
    - Polysplenia

**IMAGING FINDINGS**

**Ultrasoundographic Findings**
- Abnormal nuchal translucency: Nonspecific but concerning in at-risk family
- Abnormal posterior fossa: Cerebellar cleft
- Additional findings with "Joubert-plus"
  - Ventriculomegaly/enlarged fourth ventricle
  - Polydactyly/micropector

**MR Findings**
- "Molar tooth" sign
- Deepening of interpeduncular fossa

**Imaging Recommendations**
- Best imaging tool: Fetal MRI
- Careful posterior fossa evaluation
- Look at face-breathing pattern
- Episodic fetal hyperpnea (140-160 breaths/min) reported

**DIFFERENTIAL DIAGNOSIS**

**Dandy-Walker continuum (DWC)**
- 4th ventricle communicates with cisterna magna
  - "Molar tooth" sign not a feature
  - Midsagittal normal in DWC, thinned in Joubert

**Arnold Chiari malformation**
- Obliteration of cisterna magna
- Herniation of cerebellar tonsils with "pancake" appearance to cerebellum

**Mega cisterna magna**
- Cisterna magna >10 mm in depth
- No associated structural malformation

**DDx: Abnormal Posterior Fossa**

- DWC
- Chiari II
- Encephalocoele
- Mega Cisterna Magis
# JOUBERT SYNDROME

## Imaging Findings
- "Molar tooth" sign
- Abnormal nuchal translucency: Non-specific but concerning in at-risk family

## Top Differential Diagnoses
- Dandy-Walker continuum (DWC)
- Arnold Chiari malformation
- Occipital encephalocele

## Occipital encephalocele
Defect in occipital cortical bone
Herniation of meninges/brain parenchyma through defect

## PATHOLOGY

### General Features
Genetics: Autosomal recessive
Epidemiology
- True incidence unknown: Many cases likely undiagnosed
- Genetic clinical diagnosis of "cerebral palsy"
- Most common diagnostic imaging error is to label as DWC
Embryology
- Defect thought to occur at 6-8 weeks gestation

### Gross Pathologic & Surgical Features
- Abnormal deep cerebral nuclei and midbrain
- Abnormal fibers in cerebellar peduncles
- Volume of occulomotor nuclei
- Verminous hypoplasia/aplasia

## CLINICAL ISSUES

### Natural History & Pregnosis
- Affected children have spectrum of abnormalities
- Developmental delay/mental retardation
- Occulomotor apraxia: Characteristic for Joubert syndrome
- Hypotonia
- Variable respiratory difficulties
- Hyperpnea/apnea
- Typical facies
- High rounded eyebrows, upturned nostrils, triangular-shaped mouth, low-set ears
- Recurrence risk 25%
- Outcome independent of severity imaging findings
- Affected siblings vary widely in presentation

### Treatment
- No specific treatment
- Decreased life expectancy
- Sudden infant death attributed to apneic attacks

## Key Facts

### Clinical Issues
- Recurrence risk 25%
- Outcome independent of severity imaging findings
- Affected siblings vary widely in presentation

### Diagnostic Checklist
- Fetal MR to characterize central nervous system anomalies particularly of posterior fossa

## DIAGNOSTIC CHECKLIST

### Consider
- Fetal MR to characterize central nervous system anomalies particularly of posterior fossa

### Image Interpretation Pearls
- Massive portal is Dandy-Walker continuum
  - "Molar tooth" sign not seen in DWC
  - Present in 85% Joubert cases
- Accurate diagnosis important as prognosis/recurrence risk are different
  - "Molar tooth" sign is not pathognomonic
- Infants need complete neurological evaluation including ophthalmologic assessment of occulomotor apraxia

## SELECTED REFERENCES

## IMAGE GALLERY

![Image Gallery](image-url)
MECKEL-GRUBER SYNDROME

TERMINOLOGY

Abbreviations and Synonyms
- Meckel-Gruber syndrome
- Meckel syndrome
- Gruber syndrome
- Dysencephalia sphenocerebica

Definitions
- First described in 1832 by Johann Meckel
- Triad of findings
  - Renal cystic dysplasia in 95-100%
  - Encephalocoele in 60-80%
  - Postaxial polydactyly in 55-75%

IMAGING FINDINGS

General Features
- Best diagnostic clue: At least 2 of 3 classic features in fetus with normal karyotype

Ultrasoundographic Findings
- Genitourinary
  - Renal cystic dysplasia most consistent finding
  - Variable sonographic appearance of kidneys
  - Grossly enlarged, echogenic kidneys most common

DDx: Meckel-Gruber Syndrome

- F/E Kidney
- F/T Polydactyly
- ARPKD
- Bilateral MCCK

- 1c-20x normal size
- Large, macroscopic cysts may be present
- Abdominal circumference may be significantly increased
- Bladder may be small or absent
- 2nd trimester oligohydramnios
- Often hydroureteronephrosis
- Fluid normal in 1st trimester, before kidneys become major contributor to amniotic fluid production
- Central nervous system
  - Encephalocoele
  - Variable size
  - Occipital located
  - Microcephaly common
  - Dandy-Walker continuum
  - Agenesis of corpus callosum
  - Ventriculomegaly
  - Holoprosencephaly
- Extremities
  - Postaxial polydactyly
  - Extra digit may be small or angulated
  - Usually affects all 4 extremities similarly, although this is most variable finding in classic triad
  - May be difficult to see with oligohydramnios
  - Uncommonly preaxial
  - Clubbed feet common
MECKEL-GRUBER SYNDROME

Terminology
- Triad of findings
- Renal cystic dysplasia in 95-100%
- Encephalocele in 60-80%
- Postaxial polydactyly in 55-75%

Imaging Findings
- Best diagnostic clue: At least 2 of 3 classic features in fetus with normal karyotype
- Renal cystic dysplasia most consistent finding
- Abdominal circumference may be significantly increased
- 2nd trimester oligohydramnios

Top Differential Diagnoses
- Trisomy 13 (T13)

Key Facts
- Autosomal recessive polycystic kidney disease (ARPKD)
- Encephalocele

Pathology
- Autosomal recessive
- 25% recurrence risk
- Hepatic fibrosis consistent feature in all cases

Clinical Issues
- Genetic counseling for future pregnancies
- Thorough 1st trimester endovaginal scans on all future pregnancies

Diagnostic Checklist
- Renal appearance is variable, from large, echogenic kidneys to kidneys completely replaced by microscopic cysts

- Extremities
  - Postaxial polydactyly in 75%
  - rockerbottom foot
- Cardiac
  - Cardiac defect in 80%
  - Septal defects
  - Hypoplastic left heart
  - Aortic/mitral atresia
- Other anomalies
  - Facial anomalies
  - Cyclopia
  - Hypotelorism
  - Microphthalmia
  - Median or bilateral cleft lip
  - Intrauterine growth restriction
  - Omphalocele
  - Oligohydramnios less common
  - May have polyhydramnios

Autosomal recessive polycystic kidney disease (ARPKD)
- Enlarged echogenic kidneys
- Does not have encephalocele or polydactyly
- Variable degrees of oligohydramnios

Multicystic dysplastic kidneys (MCDK)
- Consider in differential if it is bilateral
  - MCDK bilateral in ≈ 20% of cases
- Anhydramnios
- Lethal anomaly

Encephalocele
- Isolated or with other syndromes
  - Kidneys and extremities normal

DIFFERENTIAL DIAGNOSIS

Trisomy 13 (T13)
- Significant overlap in findings
  - Renal anomalies in 50%
  - Cystic dysplasia
  - Echogenic kidneys with scattered cysts
  - Kidneys may be large but typically smaller than in Meckel-Gruber syndrome
  - Hydrourephrosis
  - Central nervous system
    - Holoprosencephaly sequence in 40%
    - Encephalocele reported, but less common

Imaging Recommendations
- When one finding seen, careful search for others
- MRI helpful if oligohydramnios limits visualization
- Endovaginal ultrasound in 1st trimester, if there is a positive family history
- Early normal scan does not completely exclude Meckel-Gruber syndrome
- Follow-up scan at 18-20 weeks

PATHOLOGY

General Features
- Genetics
  - Autosomal recessive
  - 25% recurrence risk
- Several loci have been mapped
  - MKS1 on 17q21-q22
MECKEL-GRUBER SYNDROME

**diagnostic checklist**

**Consider**

- MRI when anatomic visualization compromised by oligohydramnios
- Look carefully for other findings when one of the major abnormalities is seen

**image interpretation pearls**

- Significant overlap in imaging features with trisomy 13
- Amniocentesis should be done for karyotype to appropriately counsel for future pregnancies
- 1% recurrence risk for trisomy 13 vs. 25% for Meckel-Gruber syndrome
- Retail appearance is variable, from large, ectodermal kidneys to kidneys completely replaced by macroscopic cysts
- Renal size is often massive, causing an enlarged abdominal circumference

**selected references**


**clinical issues**

**presentation**

- Most common signs/symptoms
  - Oligohydramnios
  - Polyhydramnios
  - May have history of prior affected child
  - Polyhydramnios may be normal if covered by membrane
  - Diagnosed possible in first trimester
  - Wide phenotypic variability
  - Associated findings vary significantly between cases

**natural history & prognosis**

- Legal
  - Polyhydramnios leads to pulmonary hypoplasia
  - Most stillborn or die within a few hours

**treatment**

- Early termination offered
- Fetoscopy and cesarean section to be avoided if pregnancy continues
- Enlarged abdominal circumference may cause abdominal distoxia
- External examination and autopsy by experienced pathologist requested to confirm diagnosis
- Genetic counseling for future pregnancies
- 2% recurrence risk
- Thorough 1st trimester obstetrical scans on all future pregnancies
MECKEL-GRUBER SYNDROME

IMAGE GALLERY

**Typical**

(Left) Sagittal ultrasound shows a massively enlarged, ectopic kidney (arrows) with a few scattered macroscopic cysts. Additional findings include oligohydramnios, small chest (open arrows), and hypertensive abdomen (arrow). Right: Sagittal brain ultrasound and gross specimen in a newborn with Meckel-Gruber syndrome shows a very similar appearance, with greatly enlarged, ectopic kidneys. Histology confirmed diffuse cystic dysplasia.

**Typical**

(Left) Axial ultrasound of the kidneys in a case of Meckel-Gruber syndrome shows bilateral enlargement with the renal parenchyma replaced by multiple microscopic cysts (arrows). Right: Gross pathology from this case confirms bilaterally enlarged kidneys with multiple, large cysts. Renal cystic dysplasia is the most commonly seen feature of Meckel-Gruber syndrome. Appearance may vary from dilated ectopic kidneys to well-defined cysts.

**Typical**

(Left) Ultrasound shows a cerebral defect (arrows) with an occipital encephalocele (open arrows). There is oligohydramnios secondary to renal dysplasia, which compromises visualization of intracranial structures. Right: Ultrasound of the feet in the same case shows polydactyly (arrows).
PIERRE ROBIN SYNDROME

TERMIOLOGY

Abbreviations and Synonyms
- Pierre Robin sequence
- Robin sequence
- Pierre Robin malformation sequence

Definitions
- Association of micrognathia (often severe), glossoptosis and cleft palate or high arched palate
- Glossoptosis: Posterior displacement of tongue

IMAGING FINDINGS

General Features
- Best diagnostic clue
  - Detection of micrognathia on mid-sagittal view in mid-trimester
  - 1st trimester diagnosis has been reported
  - Cleft palate often not detectable cytographically
  - Primaquine affects posterior palate

Imaging Recommendations
- Protocol advice
  - Careful evaluation of fetal anatomy given significant association of other anomalies with micrognathia
  - Fetal karyotype when other anomalies present

DIFFERENTIAL DIAGNOSIS

Cleft palate, isolated
- "U" shaped defect as opposed to characteristic "U" shape seen in Pierre Robin

Micrognathia, isolated
- Palate intact

Chromosome aneuploidy
- Trisomy 13, triploidy
  - Multiple anomalies, growth restriction (UGR)

Genetic syndromes
- Stork syndrome
  - Pierre Robin sequence + additional findings
  - Severe myopia with retinal detachment, cataracts
  - Spoddyhypophysial dysplasia, progressive arthrogryposis
  - Autosomal dominant: mutations in type II collagen gene (COL2A1)
  - Treacher Collins syndrome

DX: Orofacial Anomalies

- Triploidy
- Micrognathia
- Cleft Palate
- Cleft Lip/Palate
PIERRE ROBIN SYNDROME

Terminology
- Pierre Robin sequence
- Association of micrognathia (often severe), glossoptosis and cleft palate or high arched palate
- Glossoptosis: Posterior displacement of tongue

Imaging Findings
- Cleft palate often not detectable sonographically
- Primarily affects posterior palate
- MRI may be helpful in evaluating profile/palate

Key Facts

Top Differential Diagnoses
- Micrognathia, isolated
- Chromosomal aneuploidy
- Stickler syndrome

Clinical Issues
- Most common signs/symptoms: Micrognathia
- Airway obstruction due to glossoptosis
- "U" shaped cleft palate
- Up to 30% mortality with severe defects

Natural History & Prognosis
- Mandibular growth often improves over time
- Airway obstruction may lessen with development of the mandible
- Chronic hypoxia in some children may lead to cor pulmonale
- Up to 30% mortality with severe defects
- Feeding difficulties, hearing loss, sleep apnea

Treatment
- Airway protection critical in infant
- Delivery in a tertiary care center
- Lip, tongue adhesion as temporizing procedure to protect the airway
- Intubation, tracheostomy for severe airway obstruction
- Surgical repair of cleft palate
- Distraction procedures to lengthen mandible

SELECTED REFERENCES

PATHOLOGY

General Features
- Genetics
- Usually sporadic, but does not exclude mendelian inheritance in some cases
- Approximately 80% of cases are syndromic
- In syndromic cases, inheritance-dependent upon underlying diagnosis
- Endocrinology
- Unknown, but likely causally heterogeneous
- Hypoplasia of mandible prior to 9 wk gestation with posterior displacement of tongue
- Prevents tongue from moving out of plane of palatal shelf closure, thus resulting in palatal defect

Deformation: Mechanical forces
- Intracranial constraint
- Oligohydramnios sequence

CLINICAL ISSUES

Presentation
- Most common signs/symptoms: Micrognathia
- Polyhydramnios common in 3rd trimester
- Predicts increased potential for neonatal airway obstruction
- Potential
- Airway obstruction due to glossoptosis
- "U" shaped cleft palate

IMAGE GALLERY

(Left) Clinical photograph shows a newborn with severe micrognathia (open mouth) and a cleft palate typical of Pierre Robin, note the burn passenger (arrows) under the neck for airway stabilization. (Right) Sagittal oblique shows an abnormal profile with severe glossoptosis (arrows). This fetus had Pierre Robin sequence as part of Smith-Lemli-Opitz syndrome.
SIRENOMELIA

Clinical photograph shows a stillborn with sirenomelia. The single fused lower extremity is evident (arrow) as well as a radioulnar variant (open arrow).

Backograph of the same view shows a single femur (arrow) and shortened single bone in the distal lower extremity (open arrow).

TERMINOLOGY

Abbreviations and Synonyms
- “Mermaid” syndrome
- Synechia diplos, apus
- Sirenomelia sequence

Definitions
- Rare, lethal malformation characterized by varying degrees of lower extremity fusion, as well as other skeletal, gastrointestinal and genitourinary abnormalities.

IMAGING FINDINGS

General Features
- Best diagnostic clue: Renal agenesis with lower extremity fusion

Ultrasonographic Findings
- Mid-trimester anhydroamnios, due to bilateral renal agenesis
- Single or fused lower extremities
  - Ectodermal or extremity abnormality often very difficult due to lack of amniotic fluid
  - Single femur or single bone in distal lower extremities suggests diagnosis

MR Findings
- Absence of a normally tapered lumbaracral spine
- Third trimester and late 2nd trimester diagnosis usually hampered by lack of amniotic fluid required for adequate visualization
- At least 50% of diagnoses missed prenatally
- Diagnosis often made at autopsy

Imaging Recommendations
- Protocol advice
  - Endovaginal ultrasound particularly useful in 1st trimester
  - Color Doppler
    - Look for renal arteries
    - Look for branching of aorta
    - Frequently lacks normal bifurcation of aorta into iliac arteries
  - Amnionfusion, although invasive, has been utilized in enhancing visualization
  - 3D ultrasound has been used in early 2nd trimester diagnosis
  - Dependent on adequate amniotic fluid for visualization

DDx: Renal And Limb Anomalies

- Renal Agenesis
- Ureteropelvic junction obstruction
- Fetal trisomy
**Differential Diagnosis**

**Renal anomalies, bilateral**
- Renal agenesis
- Multicystic dysplastic kidneys
- Extremities are normal, but evaluation is difficult due to polyhydramnios

**Caudal regression sequence**
- Lower extremity is crossed-legged "Buddha" pose
- Thigh usually normal
- More common in diabetic mothers

**Lower extremity malformations**
- Forearm hypoplasia
- Tibial hemimelia
- Femoral hydronefris
- Proximal femoral focal deficiency
- Limb resection defects
- Split hand/foot malformation

**Arthrogryposis**
- Limb malposition may mimic limb fusion.
- Polyhydramnios more common than decreased fluid

**VACTERL association**
- Vertebral anomalies, cardiac malformation, tracheoesophageal fistula, esophageal atresia, renal anomalies, limb defects (radial ray)
- Several overlapping features
- Limb defects are typically upper, not lower, extremities

**Pathology**

**General Features**
- Genetics
  - Sporadic
  - No increased recurrence risk
- Etiology
  - Several theories of pathogenesis
  - Vascular steal theory
- Originally proposed by Stevenson, et al in 1986

**Key Facts**

**Top Differential Diagnoses**
- Renal anomalies, bilateral
- Caudal regression sequence
- Lower extremity malformations
- Arthrogryposis

**Pathology**
- Several theories of pathogenesis
- Vascular steal theory
- Abnormality of biogenesis

**Diagnostic Checklist**
- Renal MRI to evaluate lower extremities and renal agenesis
- 3D ultrasound may be helpful, 2 sufficient anatomic fluid
- Color Doppler ultrasound for abdominal vessels

- Alteration in early vascular development, with abnormal persistence of a vitelline artery:
  - Vessel arises from arch below diaphragm, no tributaries of sorts below this vessel
  - Resulting blood flow is diverted via this "vitelline artery" to placenta, with subsequent hypoplasia of caval embryonic structures
  - Presence or absence of kidneys predicted by whether the vessel is above or below location of renal arteries
- Limitations: Theory does not adequately explain other malformations, non-caudal anomalies (e.g., radial ray defects, anal tube defects)
- Not all sirenomelia have a pathologically demonstrable "test" vessel
- Similar vessel has been described in one of a normal fetus
- Abnormality of biogenesis
- Predisposition theory
- Very early defect, due to disruption of caudal mesoderm occurring during gastrulation (3rd gestational week)
- Interference with formation of notochord may disrupt further development of caudal structures
- Sirenomelia as a severe form of caudal dysplasia
- Recent evidence suggests that these entities are likely pathogenetically distinct
- Fusion of extremities, single umbilical artery uncommon in caudal dysplasia
- Association of diabetes much less common in sirenomelia

**Treatment**
- Diabetes is a risk factor
- Hyperlipidemia

**Epidemiology**
- 1/6,000 to 1/10,000 births
- Found in higher frequency in monozygotic twins, reflecting early timing of malformation

**Associated anomalies**
- Bilateral renal anomalies
- Renal agenesis

**15**

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SIRENOMELIA

- Multicystic dysplastic kidneys; less common than agenesis
- Other defects of midline development
- Neural tube defects
- Radial ray abnormalities
- Genital ambiguity/absence of external genitalia
- Mullerian anomalies
- Anorectal atresia
- Cloacal abnormalities
- Single umbilical artery
- Vaginal fistula
- Skin rash
- Fractures of pelvis, patella, or femur
- Varying degrees of limb reduction, soft tissue fusion of lower extremities
- Complex fusion of feet (syndrome)
- Absent feet
- Lumbar scoliosis
- Renal agenesis
- Bladder exstrophy
- Severe malformations of lower limbs
- Hip dislocation
- Less common: Cardiac, central nervous system anomalies

Gross Pathologic & Surgical Features
- In some cases, single large vessel arising from distal aorta can be demonstrated
- No aortic bifurcations seen in these cases
- Varying renal anomalies, from complete absence of kidneys to multicystic dysplastic kidneys, secondary to obstruction
- Abnormalities of bladder, rectum
- Cloacal malformations

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
- Severe oligohydramnios
- Fused lower extremities

Demographics
- Gender: Preponderance of males 2:7:1 ratio (M:F)

Natural History & Prognosis
- Majority lethal, prenatal or perinatal
- If liveborn, death from pulmonary hypoplasia within few hours
- In rare survivors, obstruction of genitourinary and gastrointestinal systems may be life-limiting

Treatment
- No prenatal treatment available
- Termination of pregnancy should be offered
- No monitoring or intervention in labor in continuing pregnancies

Diagnosis Checklist

Consider
- Fetal MRI to evaluate lower extremities and renal agenesis
- 3D ultrasound may be helpful, if sufficient amniotic fluid

Image Interpretation Pearls
- Color Doppler ultrasound for abnormal vessels
- Demonstration of absence of renal arteries
- Confirmation of lack of branching of iliac arteries, frequently seen in sirenomelia (normal in renal agenesis without sirenomelia)

Selected References
5. Lott N et al: Management syndrome: unihemiplegic may also have survival. Pediatr Surg Int. 20:67-9, 2004
Typical

(Time Left) Gross pathology shows a similar area of "soft" tissue (curved arrow) seen on the usual (arrow) is a similar area with similar findings. No renal or pelvic masses are identified. (Right) Anteroposterior radiograph shows renal tissue fusion at the lower extremities (arrow), bilateral absence of the rib/intercostal arteries and sexual agenesis (curved arrow) in sirenomelia.

(Time Left) Ultrasound shows normal development above pelvic bony margins (open arrow), abnormal lower extremities (curved arrow), and - differentiated tissues in the mid-trimester fetus with sirenomelia. (Right) Ultrasound shows a single lower extremity in another mid-trimester fetus with sirenomelia (arrow).

(Time Left) Ultrasound of the legs shows 2 limbs (curved arrow) and a single flexed foot (open arrow). The legs and feet (open arrow) could not be separated. Vascularization limited secondary to renal dysplasia and renal agenesis. Findings of sirenomelia confirmed by x-ray. (Right) Clinical photograph shows normal (curved arrow) fusion of the feet in a similar with sirenomelia. Note the deep clef between the 1st and 2nd toes on one foot (arrow).
SMITH-LEMLI-OPITZ SYNDROME

Terminology

Abbreviations and Synonyms
- SLOS
- SLOH syndrome

Definitions
- Primary diagnosis: characterized by microcephaly, multiple congenital anomalies and developmental delay
- SLOH syndrome

Imaging Findings

General Features
- Best diagnostic clue: combination of IUGR, cardiac defects, polydactyly, genital ambiguity on mid-trimester ultrasound

Ultrasoundographic Findings
- Increased nuchal translucency common in 1st trimester ultrasound
- Central nervous system (CNS)
  - Microcephaly, holoprosencephaly, hydrocephalus, agenesis of corpus callosum

Differential Diagnosis

Chromosomal aneuploidy
- Trisomy 13
  - Holoprosencephaly
  - Cardiac anomalies
  - Ophthalmolege
  - Cleft lip/palate
  - Postaxial polydactyly
  - Cryptorchidism
- Trisomy 18
  - IUGR
  - Cardiac anomalies
  - Overlapping digits, "rocker bottom" feet
  - Radial ray defects
  - Cleft palate
  - Triploidy

DDx: Chromosomal Aneuploidy
- Trisomy 13
- Trisomy 18
- T13, Holopros
- Triploidy, Semi-Corvus
SMITH-LEMLI-OPITZ SYNDROME

Key Facts
- **Pathology**: Autosomal recessive
- **Clinical Issues**: Severe perinatal presentation usually lethal
- **Diagnostic Checklist**: Low to undetectable levels of unconjugated estriol (Muller) on maternal serum screen should prompt careful sonographic evaluation for characteristic anomalies
- **Presentation**: Most common sign/symptom
  - Craniofacial: Microophthalmia (90%), narrow bifrontal diameter, ptosis (60%), downslanting palpebral fissures, antimongoloid slant, cleft palate (35-52%), tongue cysts, low set ears
  - Genitourinary (90%): Sex reversal in males or genital ambiguity, micropenis, hypospadias, renal agenesis, cystic renal dysplasia, hydrometrocolpos
  - Growth: Pre-and postnatal growth restriction

Terminology
- Disorder of cholesterol biosynthesis characterized by intrauterine growth restriction (IUGR), multiple congenital anomalies and developmental delay

Imaging Findings
- Best diagnostic clue: Combination of IUGR, cardiac defects, polydactyly, genital ambiguity on mid-trimester ultrasound
- Increased nuchal translucency common on 1st trimester ultrasound

Top Differential Diagnoses
- Chromosomal anomalies
- Hydrocephalus
- Meckel Gruber syndrome
- Holoprosencephaly

Hydrocephalus
- Hydrocephalus
- Cardiac anomalies
- Cleft lip/palate
- Polydactyly
- Cryptorchidism
- Short limbs

Meckel Gruber syndrome
- Cystic renal dysplasia
- Postaxial polydactyly
- Encephalocoele

Holoprosencephaly
- Isolated or in association with other structural anomalies

Pseudotrisomy 13
- Holoprosencephaly
- Postaxial polydactyly
- Ambiguous genitalia
- Normal karyotype

PATHOLOGY

General Features
- Genetics: Autosomal recessive
- Etiology
  - Disorder of cholesterol biosynthesis
  - Mutations in the 3 beta-hydroxysterol Delta (7) reductase gene (DHCR7) which catalyzes the reduction of 7-dehydrocholesterol (7DHC) to cholesterol
  - Results in elevated serum and tissue levels of 7DHC, low levels of circulating cholesterol
- Sterols are critical components in myelin, other central nervous system proteins, membranes. Altered sterol profile associated with abnormal intellectual, motor function
- Sonic hedgehog and Patched (embryonic signaling proteins) both rely on cholesterol for proper function; abnormalities associated with holoprosencephaly
- Decrease in testosterone and estrogen production result in hypogonadism in males, low MfSE 3 in affected pregnancies
- Carrier status may be determined by mutation analysis
- Prediction of carrier status not possible by analysis of cholesterol, 7DHC due to wide range of normal
- Epidemiology
  - 1/20,000 births in North American Caucasians
  - Rare in individuals of African/Asian descent
  - More frequent in European Caucasians with carrier frequency as high as 1/30
  - Up to 7% of stillbirths may be due to SLOS/IRSH
  - Common mutation found in about 60% of Caucasian cases (IVS8.1G→C)

Microscopic Features
- Giant cells in parietal islets
- Thymic hypoplasia

CLINICAL ISSUES

Presentation
- Most common sign/symptom
  - Craniofacial: Microophthalmia (90%), narrow bifrontal diameter, ptosis (60%), downslanting palpebral fissures, antimongoloid slant, cleft palate (35-52%), tongue cysts, low set ears
  - Genitourinary (90%): Sex reversal in males or genital ambiguity, micropenis, hypospadias, renal agenesis, cystic renal dysplasia, hydrometrocolpos
  - Growth: Pre- and postnatal growth restriction
SMITH-LEMLI-OPITZ SYNDROME

- Extremities: Postnatal polydactyly (50%), 2-3 'Y' syndactyly of toes (95%), high frequency of short dermal ridge pattern
- Cardiac: 32%. Anterior vestibular (AV) canal defect, anomalous pulmonary venous return
- Cognitive: Moderate to profound mental retardation
- Other signs/symptoms
  - Characteristic behavioral phenotype with autism, self injury, food aversions, extreme tactile sensitivities, abnormal sleep patterns, unusual upper body anchoring, irritability
  - Adrenal dysfunction, Hirschsprung disease, anorectal atresia
  - Hologenopathy

Demographics
- Gender: Excess males

Natural History & Prognosis
- Severe prenatal presentation usually lethal
- Survivors with moderate to profound mental retardation, multiple medical problems
- Rare mild phenotype with delayed diagnosis, milder course
- Prenatal level of 7DHC correlates with clinical severity
- Postnatal clinical severity inversely correlated with level of plasma cholesterol or ratio of cholesterol to total steroids

Treatment
- Dietary supplementation with cholesterol and bile acids
- Variable results in developmental improvement
- Improvement of elimination of behavioral, feeding and growth problems
- Baseline cholesterol prior to treatment better predictor of developmental potential
- Case reports of prenatal treatment
- Intravenous and intraperitoneal infusions of fresh frozen plasma
- Resulted in improvement in fetal plasma cholesterol levels
- Long term outcome unchanged but demonstrated feasibility of intratertiary treatment
- Other case of maternal dietary cholesterol supplementation less effective
- Prenatal diagnosis possible
  - Sterol analysis of amniotic fluid in mid-trimester (7DHC:total sterol ratio)
  - 7DHC content of tissue from chorionic villus sampling (CVS)
  - Molecular analysis by CVS, amniocentesis when specific mutation known
- Experimental analysis of steroids in maternal urine

Diagnosis can be confirmed by amniocentesis or CVS

SELECTED REFERENCES


DIAGNOSTIC CHECKLIST

Image Interpretation Pearls
- Low to undetectable levels of unconjugated estriol (M&G3) on maternal serum screen should prompt careful sonographic evaluation for characteristic anomalies
SMITH-LEMLI-OPITZ SYNDROME

IMAGE GALLERY

Typical

(left) Axial ultrasound of a 3rd trimester fetus with severe SLOS/RSR/ syndrome. There is an M-canal with the acoustic portion of the defect visible (open arrow) and a lateral reflection (open arrow). Right Clinical photograph shows typical 2-3 month syndrome of the toes in an older child with SLOS/RSR/ syndrome (arrows). The foot posture is a withdrawal response to tactile stimulation.

Typical

(left) Clinical photograph shows an infant with severe SLOS/RSR/. Note the short upturned nose with antverted nares (arrow), short neck, low-set ears (open arrow), and small mouth (curved arrow). (Right) Sagittal ultrasound shows an abnormal profile with short upturned nose (arrow) and microtia (open arrow) in a different case of SLOS/RSR/ syndrome.

Typical

(left) Ultrasound shows buphthalmia; slit nes (curved arrow) and antverted nares (arrow) in a fetus with SLOS/RSR/ syndrome at 30 weeks. (Right) Clinical photograph shows ambiguous genitalia (arrow) in a male infant with severe SLOS/RSR/ syndrome. (Courtesy A. Peltzer, MD, and F. Salko, MD.)
**TERMINOLOGY**

**Abbreviations and Synonyms**
- Tuberous sclerosis (TS), tuberous sclerosis complex
- Bourneville disease

**Definitions**
- Inherited tumor disorder with multigean hamartomas
- Included in spectrum of phakomatoses
- Clinical triad: Facial angiofibromas, mental retardation, seizures

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue: Cardiac rhabdomyomas; most common prenatal finding

**Ultrasonographic Findings**
- Cardiac rhabdomyoma
  - Well-defined, hyperechoic, intracardiac mass
  - Tumor typically involves ventricles or interventricular septum
  - Most often affects left ventricle
  - Often multiple
  - May detect as early as 22 weeks gestation
  - Requires close follow-up

**MR Findings**
- Primarily for evaluation of intracranial abnormalities
- MR more sensitive than ultrasound for detection of CNS lesions
- Subependymal nodules
  - Typically iso-hyperintense on T1WI
  - Low signal intensity on T2WI
- Can be mistaken for hemorrhage

**DDx: Periventricular Masses**

- Cystic Dysplasia
- Pseudotumor: Bone
- Hemorrhage
TUBEROUS SCLEROSIS

Terminology
• Inherited tumor disorder with multigorgan hamartomas

Imaging Findings
• Best diagnostic clue: Cardiac rhabdomyomas most common prenatal finding
• Central nervous system (CNS) findings may be subtle in utero
• Subependymal, echogenic nodules
• Irregularity of ventricular wall may be initial clue

Top Differential Diagnoses
• Bilateral periventricular nodular heterotopia
• Cortical dysplasias

• Located commonly along lateral ventricle margins, near caudate/thalami
• Cortical/subcortical tubers
• Most often supratentorial
• High signal on T1WI
• Low signal on T2WI
• Cortical/subcortical white matter lesions
• High signal on T2WI
• Not routinely identified on prenatal scans
• If fetal MR negative in at-risk patient, consider postnatal MRI
• May detect more subtle findings
• Gadolinium may be given
• Postnatal cardiac MRI may also be useful for characterization of cardiac tumors

DIFFERENTIAL DIAGNOSIS
Subependymal gray matter heterotopia
• Isointense to normal cortical gray matter on MRI
• Unlike hamartomas, do not calcify
• Associated with seizures
• Variable intellectual deficits

Periventricular nodular heterotopia
• Recently identified as X-linked hereditary disease
• Mutation within long arm of X chromosome, Xq28
• Sporadic or familial epilepsy with normal intelligence
• Primarily in males
• Associated with mega cisterna magna

Cortical dysplasias
• Subcortical heterotopia
• Polymicrogyria
• Focal cortical dysplasia
• Localized abnormality of lamination in cerebral cortex
• Most present postnatally with seizures and/or developmental delay

Key Facts
Pathology
• Autosomal dominant
• > 50% new mutation

Clinical Issues
• Postnatal seizures, may be intractable
• Number of CNS lesions may predict severity of cerebral dysfunction
• Watch for development of subependymal giant cell tumor

Diagnostic Checklist
• Fetal MR more sensitive than ultrasound for detection of CNS lesions
• Even if prenatal scan is normal, postnatal MRI should be considered for subtle cases
• Multiple rhabdomyomas highly suggestive of TS

Periventricular germinal matrix
• Germinal matrix prominent in early brain development up to 26 weeks gestation
• Can be confused with nodular heterotopia or subependymal nodules because of location
• Signal characteristics similar to gray matter on MRI

Germinal matrix hemorrhage
• Because of location may be confused with subependymal giant cell astrocytoma
• Look for other signs of evolving hemorrhage
• Intraventricular hemorrhage
• Decreasing echogenicity with time
• Porencephaly, hydrocephalus

PATHOLOGY
General Features
• Genetics
  • Autosomal dominant
  • > 50% new mutation
• Variable expressivity
• Two separate genes localized
• TSC1 on chromosome 9q34
• TSC2 on chromosome 16p13.3
• No difference in clinical phenotype between TSC1 and TSC2 mutations
• Genetics: Abnormal differentiation of germinal matrix cells
• Epidemiology: 1:10,000-20,000
• Cardiac
  • Rhabdomyomas
  • Benign tumors
  • 30-65% are associated with TS
  • Multiple in 50% of cases
  • > 80-90% risk of TS if multiple
  • Intracranial
  • Subependymal nodules
  • Nonprogressing hamartomas
  • Usually < 15 mm diameter
TUBEROUS SCLROSIS

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - Usually incidental finding of cardiac mass
  - Most commonly identified in second trimester
  - Family history of TS
- Other signs/symptoms
  - Arrhythmias
  - Nonimmune hypoventilation secondary to cardiac involvement
  - Postnatal work-up for TS warranted in at-risk pregnancies, even if prenatal work-up negative
  - Czech for other signs of TS after delivery
  - Renal involvement
    - Polyuria
    - Polydipsia
  - Renal lithiasis
    - Calcium oxalate
  - Renal failure
  - Cysts, angiomylipoma
  - Lymphangiomyomatosis
- Look carefully at parents for TS
  - Family history and multifacility of lesions are strongest predictor of TS
  - Size of endocardial mass not directly linked to likelihood of TS
  - Affected counseling for future pregnancies

Natural History & Prognosis
- Cardiac rhabdomyomas
  - Often have benign clinical course prenatally
  - May grow in conjunction with gestational age or remain static
  - Usually spontaneously regress postnatally
  - Poor prognostic indicator if associated with cardiac obstruction
- CNS findings
  - Postnatal seizures, may be intractable
  - Number of CNS lesions may predict severity of cerebral dysfunction
  - Risk of cognitive impairment associated with number of lesions
  - May have normal intelligence
  - Watch for development of subependymal giant cell tumor

- Slow-growing tumor
- Usually presents later in childhood
- Favorable outcome if removed
- Rare cases present as a neuroectodermal tumor of the CNS, highly aggressive in such cases

Treatment
- Cardiac rhabdomyomas
  - May require prenatal therapy with antiarrhythmics
  - Consider neonatal cocaine section if hemodynamic obstruction becomes apparent
  - Fetal resection may be warranted postnatally if affects cardiac function
- CNS abnormalities
  - Therapy directed at seizure control
  - May require tuber resection if refractory to medication
  - Close imaging follow-up for developing subependymal giant cell tumor
  - Surgical resection usually curative
- Specific counseling for parents

DIAGNOSTIC CHECKLIST

Consider
- Fetal echocardiography to monitor cardiac function
- Fetal MRI more sensitive than ultrasonography for detection of CNS lesions
- Even if prenatal scan is normal, postnatal MRI should be considered for subtle cases
- Recommended for counseling at-risk patients (family history of TS)

Image Interpretation Pearls
- Multiple rhabdomyomas highly suggestive of TS

SELECTED REFERENCES

TUBEROUS SCLEROSIS

IMAGE GALLERY

Typical

[Images of medical scans showing characteristics of tuberous sclerosis.]

Typical

[Images showing typical features of tuberous sclerosis, such as subependymal nodules and lesions.]

Typical

[Images illustrating the relationship between subependymal nodules and the ventricular system, highlighting the diagnostic value of imaging techniques.]

Typical

[Images depicting the appearance of subependymal nodules in the brains of patients with tuberous sclerosis.]

Typical

[Images showing the typical appearance of facial angiofibromas in patients with tuberous sclerosis, emphasizing their importance in diagnosis and management.]
Terminology
Abbreviations and Synonyms
- VATER/VACTERL association

Definition:
- Non-random association of 7 core abnormalities
  - Vertebral defects
  - Anal atresia
  - Cardiac anomalies
  - Tracheoesophageal fistula (TE fistula)
  - Esophageal atresia
  - Renal anomalies
  - Limb defects (radial)
- VATER includes vertebral, anal atresia, TE fistula, esophageal atresia, renal/radial defects

Imaging Findings
General Features
- Best diagnostic clue
  - Multiple anomalies on mid-trimester ultrasound
  - Renal, limb and vertebral anomalies most easily identified

Ultrasoundographic Findings
- Vertebral anomalies
- Hemivertebrae
- Best demonstrated on coronal plane
- Kyphosis
- Spina Bifida: Originates at area of hemivertebrae
- Butterfly vertebra
- Fusion of vertebral bodies or posterior elements (block vertebrae)
- Caudal dysplasia
- Anal atresia/imperforate anus
- Normal anus & echogenic ring ('anal dimple')
- Absent in atresia
- Côte can occasionally be dilated
- Often not recognized prenatally
- Imperforate anus associated with increased incidence of genital, urinary, lung/skeletal spine abnormalities
- Cardiac malformations
- Cardiac anomalies most common defect; seen in ~ 80%
- No specific type of cardiovascular malformation is typical
- Esophageal atresia + TE fistula
- Present in 30-60% of individuals with VACTERL
- Often difficult to diagnose
- Stomach absent or small
- Look for an esophageal "pouch" sign
- Transient filling of proximal esophagus with swallowing

DDX: Conditions With Overlapping Features Of VACTERL Association
- Tetralogy of Fallot
- Hidradenoma
- Anal Atresia
- Anterior Megacolon
VACTERL ASSOCIATION

Terminology
- Non-random association of 7 core abnormalities

Imaging Findings
- Multiple anomalies on mid-trimester ultrasound
- Renal, limb and vertebral anomalies most easily identified
- Cardiac anomalies most common defect, seen in >80%
- Systematic search for associated anomalies when one defect identified
- Kanye test to exclude chromosome abnormalities
- Polyhydramnios often a late finding, developing after 28 weeks

Top Differential Diagnoses
- Trisomy 18

- Polyhydramnios may be a late finding
- Rarely present < 25 wks
- Persistent absent gastric fundus associated with increased anionic fluid best sign
- Renal anomalies
  - Agenesis, may be unilateral or bilateral (lethal)
  - Multicystic dysplastic kidney
  - Hydronephrosis
  - Ectopic kidney
- Limb malformation
  - Restricted to upper limbs
  - Usually bilateral, may be asymmetric
  - Radial ray malformation common
  - Hypoplasia/aplasia of thumbs
  - Hypoplasia/aplasia of radius with radial club hand
  - Other associated malformations/abnormalities
  - Polyhydramnios
  - Most often associated with esophageal atresia
  - Rib anomalies (bifid, fused, absent)
  - Commonly associated with vertebral segmentation abnormalities
  - Single umbilical artery often associated with renal anomalies
- Genital
  - Hypoplasia, bifid scrotum, hypoplastic labia
  - More common in those with anorectal malformation
- Intrauterine growth restriction (IUGR)
- Cleft lip/palate, high arched palate
- Oligohydramnios with bilateral renal anomalies

Imaging Recommendations
- Protocol advice
  - Systematic search for associated anomalies when one defect identified
  - Dedicated fetal echo
  - Kanye test to exclude chromosome abnormalities
  - Polyhydramnios often a late finding, developing after 28 weeks
  - Repeat ultrasound in 3rd trimester to evaluate fluid and growth

Key Facts
- Anorectal atresia
- Radial ray anomalies
- Holt-Oram syndrome
- Diabetic embryopathy

Pathology
- Recurrence risk < 1%
- Not associated with chromosomal abnormality but shares many common features
- Defective differentiation of mesoderm prior to 35 days of development (mechanism unknown)
- Diagnosis of exclusion
- All features found in VACTERL are commonly found in other syndromes, as well as in isolation
- Few patients have occult features
- Average findings per patient is 3-4

DIFFERENTIAL DIAGNOSIS

Trisomy 18
- Central nervous system (CNS) malformations
- Gastrointestinal anomalies
- Significant overlap with VACTERL association with other anomalies
  - Cardiac anomalies
  - Radial ray abnormalities
  - TE fistula
  - Renal abnormalities
  - IUGR

Anorectal atresia
- Isolated vs. syndromic
- High associated rate of genitourinary, lumbar spine abnormalities

Radial ray anomalies
- Isolated vs. syndromic
- Wide range of thumb abnormalities

Syndromes with overlapping features
- Holt-Oram syndrome
  - Radial ray anomalies, upper limb phocomelia
  - Cardiac defects (atrial septal and ventricular septal defects, hypoplastic left heart)
  - Vertebral anomalies
  - Thoracic scoliosis
  - Diabetic embryopathy
  - Cardiac anomalies
  - Renal anomalies
  - CNS anomalies
  - Limb anomalies
  - Thrombocytopenia absent radius (TAR)
  - Bilateral radial ray abnormalities with normal thumbs
  - Cardiac, renal, other skeletal defects
  - High infant mortality due to hemorrhage, cardiac defects
  - MURCS association
  - Müllerian abnormalities, renal anomalies and cervicothoracic vertebral dysplasia
**VACTERL ASSOCIATION**

- CHARGE association
  - Coloboma, heart defects, craniofacial anomalies, genital anomalies, growth abnormalities, seizures
  - TE fissure +/- esophageal atresia, anal atresia

- Townes-Brocks syndrome
  - Dysplastic ears, triphalangeal thumbs, anal, and renal anomalies

- Robert's syndrome/Robert SC Pseudothalassemic syndrome
  - Tetraphocomelia (90%), osseous, clefts, IUGR
  - Wide phenotypic overlap with TAR

- Joubert-Levin syndrome
  - Multiple rib and vertebral anomalies associated with characteristic "crab claw" appearance of ribs
  - Higher incidence in individuals of Puerto Rican descent

- VACTERL with hydrocephalus
  - Separate entity
  - X-linked and autosomal recessive types
  - Often poor prognosis with severe retardation

- Anterior hypoplasia
  - Limb contractures may simulate radula utinas ray abnormalities
  - Extremities remain in fixed position during scoliosis

**PATHOLOGY**

**General Features**

- Genetic
  - Sporadic
  - Rare report of parent to child transmission

- Occasional cases of single features of VACTERL in siblings of affected individuals

- Male predominance

- Not associated with chromosomal abnormality but shares many common features

- **Etiology**
  - Defective differentiation of mesoderm prior to 30 days of development (mechanism unknown)
  - Risk factors: Maternal diabetes

- **Epidemiology:** 1 in 100,000 incidence

**Staging, Grading or Classification Criteria**

- Diagnosis of exclusion

- **No specific criteria for confirmation of diagnosis**

- **No facial phenotype to aid in pattern recognition**

- All features found in VACTERL are commonly found in other syndromes, as well as in isolation.

- **Few patients have all features**
  - Average findings per patient: 3-4
  - **No consensus on minimum diagnostic criteria, although at least one anomaly in each of the four systems (thorax and abdomen/pelvis probably needed to secure a diagnosis.**

**CLINICAL ISSUES**

**Presentation**

- Most common signs/symptoms: Multiple anomalies on mid-trimester scan

**Natural History & Prognosis**

- Variable based on type and number of anomalies
  - 28% neonatal mortality
  - Potentially life-threatening anomalies include TE fissure, anal atresia and cardiac abnormalities
  - Survivors have good prognosis for normal intelligence
  - Severe scoliosis may be progressive, difficult to treat
  - Life-long need for treatment, therapy in severely affected individual

**Treatment**

- **Early treatment to rule out trisomy**

- **Pregnancy termination an option, given multiple severe anomalies**

- **Anticipation and staged to stall disease**

- **Delivery at tertiary care facility, if pregnancy continued**

- **Complete work-up with cardiac echo, renal ultrasonogram, spine and extremity x-rays**

- **All of the core features require surgical intervention for treatment**

- **Examination of parents and siblings for common features may help elucidate diagnosis**

**DIAGNOSTIC CHECKLIST**

**Image Interpretation Pearls**

- **One or more features should prompt thorough evaluation for other associated anomalies**

- **Often abnormalities are not as obvious (e.g., esophageal atresia and cardiac defects) have potentially more serious complications**

**SELECTED REFERENCES**


VACTERL ASSOCIATION

IMAGE GALLERY

Typical

(Left) Control ultrasound of the spine shows pelvic secondary to fused vertebrae (arrow). There is also a medullary cystic injury defect (curved arrow). This finding was bilateral, resulting in severe oligohydramnios. Lack of amniotic fluid impacts amniotic visualization. (Right) four chamber view of the heart also shows a ventricular septal defect (arrow). 10% of VACTERL cases have a cardiac defect.

Typical

(Left) Transverse ultrasound shows an absent stomach bubble (arrow), which was present on all exams in this fetus with trisomy 18. Polyhydramnios is also evident. (Right) Transverse ultrasound shows omphalocele normal genitalia in the microskeletal fetus. The adrenal gland is seen in the renal fossa (open arrow) and there is mild polydactyly in the contralateral thorax (arrows). Finding one anomaly in the VACTERL association should prompt a careful search for others.

Typical

(Left) Radiograph shows a radial ray defect in a newborn with multiple anomalies, consistent with VACTERL. There is a single femoral bone (open arrow), with radial clubbed hand (arrow) and absent thumb and 2nd digit (curved arrow). (Right) Clinical photograph shows a radial clubbed hand in a newborn. Note the malpositioned thumb (arrow) with absent flexion crease (curved arrow); a subtle but important clinical finding.
SECTION 16: Infection

Cytomegalovirus 16-2
Herpesvirus 16-6
Toxoplasmosis 16-8
Varicella 16-10
**CYTOMEGALOVIRUS**

**TERMINOLOGY**

**Abbreviations and Synonyms**

- Cytomegalovirus (CMV)

**IMAGING FINDINGS**

**General Features**

- Best-diagnostic clue: hapatocarial and infrapaphecal calcifications

**Ultrasonographic Findings**

- Calcifications may be widespread
  - Brain (ventriculomalacia, cortical), diaphragm, pectici
  - Calcifications are often non-shadowing
  - Liver: most commonly affected area
  - Ventriculomegaly, microcephaly
  - Cataract formation, choroiditis
  - Hepatomegaly
  - Splenomegaly
  - Intracranial growth restriction (IUGR)
  - Hydrops with severe disease
  - Both polyhydranhes and oligohydranhes seen

**Imaging Recommendations**

- Presumptive fetal infection in documented maternal infection, when following age present
  - Progressive IUGR
  - Microcephaly
  - Hepatomegaly
  - Calcifications
  - Hydrops

**DIFFERENTIAL DIAGNOSIS**

**Parovirus B-19 (Fifth disease)**

- Maculopapular rash in adults
- Migratory, transient rash in children
- >50% of women are immune
- 20-30% fetal transmission in infected women
- Infection may be fatal in sickle cell anemia (plastic crisis)
- Parovirus attacks red blood cell precursors = anemia
- Ascites common presenting finding in fetus
- Fetal hydrops secondary to anemia
- 10-20% risk of fetal or neonatal death
- Treated with transfusions
- Spontaneous recovery has been reported

**Toxoplasmosis (Toxplasma gondii)**

- Cats are definitive hosts; Oocyst shed in feces

**DDx: Intrauterine Infections**

- Varicella, Arv
- Herpes
- Zygplasmia
- Syphilis
Imaging Findings
- Best diagnostic clue: Intracranial and intrahepatic calcifications
- Calcifications are often non-shadowing

Top Differential Diagnoses
- Varicella
- Herpes simplex (type 2 HSV)
- Echogenic bowel

Pathology
- Genetics: Susceptibility, severity of in utero infection likely influenced by host genetics
- Early exposure increases risk to fetus

- Human infection from contaminated soil, water, undercooked meats
- 15-30% fetal infection rate
- Higher infection rate in 3rd trimester but not as serious
- Intracranial calcifications
- Random distribution, echogenic non-shadowing
- Liver calcifications and hepatoplenomegaly

Varicella
- Primary infection, chickenpox
- Latent virus in dorsal root ganglia → shingles
- > 90% of women are immune
- Low incidence of transmission to fetus
- Neurotropic virus → contractures, limb hypoplasia
- Calcifications (liver, heart, renal, skin lesions)

Herpes simplex (type 2 HSV)
- Most infections from vaginal delivery with active viral shedding
- Active lesions or prodromal symptoms of impending outbreak
- Cervical shedding without evidence of lesions
- Transplacental infection rare
- Primary outbreak during pregnancy increases risk of fetal infection
- Echogenic bowel, ventriculomegaly
- Cross-reactivity with HSV-1 may cause confusion in making diagnosis

Syphilis (Treponema pallidum)
- Risk of infection related to spirochete load
- Hepatoplenomegaly, dilated bowel, bowing of long bones, abnormal epiphyses
- Hydrops with severe cases
- 50% spontaneous abortion or perinatal death
- Jarisch-Herxheimer reaction (severe response to endotoxin release from killed organism) with treatment during pregnancy
- Associated with fetal death

HIV (AIDS embroyopathy)
- 20% transplacental infection

Key Facts
- Most common congenital infection worldwide
- Congenital CMV is most common infectious cause of mental retardation, sensorineural deafness and visual impairment

Clinical Issues
- 10% of congenitally infected infants symptomatic
- Neurologic sequelae in up to 90% (sensorineural hearing loss, visual impairment, mental retardation)
- 90% of congenitally infected infants asymptomatic at birth
- Even in absence of sonographic findings in documented fetal infection, neurologic sequelae found in at least 20%
- 10-15% will subsequently have abnormal neurologic development
- 10% will develop hearing loss in early childhood

Rubella (German measles)
- Rare in developed countries
- 1st trimester most critical time for fetal infection
- Cardiac defects, microcephaly, microphthalmia, mental retardation, IUGR

Non-immune hydrops
- Many underlying causes, including fetal aneuploidy, infection, dysrhythmia

Echogenic bowel
- Underlying causes including aneuploidy, gastrointestinal anomalies including bowel obstructions, cystic fibrosis

PATHOLOGY

General Features
- Genetics: Susceptibility, severity of in utero infection likely influenced by host genetics
- Etiology
- Early exposure increases risk to fetus
- Control of passage of CMV across placenta involves multiple regulatory events including local cytokines, maternal CMV-specific neutralizing antibodies, presence of other pathogens
- Herpes virus family
- Ubiquitous in humans, other mammals
- General population infection by direct contact, exposure to secretions
- Infection also occurs via blood transfusion, organ transplantation from infected donor
- Usually restricted to immunocompromised or immunologically immature individuals
**Cytomegalovirus**

- Fetal infection via placenta (vertical transmission)
- Epidemiology
  - Most common congenital infection worldwide
  - Incidence of congenital infections with CMV approximately 1% of livebirths (0.3-2.3% worldwide)
  - Cytomegalovirus (CMV) is most common infectious cause of mental retardation, sensorineural deafness and visual impairment
  - Viral load in maternal blood, amniotic fluid and fetal blood important prognostic factors
  - Prevalence of CMV antibodies in healthy adults = 50% in most industrialized countries
  - 100% in developing countries
  - Incidence of primary infection in pregnancy = 1%-5%
  - 20%-40% vertical transmission rate to fetus
  - Non-primary infection rate in pregnancy (reactivation of previous infections) = 5%
  - Vertical transmission rate of 0.2%-8%
  - 90% of congenitally infected infants asymptomatic at birth

**Microscopic Features**

- Immunohistochemical staining with CMV-specific antibodies reveals large multinucleated cells with intranuclear and extranuclear inclusion bodies

**Clinical Issues**

**Presentation**

- Fetal
  - Microcephaly, growth retardation
  - Intracranial calcifications
  - Spontaneous abortion, preterm birth, stillbirth especially in primary infection during pregnancy
  - Neonate
    - Up to 10% are asymptomatic
    - Most common symptom is jaundice, petechiae, hepatosplenomegaly
  - Pneumonic rash, extramedullary hematopoiesis (macular lesions)
  - Ophthalmologic (optic nerve hypoplasia, coloboma, microphthalmia, chorioretinitis)
  - Sensorineural hearing loss in early childhood
  - Adult infections, asymptomatic (99%) or mononucleosis-like

**Demographics**

- Gender: Female fetal gender may be a risk factor for severe congenital infection, although males also subject to infection

**Natural History & Prognosis**

- Primary infection during pregnancy
  - 10% of congenitally infected infants symptomatic
  - Mortality 30-60% within 2 years in symptomatic infants
  - Neurologic sequelae in up to 90% (sensorineural hearing loss, visual impairment, mental retardation)
  - 90% of congenitally infected infants asymptomatic at birth
  - Even in absence of sonographic findings (documented fetal infection, neurologic sequelae found in at least 20%)
  - 10-15% will subsequently have abnormal neurodevelopment
  - 50% will develop hearing loss in early childhood

**Treatment**

- No approved prenatal treatment
- Termination of pregnancy as option when confirmed fetal infection
- Maternal serology
  - Acute and convalescent titers may suggest infection with rising titers
- Amniocentesis for diagnosis of fetal infection
  - Amniotic fluid culture
  - Polymerase chain reaction (PCR) for viral sequence
  - Fetal cell-free maternal circulation (research)
- Systemic antivirals approved for CMV treatment (postnatal)
  - Ganciclovir, (poduct, valganciclovir), foscarin, cidofovir
- Target viral DNA polymerase
- Ganciclovir therapy in symptomatic movable may prevent or ameliorate specific neurodevelopmental injury (sensorineural hearing loss)
- Vaccine development research
- Routine screening of asymptomatic pregnant infants not currently recommended

**Selected References**

Typical

(Left) Coronal ultrasound shows calcifications in the dome of the diaphragm, hepatic veins, and intrahepatic calcifications (arrows) in this fetus with CMV infection. (Right) Ultrasound shows very subtle periventricular (curved arrows) and pericardial (arrow) calcifications (arrows) in a different fetus with CMV infection. These may be seen in up to 20% of affected fetuses. Neurologic sequelae will still occur in at least 20%.

Typical

(Left) Sagittal ultrasound of a patient with congenital CMV infection shows periventricular (arrows) and subependymal (curved arrows) calcifications. (Right) Axial NECT shows prominent periventricular calcification (arrows) in this newborn with congenital CMV infection. A very high proportion of patients may be affected.

Typical

(Left) Coronal ultrasound in a 25-week fetus with CMV infection shows echogenic bowel (curved arrow) and periventricular calcifications (curved arrows). (Right) Image of the abdomen of the same fetus at the 3rd trimester shows a thin rim of ascites (arrows), mildly echogenic bowel (curved arrow), and calcification (open arrow).
PARVOVIRUS

**TERMINOLOGY**

Abbreviations and Synonyms

- Erythema infectiosum (Fifth disease)
- HPV B19

Definitions

- Erythema infectiosum (Fifth disease) is major clinical manifestation of infection with human parvovirus B19 (HPV B19)

**IMAGING FINDINGS**

Ultrasonographic Findings

- Acute most common presenting finding
- Progression to hydrops in severe cases
- Secondary to fetal anemia
- Placental mottling
- Polyhydramnios

Imaging Recommendations

- Non-invasive assessment for fetal anemia using pulsed Doppler
- Middle cerebral artery (MCA) peak systolic velocity elevated in fetal anemia
- Governor need for intraventricular transfusion

**DIFFERENTIAL DIAGNOSIS**

Other congenital infections

- Significant overlap in imaging findings
  - Intrahepatic and intracranial calcifications most common findings
  - Requires maternal/fetal sedation to make definitive diagnosis
  - Cyanomegaly
  - Most common intrauterine infection
  - Calcifications, microcephaly, echogenic bowel
  - Toxoplasmosis (Toxoplasma gondii)
  - Human infection from undercooked meats, contaminated soil, water
  - Calcifications, hepatosplenomegaly
  - Varicella
    - Primary infection, chickenpox
    - Calcification, skin lesions, limb anomalies
  - Herpes Simplex (type 2 HSV)
    - Most infections occur during vaginal delivery
    - Echogenic bowel, ventriculomegaly
  - Syphilis (Treponema pallidum)
    - Hepatosplenomegaly, dilated bowel, bowing of long bone, hydrops
  - Rubella
    - Cardiac defects, microcephaly, IUGR, microphthalmia

DDx: Conditions With Hydrops

- Rhesus Incompatibility
- Polyhydramnios
- Turner Syndrome
- Pseudox 21
PARVOVIRUS

Imaging Findings
- Ascites (most common presenting finding)

Top Differential Diagnoses
- Other congenital infections
- Hydrops

Pathology
- Parvovirus attacks red blood cell precursors ⇒ anemia
- 2/3 of adult women are immune to parvovirus

Hydrops
- Nonimmune (aneuploidy, lymphatic, arhythmia)
- Immune (alloimmunization)

Asites
- isolated, without other signs of hydrops

PATHOLOGY

General Features
- Pathology
  - Parvovirus attacks red blood cell precursors ⇒ anemia
  - Involvement of cardiac myocytes may contribute to hydrops
  - Infection route: Transplacental, transfusion

Epidemiology
- 2/3 of adult women are immune to parvovirus
- Infection more common January-June
- Main reservoir: school aged children

CLINICAL ISSUES

Presentation
- Ascites progressing to hydrops in symptomatic fetus
- Adults
  - Transient, migratory maculopapular rash
  - May be asymptomatic
  - Polyarthralgias, polyarthralgia occurs in 60% of symptomatic adults
  - Aplastic crisis in immunocompromised, chronic hemolytic anemia
- Children
  - “Slapped cheek” rash in children
  - Mild fever, ill-ill, upper respiratory symptoms in children

Natural History & Prognosis
- Infection usually self-limited in mothers
- Immuno-compromised individuals may become severely ill or die
- 20-50% of women who become infected during pregnancy transmit infection to fetus
- Risk of hydrops with fetal infection 4%
- Risk of fetal death highest (11-20%) when infection acquired < 20 wks gestation
- Stillbirth rate, with or without hydrops 0.6%

Key Facts

Clinical Issues
- 20-30% of women who become infected during pregnancy transmit infection to fetus
- Risk of hydrops with fetal infection 4%
- Risk of fetal death highest (11-20%) when infection acquired < 20 wks gestation
- Normal developmental outcome in children who survive intrauterine infection with parvovirus
- Intrauterine transfusion for fetal anemia

- Increased spontaneous abortion with early infection
- High mortality rate with severe hydrops without fetal transfusion
- Reports of spontaneous recovery without transfusion in less severe hydrops
- Normal developmental outcome in children who survive intrauterine infection with parvovirus

Treatment
- Maternal infection in pregnancy should prompt referral to high-risk specialist
- Maternal serology for HPV B19 specific IgG and IgM
- Amniocentesis for viral polymerase chain reaction
- Weekly ultrasound to exclude hydrops for 10-12 weeks following seroconversion
- Monitor fetal anemia with MCA Doppler
- Cordocentesis for fetal serology and hematocrit
- Intrauterine transfusion for fetal anemia
- Delivery if gestational age sufficiently advanced

SELECTED REFERENCES


IMAGE GALLERY

(Left) Pulsed Doppler ultrasound shows the peak systolic velocity (curved arrow) in the MCA (arrows) of a fetus with severe anemia. MCA velocity monitoring is used to screen for anemia in Parvovirus.

(Right) Clinical photograph shows asepsis (aneuploidy) typically seen in disease severely infected with Parvovirus. The border is noted by the curved areas.
**TERMINOLOGY**

**Abbreviations and Synonyms**
- Toxoplasmosis is the "T" in T.O.R.C.H. infections

**Definitions**
- Transplacental infection with the protozoan Toxoplasma gondii

**IMAGING FINDINGS**

**Ultrasonographic Findings**
- Non-shadowing intracranial and intraspinal calcifications
- Intracranial calcifications may be periventricular or random in distribution
- May be multiple and easily missed
- Intraventricular growth restriction (IVGR)
- Ventriculomegaly, echogenic bowel

**Imaging Recommendations**
- Protocol advice
- Monthly ultrasound when suspected or confirmed infection to look for brain abnormalities, calcifications, fetal growth
- Fetal MRI to evaluate brain, assist in prognostic counseling

- All positive screening tests to pregnancy should be confirmed in toxoplasmosis reference lab
- Confirm fetal infection by amniocentesis or cord blood sampling for viral polymerase chain reaction

**DIFFERENTIAL DIAGNOSIS**

- Other congenital infections
  - Significant overlap in imaging findings
  - Intracranial and intraspinal calcifications may coexist with other findings
  - Requires maternal/fetal serology to make definitive diagnosis
- Cytomegalovirus (CMV)
  - Most common in utero infection
  - Calcifications, microcephaly, echogenic bowel
- Varicella (chicken pox)
  - Calcifications, skin lesions, limb anomalies
- Herpes
  - Attacks red blood cell precursors = anemia
  - Anencephaly
- Herpes simplex (type 2 HSV)
  - Most infections occur during vaginal delivery
  - Echogenic bowel, ventriculomegaly

Echogenic bowel, abdominal calcifications
- Multiple etiologies including amnionitis, bowel obstruction, meconium ileus

**DDx: Toxoplasmosis**

- CMV
- Herpes
- Varicella
- Echogenic bowel
TOXOPLASMOSIS

Imaging Findings
- Non-shadowing intracranial and intrahepatic calcifications
- Intracranial calcifications may be periventricular or cordon in distribution
- May be subtle and easily missed

Top Differential Diagnoses
- Other congenital infections

Key Facts

Clinical Issues
- Congenital infection causes classic triad of hydrocephalus, intracranial calcifications, chorioretinitis
- 1st trimester infection: less likely to result in congenital infection (2-10%), but more likely to be severe or result in abortion
- Infection > 20 wks has much higher congenital infection rate (20-30%), but generally less severe
- Sequelae of congenital infection include blindness, epilepsy, mental retardation
- Prognosis for normal neurologic outcome is good in absence of brain abnormalities
- Effect of prenatal therapy uncertain
- May decrease fetal infection rate or ameliorate severity

Treatment
- Therapy with folate synthesis inhibitors (pyrimethamine/sulfonamide or sulfadiazine) with or without spiramycin in confirmed prenatatal and congenital infections
- Severe side effects including pancytopenia
- Termination of pregnancy is an option in confirmed prenatatal infection
- Serologic screening of all pregnant women in United States not currently recommended due to low disease prevalence

SELECTED REFERENCES

PATHOLOGY

General Features
Etiology
- Toxoplasma gondii is a unicellular protozoan
- Cats are the definitive hosts: Oocysts shed in feces
  - Soil contamination
- Ingestion = parasitemia = latent infection/infection of cysts in muscle, central nervous system
- Both humoral and cellular immunity involved in resistance to parasite
- Detection of IgM not sufficient to prove recent infection; IgM often detectable for months
- 3 principal routes of infection in humans
  - Ingestion of inadequately cooked (infected) meat
  - Ingestion of oocytes from contaminated soil or water
  - Transplacental

Epidemiology
- Estimated 400-4,000 cases per year of congenital toxoplasmosis in United States with 750 deaths
- Seroprevalence 10-30% in developed countries
- Seroprevalence in developing countries may exceed 60-75%
- Prevention of infection centers on education regarding risk factors

CLINICAL ISSUES

Presentation
- Maternal infection most often asymptomatic
  - Mild symptoms include malaise, lethargy, lymphadenopathy
- More severe if immunocompromised
  - Spleenomegaly, chorioretinitis, pneumonitis, encephalitis, multisystem organ failure
- Congenital infection causes classic triad of hydrocephalus, intracranial calcifications, chorioretinitis

Natural History & Prognosis
- 1st trimester infection less likely to result in congenital infection (2-10%), but more likely to be severe or result in abortion
- Infection > 20 wks has much higher congenital infection rate (20-30%), but generally less severe

IMAGE GALLERY

(Left) Axial oblique ultrasound shows periventricular and intraparenchymal calcifications typically seen in congenital toxoplasmosis (arrows). (Right) Coronal ultrasound shows echogenic bowel (arrow) typical of that seen in many congenital infections, including toxoplasmosis. Note the echogenic 'pseudocysts' (curved arrow).
Clinical photograph shows a zoster lesion (arrow) in a vein with fetal varicella syndrome. Pallid hypodense parenchyma was noted. The mother had chickenpox at 15 weeks gestation.

Terminology

**Definitions**
- Transplacental infection of fetus following maternal chickenpox infection
  - Usually 4-20 weeks of gestation

**Terminology**

**Abbreviations and Synonyms**
- Varicella-zoster (VZV)
- Fetal varicella syndrome/embryopathy

**Other congenital infections**
- Significant overlap in imaging findings
  - Intrathoracic and intracranial calcifications
  - Polyhydramnios due to neurologic impairment of swallowing
  - Limb hypoplasia, contractures
  - Pseudo-vacuolar hypodense parenchyma on real time sonography due to unilateral analgesia

**Imaging Recommendations**
- Monthly ultrasound for assessment of late findings of fetal varicella syndrome
- Fetal MRI to further evaluate fetus, including central nervous system (CNS)

**Differential Diagnosis**

**Ultrasoundographic Findings**
- Intrathoracic and intracranial calcifications
- May also see liver, heart, renal calcifications
- Polyhydramnios due to neurologic impairment of swallowing
- Limb hypoplasia, contractures
- Pseudo-vacuolar hypodense parenchyma on real time sonography due to unilateral analgesia

**CAUTIONS**
- Toxoplasmosis
  - Human infection from undercooked, infected meat, contaminated soil or water
  - Calcifications, hepatosplenomegaly
- Herpes simplex (type 2 HSV)
  - Most infections occur during vaginal delivery
  - Escherichia coli, ventriculomegaly

**Limb reduction defects**
- Terminal transverse defects, oligodactyly
- Arthrogryposis

**DDx: Congenital Infection**

- **Herpes**
- **Toxoplasmosis**
- **CMV**
- **CMV**
VARICELLA

Imaging Findings
- Intracranial and intracanalicular calcifications
- May also see liver, heart, renal calcifications
- Lymph hypoplasia, contractures
- Paradoxical diaphragmatic motion on real time sonography due to unilateral paralysis

Pathology
- Maternal zoster outbreak in pregnancy NOT associated with risk of fetal infection or malformation

Key Facts
- Maternal varicella infection before 20 weeks gestation
  - 6% fetal transmission
- 1/3 of infected fetuses have clinical manifestations, usually cutaneous
- 1.2% of infected fetuses will have severe clinical stigmata of fetal varicella syndrome
- Peripartum maternal chickenpox associated with 23% risk of life threatening neonatal infection
- Exposure of seronegative pregnant woman to chickenpox
  - Passive immunization with varicella-zoster immunoglobulin (VZIG)
  - Reduces maternal complications, may prevent fetal varicella syndrome
  - Serious complications at any gestational age ⇒ hospitalization, intravenous Acyclovir
  - Delivery should be delayed at least 5 days after the onset of maternal rash to decrease risk of neonatal varicella
- Treatment of infant with VZIG, if delivered less than 5-7 days after onset of maternal rash

PATHOLOGY

General Features
- Etiology
  - Neurotropic virus
  - Sequelae due to neurologic damage in utero
  - Remains dormant in the dorsal root ganglia; reactivated as shingles (herpes zoster)
- Maternal zoster outbreak in pregnancy NOT associated with risk of fetal infection or malformation
- Epidemiology
  - Majority of reproductive aged women (> 90%) immune
  - Maternal varicella infection before 20 weeks gestation ⇒ 6% fetal transmission
  - 1/3 of infected fetuses have clinical manifestations, usually cutaneous
  - 1.2% of infected fetuses will have severe clinical stigmata of fetal varicella syndrome
  - Peripartum maternal chickenpox associated with 23% risk of life threatening neonatal infection

CLINICAL ISSUES

Presentation
- Maternal pruritic papular rash
- Elevated maternal serum and amniotic fluid alpha-fetoprotein and amniotic fluid acetylcholinesterase
- May correlate with fetal skin, muscle and nerve damage from VZV
- Neonate with varicella syndrome with multiple abnormalities
  - Cutaneous lesions in dermatomal distribution, limb hypoplasia, chorionitisitis, segmental intestinal atresia, varying degrees of neurologic dysfunction

Natural History & Prognosis
- Increased incidence of fetal/neonatal death
- Asymptomatic, structurally normal children usually neurodevelopmentally normal
- Neurologic impairment dependent upon location, extent of lesions

Treatment
- Documentation of fetal infection
  - Amniocentesis/conodensent for viral polymerase chain reaction

SELECTED REFERENCES
2. Verstraeten M et al: Perinatal ultrasound and magnetic resonance imaging in fetal varicella syndrome: correlation with pathology findings. Fetal Diagn Ther. 23(8):765-9, 2005

IMAGE GALLERY

[Left] Anteroposterior radiograph shows the elevated lateral thoracic curve in a neonate with diaphragmatic paralysis secondary to fetal varicella syndrome. [Right] Radiograph shows a normal transverse fetal defect in a growth restricted newborn with fetal varicella syndrome. Note radiculo hypoplasia (arrow) and the missing fund.
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**TERMINOLOGY**

**Abbreviations and Synonyms**
- Polyhydramnios

**Definitions**
- Excessive amniotic fluid (AF)
  - Idiopathic polyhydramnios (2/3)
  - Fetal, placental or maternal disorder (1/3)

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue
  - Large than expected pockets of fluid
  - AF between anterior uterine wall and fetus

**Ultrasonographic Findings**
- Subjective diagnosis of polyhydramnios
  - 2nd trimester
  - Fluid/effusion ratio > 1:1
  - 3rd trimester
  - Excessively large pockets of fluid
  - Fetus displaced away from anterior uterine wall
  - Gravity dependent fetus
- Semiquantitative measurements
  - Maximum vertical pocket (MVP)

**DDx: Large Fluid Pockets**
- Normal AF
- Cystic Hygroma
- Cystic Hygroma
- Limb Deficiency

- Identify largest fluid pocket in uterus
- Measure depth of fluid
- Avoid fetal parts and cord
- Use color Doppler to avoid cord
- Polyhydramnios if > 5 cm
- Amniotic fluid index (AFI)
- Divide uterus into 4 equal quadrants
- Identify and measure MVP in each quadrant
- MVP = sum of 4 quadrant MVPs
- Polyhydramnios if MVP > 24 cm
- Icm MVP = 30 mL fluid (approximately)
- Can use nomogram for MVP percentiles
- Two diameter pocket (TDP)
  - Identify MVP
  - Also measure width of same pocket
  - TDP = MVP x width
  - Polyhydramnios if TDP > 50 cm²
- Idiopathic polyhydramnios (2/3)
  - Normal fetus + polyhydramnios
  - Associated with macrosomia (28%)
  - Not-diabetic mom
  - Often mild stable polyhydramnios
  - Genetic amniocentesis not indicated
- Associated with diabetes mellitus
  - Gestational diabetes most common
  - 1 AF associated with poor control
  - Fetuses at risk for macrosomia
  - Gastrointestinal (GI) anomalies
Terminology
- Idiopathic polyhydramnios (2/3)
- Nodal placental or maternal disorder (1/3)

Imaging Findings
- Polyhydramnios if AF > 24 cm
- 1cm AF = 30 mL fluid (approximately)
- Associated with diabetes mellitus
- Gastroschisis-pentalogy
- Central nervous system/facial anomalies
- Hydrops
- Mucoloskeletal anomaly
- Cardiac defects
- Twin-to-twin transfusion syndrome
- Idiopathic polyhydramnios is diagnosis of exclusion
- Frequent follow-up AFs

Key Facts

Top Differential Diagnoses
- Normal fluid
- Cystic hygroma
- Uterine duplication anomaly

Pathology
- Polyhydramnios < AF volume > 1,500-2,000 mL
- 4-3.5% of pregnancies

Clinical Issues
- Idiopathic polyhydramnios has excellent prognosis
- In diabetics, polyhydramnios improves as blood sugar is better controlled
- Therapeutic amniocentesis

Diagnostic Checklist
- Polyhydramnios > UGR = very poor prognostic sign

- Oligohydramnios
- Exsanguinal
- Duodenal
- Jejunal/skeletal less common
- Obstructed
- Diaphragmatic hernia
- Gastrochisis-pentalogy
- Mucoloskeletal
- AF often seen in late 2nd or 3rd trimester
- Central nervous system/facial anomalies
- Limb reduction/separation from amnion
- Hydrocephalus, microcephaly
- Facial defect (syndactyly)
- Neural tube defects
- Polyhydramnios is a late finding
- Hydrops
- Immune and nonimmune causes
- More prominent feature of immune hydrops
- Polyhydramnios may be early sign of hydrops
- Mucoloskeletal anomaly
- Skeletal dysplasia
- Any movement in amnion
- Myotonic dystrophy
- Cardiac defects
- Anhydramnios
- Anomalies
- Associated with heart failure
- Fetal respiratory system anomaly
- Chest mass
- Most may transmit fluid
- Tracheal stenosis
- Polyhydramnios + intrauterine growth restriction (IUGR)
- Combination is associated with poor outcome
- 95% with anomalies
- 38% with aneuploidy
- Trisomy 18 most common
- Anomelosites = warranted even if anomalies not seen
- Differentiate from idiopathic polyhydramnios
- Normal-sized or large fetus
- Ureterovaginal junction obstruction + paradoxical polyhydramnios

Imaging Recommendations
- Best imaging tool
- AF evaluated at every 3rd/5th trimester exam
- Sonographic quantitative measurement of AF
- AF index most commonly used
- Protocol advice
- Idiopathic polyhydramnios is diagnosis of exclusion
- Look carefully for fetal anomalies
- Rule out maternal diabetes
- Look for macrosomia
- Anomaly may be difficult to assess in severe cases
- Fetus too far displaced from transducer
- Assess for twin-to-twin transfusion syndrome
- Look for 'stuck' twin
- Frequent follow-up AFs
- Progressive polyhydramnios worsen worrisome

Differential Diagnosis

Normal fluid
- Umbilical cord included in AF measurement
- Use color Doppler to avoid cord
- False positive polyhydramnios
- Quantitative methods not highly accurate

Cystic hygroma
- Nuchal cystic fluid collection
- Larger cystic hygroma can mimic AF
- Look for septations
- Associated with aneuploidy
- Turner syndrome most common
- Trisomy 21
- Associated with hydrops
- Pleural effusion, ascites, anasarca
POLYHYDRAMNIOS

Uterine duplication anomaly
- Septate uterus
- Bicornuate uterus
- Fetus in one horn and fluid in another
  - Can mimic polyhydramnios
  - Difficult to quantify fluid

PATHOLOGY

General Features
- General path comment
  - Polyhydramnios < AF volume > 1,500-2,000 mL
  - Normal: 800-1,000 mL at peak (36-37 wks)
- Genetics
  - IUGR and anomalies associated with aneuploidy
  - Trisomy 18 > trisomy 13
- Etiology
  - 1 Production or 1 removal of AF
  - Normal AF removal
  - Fetus swallows 25% body weight/day
  - GI absorption: 200-1,200 cL/day near term
  - Fetal lungs: 170 cc/day near term
  - Normal AF production
  - Fetus urinates 30% of body weight/day
  - Kidneys: 800-1,200 cc/day near term
  - Lungs: 170 cc/day near term
  - Other important AF pathways
    - Placenta, membranes, umbilical cord
    - Transcutaneous diffusion
  - Fetal movement affects absorption: contributes to polyhydramnios in skeletal disorders affecting movement
  - Epidemiology
    - 0.4-3.3% of pregnancies
  - Idiopathic (65.4%)
  - Diabetes mellitus (27.7%)
  - Congenital anomalies (4.3%)
  - Multiple gestation (2.6%)
    - May be seen with maternal use of lithium
      - Fetal natriuresis

Staging, Grading or Classification Criteria
- Mild polyhydramnios
- AF > 24 cm, < 30 cm

CLINICAL ISSUES

Presentation
- Most common sign/symptoms
  - Large for dates (1 fundal height)
  - 2/3 dilapatic
  - Incidentally noted during ultrasound study
  - Normal fetus
  - Normal mom
  - 1/3 polyhydramnios as a feature of other diagnosis
  - Maternal diabetes
  - Fetal anemia
  - Twin-twin transfusion syndrome
    - Monochorionic diamniotic twins
    - One twin with polyhydramnios and other with oligohydramnios

Natural History & Prognosis
- Idiopathic polyhydramnios has excellent prognosis
  - Often mild and stable
  - 1 Cesarean section rate secondary to macrosomia
  - Severe/focal polyhydramnios
    - Preterm labor
    - Premature rupture of membranes

Treatment
- In diabetics, polyhydramnios improves as blood sugar is better controlled
  - Polyhydramnios < from 12.7% to 2.1% with early glucose control
- Therapeutic amniocentesis
  - Patient comfort
  - 1 Preterm labor risk
  - Aid with amniotic visualization
- Induction
  - Rapid placental passage
  - 1 Fetal urine production
  - 1 Fetal lung fluid production
  - Reduction of fluid within 1 week
  - Effective in > 90%
  - Risk of treatment
    - Constriction of cecum arteriosus

DIAGNOSTIC CHECKLIST

Consider
- Frequent follow-up AF
  - Is polyhydramnios stable or progressing?
- Genetic amniocentesis in minority of cases
  - IUGR
  - Fetal anomalies
  - Severe or progressing polyhydramnios

Image Interpretation Pearls
- Careful fetal survey to rule out anomalies associated with polyhydramnios
  - Polyhydramnios + IUGR very poor prognostic sign
- Idiopathic polyhydramnios is common but always a diagnosis of exclusion

SELECTED REFERENCES
POLYHYDRAMNIOSES

IMAGE GALLERY

**Typical**

*Left:* Axial ultrasound shows a minimum vertical pocket measurement of 10.6 cm in this case of polyhydramnios and macrosomia. MVP ≥ 8 cm is diagnostic of polyhydramnios. *Right:* Axial ultrasound in another case of polyhydramnios and macrosomia shows preeclampsia anastomotic fluid (amniotic fluid measured 40%) and an abdominal circumference measurement > 10th percentile. Polyhydramnios is associated with macrosomia in both elective and diabetic patients.

*Left:* Ultrasound shows polyhydramnios (calipers measure an AF pocket of 12 cm) and a posteriorly small stomach (arrow) in a fetus with congenital diaphragmatic hernia. Polyhydramnios progressively worsens throughout the pregnancy. *Right:* Frontal tomograph of the abdomen reveals an echogenic tube terminating within the congested pouch (arrow).

*Left:* Axial ultrasound shows a dilated duodenum (arrow) in this fetus with duodenal stenosis (curved arrow points to stomach) and progressive polyhydramnios (open arrow). Karyotype was normal. *Right:* Coronal ultrasound shows massive polyhydramnios surrounding an immobile, growth-dependent fetus (arrow) with anhydrogenesis. Amniotic visualization is limited when polyhydramnios is severe.
OLIGOHYDRAMNIOSES

Terminology

Definitions
- Oligohydramnios
  - Deficiency of amniotic fluid from any cause
- Anhydramnios
  - No amniotic fluid

Imaging Findings

General Features
- Best diagnostic clue
  - Smaller than expected pockets of fluid
- Fetus seems confined

Ultrasoundographic Findings
- Amniotic (AF) assessment 2 part of every 1st/3rd trimester exam
  - 2nd trimester
    - Fetus takes up 1/2 uterine volume
    - AF pockets of fluid should be easily seen
    - Experienced sonographer can judge amniotic fluid volume subjectively
  - Second trimester
    - Fetus > 1/2 uterine volume

- Third trimester
  - Diminished pockets of fluid
  - Fetal crowding

- Semi-quantitative measurements
  - Maximum vertical pocket (MVP)
  - Identify largest fluid pocket in uterus
  - Measure depth of fluid
  - Avoid fetal parts and cord
  - Use color Doppler to avoid cord
  - Oligohydramnios if MVP < 2 cm
  - Amniotic fluid index (AFI)
    - Divide uterus into 4 equal quadrants
    - Identify and measure MVP in each quadrants
    - AFI = sum of 4 quadrant MVPs
    - Oligohydramnios if AFI < 3 cm
    - 1 cm AFI = 30 mL fluid (approximately)
    - Can use normogram for AFI percentiles
  - Two diameter pocket (TDP)
    - Identity MVP
    - Also measure width of same pocket
    - TDP = MVP x width
    - Oligohydramnios if TDP < 15 cm

- Biophysical profile score (BPP) and amniotic fluid
  - BPP assesses fetal well-being
  - Score for fluid is 2 cm (0 if not allowed)
    - 2 x AF pocket ≥ 2 cm in 2 perpendicular planes
    - 0 = no AF pocket measuring ≥ 2 cm x 2 cm
  - Fluid score of 0 is highly significant finding

DDx: Subjective Low Fluid

- Normal Fluid
- Fibroid Uterus
- Uterine Duplication
OLIGOHYDRAMNIOSES

Key Facts

- Deficiency of amniotic fluid from any cause

Imaging findings

- Amniotic fluid assessment part of every 2nd/3rd trimester exam
- Experienced sonographer can judge amniotic fluid volume
- Oligohydramnios: FAI < 5 cm
- Contractures, club foot
- Oligohydramnios may be early sign of IUGR
- Look for GU anomalies
- Assess fetal growth
- Assess placental function with Doppler
- Frequent follow-up AF often indicated
- Fetal MRI if kidneys can not be documented with ultrasound

- Genitourinary tract (GU) anomalies
  - Bilateral renal agenesis
  - Color Doppler of aorta shows no renal arteries
  - Renal glands are present
  - Bladder outlet obstruction
  - Distended bladder + oligohydramnios
  - +/- Renal ureteral obstruction
  - +/- Post-obstructive renal cystic dysplasia
  - Most often from posterior urethral valves
  - Bilateral renal cystic dysplasia
  - Multicystic dysplastic kidneys
  - Autosomal recessive polycystic kidney disease
  - Post obstructive cystic dysplasia
  - Bladder, ureteropelvic junction obstruction
  - AF may be normal in early pregnancy
  - 1 AF diffusion via fetal skin until 22 wks

- Anomalies from fetal co-ordination
  - Common with early and prolonged oligohydramnios
  - Pulmonary hypoplasia
  - Oligohydramnios restricts chest expansion
  - Small bell-shaped chest
  - 1st cause of mortality from oligohydramnios
  - Externility anomalies
  - Contractures, clubfoot
  - Post term pregnancy (> 42 wks)
  - 1 Morbidity if oligohydramnios progresses quickly
  - Premature rupture of membranes (PROM)
  - Clinical diagnosis
  - Early and prolonged with wane prognosis
  - Early: PROM < 25 wks
  - Prolonged: Oligohydramnios > 14 days
  - Oligohydramnios + intramterine growth restriction (IUGR)
  - Estimated fetal weight < 10th percentile
  - EGR from placental insufficiency if fetuc normal
  - Can be associated with aneuploidy if fetus minor
  - Trolosy 18, trisomy 13, triploidy
  - Anniotic fluid reflects placental function
  - Oligohydramnios may be early sign of IUGR
  - Doppler assessment of IUGR
  - Abnormal umbilical artery (UA) waveform

Top Differential Diagnoses

- Normal fluid
- Fetal anemia
- Uterine duplication anomaly

Pathology

- I Production or I removal of amniotic fluid
- Fetal anemia in 20%
- IUGR in 30-40%

Clinical Issues

- PROM is a clinical diagnosis
- Pulmonary hypoplasia usually fatal
- Early and prolonged oligohydramnios has a poor prognosis
- Normal prognosis if bilateral renal anomaly

MR Findings

- Helpful if ultrasound imaging severely limited
- Diagnosis of renal agenesis
- MR preferable to diagnostic amniocentesis

Imaging Recommendations

- Best imaging tool
  - Subjective assessment of AF
  - Semiquantitative measurements of AF
  - AF most commonly used method
  - Protocol advice
    - Continue AF in every 2nd/3rd trimester case
    - Look for GU anomalies
    - Assess fetal growth
    - Assess placental function with Doppler
    - Frequent follow-up AF often indicated
    - Fetal MRI if kidneys cannot be documented with ultrasound

DIFFERENTIAL DIAGNOSIS

Normal fluid

- Pockets of fluid may be difficult to see
  - Obese patient, near term patient
- Excessive transducer pressure while measuring fluid
  - Minimizes pocket depth
- False positive oligohydramnios
  - Quantitative methods not highly sensitive
Oligohydramnios

Fibroid uterus
- Large fibroid-sized tumor
- Fluid pockets difficult to see
Uterine duplication anomaly
- Septate, bicoronal uteri
- Fetus in one horn and fluid in another
- More difficult to quantitate fluid

PATHOLOGY

General Features
- Pathology
  - Producing or removal of amniotic fluid
  - Normal amniotic fluid production
  - Fetus urinates 30% of body weight/day
  - Kidneys: 800-1200 cc/day near term
  - Lung: 170 cc/day near term
  - Normal amniotic removal
  - Fetus swallows 20% body weight/day
  - Gastrointestinal absorption: 200-1200 cc/day near term
  - Urine: 170 cc/day
  - Other important amniotic fluid pathways
    - Placenta, membranes, umbilical cord
    - Transcutaneous diffusion ("leaky" fetal skin) before 22 wks
- Epidemiology: 0.5-3.5% of pregnancies
- Associated abnormalities
  - Fetal anomalies in 20%
  - Mostly genitourinary
  - IUFD in 30-40%
  - Potter facies
  - Wide-set eyes, flattened palpebral fissures, prominent epicanthus, flattened nasal bridge, micrognathia, low-set ears

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - Patient may present as "small for dates"
- Oligohydramnios often seen as major feature of other diag61
  - IUFD
  - Severe GU anomalies
  - PROM
  - Post-date pregnancy
  - Maternal conditions associated with oligohydramnios
    - Hypertension
    - Preeclampsia
    - Diabetes
    - Autoimmune disorders
  - PROM is a clinical diagnosis
  - Sterile vaginal specimen <500
  - Amniotic fluid has alkaline pH and "sering"
  - Incidentally noted during routine care
  - More likely benign course
  - More common in 3rd trimester
  - Other signs/symptoms
- Twin-twin transfusion
- Membranous amniotic sac twins
- Over twin with oligohydramnios and other with polyhydramnios
- Maternal medication
- Prostaglandin synthetase inhibitors

Natural History & Prognosis
- Pulmonary hypoplasia usually fatal
- Difficult prenatal diagnosis
- Early and prolonged oligohydramnios has a poor prognosis
- < 25 wks associated with 10% survival
- Progressive oligohydramnios with worse prognosis
- Distal prognosis if bilateral renal anomaly

Treatment
- Depends on cause and severity of oligohydramnios
- Bladder outlet obstruction
- Bladder drainage procedures
- Diuretic renal function
- Bladder-amniotic shunt placement
- Can reduce incidence of pulmonary hypoplasia
- Consider early delivery for IUFD
- Fetal
t  - Induction of labor if MVP < 2 cm or AFI < 5 cm
  - Maternal hydration rarely helpful
- Amnioinfusion during active labor
  - Risk of cord compression

DIAGNOSTIC CHECKLIST

Consider
- Frequent follow-up AFI
- Twice/week AFI check if fetus is viable

Image Interpretation Pearls
- Amniotic fluid volume reflects fetal well-being
  - Perform 80T and Doppler if fetus is otherwise normal
- Idiopathic oligohydramnios is rare
  - Rule out growth and fetal abnormalities carefully
- MRI useful tool for anatomic evaluation when sonographic visualization is inadequate

SELECTED REFERENCES
OLIGOHYDRAMNIOSES

IMAGE GALLERY

Typical

(B) Sagittal ultrasound shows severe oligohydramnios in this case of posterior urethral valves. The bladder (arrow) fills the abdomen (curved arrow) and pelvis. (Right) Ultrasound performed after placement of bladder-urethral stent (arrows) into a decompressed bladder and ureter (curved arrow). The amniotic fluid volume has normalized (curved arrows). Renal function was assessed prior to stent placement.

Typical

(B) Ultrasound in a case of PPHN shows only a tiny pocket of amniotic fluid (arrows) making amniotic fluid evaluation difficult. Normal kidneys were identified (open arrows - one kidney). (Right) Sagittal T2W MR of another fetus with severe oligohydramnios in whom kidneys could not be seen by ultrasound. On MRI, a kidney (arrows) and bladder (curved arrows) are clearly seen. MRI can be very helpful in evaluating anatomy and ruling out renal agenesis.

Typical

(B) Ultrasound shows how quickly IV administration of oligohydramnios. The sum of the four maximum vertical pockets is only 5.56 cm in this late second trimester pregnancy complicated by IUGR and preeclampsia. (Right) Axial ultrasound with and without color Doppler shows what now looks like amniotic fluid (arrow) is actually a collection of cord. This "pocket" should not be measured as amniotic fluid.
**TERMINOLOGY**

**Abbreviations and Synonyms**
- Intrauterine growth restriction (IUGR)
- Small for gestational age (SGA)
- Estimated fetal weight (EFW) < 10th percentile for gestational age (GA)
- Symmetric IUGR: Abdomen ± other biometric parameters
- Symmetric IUGR: Fetus uniformly small for gestational age (GA)
- IUGR implies fetus has not reached its full growth potential
- SGA implies smaller than expected for GA but fetus may be normally grown

**IMAGING FINDINGS**

**Ultrasoundographic Findings**
- Size less than expected for dates
  - All biometric parameters equally affected
  - Structural survey more likely to be abnormal than with asymmetric IUGR

**DDx: Symmetric IUGR**

- Asymmetric-Tumour
- Wrong Case
- Placental Insufficiency

Clinical photograph of a case of twin-to-twin transfusion syndrome. US scan showed significant symmetric growth restriction with abdominal and fetal growth being equally affected.

- Multiple anomalies f suspicion for aneuploidy/syndrome
- Second trimester finding of echogenic bowel associated with IUGR in 10-20% of cases
- Pulsed Doppler is not as helpful as in asymmetric IUGR
- Usually a primary fetal abnormality, not placental insufficiency
- Does not exhibit "head sparing" flow pattern in middle cerebral artery

**Imaging Recommendations**
- Accurate dating essential for evaluation of growth disturbance
- Early ultrasound is more accurate than menstrual dating (LMP) or clinical assessment of GA
- First trimester crown-rump length (CRL) measurements accurate in +4-6.7 weeks
- CRL more accurate than mean sac diameter
- Biological variations do not manifest until after 13 weeks gestation
- Second trimester dating based on composite of several measurements
  - Biparietal diameter (BPD)
  - Head circumference (HC)
  - Abdominal circumference (AC)
  - Femur length (FL)
Terminology
- Estimated fetal weight (EFW) < 10th percentile for gestational age (GA)
- Symmetric IUGR: Fetus uniformly small for gestational age (GA)

Imaging Findings
- Multiple anomalies = suspicion for aneuploidy/syndrome
- Look at ossification centers, helps verify dating when patients present late in gestation
- Early ultrasound scan is most accurate for dating
- Triploidy may present with either symmetric or asymmetric IUGR depending on source of extra chromosomes
- Look for signs of intrauterine infection

Key Facts

Top Differential Diagnoses
- Incorrect dates
- Small but normal
- Asymmetric IUGR

Pathology
- By definition IUGR occurs in <10% of pregnancies
- Some of these will be normal, just constitutionally small

Diagnostic Checklist
- Accurate dating is essential for diagnosis of IUGR
- Never change due date based on later exam, doing so masks a growth disturbance
- IUGR = polyhydramnios = high risk of aneuploidy, especially trisomy 18

○ Second trimester dating accurate to within +/- 1.5 weeks
○ Third trimester: same parameters, measured but accuracy decreased to +/- 3-4 weeks
○ Patient presenting in third trimester at 34 weeks may have a normal fetus measuring from 31-37 weeks
○ Biological variation has maximum impact in third trimester
○ Look at ossification centers, helps verify dating when patients present late in gestation
○ Biparietal diameter (BPD) ≥ 12 weeks gestation
○ Nuchal translucency ≥ 3.5 weeks gestation
○ Earliest ultrasound scan is most accurate for dating
○ Never change due date based on later scans
○ Doing so will mask growth disturbance
○ Evaluate amniotic fluid volume
○ Use of amniotic fluid index allows objective serial assessment of fluid volume
○ IUGR = polyhydramnios ominous combination
○ High risk for trisomy 18
○ Low fluid correlates with poor outcome especially if early onset/sustained
○ Look for anomalies
○ Symmetric IUGR has strong association with aneuploidy
○ Multiple anomalies = early onset IUGR
○ Triploidy, trisomies 18,13
○ Triploidy may present with either symmetric or asymmetric IUGR depending on source of extra chromosomes
○ Dysonic triploidy (extra set of chromosomes maternal) = severely onset asymmetric IUGR
○ Diastrophic dysplasia (extra set of chromosomes paternal) = symmetric IUGR
○ Look at fetal hands
○ Cleared fingers = trisomy 18
○ Postnatal polyhydramnios = trisomy 13
○ Syndactyly = triploidy
○ Look for signs of intrauterine infection
○ Ventriculomegaly
○ Hydrops

DIFFERENTIAL DIAGNOSIS

Incorrect dates
- Menstrual history inaccurate
○ Nursing
○ Birth control pill
○ Irregular cycles
○ Normal anatomic survey
○ Normal interval growth on follow-up exam

Small but normal
- By definition 10% of pregnancies will be "too small"
○ Constitutional: look at the parents
○ Ask about birthweight of other children
○ Interval growth normal
○ Fetus remains SGA but exhibits normal growth rate

Asymmetric IUGR
- Head measurements normal for GA
○ Abdominal circumference small with poor interval growth
○ Often associated with abnormal Doppler studies
○ Usually a primary problem of placenta insufficiency
○ Often presents later in pregnancy
**PATHOLOGY**

General Features
- Genetics
  - Trisomy 18, 13, 10
  - Early onset (UGR seen in 43% trisomy 13 cases
  - Early onset UGR seen in 55% trisomy 18 cases
  - UGR not a dominant feature in trisomy 18
  - Triploidy (diandric)
- Etiology
  - Aneuploidy
  - Endocrine infection
  - Cytomegalovirus
  - Herpes
  - Rubella
  - Syndromes
- AEDs embryopathy
  - Vertical transmission
  - Characteristic fetal-tofetal abnormalities: Lateral bending, hyperechoic, short nose, flat nasal bridge
- Epidemiology
  - By definition UGR occurs in 10% of pregnancies
  - Some of these will be normal, just constitutionally small
  - UGR fetuses represent a larger percentage in aneuploidy series of stillbirths.

**CLINICAL ISSUES**

Presentation
- Fundamental problem with fetus
  - Presents earlier than symmetric UGR
  - Often early 2nd trimester

Natural History & Prognosis
- Aneuploidy = extremely poor prognosis
- Triploidy associated with severe early onset pre-eclampsia
  - May require pregnancy termination for maternal indications
- SLA fetus with normal survey, normal chromosomes and normal interval growth has good prognosis

Treatment
- Offer karyotype
  - 2.7% incidence of chromosomal abnormalities associated with IUGR
- Infection screen
- If multiple anomalies/aneuploidy
  - Offer termination
- Encourage autopsy for specific diagnosis
- If pregnancy progresses with known poor prognosis
  - No monitoring in labor
- Intervention for maternal indications only
  - Full clinical evaluation of infant to confirm diagnosis
- Encourage autopsy for fetal demise/perinatal death
- Accurate diagnosis important for recurrence risk
  - If pregnancy progresses without clear diagnoses
  - Follow as asymptomatic UGR

- Full monitoring in labor
- Intervention/encephalotomy appropriate until onset and prognosis established

**DIAGNOSTIC CHECKLIST**

Consider
- EFW percentiles are based on GA
- Accurate dating is essential for diagnosis of IUGR
- Symmetric IUGR (fetus may be completely normal
  if dates are incorrect
- Never change due to basis on lower extent, ruling out growth disturbance

Image Interpretation Pearls
- IUGR + polyhydramnios = high risk of aneuploidy, especially trisomy 18
- Triploidy associated with both symmetric and asymmetric IUGR patterns

**SELECTED REFERENCES**

Typical

Typical

Typical

Typical

**Symmetric IUGR**

**Image Gallery**

*(Left)* Ultrasound of a infant with no prenatal care who delivered at 32.5 wks by UGR but measured 13.1 wks, raising the question of inaccurate date vs. symmetric IUGR. Classification of the prenatal fetal growth retardation (Growth Retardation Index of 1.35) weeks prior to delivery, IUGR more likely. Classification criteria can be helpful in predicting neonatal outcome in gestation. *(Right)* Left ultrasound shows multiple low-lying echoes (arrow) in a fetus with symmetric IUGR from toxoplasmosis.

*(Left)* Transabdominal ultrasound shows different findings in discordant twins with one twin transverse, one transverse fused. A uterus absent (far left) with all four quadrants equally filled. *(Right)* Sagittal ultrasound shows a very small placenta with multiple cysts. The fetus cannot have severe symmetric IUGR typical for triplody of paternal origin (trisomy 18).

*(Left)* Transabdominal ultrasound shows symmetrical at the 3rd and 4th degree liver is seen in both cases. Careful evaluation of the hands can help remove the differential diagnosis in symmetric IUGR. *(Right)* Fetal MRI shows a mild polymorphic vascular anomaly with a liver with marginally 3rd left over IUGR prompt adrenalin. The parents receiving information on the liver metastases before deciding on termination.
**TERMINOLOGY**

**Abbreviations and Synonyms**
- Intrauterine growth restriction (IUGR)
- Small for gestational age (SGA)
- Intrauterine growth retardation

**Definitions**
- Estimated fetal weight (EFW) < 10th percentile for gestational age
- Asymmetric IUGR: Abdomen < other biometric parameters
- Symmetric Fetus uniformly small for gestational age (GA)
- IUGR implies fetus has not reached full growth potential
- SGA smaller than expected for GA but may be normally grown

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue: Fetus with abnormal growth and oligohydramnios

**Ultrasoundographic Findings**
- Gray-scale Ultrasound

**DDx: Growth Restriction**
- Chromosomal
- Infection
- Multiple gestation
- Maternal anomalies
- Maternal diabetes
- Maternal hypertension
- Malnutrition
- Malformations
- Other causes

**Abnormal Biochemistry**
- Head circumference (HC) and biparietal diameter are preserved
- Abdominal circumference (AC) is small and exhibits poor interval growth
- EFW calculations heavily weighted to AC
- Poor AC growth → EFW less than expected for GA
- Oligohydramnios common
- Indicative chronic fetal stress
- Blood shunted to cerebral and coronary circulations
- Renal perfusion ↓ → urine production = oligohydramnios
- Second trimester finding of choledochal flexure associated with IUGR in 10-20% of cases
- In multiple gestations look at placental cord insertion sites
- Significant increased risk of IUGR with marginal/fetal malposition of cord

**Color Doppler**
- Consider use of color Doppler when measuring amniotic fluid index (AFI)
- AFI is four quadrant measurement
- Transverse perpendicularly to tube
- Measured pockets must contain 2 either cord or fetal parts
- Pulsed Doppler
- Umbilical artery (UA) Doppler
**Key Facts**

- Cardiac work required to perfuse abnormally resistant placenta
- MCA SD ratio should be > UA SD ratio at all gestational ages
- Reversal of this pattern = "head sparing" effect

**Top Differential Diagnoses**

- Symmetric IUGR

**Pathology**

- Risk of IUGR up to 25% if past history of IUGR fetus or maternal risk factors

**Clinical Issues**

- Fourfold increase in adverse perinatal outcome for IUGR fetuses
- Long-term studies show neurodevelopmental morbidity in survivors

**Imaging Findings**

- Head circumference (HC) and biparietal diameter are present
- Abdominal circumference (AC) is small and exhibits poor interval growth
- Oligohydramnios common
- Second trimester finding of echogenic bowel associated with IUGR in 10-20% of cases
- UA SD ratio should be < 3 in third trimester
- At placental resistance > UA diastolic flow

- UA blood flow quantified by systolic-diastolic (SD) ratio = peak systolic velocity / end-diastolic velocity
- UA SD ratio should be < 3 in third trimester
- UA placental resistance > UA diastolic flow
- Absent end-diastolic flow (AEDF) = no flow into placental vascular bed during diastole
- Reversed end-diastolic flow (REDD) = vasoconstrictive resistance so high blood flow away from placenta in diastole
- Studies suggest > 70% placental vascular bed obliterated before REDD is seen
- Cardiac work required to perfuse abnormally resistant placenta
- Eventual cardiac decompensation
- Right atrial pressure
- Reversal of flow in inferior vena cava
- Reversal of "a" wave in ductus venosus
- Pulsatile flow in umbilical vein
- Middle cerebral artery (MCA) flow also quantified by SD ratio
- MCA SD ratio should be > UA SD ratio at all gestational ages
- Reversal of this pattern = "head sparing" effect
- Pulsatile flow in UV reflects breakdown of fetal circulatory compensation to fetal placental resistance
- Maternal uterine artery (UA) Doppler may predict patients at risk for IUGR
- Series of SGA fetuses with normal survey and UA Doppler
- UA and MCA Doppler performed at time of diagnosis as SGA
- Anomalous UA and MCA Doppler correlated strongly and independently with need for emergent cesarean section
- Consider delivery at lung maturity in this group

**Imaging Recommendations**

- Serial measurements taken at shorter intervals are subject to error
- Monitor fetal response to hostorial environment with biophysical profile (BPP)
- Few parameters are "scored"
- Fetal breathing
- Fetal movement
- Fetal tone
- Amniotic fluid volume
- Abruption = abnormalities of movement and tone
- Chronic hypoxia = amniotic fluid volume
- Nonstress test (NST): 5th parameter to assess fetal reaction to environment

**DIFFERENTIAL DIAGNOSIS**

- Symmetric IUGR

**Pathology**

- Hard no longer "spongy"
- All growth parameters equally effected
- Generally due to problem with fetus rather than placental insufficiency
- More likely with syndromes and aneuploidy
- Look for multiple anomalies
- More likely with infection
- Look for intracranial/abdominal calcifications
- Look for giant hydrops

**PATHOLOGY**

**General Features**

- Genetics
- Trisomy may present with either symmetric or asymmetric IUGR, depending on source of extra chromosomes
- Digeoxin triptidly (extra set of chromosomes) material = severe, early-onset asymmetric IUGR
- Digeoxin triptidly (extra set of chromosomes) paternal = abnormal thick/elective placenta with symmetric IUGR
- Triology
CLINICAL ISSUES

Presentation
- Asymptomatic IUGR presents late second to early third trimester
- Earlier presentation concerning for triplet pregnancy
- Increased risk in twins and higher order multiples

Natural History & Prognosis
- Fourfold increase in adverse perinatal outcome for IUGR fetuses
  - Additional 4.8 fold increase if IUGR + abnormal Doppler
- Long-term studies show neurodevelopmental delay in survivors
- "Fetal origins" hypothesis
  - IUGR babies have 1 risk hypertensive, diabetes, stroke as adults

Treatment
- Offer cesarean, especially if early onset IUGR
- Infection screen
- Consider maternal testing for thrombophilic disorders, especially if prior IUGR fetus or preeclampsia
- Antiphospholipid syndrome
- Protein C deficiency
- Aggressive treatment of any contributing maternal condition
  - Treat hypertension
  - Control diabetes
- Increased surveillance
  - Serial growth measurement
  - Airial fluid check
  - Frequent NST/BPP
  - Frequent Doppler assessment of UA/MCA vs. UT A
- 2nd trimester management clinical
  - Significant risks of preterm delivery balanced with significant risk of intrauterine demise
- No single parameter determines decision to deliver
- Abnormal Doppler, fluid, BPP in 3rd trimester = deliver

DIAGNOSTIC CHECKLIST

Consider
- EFW percentiles are based on GA
- Accurate dating is essential to diagnosis of IUGR
- Early US is more accurate than menstrual history or clinical findings
- Management decisions are based on multiple factors
  - Gestational age
  - Internal growth and AFI
  - Renal artery screening and BPP
- Maternal factors

Image Interpretation Pearls
- UA Doppler is "tip of the iceberg" with respect to overall neurodevelopmental status
- 70% of placental vascular bed obliterated before REDI is seen
- Addition of venous Doppler = more information of fetal response to adverse conditions

SELECTED REFERENCES
ASYMMETRIC IUGR

IMAGE GALLERY

Typical

[Images of ultrasound scans showing asymmetry]

Twin A

Twin B

Typical

[Images of Doppler waveforms]

V1 = 0.50 cm/s
V2 = 0.22 cm/s
50% = 0.41
50% = 2.56

Typical

[Images of clinical photographs]

Typical

[Images of clinical data]

CLINICAL MA = 19.98
MACROSOMIA

Axial ultrasonogram shows a greater than expected AC measurement in a 36 wk fetus. A large amount of echogenic subcutaneous fat is easily seen (arrow). Macrosomia is common with macrosomia.

TERMINOLOGY

Abbreviations and Synonyms
- Large for gestational age (LGA)

Definitions
- Estimated fetal weight > 90th percentile
- Birth weight (BW) > 4,000-4,500 g

IMAGING FINDINGS

General Features
- Best diagnostic tool: LGA fetus + ↑ abdominal circumference (AC) + polyhydramnios

Ultrasoundographic Findings
- Estimated fetal weight (EFW) > 90th percentile
- Head biometry used to estimate weight
- Biparietal diameter (BD)
- Fetal circumference (FC)
- Abdominal circumference (AC)
- Femur length (FL)
- EFW accuracy for macrosomia is 85%
- AC heavily weighted in calculation of EFW
- Macrosomia often manifests in 3rd trimester
- AC alone may be predictive of macrosomia
- Risk for macrosomia < 1% if AC < 35 cm

Imaging Recommendations
- Best imaging tool: Accurate AC measurement
- Protocol advice: Growth graphs are useful visual tools

DIFFERENTIAL DIAGNOSIS

Beckwith-Wiedemann (BW) syndrome
- Early excessive growth
- Macrosomia + anomalies common
- Enlarged kidneys (often echogenic)
- Osphalangeal

Hydrops
- Excessive fluid collection
- Skin edema more hypoechoic than fat
- Pleural effusions

DDx: Large Fetus

Hydrops
Hydrops
BW, Tongue
BW, Kidney
MACROSONIA

Terminology
- Estimated fetal weight > 90th percentile
- Birth weight (BW) > 4,000-4,500 g

Imaging Findings
- Best diagnostic clue: LG fetus + 1 abdominal circumference (AC) + polyhydramnios
- Macrosomia often manifests in 3rd trimester
- AC often first measurement to 1
- Ascites
- Immune vs. non-immune causes

PATHOLOGY

General Features
- Epidemiology
  - 6-8% in non-diabetics
  - 16-18% in diabetes
- Associated abnormalities: Thick placenta

CLINICAL ISSUES

Presentation
- Most common signs/symptom
  - Larger than expected fundal height measurement
  - Pregnancies at risk for macrosomia
  - Diabetes
  - Maternal obesity
  - Post-term pregnancy (> 42 wks)
  - Prior child with macrosomia
  - Polyhydramnios
  - Diabetes and macrosomia
  - Less risk if diabetes well controlled

Natural History & Prognosis
- Fetal complications related to delivery
  - Shoulder dystocia in 10%
  - Brachial plexus injury
  - Asphyxia
  - Hypoglycemia (risk with diabetes)
  - Low plasma calcium levels (risk with diabetes)
  - Maternal complications from delivery
  - Anal and urinary incontinence

Treatment
- Early delivery
- Elective cesarean section delivery

DIAGNOSTIC CHECKLIST

Consider
- Risk for macrosomia if AC > 90th percentile
- EFW may initially be within normal limits
- Follow fetal growth carefully in diabetics

Key Facts
- 1/3 of fetuses with idiopathic polyhydramnios are macrosomic

Pathology
- 6-8% in non-diabetics
- 16-18% in diabetics

Clinical Issues
- Shoulder dystocia in 10%
- Elective cesarean section delivery

Image Interpretation Pearls
- Look for macrosomia in patients with unexplained polyhydramnios

SELECTED REFERENCES


IMAGE GALLERY

(Left) Growth chart of a fetus with gestational diabetes shows excessive AC growth. HC growth remains normal and there is a decreased HC/AC ratio. Estimated fetal weight (EFW) is > 95th percentile in the 3rd trimester. 
(Right) HC of 38.9 cm is measured in a pregnancy with macrosomia. Polyhydramnios is often seen in association with macrosomia, regardless of cause.
**BIOPHYSICAL PROFILE**

Graphic shows the correct method for measuring amniotic fluid for the BPP. The area is completely outlined, and the largest pocket of amniotic fluid, known as the calipers, is measured.

**TERMINOLOGY**

**Abbreviations and Synonyms**

- Biophysical profile (BPP)
- Non-stress test (NST)

**Definitions**

- **BPP score**
  - Ultra sound-based method to test for fetal hypoxia
  - Total of 8 points possible
  - 4 variables tested
  - 2 points maximum/variable
  - Performed on viable fetuses only
  - Test used to decide fetal delivery

- **NST score**
  - Electronic fetal monitoring
  - Does not use ultrasound
  - NST complementary to BPP
  - Total of 2 points possible

- **BPP + NST score**
  - Used together for management decisions
  - Total of 10 possible points
  - 8 points from BPP
  - 2 points from NST

**IMAGING FINDINGS**

**General Features**

- Best diagnostic tool: BPP + NST score of < 6/10 associated with fetal acidemia

**Ultrasonographic Findings**

- **Biophysical profile score**
  - 4 ultrasound variables observed
  - Fetal breathing
  - Gross body movement
  - Fetal tone
  - Amniotic fluid
  - Observation time = 30 minutes
  - Fetal sleep state = 20 min
  - Abnormal score cannot be given in < 30 min
  - Normal BPP possible in < 30 min
  - Scoring
    - Each variable scored 0 or 2 points
    - 2 points awarded if fetus meets criteria
    - No "T"s allowed
    - Total of 8 points possible
  - Normal result is BPP score of 8/8
  - BPP + NST score ≥ 8/10
  - NST score less important than BPP
  - Abnormal result is BPP score ≤ 4/6
  - If NST is 2 then 6/10 score is equivocal
  - If NST is 0 then ≤ 4/10 score is abnormal

**DDx: Oligohydramnios From Fetal Anomalies**

- Renal agenesis
- Renal agenesis
- Renal cystic dysplasia
- Bladder obstruction
BIOPHYSICAL PROFILE

Key Facts
- Ultrasound-based method to test for fetal hypoxia
- Total of 8 points possible

Imaging Findings
- Best diagnostic clue: BPP + NST score of < 6/10 associated with fetal acidemia
- Fetal breathing
- Gross body movement
- Fetal tone
- Amniotic fluid
- Observation time = 36 minutes
- Each variable scored 0 or 2 points
- Normal result is BPP score of 8/8
- Abnormal result is BPP score ≤ 4/8
- Equivocal result is BPP score 6/8

○ Equivocal result is BPP score 6/8
  - If NST is 2 then 6/10 is normal
  - If NST is 0 then 6/10 is equivocal
- Fetal breathing
  - Sustained diaphragm movement
  - Diaphragm excursion
  - Chest expansion
  - Movement of diaphragm can show movement
  - Scoring
    - ≥ 1 episode of “breathing” ≥ 30 sec = 2 point
    - No episode of “breathing” ≥ 30 sec = 0 points
- Gross body movement
  - Trunk roll
  - Spine flexion or extension
  - Gross limb movement
  - Scoring
    - ≥ 3 trunk or limb movements = 2 points
    - < 3 trunk or limb movements = 0 points
- Fetal tone
  - Active limb movement
  - Flexion = extension = fixation
  - Hand opens and closes
  - Scoring
    - ≥ 1 episode = 2 points
    - 0 episodes = 0 points
- Amniotic fluid (AF) volume
  - Largest AF pocket is found
  - Vertical and transverse measurements
  - Different than 4-quadrant amniotic fluid index
  - Scoring
    - ≥ 1 pocket of fluid ≥ 2 cm x 2 cm = 2 points
    - No pocket of fluid ≥ 2 cm x 2 cm = 0 points

Other Modality Findings
- NST
  - Non-ultrasound based testing
    - Cardiac activity
    - Fetal movement
    - Uterine contractility
    - Observation time = 20 minutes
    - Heart rate acceleration criteria
    - ≥ 15 beats per minute for 15 sec
    - Scoring

○ ≥ 2 accelerations in 20 min = 2 points
○ ≥ 1 acceleration in 20 min = 0 points
- Unilateral artery (UA) Doppler
  - Complimentary to BPP
  - Normal UA Doppler
  - Antegrade flow throughout diastole
  - Low resistive waveform pattern
  - Absent or reversed diastolic flow
  - Associated with hypoxia

Imaging Recommendations
- Best imaging tool
  - Experienced sonographer
  - Careful fetal observation
  - Accurate amniotic fluid assessment
  - Assess for intrauterine growth restrictions (IUGR)
  - Associated with abnormal BPP
- Protocol advice
  - BPP < 8/8
  - Observe at least 30 minutes
  - Send patient for NST
  - Perform UA Doppler
  - Use color Doppler for AF assessment
- Helps avoid measurement of cord in AF pockets

Differential Diagnosis

Oligohydramnios 2nd to fetal anomaly
- Renal agenesis
  - Anuria
  - Pulmonary hypoplasia
  - Fetal
- Bilateral renal anomalies
  - Bilateral cystic dysplasia
  - Sever autosomal recessive polycystic kidney disease
- Genitourinary tract obstruction
  - Bilateral renal obstruction
  - Bladder outlet obstruction
  - Posterior urethral valves

Top Differential Diagnoses
- Oligohydramnios 2nd to fetal anomaly
- Arthrogryposis

Pathology
- Tissue hypoxia = loss of function
- Oligohydramnios reflects chronic hypoxia
- Fetal breathing lost first
- Fetal tone lost second
- Gross body movement: lost last

Clinical Issues
- Normal BPP almost never associated with acidemia
- Early delivery of fetus if abnormal BPP/NST
BIOPHYSICAL PROFILE

Anomaly

- BP not designed for abnormal fetuses
- False-positive results more likely
- Cordal nervous system anomalies
- Cardiac defects
- IUGR common

PATHOLOGY

General Features

- General pathology
  - Tissue hypoxia = loss of function
  - Neuronal tissue more sensitive
  - Hypoxia \( \Rightarrow \) cardiac output redistribution
  - Chromonemocytes in amniotic fluids
  - Hypoxia \( \Rightarrow \) UGRR
  - Placental insufficiency
  - Biology
    - Variables affected by acute hypoxia
    - Fetal breathing
    - Gross body movement
    - Fetal tone
    - Fetal heart rate accelerations
    - Oligohydramnios reflects chronic hypoxia
  - Blood shunted away from head, body
  - Blood shunted away from lungs
  - Fetal swallowing \( \Rightarrow \) with hypoxia
  - \( \approx \) 3 risks for significant oligohydramnios to develop
  - Predictable order of function loss
    - Fetal breathing last first
    - Fetal heart rate second
    - Gross body movement next last
  - Epiglomeropathy
    - Low birth rate following normal birth
    - 0.4-0.6,1,000 high-risk pregnancies
  - Associated anomalies: IUGR

Staging, Grading or Classification Criteria

- Normal BP = 6/8 or 8/10 with NST
- Equivalent BP = 6/8 or 6/10 with NST
- Abnormal BP = 6/8 or < 6/10 with NST

CLINICAL ISSUES

Presentation

- Most common signs/symptoms
  - BP/NST to assess fetal health in high-risk cases
  - Intrauterine growth restriction (IUGR)
  - Fetal movement
  - Maternal hypertension
  - Maternal diabetes
  - Past dates
  - Premature rupture membranes

Natural History & Prognosis

- BP/NST used to avoid stillbirths
  - \( \approx \) 70% of birth fetuses with IUGR
  - \( \approx \) 90% show evidence for chronic hypoxia
  - Use of BP/NST with 1 primordial mortality from 1%
    - \( \approx \) 2%
  - BP/NST \( \approx \) 8/10 accurately predicts normal tissue oxygenation
  - Normal BP almost never associated with acidemia
  - False negative rate \( \approx \) 0%
  - BP/NST \( \approx \) 6/10 relatively accurate predictor of acidemia
  - \( \approx \) 6/10 is an equivocal score
  - \( \approx \) 75% false positive rate for acidemia
  - May select fetal ability to compensate for hypoxia
  - \( \approx \) 6/10 near 100% predictive for acidemia
  - Specific test results
    - Normal acute variables + normal fluid
    - Normal blood gas + normal pH
    - Normal acute variables + abnormal fluid
    - Normal blood gas + normal pH + hypoxia with compensation
    - Abnormal acute variables + normal fluid
    - Abnormal blood gas + abnormal pH in acute setting
    - Abnormal acute variables + abnormal fluid
    - Abnormal blood gas + abnormal pH in chronic setting

Treatment

- Early delivery of fetus if abnormal BP/NST
- Avoid stillbirths
- Repeat noninvasive testing for equivocal results

DIAGNOSTIC CHECKLIST

Consider

- Correlate BP score with NST score
- BP exam to viable fetuses with IUGR
- IUGR in viable fetuses with oligohydramnios

Image Interpretation Pearls

- Obtain cord Doppler if BP is abnormal
- Most observe fetus for 30 minutes before giving score for any acute variable

SELECTED REFERENCES

** Typical **

- (Left) Condom ultrasound shows a clear placement in order to observe fetal thoracic movements. The area to be scanned passes through the diaphragm (arrow) and fetal breathing can be documented. **(Right)** Condom ultrasound shows fetal breathing. The endulaing fetal mouth (arrow) is from the diaphragm and lung motion.

- (Left) Condom ultrasound shows normal fetal type. The fetal leg (arrow) was seen extending from a shallow position. **(Right)** Condom ultrasound in the same case shows the leg (arrow) requiring a closed or open position without movement of the fetal arm (arrow) points to knees. At least 1 type of flexion occurs and back to the arm is required for a score of 2 for knees. Opening and closing of a femur could also be as well.

- (Left) An abdominal NST strip shows lack of cardiac acceleration (arrow) and a mild deceleration (curved arrow) during a period contractions (open arrow) in a non-laboring patient. The NST scale here is 0. **(Right)** Velot Doppler ultrasound of the umbilical artery in a fetus with IUGR and a BP record of 4/9 shows normal fetal flow (arrows). UA Doppler can also help identify foetal acidosis for Hypoxic.
**TERMINOLOGY**

**Abbreviations and Synonyms**
- Middle cerebral artery (MCA)
- Peak systolic velocity (PSV)
- End diastolic velocity (EDV)
- Systolic-diastolic (S/D) ratio
  - PSV/EDV/PSV
- Umbilical artery (UA)

**Definitions**
- MCA Doppler is a useful tool in assessing fetal well-being in varying clinical conditions, including intrauterine growth restriction and fetal anemia.
- 2nd trimester growth restriction (UGR)
- Estimated fetal weight < 10th percentile for gestational age.
- Most useful for asymmetric UGR
- Fetal anemia
- Fetal anemia varies with gestational age
- Characterized as severe when fetal hematocrit <15%, hematoglobin 4-5 g/dL.
- Color Doppler of circle of Willis and branches help in evaluation brain malformations.

**IMAGING FINDINGS**

**Ultrasoundographic Findings**
- Asymmetric UGR
- SD ratio of MCA should be > SD ratio of UA throughout gestation.
- Reversal of this ratio in UGR is called "head sparing" pattern.
- Abdominal circumference less than other biometric parameters
- Estimated fetal weight less than < 10th percentile
- Oligohydramnios common
- Fetal anemia
- Anemia caused by red cell alloimmunization syndromes and infection, particularly parvovirus.
- May see signs of hydrops.
- Color Doppler of circle of Willis and branches helpful in evaluation brain malformations.
- Hydrocephaly
- Cerebral atrophy due to vascular catastrophe
- No flow seen in circle of Willis
- Holoprosencephaly
- Brain malformation associated with abnormal development of prosencephalon
- Lobar holoprosencephaly associated with arteria anterior central artery
- Single vessel seen just beneath skull vault
- Agenesia of corpus callosum.

**DDx: Errors In MCA PSV Measurement**

- Wrong Vessel
- Wrong Angle
- Real Breathing
Key Facts

**Top Differential Diagnoses**
- Wrong vessel
- Wrong sample site
- Wrong angle
- Fetal breathing

**Clinical Issues**
- Most data supports performance of intravascular blood transfusion based on velocity data

**Diagnostic Checklist**
- Use of MCA Doppler has changed management of pregnancies complicated by alloimmunization
- Serial measurements showing differing velocities, repeat before making management decision
- Hydrops and massive ascites may cause MCA PSV in the absence of anemia

**Differential Diagnosis**

**Wrong vessel**
- Management criteria based on MCA flow velocities
- Anterior/posterior cerebral arteries have different velocity profile
- Cannot use measurements from these vessels

**Wrong sample site**
- Best to sample within 2 mm of origin MCA from circle of Willis
- Statistically significant differences seen in measurements from proximal and distal parts of vessel
- Incorrect measurements = incorrect management decisions

**Wrong angle**
- Flow calculations are affected by angle of insonation
- Frequency shift proportional to cosine of angle of insonation
- Keeping angle at 90° avoids need for angle correction
- Technically feasible in most cases
- Scan plane skin to that for head measurements therefore easily reproduced

**Fetal breathing**
- Alter flow in all fetal vessels
- Variable height of waveforms
- Velocity measurements unreliable
- Incorrect measurements = incorrect management decisions

**Imaging Findings**
- Use color Doppler to identify circle of Willis
- "Zoom" image to see entire length MCA
- Place cursor close to origin of MCA
- Statistically significant differences seen in measurements from proximal and distal parts of vessel
- Angle of insonation should be zero
- Avoid sampling during periods of fetal breathing and increased activity
- Fetal breathing causes highly variable waveform with beat-to-beat PSV variations
- Fetal activity causes mean PSV to increase by 4cm/sec
- Potential pitfalls in assessment of anemia
- Massive fetal ascites
- Reported case with elevated MCA PSV but normal hematocrit at birth
- MCA PSV correlates with volume of ascites

**Imaging Recommendations**
- Protocol advice
  - Assessment of IUGR
  - Measure MCA SD ratio and compare to that of UA
  - Assessment of anemia
    - Use color Doppler to identify circle of Willis
    - "Zoom" image to see entire length MCA
    - Place cursor close to origin of MCA
    - Statistically significant differences seen in measurements from proximal and distal parts of vessel
    - No significant difference in velocities of near/far-field MCA if proximal sample site used
    - Angle of insonation should be zero
    - Do not use angle correction
    - Take several measurements (at least three) with 15-30 waveforms
    - Velocities should be similar
    - Take best measurement
    - Do not average several velocities
    - Avoid sampling during periods of fetal breathing and increased activity
  - Fetal breathing causes highly variable waveform with beat-to-beat PSV variations
  - Fetal activity causes mean PSV to increase by 4cm/sec
  - Potential pitfalls in assessment of anemia
    - Massive fetal ascites
    - Reported case with elevated MCA PSV but normal hematocrit at birth
    - MCA PSV correlates with volume of ascites

**Terminology**
- MCA Doppler is a useful tool in assessing fetal well-being in varying clinical conditions, including intravascular growth restriction and fetal anemia
- Color Doppler of circle of Willis and branches also aids in evaluation of cerebral malformations

- Corpus callosum induces formation of pericallosal and callosomarginal branches of anterior cerebral artery
- Sagittal view with color Doppler used to demonstrate flow
- Presence of vessels implies presence of corpus callosum
- Anterior/axial malformations
- Neck and cerebral vessels increased in size in presence of shuttler flow
PATHOLOGY

General features
- **Anatomy:**
  - **IUGR**
  - **By definition occurs in 10% of pregnancies**
  - Rheus (Rh) alloimmunization
  - 10.2:10,000 stillbirths
  - Other autoimmune conditions (e.g., HLA, Duffey, C, c, E
d and others)
  - 15'-15,000 live births
  - Fetal virus
  - Transplacental transmission in 3% of cases

- **Physiology:**
  - IUGR
  - Intravascular environment becomes hostile to fetus
  - Most common cause is placental insufficiency
  - Protective mechanism allows 1 proportion of umbilical blood flow to go to brain
  - Normally 20-30% of ductus venous blood shunts across uniovular to supply coronary arteries and brain.
  - With IUGR/hypoxia up to 70% of flow is diverted to brain/ovaries
  - Diastolic flow ↑ = SD ratio ↑
  - U/A SD ratio ↑ = Placental resistance ↑
  - Eventually U/A SD ratio > MCA SD ratio = "head sparing" pattern
  - Fetal anemia
  - Blood viscosity ↑ = Velocity of flow even if vessel diameter stable
  - Hypoxia ↑ = 1 cerebral blood flow as protective mechanism

**CLINICAL ISSUES**

**Presentation**
- Infarcted directly to monitor at-risk pregnancies

**Treatment**
- **Anemia**
  - Monitor velocities
  - Plot measurement of MCA PSV in cm/sec against gestational age in weeks
  - Intervention, based on relationship of velocity to GA
  - Zone A: Inactive
  - Zone B: Repet measurement in 5-7 days
  - Zone C: Repeat measurements in 7-10 days
  - Zone D: Repeat measurements in 2-3 weeks
  - Follow-up interval must be adjusted based on
  - Maternal antibody titers
  - Prior history of affected infants
  - Moderate anemia detected with 100% sensitivity and 12% false positive rate
  - Using cutoff of PSV values at 1.5 multiples of the median 36MoM for GA
  - Severe anemia detected with 100% sensitivity and 15% false positive rate with cut off of 1.55 MoM
  - Number of false-positives increase after 35 weeks gestation but delivery is safe up to that GA
  - Intervention

- Most data supports performance of intrauterine blood transfusion based on velocity data
- Intrauterine route preferred but interuterine route may be performed if IV route not available
- Report MCA Doppler after transfusion shows increased MCA PSV
- Fetal anemia may cause fetal anemia
- Transplacental transmission estimated to occur in 20-30% of cases
- Anhydrotic fetuses occur within 4 wks of symptomatic maternal infections, rare after 8 wks
- No reported fetal deaths > 12 wks post exposure
- Optimal interval uncertain: many centers use weekly Doppler checks for signs of cord
  - Follow for 12 weeks then return to routine obstetric care

**DIAGNOSTIC CHECKLIST**

**Consider**
- **Use of MCA Doppler has changed management of pregnancies complicated by alloimmunization:**
  - Serial anemia tests no longer required
  - Less risk of procedure-related pregnancy loss
  - Less risk of fetal infection and miscarriage

**Image Interpretation Pearls**
- **Check all waveforms and select best measurement**
  - If serial measurements show differing velocities, repeat before making management decisions
  - Fetal Breathing
  - Poor technique
  - Hydrops and chorioi defects may cause 1 MCA PSV in the absence of anemia

**SELECTED REFERENCES**

**Typical**

(Left) Pulsed Doppler ultrasound shows normal high-resistance circulation in the MCA. The SD ratio in this second trimester fetus is normal at 3.2. Note: Sharp upstroke and little integrative diabetic flow (arrow).  
(Right) Pulsed Doppler ultrasound shows abnormal low-resistance flow in the MCA in a fetus with growth restriction. The SD ratio of 2.79 was less than that of the UA. Note the prominent integrative diastolic flow (arrow).

**Typical**

(Left) Graphic of MCA PSV plots in a fetus-only patient. The length of interval follow-up is based on the zone in which the PSV plots. Intrauterine transfusion (IUT) was performed when the PSV was in zone A with a subsequent drop in PSV.  
(Right) Pulsed Doppler ultrasound shows a PSV of 40 cm/s, which plotted in zone C. The appropriate follow-up interval in zone C is 7-10 days.

**Typical**

(Left) General ultrasound shows features of hydrops. It is important to be aware that hydrops may cause elevations in the PSV without anemia. This fetus was anemic and improved after translation.  
(Right) Sagittal socal Doppler ultrasound shows the anterior cerebral artery (arrows) branching into the precentral and callosomarginal branches as it runs over the corpus callosum. Doppler of the major cerebral vessels helps evaluate for vascular anomalies.
**TERMINOLOGY**

**Abbreviations and Synonyms**

- Uterine Artery (Ut A) Doppler
  - Resistive index (RI)
    - Diastolic velocity (PSV) - end-diastolic velocity (EDV)
  - Pulsatility index (PI)
    - PSV-EDV/average velocity (average flow velocity over a complete cardiac cycle)
  - Systolic to diastolic (S/D) ratio
    - PSV/EDV

**Definitions**

- Doppler interrogation of uterine artery flow
- Clinical applications of uterine artery Doppler
  - In vitro fertilization
  - Uterine receptivity for implantation
  - Risk assessment for maternal complications of pregnancy
  - Pregnancy-induced hypertension
  - Pre-eclampsia toxemia
  - Risk assessment for poor fetal outcome
  - Intrauterine growth restriction (IUGR)
  - Small for gestational age (SGA) infant

**IMAGING FINDINGS**

**General Features**

- Ut A spectrum changes early in normal pregnancy
  - Switch from high to low resistance usually occurs in first trimester
  - May be delayed until second trimester
  - Little change after 24 weeks
  - Abnormal Ut A Doppler implies abnormal placentation
  - Umbilical artery (UA) Doppler reflects fetal response to abnormal placentation
  - As fetus grows, abnormal placenta becomes non-functional
  - Causes tissue hypoxia, Doppler reflects fetal response to stress of hostile intratissue environment
  - Changes more likely to develop and progress in third trimester
    - Normal values for uterine artery RI at 11-14 weeks
      - 10th percentile = 0.33
      - 50th percentile = 0.71
      - 90th percentile = 0.85
  - Abnormal findings
    - Persistent diastolic notch beyond first trimester
    - Conversion from high to low resistance delayed until second trimester

**DDx: Pitfalls in Measuring Uterine Artery Doppler**

- External Iliac artery
- Internal Iliac artery
- Myometrial branches
UTERINE ARTERY DOPPLER

Key Facts

- Imaging Findings
  - Switch from high to low resistance usually occurs in the first trimester
  - Abnormal Ut A Doppler implies abnormal placenta
tion
  - Umbilical artery (UA) Doppler reflects fetal response to abnormal placenta
tion
  - Salsa just cephalad to where Ut A appears to cross internal iliac artery
  - Obtain 3 similar consecutive waveforms
  - Measure RI (PI and SD ratio) also used in some studies
  - Evaluate both vessels and average measurement.
  - Document presence of "notch".

- Top Differential Diagnoses
  - Wrong vessel

Pathology

- Pathologic changes found in 79% of placental bed biopsies in IUGR abnormal Ut A Doppler normal
- Control cases had 0% pathologic findings in placental bed biopsies

Diagnostic Checklist

- Use results in addition to other information including ultrasound and Doppler and tests of fetal well-being
- Data established for high-risk singleton pregnancies
- Low sensitivity for adverse outcome in multiple pregnancies despite use of twin-specific nomograms
- Diastolic notch beyond the first trimester is abnormal

Imaging Findings

- Abnormal findings with 71.4% positive predictive value for adverse outcome in selected high-risk group
  - Unilateral notch and mean RI ≥ 0.65 at 20 weeks
  - Bilateral notches and mean RI ≥ 0.55 at 20 weeks
  - High-risk women with normal values at 20 weeks had similar outcome to controls
  - Normal result in this study had a negative predictive value of 93.4%

Imaging Recommendations

- Protocol advice
  - Transabdominal or endovaginal (EV) approach
  - EV may be necessary with obese maternal habitus
  - Find cervical canal for mid-cervical plane
  - Move transducer laterally to find paracervical planes
  - Sample just cephalad to where Ut A appears to cross internal iliac artery
  - Obtain 3 similar consecutive waveforms
  - Measure RI (PI and SD ratio) also used in some studies
  - Evaluate both vessels and average measurements
  - Avoids bias from lateral placental implantation
  - Document presence of "notch".
  - Defined as decreased velocity in early diastole (less than peak diastolic velocity)
  - Is notch unilateral or bilateral?

DIFFERENTIAL DIAGNOSIS

Wrong vessel

- Internal iliac artery
  - Sharp systolic upstroke
  - Very low diastolic velocity
  - Early diastolic flow reversal is normal
- External iliac artery
  - Early diastolic flow reversal is normal
  - Much higher velocity than uterine artery
- Spiral artery
  - Very low velocity
  - Very low resistance

PATHOLOGY

General Features

- Etiology: Impaired trophoblastic invasion of spiral arteries > increased impedance to flow in uterine arteries

- Epidemiology
  - Incidence abnormal Ut A Doppler in general population not known
  - IUGR in 10% depending on definition

- Normal development of maternal circulation
  - Placental trophoblast cells invade maternal spiral arteries
  - Vessel walls transformed from non-pregnant smooth muscle to fascial channels without smooth muscle properties
  - Uterine artery blood flow in early pregnancy 60 ml/min
  - Uterine artery blood flow at term reaches 700 ml/min

- Spiral artery impedance decreases between 15th and 20th week gestation
- Uterine and arterial impedance decreases after 8th week
- Uterine artery Doppler reveals information about maternal side
- Umbilical artery Doppler reveals information about fetal side

Gross Pathologic & Surgical Features

- Series of pregnancy complicated by IUGR with abnormal Ut A and UA Doppler
  - 82% abnormal placental biopsy
  - Villous edema
  - Cytotrophoblast proliferation
  - This villous trophoblastic basal monolayer
  - 95% abnormal placental bed biopsies
  - Inadequate endovascular trophoblast invasion
  - Thrombosis or minimal obliteration of spiral arteries
  - Increased extravillous trophoblasts
• Atherosclerosis (fibrinoid necrosis of vessel walls with subintimal accumulation of lipid laden cells)
• Pathologic changes found in 79% of placental bed biopsies in IUGR + abnormal Ut A Doppler (Ut A Doppler normal)
  • Control cases had 0% pathologic findings in placental bed biopsies

CLINICAL ISSUES

Presentation
• Infertility especially in older women
  • Ut A impedance increases in women > 35 yrs of age
  • May partly explain increase in pregnancy complications in this age group
• Prior history of complicated pregnancy
  • Prior pre-eclamptic toxemias
  • Prior IUGR/SGA fetus
• Risk assessment for preterm delivery
  • Defective placentation thought to increase risk for preterm delivery, however Ut A Doppler has not been shown to reliably predict recurrence

Natural History & Prognosis
• In vitro fertilization patients
  • Ut A PI > 3.26 = very low chance of achieving pregnancy
  • Measures to decrease vascular impedance might enhance uterine receptivity in this group
• Abnormal uterine placental vascular resistance (Ut A Doppler) associated with
  • Preterm delivery
  • Operative delivery
  • SGA infants
• Patients with abnormal Ut A and UA Doppler
  • Deliver early
  • Lower mean birth weight
  • Lower placental weight
• Abnormal Ut A Doppler in patients with pre-eclamptic toxemias (PET) predicts adverse outcome in future pregnancies
  • 3.4x likelihood of PET again in subsequent pregnancy
  • 9.7x likelihood of delivering SGA infant in subsequent pregnancy
• Individualized risk assessment in inner city population in London
  • Mean PI = 1.45 at 23 weeks = 5x likelihood ratio of PET
  • Maternal smoking doubled the risk for any given PI
• Pregnant women with chronic hypertension at risk for PET
  • Ut A and UA Doppler abnormal in all who developed PET
• IUGR significant risk factor for adverse perinatal outcome
• Abnormal Ut A Doppler implies worse prognosis
• Bilateral Ut A notchings or mean PI > 0.58 = 4-fold risk of admission to new born intensive care unit
• Series of IUGR fetuses delivered at 24 weeks gestation
• Abnormal Ut A Doppler correlates with SGA infant even after correction for confounding variables including maternal smoking

Treatment
• Randomized controlled trials are currently in progress
• Aim to see if abnormal uterine artery Doppler in early pregnancy can be effectively treated before onset of pregnancy complications
• Treatment options
  • Aspirin
  • Vitamins C/E
  • Low molecular weight heparin

DIAGNOSTIC CHECKLIST

Consider
• Studies use different criteria for 'adverse outcome' and for normal/abnormal values of uterine artery Doppler
• If applying in practice establish consistent technique
• When to measure: First or second trimester
• Define normal for population: Absolute values, percentile range, which Doppler parameters
• Use results in addition to other information including umbilical artery Doppler and tests of fetal well-being
• Data established for high-risk singleton pregnancies
• Low sensitivity for adverse outcome in multiple pregnancies despite use of twin-specific nomograms
• Benefit not clearly proven in low-risk population

Image Interpretation Pearls
• Diastolic notch beyond the first trimester is abnormal

SELECTED REFERENCES
**UTERINE ARTERY DOPPLER**

**IMAGE GALLERY**

**Typical**

- **Left**: Pulsed Doppler ultrasound shows measurement of various Doppler parameters including RI, PI and S/D ratio. With visual assessment, the mean measurement is used by the examiner. **Right**: Pulsed Doppler ultrasound shows normal diastolic flow in the uterine artery at 20 weeks gestation. Uterine artery flow increases from 70 to 150 m/s by term.

**Typical**

- **Left**: Pulsed Doppler ultrasound shows the typical features of a normal uterine artery waveform in early pregnancy after converting from high to low resistance. This usually occurs in the first trimester. **Right**: Pulsed Doppler ultrasound of the uterine artery shows an early diastolic notch (N) waveform. This pattern is abnormal, as the uterine arteries should have converted to a low-resistance vascular bed.

**Typical**

- **Left**: Pulsed Doppler ultrasound of the umbilical artery shows reversed and electrocardiogram-like flow in a fetus with RUQ syndrome. **Right**: Pulsed Doppler ultrasound of the umbilical artery in a fetus with RUQ syndrome shows low resistance (RI) which implies lesions (or lesions) and significant dilatation.


**HYDROPS**

Digital ultrasound shows intravascular findings from red cell iso-immunization. The presence of ascites (open arrow), pleural effusion (arrowhead) and edema (curved arrow) are diagnostic of hydrops.

**TERMINOLOGY**

**Abbreviations and Synonyms**
- Hydrops fetalis
- Erythroblastosis fetalis

**Definitions**
- Excessive fetal body fluid
- Immune hydrops (10%)
- Hereditary disease ⇒ fetal anemia
- Nonimmune hydrops (90%)
- Any other cause besides immune

**IMAGING FINDINGS**

**General Features**
- Best diagnostic clue
  - Fluid accumulation at 2 or more body cavities
- Anasarca • body cavity fluid

**Ultrasoundographic Findings**
- Body cavity fluid collections
  - Ascites
  - Anomalous fluid
- Best seen between liver and abdominal wall
- Bilateral pleural effusions
- Hydrothorax

- Pericardial effusion
  - Associated with cardiac defects
  - < 2 mm considered physiologic
- Anasarca
  - Skin/scleral edema
  - Hypoechoic fluid
  - Scalp edema often first sign
- Jaundice + cutaneous hydrops
- Turner syndrome
- Trisomy 21 (Down's)
- Placentomegaly
  - Fetal placental edema
  - Placenta thickness > 40 mm
  - More often with immune hydrops
- Amniotic fluid dynamonomes
  - Polyhydramnios
  - More common with immune hydrops
  - May be early isolated finding
- Oligohydramnios
  - More often seen with fetal anomalies
- Fetal cardiac abnormalities
  - 22% of nonimmune hydrops with cardiac defect
  - Poor contractility ⇒ heart failure ⇒ hydrops
  - Tachyarrhythmia
  - > 280-200 bpm
- Non-cardiac causes of high-output cardiac failure
  - Vascular fetal mass
  - Placental aneu (chooroangioma)

**DDX: Hydropic Fetus**

- Isolated Ascites
- Chylothorax
- Pericardial Effusion
- Reduced Skin

Clinical photograph from a fetus with syndrome 21 and hydrops. Below left and torn amnion seen. The abdomen is distended from ascites. Nonimmune hydrops is associated with aneuploidy.
HYDROPS

Terminology
- Excessive fetal body fluid
- Immune hydrops (10%)
- Nonimmune hydrops (90%)

Imaging Findings
- Ascites
- Bilateral pleural effusions
- Skin/subcutaneous edema
- Placental megalgy
- Polyhydramnios
- MCA Doppler screening for fetal anemia
- M-mode to rule out tachyarrhythmia

Top Differential Diagnoses
- Isolated ascites
- Chylothorax

- Twin-twin transfusion syndrome
- Aneuplody and fetal syndromes
- 16% of nonimmune hydrops
- Turner syndrome
- Hydrops + cystic hygroma
- Trisomy 18 and trisomy 13
- Lead likely to present with hydrops
- Severe intrauterine growth restriction (IUGR)
- Other typical anomalies often seen
- Noonan syndrome
- Normal chromosomes
- Phenotypic features of Turner syndrome
- Other hereditary and metabolic syndromes
- Family history helpful
- First trimester hydrops
- Increased nuchal translucency + anasarca
- Fetal effusion and ascites can be seen
- Highly associated with aneuplody
- Turner, T21 most common
- Middle cerebral artery (MCA) Doppler
- 1 MCA peak systolic velocity (PSV)
- Non invasive way to screen for anemia
- Red cell alloimmunization, screening
- MCA Doppler technique
- MCA easily seen with color Doppler
- MCA sampled near origin
- 0° Doppler angle necessary
- Peak systolic velocity (PSV) compared with gestational age
- > 1.5 multiples of median considered abnormal
- Abnormal MCA PSV
- Anemia confirmed with cordocentesis
- Treatment with in utero transfusion

Imaging Recommendations
- Best imaging tool
  - MCA Doppler screening for fetal anemia
- Careful ultrasound to detect early hydrops
- Protocol advice

Key Facts
- Isolated pericardial effusion
- Redundant skin

Pathology
- Turner syndrome (45,XO)
- Trisomies: 21 > 18, 13
- Maternal Rh sensitization
- Atrial antibodies
- Fetal anemia leads to hydrops
- Variety of causes for nonimmune hydrops
- No underlying cause found in 50-80% of cases

Clinical Issues
- Hydrops + fetal anomaly nearly 100% fatal

Diagnostic Checklist
- Look forreatable causes of hydrops
- Look for additional fluid collections when one collection seen.
- Search for cause of nonimmune hydrops
- M-mode to rule out tachyarrhythmia
- Fetal anomalies

DIFFERENTIAL DIAGNOSIS

Isolated ascites
- Urinary ascites
  - Other signs of obstruction often seen
  - Hydroureter
  - Ureteral obstruction
  - Distended bladder
  - Gastrointestinal perforation
  - Meconium peritonitis
  - Ascitic fluid often complex
  - Better prognosis than hydrops

Chylothorax
- Unilateral pleural effusion
- Thoracic duct anomaly
- Can progress to hydrops
- Associated with T21 and Turner syndrome

Isolated pericardial effusion
- Often a transient normal finding
- < 2 mm considered normal
- Associated with cardiac abnormality
- Often early sign of hydrops

Redundant skin
- Lethal skeletal dysplasia
  - Extremely short bones
  - Excess echogenic skin
- Macrocephaly
  - Excessive subcutaneous fat
  - More echogenic than edema
HYDROPS

PATHOLOGY

General Features
- Genetics
  - Turner syndrome (45,X0)
- Triomies: 21 > 18, 13
- Etiology
  - Maternal Rh sensitization
    - Maternal lack of D antigen
    - Fetal D antigen causes antibody response
    - Maternal antibodies attack fetal red blood cells
    - Sensitization 2nd to fetal-maternal hemorrhage
    - < 1% fetal cells can lead to anti-D antibody
  - Maternal LEA causes immunization
    - Anti-Kel, anti-C, anti-e most often detected
    - Becoming more common
  - Fetal anemia leads to hydrops
  - Anemia from any cause
  - Extramedullary erythropoiesis
  - Hepatomegaly
  - Cardiac output = cardiac failure
  - Nonimmune hydrops and infection
    - Infection = myocarditis, anemia
  - Parvovirus most common
  - Variety of causes for nonimmune hydrops
    - Primary cardiac anomaly
    - Large thoracic mass displaces heart
    - High-output heart failure from extrathoracic mass
    - Heart failure from tachyarrhythmia
    - Congenital obstruction
    - Maternal-fetal hemorrhage = anemia
  - No underlying cause found in 50-80% of cases
- Epidemiology
  - Rh negative
    - 15% Caucasians
    - 5% African-American
  - Rh sensitization
    - 6,7,1,000 births
    - 20-25% develop fetal anemia if untreated
  - 50% of anemic fetuses develop hydrops
  - Non-D antibody sensitization
    - Develops 5% after blood transfusion
  - 2% immune hydrops cases
  - Nonimmune hydrops in 1-3% births
  - 22% cardiac abnormality
  - 16% aneuploidy
  - 10% alpha fetoprotein
  - 6% twin-twin transfusion
  - 5% congenital infection
- Associated abnormalities: Cystic hygroma

Staging, Grading or Classification Criteria
- Immune hydrops
- Nonimmune hydrops

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - Large fetus from hydrops
  - Exposure to parvovirus
  - Red cell alloimmunization
  - Cystic hygroma

Natural History & Prognosis
- Hydrops = fetal anomaly nearly 100% fatal
- Hydrops = tachyarrhythmia
- Treatable w/ good prognosis
- Fetal anemia
  - 75% survival if treated after onset of hydrops
  - 95% survival if treated before onset of hydrops
- MCA PSV can identify anemic fetus

Treatment
- Rh immunoglobulin (RhGAM)
  - Blocks antigen sites on fetal blood cells
  - Given after every pregnancy/procedure
  - Only useful for D antibodies
- Antiparvoviral antibody reimmunization
  - No pharmaceutical immunoglobulins yet
  - Identify fetal anemia prior to onset of hydrops
  - MCA Doppler
  - Treatment w/ in utero transfusion
  - Immune hydrops
  - Treat anemia w/ in utero transfusion
  - Nonimmune hydrops
  - Treat cause if possible
  - Tachyarrhythmia treated pharmacologically
  - Anemia from any cause
  - In utero transfusion

DIAGNOSTIC CHECKLIST

Consider
- Hydrops is a nonspecific ultrasound diagnosis
- Immune causes ruled out with history and serology
- Infections causes often ruled out by serology

Image Interpretation Pearls
- Look for treatable causes of hydrops
- Tachyarrhythmia, anemia
- Look for causes of nonimmune hydrops
- Fetal anemias, aneuploidy

SELECTED REFERENCES
HYDROPS

IMAGE GALLERY

Typical

(Left) Axial ultrasound shows bilateral small pleural effusions (arrows) as an isolated finding at 18 weeks.

(Right) Coronal oblique ultrasound in the same patient 6 weeks later shows left pleural hydrops. A large pleural effusion (arrows) and ascites (arrowhead) have developed. We were unable to find a cause for hydrops in this case. Many nonimmunologic hydrops cases are unexplained.

Typical

(Left) Coronal ultrasound shows bilateral pleural effusions (arrows) in a fetus with lowcord hydrops of unknown etiology. The lungs (open arrows) are surrounded by pericardial effusion. (Right) Frontal radiograph after delivery shows bilateral pleural effusions (arrows) and also ascites (open arrow). A small amount of sputum was also present. This neonate died five after birth.

Typical

(Left) Axial ultrasound shows pleomorphic cysts (arrows) and polyhydramnios (curved arrow) in a pregnancy with twin hydrops. The placenta measures 7 cm thick. (Right) Axial and sagittal ultrasound through the fetal head and neck shows extramedullary hematoma (arrow) and cystic hygroma (open arrow) in a fetus with Down's syndrome. Cystic hygroma is highly associated with both hydrops and aneuploidy.
SECTION 18: Maternal Conditions in Pregnancy

Uterus

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INCOMPETENT CERVIX

Terminology

Abbreviations and Synonyms
- Short cervix
- Decreased cervical length
- Cervical effacement
- Internal os funneling
- Internal os bridging

Definitions
- Cervical incompetence
  - Cervical length (CL) ≤ 25 mm at 16-24 wks
- Preterm labor
  - CL ≤ 25 mm at 24-36 wks and patient is having uterine contractions
  - Internal os (IO) funneling
  - IO dilation with membranes bulging into cervical canal

Imaging Findings

General Features
- Best diagnostic clue: Short cervix +/- IO funneling by transvaginal ultrasound (TVUS)

Ultrasoundographic Findings
- Normal cervix

DDx: Atypical Cervical Appearance

- Nabothian Cyst
- Hypoechoic Canal
- Vaginal Air
INCOMPETENT CERVIX

**Key Facts**
- **Pathology**
  - 1% ofsingleton pregnancies
  - 60% of twins
  - 20% of triplets
- **Clinical Issues**
  - Ultrasonic more sensitive than manual exam
  - Risk of preterm birth increases with shorter CL
  - Worse prognosis if short cervix + funneling
  - Fetal fibronectin (FN) test on vaginal mucous helpful in clinical management
  - FN and CL < 25 mm: ~ 64% risk for preterm birth (~35 wks)
  - FN and CL < 25 mm: ~ 15% risk for preterm birth
  - Current studies cast doubt on utility of cerclage

- **Differential Diagnosis**

**Normal cervix**
- Hypotonic cervical canal
- Can mimic fluid in canal
- CL otherwise normal
- No funneling
- Air in vagina adjacent to cervix
- Can mimic cerclage sutures

**Nabothian cyst**
- Cervical cyst
  - Common, benign finding
  - Can mimic fluid in cervical canal
  - EVUS helpful
  - Shows cyst in cervical muscle not canal

**Focal myometrial contraction (FMC)**
- Thick myometrium 2+ to contraction
  - Open asymmetric
  - FMC in lower uterine segment (LUS)
  - Distorts LUS morphology
  - May mimic IO funneling
  - FMC will change/resolve with time
  - EVUS shows normal cervix, inferior to FMC

**Terminology**
- Cervical length (CL): ≤ 25 mm at 16-24 wks

**Imaging Findings**
- IO dilatation
- Determine percentage of open CL
- Bulging membranes
- Increased amniotic fluid
  - Ultrasound more sensitive than manual exam
- Cervical canal:
  - Short: ≤ 25 mm
  - Long: > 25 mm
- Conical cervix:
  - Short: ≤ 25 mm
  - Long: > 25 mm
- Funneling:
  - Closed: ≤ 10 mm
  - Open: > 10 mm
- Multiple gestation pregnancy
- Prior preterm birth
- Prior cervical surgery
- Performed every 2 wks between 16-24 wks
- Prior cervical surgery
- Performed transvaginal ultrasound if EVUS is contraindicated
- Ruptured membranes
- Known funneling
- Known funneling
- Active bleeding
  - Transvaginal technique for clinical measurement
  - Elevate maternal hips to minimize bowel artifact
  - Use covered 3.5-MHz sector probe
  - Place probe on perineum, over labia minora
  - Use collapsed vagina as acoustic window to cervix
  - Same measurement technique at with EVUS

** Imaging Recommendations**
- Protocol advice
  - IO dilatation technique for CL measurement
  - Scan within carefully inserting probe
  - Find midline sagittal plane
  - Angle for both long-axis view
  - Pull probe back until EO seen
  - Avoid pressure on cervix
  - Measure from IO to EO
  - Obtain measurements over 1-5 minutes
  - Apply fundal pressure for 15 seconds
  - EVUS technique for measuring IO funneling
  - Measure diameter and length of funneling portion
  - Measure length of closed cervix (functional cervix)
  - Obtain EVUS CL in high-risk patients (16-24 wks)

- Normal cervical
- Cervical cyst
- Prior preterm birth
- Prior cervical surgery
- Perform every 2 wks between 16-24 wks
- Procedure performed transvaginal ultrasound if EVUS is contraindicated
- Ruptured membranes
- Known funneling
- Known funneling membranes
- Active bleeding
  - Transvaginal technique for CL measurement
  - Elevate maternal hips to minimize bowel artifact
  - Use covered 3.5-MHz sector probe
  - Place probe on perineum, over labia minora
  - Use collapsed vagina as acoustic window to cervix
  - Same measurement technique at with EVUS
PATHOLOGY

General Features
- **Etiology**
  - Loss of cervical stromal resistance
  - Intrinsic weakness
  - Connective tissue disease
  - Fetal origin: from many different causes
  - Infection
  - Inflammation
  - Uterine overdistension
  - Cervical trauma/surgery
- **Epidemiology**
  - 1% ofsingleton pregnancies
  - 6% of twins
  - 20% of triplets

CLINICAL ISSUES

Presentation
- Most common signs/symptoms:
  - Incessant ultrasound diagnosis
  - Asymptomatic patient
  - High-risk patient
  - Prior preterm delivery
  - Multiple gestation
  - Cone biopsy or other cervical surgery
  - Ultrasound more sensitive than manual exam
  - 75% with no appreciable change by manual exam

Natural History & Prognosis
- CL ≤ 25 mm at 16-24 wks associated with 1 preterm birth rate
  - 18% in low-risk patients
  - 55% in high-risk patients
  - 60% in twins
  - Risk of preterm birth increases with shorter CL
    - 0.24% risk at CL ≥ 40 mm
    - 92% risk at CL ≤ 5 mm
  - Worse prognosis if short cervix + funneling
    - FHR 110-160 at 20-21 wks
  - Fetal fibroinjection (FI) test on vaginal mucous helpful in clinical management
    - Speculum test of vaginal mucus for IFN
    - IFN from chorion/descent disruption
    - IFN and CL < 25 mm → 94% risk for preterm birth
    - < 25 wks
    - IFN and CL ≤ 25 mm → 25% risk for preterm birth
    - Can not do IFN if EVUS in last 24 hrs. Therefore do not start EVUS

Treatment
- Cerclage
  - Pursuing stitch around cervix
  - Sutures placed as cranial as possible
  - Give largest possible CL
  - Prophylactically placed after 1st trimester in high-risk patient
  - Emergency cerclage in 2nd trimester
  - 2st to abnormal EVUS
  - Transvaginal cerclage placement

- Most commonly performed procedure
- Modified Shirodkar technique common
- Cerclage removed at 36-38 wks
- Transabdominal sutures placement
- Requires abdominal incision
- Must placed around lower uterine segment
- Obliteration
- Current studies cast doubt on utility of cerclage
  - Fail to show significant & in preterm birth rate
  - Compared to Bedrest
  - Cerclage not helpful for multiple gestations
  - Risks of cerclage placement
    - Premature rupture of membranes (1-9%)
    - Chorionic previa (1-2%)
    - Preterm labor
    - Cervical laceration
  - Bedrest
  - Contraction monitoring

DIAGNOSTIC CHECKLIST

Consider
- EVUS of CL in all patients at high-risk for preterm birth

Image Interpretation Pearls
- Do not make diagnosis of a CL or funneling with transabdominal ultrasound
- Normal CL by transabdominal ultrasound alone does not rule out short cervix
- Look for the T → Y → U progression of IO dilatation
- Evaluate cerclage sutures carefully
- Determine if sutures adequately placed
- Should see circumferential sutures
- Look for funneling beyond sutures

SELECTED REFERENCES

**INCOMPETENT CERVIX**

**IMAGE GALLERY**

**Typical**

*Left* Sagittal endocervical ultrasound shows maximal internal os funneling (arrow) at 32 wks. The closed portion of the cervix (open arrow) measured 3.3 cm and in the case, the finding did not progress.  
*Right* Sagittal endocervical ultrasound shows 3 funneling (arrows) that involved > 50% of the cervical canal. The closed portion of the cervix (open arrow) is the functional cervix and is quite short.

**Variant**

*Left* Sagittal endocervical ultrasound shows cervical incompetence and basofixation measured at 20 wks. The cervical canal is wide open (open arrow) and the membranes blend with the upper vagina (arrow).  
*Right* Sagittal endocervical ultrasound shows cervix rupture (arrow) in 1 case. The cervical length is normal in the upper case. In the lower case, 2D laminaria (calipers) is present but does not extend beyond the uterus, suggesting the cervix is working.

*Left* Sagittal endocervical ultrasound suggests cervix failure as scar tissue is seen only in the anterior cervix (arrow). The cervical length is short (calipers) and an IUD is dilated open (arrow).  
*Right* Axial endocervical ultrasound confirms cervix sutures in the anterior tip of the cervix (calipers). The open arrow points to the endocervical canal. The sutures should extend circumferentially around the canal.
**TERMINOLOGY**

**Abbreviations and Synonyms**
- Müllerian duct anomalies

**Definitions**
- Spectrum of congenital uterine malformations
- Agenesis/hypoplasia 10%
  - Combined agenesis of uterus, cervix, and upper portion of vagina most common
  - Presents as primary amenorrhea
- Unicorinate uterus 20%
  - Single uterine horn, may have rudimentary horn
- Uterus didelphys 5%
  - Two separate, non-communicating horns
- Bicornuate uterus 10%
  - Concave or heart-shaped external contour
- Septate uterus 35%
  - Normal internal contour
  - Septum may extend for variable lengths
  - Complete (to external os) or partial
- Acrisiate
  - Argued whether should be classified as congenital anomaly or anatomic variant
  - Smooth, broad fundal indentation

**IMAGING FINDINGS**

**General Features**
- Unicorinate uterus may not be distinguishable from a normal uterus in pregnancy
- Uterine duplication anomalies (didelphys, bicornuate, septate) are primary differential consideration for amenorrhea seen in pregnancy
- Key to diagnosis is visualization of external uterine contour
  - Didelphys
    - Two separate uteri that never join together
  - Bicornuate
    - Concave or heart-shaped external fundal contour
  - Septate
    - Fundus mildly convex to mildly concave
    - Mildly concave defined as < 1 cm external indentations and at least 5 mm of myometrium above funnelling tubal ostia

**Ultrasonographic Findings**
- Primary modality of evaluating uterine duplication in pregnancy
- Reported accuracy 90-92%
- 3D ultrasound provides improved spatial delineation
  - Sensitivity 95%, specificity 100%

**DDx: Duplicated Uterus**

- Interstitial Ectopic
- Intramural Ectopic
- Placenta
- Degenerated Uterus
TERMINOLOGY
- Spectrum of congenital uterine malformations
- Agnathan/ujeroplast 10%
- unicornuate uterus 20%
- Uterus didelphys 5%
- Bicornuate uterus 10%
- Septate uterus 55%
- Acracate

IMAGING FINDINGS
- Key to diagnosis is visualization of external uterine contour
- Top Differential Diagnoses
- Intralithall ectopic
- Leiomyoma

MR FINDINGS
- Not recommended in first trimester
- Unknown effects on ontogenesis
- Study of choice for evaluating non-pregnant patient
- Accuracy approaching 100%
- Image plane parallel to long axis of uterus
- Optimal assessment of endometrial contour
- T1WI
  - High signal endometrium
  - Low signal functional zone
  - Intermediate signal myometrium
- T2WI:
  - Occasionally useful
  - High signal fat may outline low signal uterus
  - Structures may have high signal blood products

IMAGING RECOMMENDATIONS
- Best imaging tool
- 3D ultrasound in pregnant patient
- MII in non-pregnant patient
- Protocol advice
- Check kidneys in every patient with a Müllerian duct anomaly
- High association with renal anomalies

DIFFERENTIAL DIAGNOSIS

Interstitiail ectopic
- May give false appearance of a septate or bicornuate uterus
- Interstitial line sign
- Interstitial line can be followed from endometrium to ectopic sac
- Myometrium thinned over gestational sac
- Color Doppler shows neoplastic flow around sac

Leiomyoma
- May distort endometrial cavity, giving appearance of duplication
- Hypoechoic, well-defined mass

PATHOLOGY

General Features
- Genetics: Sporadic, although polygenic inheritance described in some
- Etiology:
  - Primary congenital malformation
  - Prunebellum defects form uterus and majority of vagina
  - Distal vaginials from urogenital sinus
  - Prolapsing vaginal from genitai ridge and are not affected by abdominal uterine development
  - Uterus forms form paired, paramesonephric (mullerian) ducts
  - Failure of both or one to form = agenesis or unicornuate
- Does grow in a bidirectional manner and join
- Failure to fuse = didelphys
- Partial lower fusion = bicornuate
- Septal resorption occurs between fused horns
- Failure of septation = septate uterus
- Exposure is 5% implicated
- Diethylstilbestrol (DES), thalidomide, radiation, intrauterine infection
- Epidemiology
  - 1% of general population
  - 3% of women with reported pregnancy loss
  - 25% of women with uterine anomalies have reproductive problems
- Associated abnormalities
  - Renal anomalies in 30%
  - Renal agenesis in majority
  - Crossed fused ectopy, pelvic kidney, horseshoe kidney, duplications and cystic dysplasia also reported
  - Most common with didelphys and unicornuate
- Vaginal septum
  - Sacral men incontinence in didelphys, 75%
  - Complex variations with obstructions frequent
  - Hematometra, hematometrostosis
  - May involve only a single horn of a duplicated system
CLINICAL ISSUES

Presentation
- Little difficulty with conception
- Inconsistency of spontaneous abortion, premature delivery, abnormal fetal lie, cervical incompetence, dystocia
- Unicornuate
  - Spontaneous abortion rate 50%
  - Premature birth rate 15%
  - Fetal survival 40%
- Didelphys
  - Spontaneous abortion rate 45%
  - Premature birth rate 38%
  - Fetal survival 55%
- Bicornuate
  - Spontaneous abortion rate 30%
  - Premature birth rate 20%
  - Fetal survival 60%
- Septate
  - Spontaneous abortion rate 65%
  - Length of septum and composition (fibrous vs. myometrial) does not necessarily correlate with outcome
  - Shorter myometrial septae may cause recurrent abortion

Natural History & Prognosis
- Causes likely multifactorial: Abnormal vasculature, decreased connective tissue, abnormal overlying endometrium
- Preterm birth rate 20%
- Fetal survival 30%
- Accurate
- Risk based on size of orionation
- Draw a line between top of horns and measure length of the line
- Height is measured from that line to bottom of myometrial indentation
- Calculate ratio of height:length
- If ratio is <10% no adverse effects

TREATMENT
- Need to follow patients carefully for preterm labor
- Uterine septum treated with hysterectomy or resection
- Decrease in spontaneous abortion rate to 6.9%
- Treatment for bicornuate uterus usually not reported
- Strassman myometroplasty may be done for recurrent pregnancy loss
- Wedge resection of medial portion of uterus, creating single cavity
- No treatment options for unicominate or didelphys

DIAGNOSTIC CHECKLIST

Consider
- Septate uterus is most common congenital anomaly and has worst obstetric outcome
- Rejection of septum results in marked decrease in spontaneous abortion rate

Image Interpretation Pearls
- 3D ultrasound very helpful in first trimester to define uterine malformation and exclude an intestinal ectopic pregnancy

SELECTED REFERENCES
(Left) Ultrasound of a uterus didelphys shows a fetus (open arrow) in the right uterine cavity. A separate, uniloculated horn (curved arrow) is also seen. (Right) Nephrogram abdominal image in the same patient shows the liver but no kidney in the expected location (right). There is compensatory hypertrophy of the left kidney (b箭头). Mild renal duct anomalies are commonly associated with renal anomalies, particularly agenesis, as seen in this case.

(Left) Transabdominal ultrasound shows a twin pregnancy (open arrows) in a woman with a known bicornuate uterus. Note the concave external contour (arrows). (Right) Intraoperative photograph from a different case shows the characteristic bean-shaped contour of a bicornuate uterus.

(Left) Coronal ultrasound shows a septate uterus with a mildly concave external contour (curved arrow) and a prominent, zonular septum. Two distinct cavities are easily identified, with the fetus located on the right (open arrow). (Right) 3D US in the first trimester shows a septate cavity. The embryo (open arrow), external contour (curved arrow), and septum (arrows) are well distinguished. 3D US provides improved spatial resolution, distant to pelvic anatomic defects.
LEIOMYOMA

TERMINOLOGY

Abbreviations and Synonyms
- Leiomyoma
- Fibroid
- Uterine fibroma
- Fibroid leiomyoma

Definitions
- Benign uterine tumor composed of smooth muscle
- Multiple types of degenerated fibroids
  - Usually occurs in large fibroids (≥ 8 cm)
  - Hyaline
  - Very common, present to some extent in most fibroids
  - Hemorrhagic degeneration
  - Also called carious or red degeneration
  - Presents acutely
  - Increased incidence in pregnancy
  - Cystic
  - Chronic changes from necrosis
  - May see both cystic and hemorrhagic components
  - Myxoid
  - Liquified hyaline degeneration
  - Fatty
  - Associated with advanced hyaline degeneration
  - Calcific
  - Usually older women

- Sarcomatous
  - Rare, occurs in < 0.05%
  - More common in perimenopausal women

IMAGING FINDINGS

General Features
- Best diagnostic clue: Well-defined, hypoechoic myometrial mass
- Location
  - Most commonly involves myometrium
  - Subserosal
  - Intramural
  - Submucosal
  - Pedunculated
- Can involve cervix
- Size
  - Variable, but can be large
  - Large fibroids more likely to cause complications

Ultrasonographic Findings
- Typically well-delineated
- Homogeneous, hypoechoic
- Degenerated fibroids (more heterogeneous and variable in appearance)
- Borders often less well-defined
- Hypoechoic with hemorrhage
- Cystic, often with thick, irregular septations

DDx: Apparent Myometrial Masses

- Contraception
- Contraception
- Amenorrhea
- Chronic ovarian cysts
LEIOMYOMA

Imaging Findings
- Typically well-circumscribed
- Homogeneous, hypoechic
- Look for relationship of fibroids with placenta
- Look for relationship with cervix
- Fibroids may grow or degenerate during pregnancy
- Consider MR if any difficulty differentiating from an adnexal mass

Top Differential Diagnoses
- Focal myometrial contraction
- Placental abruption
- Chorioangioma

Pathology
- Hemorrhagic degeneration occurs in 1-8% of fibroids during pregnancy

- Cystic
- Low signal T1WI, high signal T2WI

MR Findings
- Non-degenerated fibroid
  - Intense intermediate signal T1WI
  - Intense intermediate to slight signal T2WI
  - Degeneration causes variable signal
    - Hemorrhagic
  - T1WI: Diffuse high signal (early), high signal rim (late)
  - T2WI: Variable, usually low signal intensity with low signal rim

Imaging Recommendations
- Document all fibroids
  - Size
  - Location
  - Number
  - Appearance
- Look for relationship of fibroids with placenta
  - Increased complications if placental implantation is on fibroid
- Abruption
- Spontaneous abortion
- Premature labor
- Intrauterine growth restriction
- Postpartum hemorrhage
- Look for relationship with cervix
  - Cervical or lower uterine fibroids may obstruct delivery
- Consider follow-up examination, particularly if large or inferioiy located
  - Fibroids may grow or degenerate during pregnancy
  - Consider MR if any difficulty differentiating from an adnexal mass

Differential Diagnosis

Focal myometrial contraction
- Transient myometrial thickening
  - Will resolve with time
  - Appears mass-like
  - Inner myometrium affected more than outer

Placental abruption
- Initially isoechoic to placenta
- Echogenicity decreases over time
  - Size decreases over time
  - Often begins at placental margin

Chorioangioma
- Placental mass
  - More commonly on fetal side of placenta, near cord insertion
  - Vascular

Focal adenomyosis/adenomyoma
- Extensive endometrial glands and stroma within myometrium
  - US: Heterogeneous thickening of myometrium
    - Poorly-margined, ovoid masses as opposed to well-defined, round fibroids
    - May see small cysts
  - MRI: Irregular, low-intensity area, directly contiguous with junctional zone

Solid adnexal masses
- Sex-cord stromal tumors
  - Fibroma, fibrothecoma must be confused with pedunculated leiomyoma
  - Consider MR if can not differentiate uterine vs. ovarian origin

Pathology

General Features
- Genetics: No hereditary factor clearly defined, however, does run in families
LEIOMYOMA

- Epidemiology
  - Increasing incidence with age
  - > 20-30% of women > 30 yrs have fibroids
  - True incidence in pregnancy not known
  - Reported range 6.1-12.5%
  - 2:1x more common in African-American women
  - Premenstrual degeneration occurs in 54% of fibroids during pregnancy
  - Larger fibroids are at greatest risk
  - Associated abnormalities
    - infertility
    - Recurrent pregnancy loss
    - Least common with submucosal fibroid

Cross Pathologic & Surgical Features
- Benign, smooth muscle tumor
- Muscle bands separated by fibrous connective tissue
- Discrete mass with pseudocapsule
- Cells surface have characteristic wolv-like, trabeculated appearance
- May be cystic or hemorrhagic if degenerated

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - Involuntary finding on routine scan
  - Acute pelvic pain and low grade fever associated with hemorrhagic degeneration
- Other signs/symptoms
  - Spontaneous abortion
  - Placental abruption
  - Fetal malposition
  - Premature labor
  - Prolonged/disfunctional labor
  - Uncommon complications
    - Prolapse into vagina
    - Ileal venous thrombosis
    - Polythecnemia
  - Aspects

Natural History & Prognosis
- Elevated estrogen level in pregnancy promotes growth of fibroid
- May outgrow vascular supply, resulting in hemorrhagic infarction and necrosis
- Stretching of uterine wall may also contribute to compromised blood supply
- Complications directly related to size and location
  - Cervical/dor peritoneal segment increases likelihood of malpresentation, cesarean section and postpartum hemorrhage
  - Retropelvic location increases likelihood of placental insufficiency, spontaneous abortion, prematurity, labor, abortion and postpartum hemorrhage
  - In one series, 57% had a placental abruption with leiomyoma volume > 200 cc (30% fetal demise in this group)
- Majority of fibroids remain asymptomatic throughout pregnancy

Treatment
- Medical management for symptomatic patients
  - Analgesics, bed rest
- Surgery during pregnancy
  - Considered only in symptomatic patients whose pain can not be controlled medically
  - Successfully performed in select group of patients
  - Consider resection prior to next pregnancy for those with fibroid-related complications
- Uterine artery embolization currently not recommended for women wishing to preserve fertility
- Complications including placenta previa, accreta, postpartum hemorrhage and increased incidence of cesarean section reported
- Normal pregnancies and deliveries have been reported after embolization treatment

DIAGNOSTIC CHECKLIST

Consider
- MRI if difficulty differentiating a pedunculated fibroid from an adnexal mass

Image Interpretation Pearls
- Critical factors determining effect of fibroids on pregnancy include size, number, location and relationship to placenta

SELECTED REFERENCES
**IMAGE GALLERY**

**Typical**

(Left) Sagittal T2W MRI shows a very large, complex fibroid with cystic degeneration. The lower portion (black arrow) has both cystic and solid components, while the upper portion (white arrow) is completely cystic with prominent septations. (Right) Sagittal endovaginal ultrasound in a patient with acute pelvic pain shows a bilaterally hyperechoic, wall-intruded mass (mass). Pathology showed a fibroid with hemoragic (red) degeneration.

(Left) Ultrasound shows implantation of the placenta on a subserosal fibroid (arrow). (Right) Ultrasound from a different case also shows placental implantation on a subserosal fibroid (arrow). These patients are at increased risk for placental abruption, pregnancy loss, growth restriction, preterm labor and preterm birth.

(Left) Ultrasound shows a very large fibroid (clipping) involving the lower uterine segment and cervix (arrow). (Right) Sagittal ultrasound in another patient shows a cervical fibroid (arrow) (cervix - caliper). Ultrasound in this location can obstruct delivery. Both of these patients were delivered by cesarean section.
SYNECHIAE

Terminology

Abbreviations and Synonyms
- Amniotic sheets

Definitions
- Created when amnion and chorion drape over fibrous band (synchieae)

Imaging Findings

General Features
- Best diagnostic clue: Shelf or band-like structure, which does not restrict fetal movement
- Location
  - Appears to be within amniotic cavity but actually is extra-amniotic
  - Membranes wrap over synchieae

Ultrasoundographic Findings
- Band-like structure crossing endometrial cavity
- Straight, bulboous free edge with thinned sheet extending to endometrial surface
  - Hyperechoic central area (synchieae) between more hyperechoic layers (membranes)
- Y-shaped notch at endometrial base, created by membranes separating endometrial margin

Differential Diagnosis

Amniotic bands
- Distortion of amnion
- Fetus becomes entangled = constrictions, amputations, "slit" defects
- Bands are thinner than synchieae
- Often difficult to see
- Do not attach to both uterine walls

Circumvallate placenta
- Margin of placenta is elevated off uterine wall
- Creates a "marginal shelf" when scanning parallel to edge
  - Scanning longitudinally shows "vandy lip" of placental margin

Uterine septum
- Midline, fundal
- May be fibrous or composed of myometrium

DDx: Uterine Bands/Membranes

- Circumvallate, long
- Circumvallate, axial
- Amniotic Bands
- Uterine Septum
SYNECHIAE

Terminology
- Amniotic Sheets
- Created when amnion and chorion drape over fibrous band (synechiae)

Imaging Findings
- Band-like structure crossing endometrial cavity
- Straight, bulbous free edge with thinner sheet extending to endometrial surface
- Thicker than synechiae
- Two distinct endometrial cavities

Chorioamniotic separation
- Amnion forms sac aroundetus
  - Does not go wall-to-wall
- Normally fuse 12-14 weeks
- Delayed fusion associated with aneuploidy
- Trisomy 21 most common

Twins
- 2 fetuses
- Dichorionic, diamicotic = thick membrane
- Monochorionic, diamicotic = thin membrane

PATHOLOGY
General Features
- Etiology
  - Instrumentation, trauma or infection causing destruction of basilar layer of endometrium
  - Adhesions form between opposing uterine walls
  - Most often from prior dilation and curettage
  - Curettage denudes basal layer
  - Retained placental/villous elements at-risk (abortion or postpartum)
  - Promotes fibrinolysis proliferation before endometrial regeneration can occur
- Epidemiology: 0.43-0.47% of pregnancies
- Associated abnormalities
  - Abnormal fetal lie
  - Sheets oriented perpendicular to placental surface more likely to have abnormal fetal lie
  - Synechiae may cause infertility and amenorrhea

CLINICAL ISSUES
Presentation
- Incidental finding in 2nd trimester
  - May no longer be visible in 3rd trimester
  - Rupture
  - Compression
- Ultrasound or radiographic finding during infertility work-up

Natural History & Prognosis
- Higher incidence of cesarean section for abnormal fetal lie

Key Facts
- Hypocoelic central area (synechiae) between more hypercoelic layers (membranes)
- Y-shaped notch at endometrial base, created by membranes separating at endometrial margin
- Pesus moves freely around sheet

Top Differential Diagnoses
- Amniotic bands
- Circumvallate placenta
- Uterine septum

- Otherwise no impact on pregnancy

Treatment
- Lysis of adhesions for those with infertility

DIAGNOSTIC CHECKLIST
Consider
- Synechiae do not cause fetal structural defects
- Generally incidental finding but important to differentiate from other more serious entities

SELECTED REFERENCES

IMAGE GALLERY
(Right) Ultrasound shows partial implantation of the placenta on a synechiae (arrows). This is frequently seen and does not negatively impact outcome. (Right) Ultrasound shows a synechiae (white arrow) on the left border of a separate uterine. The base of the synechiae has the typical Y-shaped configuration (black arrow). Compare to appearance of the synechiae in the broad mesometrial region (gray arrows). The left end (arrows) moved freely about the sheet.
TERMINOLOGY

Definitions
- Uterine rupture: Full thickness tear of uterine wall
- Uterine dehiscence: Incomplete rupture, with disrupted myometrium but intact serosa
- May occur during pregnancy, labor or postpartum

IMAGING FINDINGS

General Features
- Best diagnostic clue
  - Fetus seen in peritoneal cavity with defect in myometrium
  - Non-pregnant patient
  - Free intraperitoneal fluid after recent delivery or uterine instrumentation
- Location
  - Rupture most commonly occurs in anterior lower uterine segment
  - Thinnest portion of myometrium in pregnant uterus
  - Level of scar from prior low transverse cesarean section

Ultrasoanographic Findings
- Free pelvic fluid may be most obvious finding
  - May be most apparent anterior to cesarean section scar
  - If elevated, consider uterine dehiscence
  - Fluid/hemorrhage contained by uterine serosa
  - Fluid may be echogenic if significant hemorrhage
  - Disrupted myometrium
  - Usually in anterior lower uterine segment
  - If history of myomectomy or septoplasty, may be elsewhere
  - Look for continuity of extraperitoneal fluid with endometrial cavity

MR Findings
- T2W1
  - Full thickness defect of myometrium in rupture
  - Helpful in cases of congenital uterine anomaly, fibroid, or any cases when anatomy is not clearly delineated by ultrasound (US)
  - Potential pitfalls with MR
    - Normal early post-operative appearance
    - Bladder flap hematomata
    - Degenerating fibroid
    - Abscess or hematoma

DDx: Maternal Bleeding And/Or Pain
- Vasa Previa
- Placental Abruption
- Placenta Previa
- PIPE
CT Findings:
- Study of choice to evaluate maternal organs in setting of trauma
- Also look for uterine rupture
- Fetus in peritoneal cavity
- Normal myometrium not visible
- Defect seen in myometrium at site of tear
- Free intraperitoneal fluid
- Amniotic fluid $\rightarrow$ blood

Imaging Recommendations:
- Uterine rupture in labor
- Imaging seldom performed
- Clinical diagnosis with simultaneous acute maternal
  and fetal distress
- Diagnosis made in operating room

Rupture/dehiscence during pregnancy:
- US for evaluation of anterior myometrium
  - May be sufficient for complete myometrial survey in early gestation
  - By late 2nd/3rd trimester, uterus often obscures complete evaluation
  - MRI if patient clinically stable
  - CT faster if patient is unstable

Pregnancy rupture:
- Ultrasound is excellent
- If any uncertainty use MRI

Ultrasound technique:
- Anterior myometrium
  - High frequency, linear transducer much better than curved or vector
  - Look for continuous myometrial band
  - Measure thickness
  - Posterior myometrium
  - Need greater penetration
  - Curved, vector transducers are necessary
  - Endovaginal may be helpful in early pregnancy

CT:
- May be used in setting of abdominal trauma or acute abdomen
- Always check myometrial integrity
- Uterus shows symmetric enhancement

Highly vascular, receiving 25% of cardiac output
- Any defect should be regarded as highly suspicious
- Sagittal reconstructions recommended if using multidetector scanner
- MRI
  - Rapid sequences prevent image degradation due to fetal motion
  - Axial and sagittal through uterine are most helpful
  - T1W1: Blood products are high signal
  - T2W1: Signal intensity of placenta $>$ myometrium
  - Detailed views of cesarean section scar
  - Center pelvis coil over scar
  - Scan plane perpendicular to incision
- If other prior uterine surgery, try to set scan plane perpendicular to expected scar

Differential Diagnosis:
- Prenatal maternal bleeding $\pm$ pain
  - Placental abruption
  - Vasal/placenta previa
  - Placenta accreta spectrum
- Postpartum bleeding $\pm$ pain
  - Retained products of conception (RPOC)
  - Endometritis
  - Post-operative infection
- Abnormal myometrium
  - Placenta accreta spectrum
  - Hamartitic/degenerated fibroid
  - Uncomplicated fibroid
  - Isointense to uterus on T1WI, low signal T2WI
  - Hemorrhagic fibroid
  - Usually mixed to high signal intensity on both sequences
  - May be difficult to differentiate from dehiscence with hematoma
  - Cesarean section scar without rupture or dehiscence
**PATHOLOGY**

- **General Features**
  - **Stiology**
    - Prior cesarean section in majority of cases (80%)
    - Classical vertical incision greater risk than low transverse incision
    - Risk 1% that of unscarred uterus
    - Other sources of uterine scar
      - Myomas, septum, submucous, prior rupture or dehiscence
    - Trauma may cause rupture of normal uterus
    - Congenital uterine anomaly
    - Especially if pregnancy in rudimentary horn
    - Postpartum rupture
    - Patient has undergone vaginal birth after prior cesarean section (VBAC)
    - Inadequate treatment of endometritis
    - Non-pregnant patient
    - Uterine instrumentation
    - Other risk factors
      - Obstetric labor may cause spontaneous rupture in an unscarred uterus
    - Grand multiparity (≥ 4)
    - Abruption placenta
    - Multiple fetuses delivery
    - Breach extraction
    - External cephalic version
  - Epidemiology: incidence < 0.1% in developed countries

- **Clinical Issues**
  - Most common signs/symptoms
    - Abdominal pain
    - Bleeding - hypotension - hypovolemic shock
    - Uterine rupture in labor
    - Abdominal pain - fever - chills - hypotension
  - Uterine rupture during labor may result in death
  - Most patients encouraged to attempt VBAC if no contraindications
  - Uterine rupture during labor has worst prognosis
    - High blood flow to uterus and placenta - catastrophic hemorrhage
    - Severe maternal morbidity and mortality
    - Significant risk of neonatal asphyxia
    - Fetal ex utero survival
  - Uterine dehiscence is contained, therefore much lower maternal and neonatal morbidity/mortality

- **Treatment**
  - Obstetrical emergency
    - Emergency exploratory laparotomy and delivery for rupture
    - Large bowel IV access
    - Vigorous fluid resuscitation
    - Blood transfusion
    - Often requires hysterectomy
    - Repairs of rupture with dehiscence with continuation of pregnancy
    - Requires hemodynamically stable patient
    - Complications of uterine repair
      - Vesicouterine fistula
    - When attempting VBAC
      - Prepare for possible repeat cesarean section
      - Use caution with induction and augmentation of labor

**Diagnostic Checklist**

- **Consider**
  - Always consider diagnosis if patient has history of prior cesarean section
  - Labor complications
    - Sudden abnormal fetal heart tracing
    - Severe maternal pain and bleeding
    - Maternal hypotension
    - Persistent postpartum bleeding

**Selected References**

3. Locatelli A et al: Risks of induction of labour in women with a uterine scar from previous low transverse cesarean sections. BJOG. 2014;111(12):1299-1304, 2004
UTERINE RUPTURE

IMAGE GALLERY

Typical

(Left) Sagittal ultrasound in a patient presenting with persistent low-VG pressure. USG shows a myometrial defect (arrows) in the lower uterine segment. Fluid in the uterus (open arrow) is contiguous with fluid in the endometrial cavity (curved arrow). (Right) Sagittal ultrasound of a posterior uterine rupture at the site of a previous cesarean section (arrow). Fluid reflects anteriorly (open arrow) and communicates with the endometrial cavity (curved arrow).

Typical

(Lefl) Axial CT scan performed for abdominal trauma shows rupture of the uterine wall (arrow), with the fetal skull (open arrow) within the maternal pelvis. A large amount of free fluid (curved arrow) is seen and represents hematoma + amniotic fluid. (Right) Intraoperative photograph shows the placenta and membranes through the large uterine defect (arrow).

Typical

(Lefl) Sagittal T2W MR shows a heterogeneous "mass" with mixed signal intensity (arrows) in the region of a previous cesarean section scar. This is hematoma secondary to uterine dehiscence. The serosa (curved arrow) is intact. (Right) Intraoperative photograph shows a large hematoma (arrows) contained by the serosa in a case of posterior uterine dehiscence. Apical uterine myometrium (arrow) is seen superior to the hematoma.
RETAINED PRODUCTS OF CONCEPTION

Terminology

Abbreviations and Synonyms
- Retained products of conception (RPOC)
- Retained placenta
- Retained trophoblastic tissue

Definitions
- Incomplete uterine evacuation, with retention of placental tissue within endometrial cavity
  - Occurs after delivery or abortion

Imaging Findings

General Features
- Best diagnostic clue: echogenic endometrial mass with low-resistance, high-velocity flow
- Significant overlap in ultrasound findings between normal postpartum uterus and RPOC
  - Overall false positive rate for RPOC is 34%
  - 28.9% after delivery
  - 5.5% after abortion

Ultrasonographic Findings
- Solid, heterogeneous, echogenic mass
- Irregular interface between endometrium and myometrium
- Intrauterine fluid collection
- Persistent, thickened endometrium
- Color Doppler
  - High-velocity, low-resistance flow
  - Peak velocity ≥ 21 cm/sec
- Lack of increased flow does not rule out RPOC

MR Findings
- Echogenic intracavitary mass with myometrial thinning and obliteration of junctional zone
- T1WI: isointense to uterus
- T2WI: Heterogeneous: high-signal intensity
- Variable gadolinium enhancement

Differential Diagnosis

Normal postpartum uterus
- Highly variable, from smooth to irregular endometrium
- Small echogenic focus and fluid common
- Foet of gas may be seen in up to 21%
- Endometrial thickness < 2 cm and should decrease to < 8 mm with uterine involution

Uterine atony
- Primary differential consideration for immediate postpartum hemorrhage

DDx: Abnormal Postpartum Endometrium

- Cervix
- Cervix
- Endometritis
- Endometritis
**Imaging Findings**
- Significant overlap in ultrasound findings between normal postpartum uterus and PFOC.
- Overall false negative rate for PFOC is 34%.
- Solid, heterogeneous, echogenic mass.
- Irregular interface between endometrium and myometrium.
- High-velocity, low-resistance flow.
- Lack of increased flow does not rule out PFOC.

**Pathology**
- 1-2% of all pregnancies.
- More frequent following termination.

**Clinical Issues**
- Delayed postpartum bleeding.

**Key Facts**
- Top Differential Diagnoses:
  - Normal postpartum uterus.
  - Infarcted blood clot.
- Pathology:
  - 1-2% of all pregnancies.
  - More frequent following termination.

**Treatment**
- May monitor 24-48 hours, especially if ultrasound findings are equivocal.
- May repeat ultrasound to re-evaluate.
- Dilatation and curettage for persistent bleeding or obvious PFOC.

**DIAGNOSTIC CHECKLIST**
- Ultrasound anatomy vs. PFOC: primary differential for immediate postpartum hemorrhage.
- Atrophy: normal appearing cavity.
- PFOC: Echogenic, intrauterine mass.
- If no mass or fluid and endometrial thickness <10 mm, PFOC extremely unlikely.

**SELECTED REFERENCES**

**IMAGE GALLERY**
- [Image: Abnormal Color Doppler ultrasound of the uterine cavity shows color flow within an echogenic, nodular mass. Doppler echocardiography helps to differentiate PFOC from clot. Right: Sagittal transabdominal ultrasound shows calcified PFOC in a woman who had a very delayed onset of postpartum bleeding. The endometrium is filled with a solid, echogenic mass with multiple echogenic white areas. The endometrial wall (black, arrowhead) is thinned.](image-url)
**TERMINOLOGY**

Definitions
- Endometrial infection most commonly occurring after delivery or termination

**IMAGING FINDINGS**

General Features
- Best diagnostic clue: Endometrial gas bubbles in a patient with postpartum fever and pelvic pain

Ultrasoundographic Findings
- Endometrium may appear normal
- Nonspecific findings
  - Findings overlap with retained products of conception (RPOC)
  - RPOC is a risk factor for endometritis, may see both
  - Thickened, heterogeneous endometrium
  - Hyperechoic foci within endometrial cavity +/- shadowing
  - Intracavitary gas, inflammatory debris
  - Gas bubbles alone are not diagnostic
  - Endometrial gas is seen in up to 2% of healthy patients in postpartum period
  - Large amount of echogenic fluid concerning for pyometra

CT Findings
- Nonspecific, most useful for complications (abcess) or alternative diagnosis
  - Ultrasound enlargement, heterogeneous density
  - Detected endometrial cavity
  - May see air-fluid or fluid-fluid level (pus, hematomas)
  - Inflammatory changes around uterus

**DIFFERENTIAL DIAGNOSIS**

Retained products of conception
- Echogenic endometrial mass
- Significant overlap in findings with endometritis
- Presents with postpartum bleeding
- Simple RPOC should not have fever, 1 white count
- May have RPOC with superimposed infection

**DDx: Endometritis**

- Postpartum Ces
- Postpartum Ces
- Cot
- RPOC
### Imaging Findings
- Best diagnostic clue: Endometrial gas bubbles in a patient with postpartum fever and pelvic pain
- Findings overlap with retained products of conception (RPC)
- RPC is a rare factor for endometritis, may see both
- Gas bubbles alone are not diagnostic
- Endometrial gas is seen in up to 21% of healthy patients in postpartum period

### Intrauterine blood/clot
- Seen in up to 23% of asymptomatic postpartum patients
- May also be seen with endometritis

### Postpartum fever
- Ovarian vein thrombosis
- Atelectasis, pneumonia
- Pyelonephritis, appendicitis

### PATHOLOGY

**General Features**
- Epidemiology
  - Ascending infection of vaginal/cervical flora
  - May progress from chorioamnionitis
  - Noninfectious infection, group B Streptococcus
- Occurs in first 24-48 hrs
- Polybacterial, both aerobic and anaerobic
- Occurs in first 48 hrs

**Etiology**
- Most common cause of postpartum fever
- Occurs in 1-3% of vaginal deliveries
- Much more common following cesarean section (15-20%)
- Prophylactic antibiotics highly effective in reducing risk
- Risk factors
  - Cesarean section
  - Preexisting lower genital tract infection
  - Prolonged labor
  - Prolonged rupture of membranes
- Associated abnormalities: RPOC, retained clots

### CLINICAL ISSUES

**Presentation**
- Most common signs/symptoms
  - Fever within 36 hours following delivery
  - Pelvic/abdominal pain, tenderness
  - T White blood cell count
- Other signs/symptoms: Malodorous lochia

**Natural History & Prognosis**
- Current rates approach 95% with appropriate therapy

### Top Differential Diagnoses
- Retained products of conception

### Pathology
- Most common cause of postpartum fever
- Occurs in 1-3% of vaginal deliveries
- Much more common following cesarean section (15-20%)
- Prophylactic antibiotics highly effective in reducing risk
- May extend to periotometrium/parametrium

### Treatment
- Parenteral broad spectrum antibiotics
  - 90-95% decrease with 48-72 hrs
- Persistent fever
  - Resistant organism => triple antibiotic therapy
  - Abscess => surgical or percutaneous drainage

### DIAGNOSTIC CHECKLIST

**Image Interpretation Pearls**
- In the appropriate clinical setting (postpartum fever and pain), the presence of endometrial gas bubbles is highly suggestive

### SELECTED REFERENCES

### IMAGE GALLERY

*Left* Sagittal transabdominal (transvaginal in a pregnant woman with fever shows: multiple loculated loops within the endometrial cavity (arrows). Endometrial gas may normally be seen postpartum, but in the setting of pain and fever, is very suggestive for endometritis (right). Color Doppler ultrasound in another case shows a thickened, irregular endometrial cavity (arrows) but without increased blood flow. Lack of increased flow does not rule out endometritis. In some cases, the uterine may appear normal by ultrasound. The patient improved with antibiotic treatment.
CORPUS LUTEUM CYST

**Terminology**

**Definitions**
- Formed from graafian follicle following ovulation

**Imaging Findings**

- Ultrasonographic findings:
  - Thick, hyperechoic wall
  - Central anechoic/hypoechoic cavity
  - Communally complicated by hemorrhage
  - Look for fluid-fluid level
  - Thin septations with radiating, reticular pattern
  - No internal flow with Doppler imaging
  - May appear solid if significant hemorrhage or sac collapse
  - Retracing clot seen on follow-up scans
  - Doppler findings
    - Marked vascular flow within cyst wall
    - "Ring of fire" appearance
    - Low-resistance waveform on pulsed Doppler

**Imaging Recommendations**
- Doppler all lesions to exclude solid components
- Blood flow in solid tissues, not in clot
- Ring of fire classical for corpus luteum

**DDx: Adnexal Masses**
- Ectopic
- Ruptured Ectopic
- Dermoid
- Malignant Tumor

**Differential Diagnosis**

- Ectopic pregnancy
  - Echogenic tubal ring
  - Also shows "ring of fire" but separate from ovary
- Intrasacral ectopic extremely rare
- Adnexal mass (hematoma) with echogenic free fluid

- Ovarian neoplasm
  - Cystic tumors
    - Serous cystadenoma
    - Mucinous cystadenoma
  - Solid tumors
    - Thecoma-fibroma
  - Ovarian malignancy

- Follow-up masses of concern in 6-8 weeks
- Decreasing size and clot retraction confirm corpus luteum diagnosis
- Exophytic corpus luteum (CL) cyst may be difficult to differentiate from ectopic pregnancy
- Use ultrasound probe with gentle abdominal pressure to better evaluate adnexa
- CL cyst remains with ovary, whereas a tubal ectopic can be separated from ovary
**Imaging Findings**
- Thick, hyperechoic wall
- Commonly complicated by hemorrhage
- May appear solid if significant hemorrhage or sac collapse
- Marked vascular flow within cyst wall

**Top Differential Diagnoses**
- Ectopic pregnancy
- Ovarian neoplasm

**Key Facts**

**Clinical Issues**
- May enlarge minimally with fertilization and pregnancy
- Should diminish in size with progression of pregnancy

**Diagnostic Checklist**
- Even if CL is persistent, may monitor through pregnancy if no malignant features
- Beware of incorrectly diagnosing ectopic or heterotopic pregnancy

**Heterotopic pregnancy**
- Usually history of fertility treatments
- Heterotetene pregnancy documented
- Ectopic pregnancy, usually tubal

**PATHOLOGY**

**Gross Pathologic & Surgical Features**
- Corpus luteum: mean "yellow body"
- Central cystic cavity with fluid and fibrin
- Often with hemorrhage
- Highly variable in size
- Greater than 3 cm is considered cystic by pathologic criteria
- Obolization begins by 5th month of pregnancy and is complete by term
- Converts to corpus albicans

**Microscopic Features**
- Contains luteinized granulosa cells
- With coarse granules, granulosa-lutein cells enlarge
- Micellar human chorionic gonadotropin (HCG) stimulates CL progesterone production by granulosa-lutein cells
- CL progesterone production declines by end of 2nd month of gestation
- Placenta takes over production of progesterone
- CL present throughout pregnancy, though significantly reduced in metabolic activity

**CLINICAL ISSUES**

**Presentation**
- CL incidentally noted on first trimester scan
- Pelvic pain
- May result from large size, rupture or torsion

**Natural History & Progrosis**
- May resolve initially with fertilization and pregnancy
- Peak size usually around 7 weeks
- Should diminish in size with progression of pregnancy
- Most are no longer seen by sonography by early second trimester
- If persists after pregnancy, may represent ovarian neoplasm

**DIAGNOSTIC CHECKLIST**

**Image Interpretation Pearls**
- Even if CL is persistent, may monitor through pregnancy if no malignant features
- Most likely a persistent functional cyst
- May have "ring of fire" appearance
- Beware of incorrectly diagnosing ectopic or heterotopic pregnancy

**SELECTED REFERENCES**


**IMAGE GALLERY**

(Left) Endosalpingeal ultrason of a corpus luteum cyst appearing as a solid mass. Sagittal image of the left ovary during a 10-week gestation scan shows a 7.5 cm solid-appearing left ovarian mass (cyst). No flow was seen within this area on Doppler imaging. The fluid filled a cystic area that was noted (open arrow). (Right) Endosalpingeal ultrason is weeks later shows regression of the mass. Peritoneal nodes are not seen (arrows) within the cyst. A follow-up scan should always be performed on large or complex mass to ensure resolution.
HYPERSTIMULATION SYNDROME

**TERMINOLOGY**

**Abbreviations and Synonyms**
- Ovarian hyperstimulation syndrome (OHSS)

**Definitions**
- Clinical syndrome generally associated with ovulation induction
  - Hyperstimulated, enlarged ovaries
  - Increased vascular permeability
  - Ascites
  - Pleural effusion

**IMAGING FINDINGS**

**General Features**
- Bilaterally enlarged, cystic ovaries
  - > 5-10 cm diameter
- Ascites
- Can have internal echoes due to high protein content
- Pleural effusion

**MR Findings**
- Not usually required for diagnosis
- Most often used to distinguish hyperstimulated ovaries from ovarian neoplasia

**DIFFERENTIAL DIAGNOSIS**

**Theca lutein cysts**
- Multiple cysts with enlarged ovaries
- Not associated with ascites, pleural effusion or oliguria
- Multiple etiology
- Exogenous hormonal stimulation
- Gestational trophoblastic disease
- Torsion

**DDx: Functional Ovarian Cysts**
- Corpus Luteum
- Polycystic Ovary
- Theca Lutein Cysts
HYPERSTIMULATION SYNDROME

Terminology
• Clinical syndrome generally associated with ovulation induction

Imaging Findings
• Bilaterally enlarged, cystic ovaries
• Ascites
• Pleural effusion

Top Differential Diagnoses
• Theca-lutein cysts

Pathology
• Moderate OHSS: 3-6% of in vitro fertilization (IVF) cases
• Severe OHSS: 0.1-2% of IVF cases
• Exaggerated response to ovulation induction

Key Facts
• Increased permeability of peritoneal and pleural surfaces
• Protein-rich fluid leaks out of intravascular space

Clinical Issues
• Polycystic ovarian syndrome major risk factor
• Early type occurs < 5 days after oocyte retrieval
• Late type occurs ≥ 5 days (range 5-15 days) after oocyte retrieved
• Late type always associated with pregnancy
• Should be self-limiting as long as supportive care started early in process
• More severe in patients who become pregnant
• Severe OHSS potentially life-threatening
• No known therapy to immediately reverse OHSS
• Conservative therapy with observation warranted

Hyperreactio luteinalis
• More mild, indolent course within spectrum of OHSS
• Bilateral ovarian enlargement with multiple theca lutein cysts
• Always associated with pregnancy
• High maternal human chorionic gonadotropin (hCG) serum levels
  ○ No exogenous hCG administered
  ○ May be a response to chronic exposure to elevated hCG levels
  ○ Most cases identified in third trimester or immediately postpartum

Cystic ovarian neoplasm
• Usually unilateral
• Serous cystadenoma/cystadenocarcinoma
• Mucinous cystadenoma/cystadenocarcinoma
• Cystic germ cell tumors

Polycystic ovarian syndrome
• Bilateral enlarged ovaries with hyperplastic central stroma
• Multiple small peripheral follicles ("string-of-beads")
• Chronic aromatization
• Associated with obesity and insulin resistance

Ectopic and heterotopic pregnancy
• Echogenic peritoneal fluid
• Adnexal mass
• Higher risk in women undergoing ovulation induction

PATHOLOGY

General Features
• Epidemiology:
  ○ Moderate OHSS: 3-6% of in vitro fertilization (IVF) cases
  ○ Severe OHSS: 0.1-2% of IVF cases
  ○ Exaggerated response to ovulation induction
  ○ Almost exclusively associated with exogenous gonadotropin use
  ○ Numerous potential pathophysiologic mediators

• Cytokines
• Growth factors
• Most likely associated with vascular endothelial growth factor (VEGF)
  ○ Granulosa cells are one site of production
  ○ hCG and VEGF serum levels correlate with severity of OHSS
  ○ Paradoxical arteriolar dilatation and i peripheral vascular resistance
  ○ Leads to compensatory release of vasoactive substances
  ○ Aldosterone
  ○ Antidiuretic hormone
  ○ Norepinephrine
  ○ Renin
  ○ Increased permeability of peritoneal and pleural surfaces
  ○ Protein-rich fluid leaks out of intravascular space
  ○ Leads to ascites and effusions

Gross Pathologic & Surgical Features
• Ovaries appear similar to changes seen with theca lutein cysts
• Bilaterally enlarged
• Multiple follicular cysts with prominent luminalization of theca interna layer
• Corpus luteum present
• May be more than one

CLINICAL ISSUES

Presentation
• Most common signs/symptoms
  ○ Abdominal pain
  ○ Nausea/vomiting/diarrhea
  ○ Weight gain
  ○ Oliguria
  ○ Other signs/symptoms
  ○ Abdominal distention from ascites
  ○ Shortness of breath from pleural effusion
  ○ Hypotension
  ○ Electrolyte imbalances
HYPERSTIMULATION SYNDROME

- Typically seen in women undergoing ovulation induction
  - Follicle-stimulating hormone (FSH) followed by hCG
  - Relative hyperstimulation due to fluid leaking into peritoneal/plural spaces
  - Increased risk of thromboembolism
  - Oliguria

Demographics
- Risk factors
  - Polycystic ovarian syndrome: Major risk factor
  - May be related to increased number of follicles/ovaries produced when stimulated
  - Oligomenorrhea itself also a risk factor
  - Younger age
  - Previous OHSS history
  - Risk correlates with increasing
  - Ovarian volumes
  - Number of oocytes retrieved
  - Number of baseline follicles
  - Number of developing follicles during FSH stimulation
  - Especially immediate size (10-15 mm)
  - Serum estradiol concentrations

Natural History & Prognosis
- Occurs after ovulation
  - Early type occurs < 5 days after oocyte retrieval
    - Induced by exogenous FSH administration
  - Late type occurs ≥ 5 days (range 5-15 days) after oocyte retrieval
    - Induced by endogenous hCG from implanted pregnancy
  - Late type always associated with pregnancy
  - Should be self-limiting, as long as supportive care started early in process
  - Usually resolves over 10-14 days unless pregnancy implantation occurs
  - Subsequently can have increase in endogenous hCG
  - May prolong OHSS or initiate late form of OHSS
  - More severe in patients who become pregnant
  - Severe OHSS potentially life-threatening
  - Mortality estimated at 1:45,000 cases of OHSS

Treatment
- No known therapy to immediately reverse OHSS
- Avoid pelvic trauma to ovaries
- No intercourse, pelvic exams, strenuous exercise
- Conservative therapy with observation warranted
  - May be managed as an outpatient
  - Frequent vital sign and electrolyte checks
  - Maintain intravascular volume and urine output
  - 24 urine volume measurements
  - Daily weights
  - Cevider ultrasound guided paracentesis or thoracentesis
  - Serial abdominal girth measurements
  - Pneumoperitoneum
  - Useful due to relative hyperstimulation
  - Some advocate aggressive management to shorten course of symptoms
  - Most often controlled if moderate to severe OHSS
  - Actively administer fluids and/or albumin
- Diuretics considered when adequate intravascular volume achieved
- Benefits of ultrasound guided paracentesis
  - ± Hospitalizations
  - ± Hematocrit
  - ± Urine output
  - ± Acidosis, electrolyte abnormalities
- Hospitalization criteria
  - Intractable pain
  - Intractable nausea/vomiting
  - Respiratory difficulties
  - Suspected infection/abscess
  - Hypertension
  - Electrolyte imbalance
  - Leukocytosis
  - HCT > 45%
  - ± Liver function tests
  - Oliguria
  - Creatinine > 1.2 or creatinine clearance < 50
  - ± Surgical intervention only rarely required
  - Ovarian cystotomy
  - Cyst rupture with hemorrhage
  - Partial oophorectomy for severe cases reported

DIAGNOSTIC CHECKLIST

- Avoid aggressive transvaginal imaging as ovaries can be fragile
- Correlate imaging appearance of ovaries with clinical history foe diagnosis

SELECTED REFERENCES
HYPERSTIMULATION SYNDROME

IMAGE GALLERY

Typical

Ovulation or
Egg Retention

0 days 5 10 15

Typical

(Left) Ovarian ultrasound showing the typical late course for early and late OHSS. Early OHSS occurs 1-5 days after ovulation, whereas late OHSS occurs 5-11 days. Following ovulation and is associated with pregnancy.

(Left) Axial CECT shows an IVF patient presenting to the emergency room for pelvic pain. She recently had egg retrieval, and a hyperstimulated left ovary (arrows) is seen in the pelvis with a small amount of free fluid (open arrow).

Typical

(Left) Transabdominal ultrasound of a patient with late OHSS and confirmed pregnancy shows a hyperstimulated right ovary measuring 10 x 15 cm (collapse). The left ovary is enlarged as well and also the right ovary (arrows).

(Left) Axial CECT shows an IVF patient presenting to the emergency room for pelvic pain. She recently had egg retrieval, and a hyperstimulated left ovary (arrows) is seen in the pelvis with a small amount of free fluid (open arrow).

(Left) An axial T2-weighted image shows the hyperstimulated right ovary (arrows) with surrounding slightly dense proteinaceous fluid (open arrow).

(Left) Transabdominal ultrasound of a patient with late OHSS and confirmed pregnancy shows a hyperstimulated right ovary, measuring 10 x 15 cm (collapse). The left ovary is enlarged as well and also the right ovary (arrows).

(Left) Axial CECT shows an IVF patient presenting to the emergency room for pelvic pain. She recently had egg retrieval, and a hyperstimulated left ovary (arrows) is seen in the pelvis with a small amount of free fluid (open arrow).

(Left) Transabdominal ultrasound of the retroverted uterus shows the cavity around the low (arrow). She delivered live dichorionic twins at 31.5 weeks following spontaneous membrane rupture.
THECA LUTEIN CYSTS

TERMINOLOGY

Abbreviations and Synonyms
- Hyperreactio luteinalis

Definitions
- Ovarian enlargement caused by multiple luteinized follicular cysts
- Secondary to excessive human chorionic gonadotropin (hCG) stimulation

IMAGING FINDINGS

Ultrasoundographic Findings
- Enlarged ovaries with multiple cysts
  - Most often bilateral
  - Occasionally will see unilateral enlargement
  - Intertwining septae
  - Should be thin
  - No papillary excrescences
  - No wall nodularity
  - Cysts can rupture
  - May see acines fluid in cul-de-sac
  - Can contain echogenic debris if hemorrhagic

MR Findings
- Multiple simple-appearing cysts
  - Thin septae separating cysts
  - High signal on T2WI
  - "Spoke-wheel" appearance described
  - Large, peripherally located cysts
  - Central ovarian stroma
  - May appear partially solid
  - May have hemorrhagic components

Imaging Recommendations
- Need to evaluate for underlying cause
- Infertility treatment
  - Exogenous hormone administration
  - Ovaries hypersensitized in response to hormones
- Underlying diagnosis of polycystic ovarian syndrome may predispose to theca luteum cyst formation
- Gestational trophoblastic disease (GTD)
  - Hydatidiform mole, invasive mole, choriocarcinoma
  - High levels of circulating hCG hormone cause stimulation of ovaries
- < 50% of hydatidiform mole cases have theca lutein cysts
  - Cysts < 13 weeks
  - Complex, echogenic endometrial mass with scattered cysts ('Swiss cheese' appearance)
  - Risk for metastatic disease

DDx: Ovarian Cystic Lesions
- Corpus Luteum
- Hemorrhagic CL
- Cystadenoma
- Deciduall
THECA LUTEIN CYSTS

Terminology
- Ovarian enlargement caused by multiple luteinized follicular cysts
- Secondary to excessive human chorionic gonadotropin (hCG) stimulation

Imaging Findings
- Enlarged ovaries with multiple cysts
- Need to evaluate for underlying cause

Top Differential Diagnoses
- Hyperstimulation syndrome
- Corpus luteum (CL) cyst

Pathology
- Associated with clomiphene with high levels of hCG
- Gestational trophoblastic disease

Key Facts
- Multiple gestation
- Infertility treatments
- Immune hydrops

Clinical Issues
- Theca lutein cysts seen with GTD may not regress immediately after treatment
- Observation without intervention usually sufficient
- Surgical management rarely required unless complication occurs

Diagnostic Checks:
- If presenting with pain, check for rupture or ovarian torsion
- Ovaries may remain enlarged in the postpartum period and regress slowly

- Electrolyte imbalances
- Extravascular fluid leaking
- Maternal ascites and pleural effusion

Corpus luteum (CL) cyst
- Usually unilocular
- Can have internal hemorrhage
- “Lace-like” sonographic pattern
- Indicates debris
- May have thick, echogenic rts of ovarian parenchyma
- Doppler flow often shows hypervascularity
- Other adjacent follicles may be seen

Dermoid cyst
- Pure sebum is hypoechogenic/anechoic
- If predominate component, lesion appears cystic
- Often will see other component as well
- Dermoid "plug" of keratin
- Echogenic tooth
- Thin, echogenic strands of hair

Cystadenoma
- Usually unilocular
- No papillary projections or nodularity
- Unlike typical CL, will not resolve in second trimester
- Increased risk of ovarian torsion if large
- If suspect benign etiology, may be followed during pregnancy
- Surgical removal can be performed at cesarean section
- Postpartum surgery also an option

Cystadenocarcinoma
- Usually presents as complex ovarian mass
- Mural nodularity
- Papillary projections
- Thick, irregular septations
- Low malignant potential (borderline) tumors can appear mostly cystic
- Low-impedance Doppler flow
- Not specific for malignancy

DIFFERENTIAL DIAGNOSIS

Hyperstimulation syndrome
- Clinical syndrome helps to distinguish from isolated theca lutein cysts
- Associated with exogenous hormone stimulation
- Oliguria
THECA LUTEIN CYSTS

PATHOLOGY

General Features
- Associated with disorders having high levels of hCG
  ○ Gestational trophoblastic disease
  ○ Multiple gestations
  ○ Inflammatory processes
  ○ Immune hydrops
- May have elevated plasma testosterone levels
  ○ Levels directly proportional to ovarian enlargement

Gross Pathologic & Surgical Features
- Bilateral cysts
  ○ Fluid-filled
  ○ Can be hemorrhagic
- Moderate to massive ovarian enlargement
  ○ Ovarian enlargement up to 26 cm reported

Microscopic Features
- Multiple follicular cysts
- Prominent internalization of theca interna layer
- Granulosa cells may also be involved
- Granulosa stromal cells
- Stromal luteinization

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  ○ Pelvic pain
  ○ Palpable abdominal mass
- Incidentally noted during anatomic survey
- May present with complications
  ○ Torsion
  - Especially in late first/triangular second trimester
  - Occurs when uterus has rapid growth
  - Causes displacement of enlarged ovaries with possible twisting of pedicle
  ○ Cyst rupture in postpartum period as uterus involutes
  ○ Rupture with hemoperitoneum
  ○ Thin-walled
  ○ Cause periluteal signs
- Ascites
- Virilization reported in up to 25% of patients, in cases not associated with GTD
  ○ Due to cyst production of androgens
- Has no effect on female fetuses

Natural History & Prognosis
- Typically cysts will regress spontaneously without treatment
  ○ May regress during pregnancy
  ○ Complete involution usually occurs in postpartum period
  ○ Rarely will take months to resolve after delivery
- Theca lutein cysts seen with GTD may not regress immediately after treatment
  ○ Initial treatment performed with dilation and curettage
- Associated cysts can take up to 3 months to resolve
  ○ Do not assume persistent or recurrent disease if seen within 3 months
- Following hCG levels will help exclude recurrence
- Levels should readily decline

Treatment
- Observation without intervention usually sufficient
- Clinical assessment for acute pelvic pain
  ○ Watch for secondary sequelae of enlarged ovaries
  ○ Torsion
  - Rupture
- Surgical management rarely required unless complications occur
  ○ Massive enlargement with torsion or rupture
  ○ Oophorectomy reported
- Ovaries not required to sustain pregnancy beyond first trimester
- Placental hormones sufficient if oophorectomy necessary

DIAGNOSTIC CHECKLIST

Consider
- MRI & ultrasound indeterminate for ovarian malignancy

Image Interpretation Pearls
- Access for underling associated etiology
- T present with pain, check for rupture or ovarian torsion
- Ovaries may remain enlarged in the postpartum period and regress slowly

SELECTED REFERENCES
(Left) Sagittal ultrasound of a complete hydatidiform mole (CHM) shows expansion of the endometrial cavity with a hemorrhagic mass containing multiple small cysts. (Right) Sagittal ultrasound images of both ovaries show large theca lutein cysts expanding and replacing the normal parenchyma. Theca lutein cysts are present in only 50% of CHM cases and are most common before 12 weeks gestation.

(Left) Ultrasound in the 2nd trimester shows a 1.4 cm left ovary with multiple theca lutein cysts. The right ovary had a similar appearance. The patient was pregnant with monochorionic twin. (Right) Ultrasound of the same patient in the 3rd trimester shows a normal appearing left ovary (calipers). In this case, the cyst reached spontaneously during pregnancy, but in some cases they may not regress and after delivery.

(Left) Transabdominal ultrasound shows large theca lutein cysts in a patient who had undergone hormonal stimulation for in vitro fertilization. No nausea or other signs of hyperemesis gravidarum were seen. (Right) Transabdominal ultrasound of the uterus in the same patient shows non-gestational sac(s) (calipers).
INCIDENTAL OVARIAN MASS

TERMINOLOGY

Definitions
- Ovarian mass discovered incidentally during routine obstetric ultrasound

IMAGING FINDINGS

General Features
- Best diagnostic clue
  - "Cline" sign present within ovary
  - Curvilinear rim of ovarian tissue partially surrounding mass
- Indicates ovarian origin of lesion

 Ultrasonographic Findings
- Mass in adnexa
- Variable appearance, from purely cystic to completely solid

MR Findings
- Use for further characterization of mass
  - Important to distinguish it more likely benign or malignant
  - Impacts clinical management of mother and potentially fetus

Imaging Recommendation
- Must determine source of adnexal mass (ovarian vs. uterine vs. surrounding structures)
- Look for "Cline" sign
- If mass is large, inability to identify ovary can indirectly suggest ovarian origin
- Perform MRI if ultrasound can not fully evaluate

DIFFERENTIAL DIAGNOSIS

Benign functional cyst(s)
- Corpus luteum of pregnancy
- Can have bronchialhage and appear solid
- Theca-lutein cyst
- Look for twin pregnancy

DDx: Adnexal Mass

- Ectopic
- Parametrial Cyst
- Degenerative Endometriosis
- Appendicitis
INCIDENTAL OVARIAN MASS

Imaging Findings
- "Claw" sign present within ovary
- Irregular mass, inability to identify ovary can indirectly suggest ovarian origin
- Perform MRI, ultrasound can not fully evaluate

Top Differential Diagnoses
- Benign functional cyst(s)
- Dermoid
- Cystadenoma
- Ovarian stromal tumor
- Parovarian cyst
- Pedunculated fibroid
- Hydrosalpinx
- Tubo-ovarian abscess
- Ruptured appendicitis

- Exclude molar pregnancy
- Exclude gestational trophoblastic disease
- Exclude endometrioma in reproductive age group
- Hypothalamic/pituitary derangement in menstrual dysfunction

Sex-cord, stromal tumor
- Sertoli-Leydig cell tumors
- Granulosa cell tumors
- Mullerian-derived tumors
- Sertoli-Leydig cell tumors
- Granulosa cell tumors
- Mullerian duct remnant tumors
- Granulosa cell tumors
- Mullerian duct remnant tumors

Epithelial ovarian carcinoma
- Malignant tumors
- Metastatic disease
- Malignant tumors
- Metastatic disease
- Malignant tumors
- Metastatic disease
- Malignant tumors
- Metastatic disease

Key Facts

Clinical Issues
- May present with abdominal or pelvic pain
- Increased risk of torsion most common during periods of rapid uterine expansion or implantation
- Most ovarian "mases" discovered during pregnancy
- Corpus luteum cysts
- Dermoid cyst is most common ovarian neoplasm discovered incidentally during pregnancy
- Optimal time for surgical exploration during pregnancy is early second trimester
- Unilocular masses < 6 cm may be followed
- Surgical management appropriate for malignancy staging, regardless of pregnancy status

Doppler flow does not exclude ovarian torsion

Sex-cord, stromal tumor
- Fibroma, thecoma, fibrothecoma, Sertoli-Leydig cell
- Granulosa cell
- Most often present as solid mass
- Large masses may have cystic components
- Fibroma
- Associated with Stein-Leventhal syndrome
- Pleural effusion, ascites
- Can be seen with other ovarian tumors as well

Adnexal masses, not ovarian origin
- Parovarian cyst
- Congenital cyst
- Paramesonephric embryonic remnant in broad ligament
- Ovary identified adjacent to cystic adnexal mass
- Does not change in size with hormonal stimulation or menstrual cycles
- Can undergo torsion and rupture if large
- Pedunculated fibroid
- Can be diagnostic dilemma, if large and extends into adnexa
- If degenerated, can have cystic areas
- Should move with uterus, if palpate while scanning
- Look for separate ovary
- Ectopic pregnancy
- Tubal ectopic most common location
- May visualize extraluminal gestational sac +/- embryo, yolk sac
- Adnexal hematomas
- Echogenic free fluid
- Hydrosalphinx
- Can be confusing, if dilated and tortuous
- Look for tubular configuration
- Correlate with history of pelvic inflammatory disease or endometriosis
- Abscess
- Correlate with clinical history of fever and leukocytosis
- Tubo-ovarian abscess
- Ruptured appendicitis
INCIDENTAL OVARIAN MASS

Ovarian metastasis
- Primary malignancy elsewhere
- Local spread from pelvic tumor
- Distant spread
  - Breast
  - Gastrointestinal tract
  - Kinking tumor: Bilateral metastases to ovaries
- Most often gastric origin

PATHOLOGY

Microscopic Features
- Germ cell tumors
  - Arise from germ cells
  - Stratified squamous epithelium with sebaceous glands, hair shafts
  - Other germ layers also often involved
    - Cartilage, bone, thyroid tissue
- Sex-cord, stromal tumor
  - Arise from ovarian stroma
  - Originates from sex cords of embryonic gonad
  - Some of these cells normally secrete hormones
    - Corresponding tumors may also produce hormones
  - Thecal cells → estrogen
    - Leydig cell → androgen
- Epithelial tumors
  - Arise from epithelium and adjacent stroma
  - Serous and mucinous most common subtypes
  - Benign tumors: Smooth walls, columnar epithelium
  - Increasing number of papillary projections and solid components with malignancy

CLINICAL ISSUES

Presentation
- Incidentally seen on routine ultrasound
- May present with abdominal or pelvic pain
- Rupture of cyst
- Rupture into cyst/nas
- Torsion of mass/ovary/three

Natural History & Prognosis
- Increased risk of torsion most common during periods of rapid uterine expansion or involution
  - Most frequent during 8th-14th week of gestation
  - Uterus enlarges rapidly
  - Displaces ovary and mass
  - Also occurs during pregnancy, with uterine involution
- Most ovarian "masses" discovered during pregnancy are corpus luteum cysts
- Dermoid cyst is most common ovarian neoplasm discovered incidentally during pregnancy
- Dermoid cysts + serous-cystadenomas = 85% of ovarian neoplasms during pregnancy

Treatment
- Management depends on several factors including gestational age, clinical symptoms and ultrasound features
- Optimal time for surgical exploration during pregnancy is early second trimester
- Typically 14-18 weeks gestation
- Decreased risk of miscarriage
- Probable benign lesion
- Conservative management
- Unilocular mass, ≤ 6 cm, may be followed
- Close clinical follow-up for signs of torsion
- No adverse effect on pregnancy
- Can undergo treatment after delivery
  - Could consider removal at time of delivery if cesarean section performed
- Some benign lesions, such as dermoids, may be followed without resection
- Indeterminate lesion
  - Consider surgical exploration if mass is
    - Solid
    - Bilateral
    - > 6 cm diameter
    - Persist for second trimester (not a complex corpus luteum cyst)
- Consider MRI to characterize
- Malignant lesions
  - Surgical management appropriate for malignancy staging, regardless of pregnancy stage
  - Would also consider chemotherapy depending on stage and tumor histology

DIAGNOSTIC CHECKLIST

Consider
- MRI to characterize ovarian mass
  - More useful than ultrasound alone to assess for probability of malignancy

Image Interpretation Pearls
- Use Doppler ultrasound to check for arterial and venous flow in surrounding ovarian parenchyma
- Doppler flow does not exclude ovarian torsion

SELECTED REFERENCES
INCIDENTAL OVARIAN MASS

IMAGE GALLERY

Typical

B: Endovaginal ultrasound shows a corpus luteum cyst (arrow) with "nacreous" hummingshoe. Contents of large, a follow-up scan may be performed to document resolution. This is the most common ovarian "tumor" seen in pregnancy.

R: Pelvic ultrasound shows an enlarged right ovary with multiple theca lutein cysts in association with a (spontaneous) monochorionic twin gestation. The ovary measured over 13 cm.

Typical

B: A 32-week gestation ultrasound shows an incidentally detected, echogenic mass (arrow) in the ovary, typical of a small dermoid. The pregnancy was uncomplicated and the ovary was resected after delivery. The histopathological analysis shows the dermoid (open arrow). Right: Sagittal (T2W) MRI shows right ovarian mass (arrow). Given its benign appearance, immediate surgery was not indicated. A minimally invasive cystectomy was performed at ovarian section.

Typical

B: Sagittal (T2W) MRI of a 2nd trimester pregnancy shows a complex, cystic mass with solid components (arrows). The pathologic diagnosis was an immature teratoma. Right: Ultrasound shows a complex, multiloculated, ovarian mass (calipers). Hypoechogenic material seen within some cysts is mucin. In this benign mass, cystadenofibroma. When masses appear complex, malignancy cannot be excluded and they must be resected.
TERMINOLOGY

Abbreviations and Synonyms
- Tubo-ovarian torsion
- Adnexal torsion

Definitions
- Partial or complete rotation of vascular pedicle, compromising lymphatic and venous drainage and ultimately arterial inflow
- Usually involves both ovary and tube

IMAGING FINDINGS

General Features
- Best diagnostic clue: Enlarged ovary on symptomatic side with loss of arterial and/or venous flow
- Location: Right > left (3:2)
- Morphology
  - Findings vary according to degree of vascular compromise, duration and coagulase of mass
  - Pre-existing ovarian masses act as factor for torsion

Ultrasoundographic Findings
- Large ovary with small, peripheral cyst
  - Reflects central edema

DDx: Adnexal Pain in Pregnancy

- Appendicitis
- Ectopic
- Hemorrhagic CI
- Hemorrhagic CI

MR Findings
- Ovarian enlargement: From edema and/or ovarian mass
  - Look for twisted pedicle forming “beak” towards mass
  - Distended, thickened fallopian tube may be seen
  - Cystic masses show smooth wall thickening
  - Edema
    - Low signal T1WI, high signal T2WI
  - Hemorrhagic infarction
    - High signal T1WI, may form peripheral rim
    - Low or high signal on T2WI

Ultrasound of a 3rd trimester patient presenting with acute pain shows an enlarged, solid-appearing ovary with small peripheral cyst (arrows). No flow was seen on Doppler imaging.

Torsion of the ovary and tube seen confirmed at surgery. The twisted ovary shows marked edema and hemorrhagic infarction. Small cystic areas can be seen in the periphery.
**TORSION**

**Imaging Findings**
- Findings vary according to degree of vascular compromise, duration and coexistence of mass.
- Distended, thickened fallopian tube may be seen.
- Cystic masses show smooth wall thickening.
- Large ovary with small peripheral cysts.
- Presence of blood flow does not exclude torsion.

**Top Differential Diagnoses**
- Hemorrhagic corpus luteum (CL).

**DIFFERENTIAL DIAGNOSIS**

**Adnexal mass without torsion**
- Hemorrhagic corpus luteum (CL)
  - May cause acute pain.
  - Echogenic fluid, fluid-fluid level, "lace-like" appearance.
  - Increased flow around periphery.
- Masses (teratomas, cystadenomas) present as incidental findings.

**Ectopic pregnancy**
- Echogenic ring or mass, separate from ovary.
- Ovary is normal.
- Very rare cases of intraovarian ectopic reported.
- No intrauterine gestational sac.

**Appendicitis**
- Thickened, blunted tubular structure.
- Surrounding inflammatory changes on CT.

**PATHOLOGY**

**General Features**
- Etiology:
  - Pre-existing mass major risk factor for torsion.
  - CL cyst most common ovarian "mass" in pregnancy, followed by dermoid cyst and serous cystadenoma.
  - Always be suspicious of torsion if known ovarian mass becomes acutely painful.
- Epidemiology: 0.06% of pregnancies.
- Pathophysiology:
  - Torsion of vascular pedicle → venous and lymphatic obstruction → edematous ovary.
  - Edema increases "wringing" of fluid and further compromise of blood flow.
  - Finally arterial flow compromised → ovarian infarction.

**CLINICAL ISSUES**

**Presentation**
- Acute pelvic pain, nausea, vomiting.
- Torsion typically occurs during periods of rapid uterine expansion or involution.
  - 8-16 weeks gestation.
  - During piuoration.

**Key Facts**
- Ectopic pregnancy.

**Pathology**
- Pre-existing mass major risk factor for torsion.
- Always be suspicious of torsion if known ovarian mass becomes acutely painful.

**Clinical Issues**
- Torsion typically occurs during periods of rapid uterine expansion or involution.

**Treatment**
- Torsion without infarction
  - Laparoscopic "detorsion".
  - Rejection of any mass.
- Torsion with infarction
  - May require salpingo-oophorectomy.

**DIAGNOSTIC CHECKLIST**

**Consider**
- Presence of blood flow does NOT exclude torsion.
- Preservation of central venous flow in a twisted ovary is predictive of ovarian viability.

**SELECTED REFERENCES**

**IMAGE GALLERY**

(Left) Sagittal T2W MR of the right ovary shows diffuse low signal intensity with small peripherial, high signal cysts and surrounding free fluid (open arrow). Torsion with hemorrhagic infarction found at surgery. (Right) Unenhanced CT of the right adnexa shows a complex, cystic mass with hypodense fluid and an echogenic nodule (arrows), typical of a teratoma. Always be suspicious of torsion when a patient presents with a preceding mass presents with acute pain. (Sagittal CT confirmed at surgery.)
FETAL ALCOHOL SYNDROME

Clinical photograph shows typical features of FAS including short palpebral fissures (arrow), smooth philtrum (upper arrow), and anophthalmia. (Courtesy M. Leguee/Harrist, MD.)

TERMINOLOGY

Abbreviations and Synonyms

- Fetal alcohol syndrome (FAS)
- Fetal alcohol spectrum disorder (FASD)
- Alcohol related neurodevelopmental disorder (ARDN)
- Alcohol related birth defects (ARBD)

Definitions

- FAS: Physical and central nervous system (CNS) abnormalities resulting from maternal alcohol ingestion during pregnancy
- FASD: Umbrella term encompassing spectrum of effects occurring in an individual with prenatal alcohol exposure

IMAGING FINDINGS

General Features

- Best diagnostic clue
  - History of prenatal alcohol exposure with
    - Growth restriction, microcephaly
    - Structural anomalies (cardiac, skeletal, renal)

Imaging Recommendations

- Protocol advice
  - Serial ultrasounds for interval growth, anatomy

DIFFERENTIAL DIAGNOSIS

- Symmetric intrauterine growth restriction
- Multiple causes, including aneuploidy, infection and syndromes

Aneuploidy

- Trisomy 21, 18, 13

 Syndromes with overlapping features of FAS

- Other trisomies exposure
- Fetal anticoagulant syndromes
- Hydrantin, vdroionate
- Neuromuscular phenylketonuria (PKD)
- Trisomy Down syndrome
- Velocardiofacial syndrome (deletion 22q11)
- Williams syndrome
- Patau syndrome
- Cornelia de Lange syndrome

PATHOLOGY

General Features

- Etiology

DDx: Similar Facial Features

- Hydrantin
- Cornelia de Lange
- Deletion 22q11
**FETAL ALCOHOL SYNDROME**

### Key Facts

**Pathology**
- No lower threshold of safety for alcohol use
- One of the most common, preventable causes of birth defects and mental retardation
- 1 in 1000 live births with FAS in the United States
- ≥ 1% of live births with FASD (includes more minor findings)
- 10% report drinking alcohol during pregnancy

**Natural History & Prognosis**
- Behavioral/cognitive profile
  - Learning disabilities, poor language control, problems in social adjustment and school performance, deficits in memory, attention, judgment, receptive and expressive language, hyperactivity, sleep disturbance
- Seizures, visual/hearing impairment, mental retardation

**Treatment**
- Screen all pregnant women for alcohol use
- Advise total abstinence during pregnancy
- Recognition of disorder, early diagnosis, appropriate treatment critical
- May decrease secondary disabilities and recurrence in future offspring

### Terminology
- FAS: Physical and central nervous system (CNS) abnormalities resulting from maternal alcohol ingestion during pregnancy

### Top Differential Diagnoses
- Symmetric intrauterine growth restriction
- Anencephaly
- Other teratogenic exposures
- Velocardiofacial syndrome (deletion 22q11)

### Clinical Issues

**Presentation**
- FAS with confirmed maternal alcohol exposure
  - Characteristic facial phenotype
  - Short palpebral fissures, epicanthus, hypertelorism, smooth philtrum, thin upper lip
  - Pre- and postnatal growth restriction
  - CNS/neurodevelopmental anomalies
    - Microcephaly, agenesis of corpus callosum, cerebellar hypoplasia, abnormal neurolog exam
  - FAS without confirmed maternal alcohol exposure
    - May not have maternal history (adoptive, foster care)
  - Diagnosis can still be made based on above findings
- Alcohol-related birth defects
  - Cardiac
    - Atrial and ventricular septal defects, aberrant great vessels, conotruncal heart defects
  - Skeletal
    - Radial/club hands, contractures, vertebral segmentation abnormalities, scoliosis
  - Renal
    - Aplastic/hypoplastic/dysplastic kidneys, horseshoe kidneys, hydronephrosis
  - Ophthalmologic
    - Strabismus, retinal vascular abnormalities, ptosis, optic nerve hypoplasia
  - Hearing loss: Neurosensory and conductive
  - Minor anomalies
    - Nasal hypoplasia, "hockey stick" palmar crease, abnormal ears, camptodactyly
- Alcohol-related neurodevelopmental disorder
- Evidence of abnormal birth weight or structure
- Behavioral/cognitive abnormalities
- Increased spontaneous abortion, preterm mortality

### Selected References

### Image Gallery

(Left) Clinical photograph of a teenager with FAS. Note the small philtrum (center), epicanthal folds (lateral arms), strabismus (open arrows). Behavioral and cognitive abnormalities were prominent. (Right) Radiograph shows vertebral segmentation defects (arrows), typical of those found in FAS.
**TERMINOLOGY**

**Abbreviations and Synonyms**
- Diastematomyelia
- Phenytin
- Phenytoin
- Phenytoin syndrome
- Fetal hydantoin syndrome

**Definitions**
- Fetal effects of maternal exposure to phenytoin, characterized by growth restriction, microcephaly, mental deficiency, and craniofacial malformations.

**IMAGING: FINDINGS**

**General Features**
- Best diagnostic clue: Intrauterine growth restriction.
- **IUGR**: +/- other structural malformations in fetus exposed to anticonvulsants.

**Ultrasoundographic Findings**
- Microcephaly
- Cardiac anomalies: Septal defects, coarctation of aorta, valvarular stenosis
- Cleft lip/palate
- Genitourinary abnormalities: Hypoplasia

**Imaging Recommendations**
- Serial ultrasounds to assess fetal growth, anatomy in patients on antiepileptic medication.

**DIFFERENTIAL DIAGNOSIS**

**Embryopathy from other anticonvulsants**
- Antiepileptic drugs, including carbamazepine, trimethadione and phenobarbital, all with similar pattern of malformations.
- **IUGR**, microcephaly, craniofacial abnormalities, developmental delay.
- **Vaginal embryopathy**: 1-2% risk of neural tube defect (NTD)
- Uncommon in phenytoin

**Aneuploidy**
- Variable structural malformations, IUGR

**Intrauterine growth restriction (IUGR)**
- Multiple causes including uteroplacental insufficiency, maternal medical conditions, aneuploidy.

**Congenital heart defects**
- Isolated vs. syndromal
- Cleft lip/palate
  - Isolated vs. syndromal

**DDx: Fetal Hydantoin Syndrome**

- Isolated Cleft
- Vaginoplasty (NTD)
- IUGR
HYDANTOIN

Terminology
- Fetal hydantoin syndrome
- Fetal effects of maternal exposure to phenytoin, characterized by growth restriction, microcephaly, mental deficiency and craniofacial malformations

Top Differential Diagnoses
- Encephalopathy from other anticonvulsants
- Acrocephaly

Key Facts
Pathology
- 6.10% of exposed fetuses will develop fetal hydantoin syndrome
- Additional 1/3 with some degree of clinical effects from exposure
- No clear cut dose-response curve, with no "safe" lower dose

Clinical Issues
- Psychomotor delays, learning and memory problems

Intrauterine infections
- IUGR, microcephaly
- Intertinal and liver calcifications
- Not seen in phenytoin
- Structural malformations uncommon

PATHOLOGY
General Features
- Genetics: Recurrence in siblings (variable severity), due to repeated exposure in subsequent pregnancy
- Etiology
  - Epilepsy is the most common neurologic disorder in reproductive age women
  - Dilantin is a commonly prescribed antiepileptic drug used to treat focal/toxic-clonic seizures
  - Bioactivation of phenytoin to toxic metabolites and generation of reactive oxygen species implicated in pathogenesis of phenytoin toxicity
  - Blockage of ion channels by phenytoin in embryonic heart may result in bradyaryrhythmias, hypoxic ischemic injury
  - Lower microsomal epoxide hydroxase activity in chronic phenytoin therapy supports putative oxidative metabolism mechanism
- Epidemiology
  - 6-10% of exposed fetuses will develop fetal hydantoin syndrome
  - Additional 1/3 with some degree of clinical effects from exposure
  - No clear cut dose-response curve, with no "safe" lower dose

CLINICAL ISSUES
Presentation
- Prenatal evaluation for known exposure
  - IUGR, microcephaly, cardiac defects
  - Typical facial appearance at birth
    - Broad, depressed nasal root, hypertelorism
    - Thin lips, often with bowed upper lip
    - Cleft lip/palate, long philtrum
    - Distal phalangeal and nail hypoplasia, most severe on wrist side
    - Hair thinning, coarse hair
  - Rib anomalies
- Natural History & Prognosis
  - Risk of fetal death
  - Psychomotor delays, learning and memory problems
  - Incidence of tumor (nuclear crest origin)
  - Risk of seizure disorders in offspring of epileptics

Treatment
- Seizure control in maternal epilepsy is paramount for optimal pregnancy outcome
  - Single drug at lowest possible dose
  - Avoidance of polytherapy when possible

Diagnostic Checklist
Consider
- Always perform karyotypic analysis for aneuploidy in patient with known phenytoin exposure

SELECTED REFERENCES

IMAGE GALLERY
(left) Central ultrasound shows a malformed left lip, (arrow) and palate. (Right) Four chamber view shows a ventricular septal defect (arrow). These findings are non-specific for hydantoin exposure and can also be caused by other anticonvulsant drugs.
VALPROIC ACID

Terminology

Abbreviations and Synonyms
- Valproic acid (VPA), Depakene, Depakote
- Fetal valproate syndrome

Definitions
- Fetal exposure to the antiepileptic drug valproic acid, characterized by dysmorphic facial appearance, major and minor anomalies, central nervous system dysplasia.

Imaging Findings

General Features
- Best diagnostic clue: Neural tube defect (NTD), facial anomalies and growth restriction in an exposed fetus.

Imaging Recommendations
- Protocol advice
  - Monthly ultrasounds for interval growth, anatomy
  - Consider 3D ultrasound to assess more subtle facial findings

DDx: Fetal Valproate Syndrome

- NTD, isolated
- Polydactyly
- Cleft lip/plate
- Radial ray

Differentiation Diagnosis

Embryopathy from other anticonvulsants
- Characteristic pattern of malformations, intrauterine growth restriction (IUGR) and developmental delay seen in phenytoin, trimethadione, carbamazepine, phenobarbital.

Neural tube defects
- Isolated vs. syndromic

Aneuploidy
- IUGR, other structural malformations

Cardiac defects
- Isolated vs. syndromic

Cleft lip/palate
- Isolated vs. syndromic

Intrauterine growth restriction (IUGR)
- Multiple causes: Aneuploidy, infection, maternal medical condition, uteroplacental insufficiency

Limb defects
- Radial ray abnormalities, polydactyly

Intrauterine infections
- Intracranial/liver calcifications
- Not seen in valproate exposure
**VALPROIC ACID**

**Key Facts**
- VPA exposure occurring at 17-30 days post-fertilization confers risk of spina bifida of 1-2%.
- Risk of other major malformations - 10% (2-3x that of unexposed pregnancy).
- Increased risk of embryopathy with higher doses of VPA and >1 antiepileptic drug.

**Pathology**
- Mechanism of teratogenesis related to impairment of folate absorption and metabolism.

**PATHOLOGY**

**General Features**
- Genetics: Recurrence in siblings due to repeated exposures in subsequent pregnancies.
- Epidemiology:
  - VPA most effective drug for petit mal seizures; also effective for bipolar disorder, migraine.
  - Mechanism of teratogenesis related to impairment of folate absorption and metabolism.
  - Epidemiology:
  - VPA exposure occurring at 7-30 days post-fertilization confers risk of spina bifida of 1-2%.
  - Risk of other major malformations - 10% (2-3x that of unexposed pregnancy).
  - Minor anomalies in 1/3 of fetuses.
  - Increased risk of embryopathy with higher doses of VPA and >1 antiepileptic drug.

**CLINICAL ISSUES**

**Presentation**
- Most common signs/symptoms:
  - Neural tube defects 1-2%: Sacral, lumboSacral.
  - Microcephaly 15%.
  - Congenital heart defects 25%.
  - Left-sided lesions, interrupted arch, septal defects.
  - IUGR.
  - Craniofacial:
  - Bilateral narrowing, midface hypoplasia, broad flat nasal bridge.
  - Small palpebral fissures, hypertelorism, epicanthal folds, microphthalmia, hypoplasic optic nerves.
  - Long flat philtrum, small mouth with thin lips, micrognathia.
  - Cleft lip/palate.
  - Limb abnormalities 45-65%.
  - Thin fingers, hypoplastic nails, polydactyly.
  - Radial ray defects.
  - Gerontourinary (20%): Hyphenadias.
  - Developmental delay.
- Other signs/symptoms: Neonatal hyperglycemia, afibrinogenemia, hyperbilirubinemia.

**Natural History & Prognosis**
- Infant mortality 12%.
- Mental retardation 29%.
- Variable severity among affected sibs.

**Treatment**
- Seizure control in pregnancy is paramount.
- Use of a single drug at lowest possible dose.
- Preconceptional folic acid 0.4-4 mg per day.
- Efficacy not conclusively established; controversy exists regarding whether folic acid supplementation might impair effectiveness of valproic acid.
- Preconceptional folic acid 4 mg per day with history of previous affected child with NTD.
- Pregnancy termination an option.

**SELECTED REFERENCES**

**IMAGE GALLERY**

(Left) Cranial ultrasound of the lumbarn spine shows a metacranial defect with widening of the posterior elements (arrows). (Right) Clinical photograph of the back shows the curvilinear spine appearance (arrows). Seizure control in maternal epilepsy is paramount for optimal pregnancy outcome for antiepileptic drugs have a teratogenic risk. Therapy should be directed at using a single drug at the lowest dose possible to control seizure activity.
TERMINOLOGY

 Abbreviations and Synonyms
 - Warfarin (Coumadin) embryopathy
 - Fetal warfarin (Coumadin) syndrome

 Definitions
 - Fetal effects of early gestational exposure to warfarin, a vitamin K antagonist

 Imaging Findings

 General Features
 - Best diagnostic clue
   - Severe nasal hypoplasia, rhizomelia, exposed fetus
   - Stepped epiphyses may be seen in 3rd trimester in A-P radiographs of large joints

 Imaging Recommendations
 - Best imaging tool
   - 2nd-3rd trimester 3D ultrasound of fetal face
 - Postnatal radiography
 - Protocol advice
   - Careful search for corroborative epiphyseal calcifications in suspected embryopathy
   - Fluoroscopic spot views of large joints in 3rd trimester looking for stepped epiphyses

 DIFFERENTIAL DIAGNOSIS

 Chondrodysplasia punctata (CDP)
 - Heterogeneous group of skeletal dysplasias
 - Expanded epiphyses with punctate calcifications
 - Rhizomelia, nasal hypoplasia
 - Congenital heart disease in 10%

 Skeletal dysplasias
 - Achondroplasia: Short limbs, mid-face hypoplasia
 - Achondrogenesis: Severe rhizomelia, nassa hypoplasia, lethal
 - Thanatophoric dysplasia: Micromelia, cloverleaf skull, short upturned nose, lethal

 Trisomy 21
 - Absent or hypoplastic nasal bone
 - Mild hemihypertrophy shortening

 Pseudo-warfarin embryopathy
 - Epoxyde reductase deficiency

 Vitamin K deficiency
 - Acquired abnormality from severe maternal malabsorption

 Binder syndrome
 - Maxillaronal dysostosis

 DDx: Conditions With Nasal Hypoplasia

 Achondrogenesis
 Trisomy 21
 Thanatophoric
 CDP
**WARFARIN (COUMADIN)**

**Terminology**
- Warfarin (coumadin) embryopathy
- Fetal effects of early gestational exposure to warfarin, a vitamin K antagonist

**Imaging Findings**
- Severe nasal hypoplasia, rhizomelia in exposed fetus
- Fluoroscopic spot views of large joints in 3rd trimester looking for stippled epiphyses

**Iatrogenic**
- Off-axis imaging of fetal profile can give impression of nasal hypoplasia

**PATHOLOGY**

**General Features**
- Etiology: Inhibition of vitamin K-dependent carboxylation of bone proteins
- Critical period is 6-9 weeks post-fertilization
  - Lower risk may extend into 2nd and 3rd trimesters (optic, central nervous system effects)
  - Risk is higher with doses over 5 mg/day
- Epidemiology: Embryopathy with 1st trimester exposure in 6%
- Central nervous system abnormalities
  - Dandy-Walker continuum, agenesis of corpus callosum, microphthalmia, optic atrophy
- Congenital heart defects

**CLINICAL ISSUES**

**Presentation**
- Postnatal presentation
  - Neonatal respiratory distress
  - Severe nasal hypoplasia with depressed nasal bridge, deep grooves between alae nasi and nasal tip
  - Skeletal: Stippled epiphyses, short limbs, nail hypoplasia, vertebral abnormalities
  - Ectopic calcifications of nose, tracheobronchial tree

**Natural History & Prognosis**
- Spontaneous abortion (25%), stillbirth (7%)
- Fetal intracranial hemorrhage
- Rare, often fatal, occurs in 2nd or 3rd trimester
- Neonatal airway obstruction from nasal hypoplasia
- Increased risk of neonatal death
- Nasal hypoplasia significant cosmetic problem
- Stippled epiphyses not usually clinically significant
- Cervical vertebral abnormalities ⇒ myelopathy, spinal cord compression

**Treatment**
- Options, risks, complications
  - Indications for anticoagulation during pregnancy
    - Prosthetic heart valves

**Top Differential Diagnoses**
- Chromodysplasia punctata (CDP)

**Pathology**
- Critical period is 6-9 weeks post-fertilization
- Lower risk may extend into 2nd and 3rd trimesters (optic, central nervous system effects)
- Risk is higher with doses over 5 mg/day
- Epidemiology: Embryopathy with 1st trimester exposure in 6%

- Prevention and treatment of venous thromboembolism
- Unfractionated heparin and low-molecular weight heparin (LMWH) are mainstays of therapy in pregnancy
- LMWH not approved for use with prosthetic valves
- Unfractionated heparin is associated with increased thrombotic risk with mechanical valves
- No controlled trials to establish optimal anticoagulation regimen
- To decrease thrombotic risks of warfarin, common practice is to switch to unfractionated heparin for weeks 6-12 post-fertilization, and again just prior to delivery

**SELECTED REFERENCES**

**IMAGE GALLERY**

Left: Coronal ultrasound shows a hypoplastic nasal tip (arrow) in a 3rd trimester fetus with warfarin embryopathy. Note the grooves needed to the alae nasi open anteriorly. Right: Anteroposterior radiograph shows punctate calcifications in the left lateral epiphysis (arrows) in a newborn with total warfarin syndrome.
ACUTE ABDOMEN IN PREGNANCY

**IMAGING FINDINGS**

**General Features**
- Almost any cause of an acute abdomen can occur in a pregnant patient
- Some causes of pain are specific to pregnancy
  - Acute cholecystitis
  - Uterine rupture
  - Abruptio placentae
  - Ectopic pregnancy
- Abdominal pain + abnormal lab tests without apparent cause:
  - Pre-eclampsia
  - HELLP syndrome (Hemolysis, Elevated Liver function tests, Low Platelet count)

**Physiologic changes in pregnancy**
- Pulse rate 1 by 10-20 beats per min
- Blood pressure 1 by 5-15 mm Hg by mid gestation
- White cell count↑
- Alkaline phosphatase↑
- Physiologic changes alter intra-abdominal anatomy → impaired diagnostic accuracy

**Imaging Recommendations**
- Use ultrasound as first line for abdominal imaging
- MRI next line in many conditions
- Rapid sequences overcome image degradation due to fetal movement

**DIAGNOSTIC DIFFERENTIATION**

- **Appendicitis**
  - Most common non-obstetric indication for surgery during pregnancy
  - Appendis elevated out of pelvis by gravid uterus → site of maximal tenderness in pelvis, particularly in third trimester
  - If pain persists localized to one spot when patient moves → perforated rupture, not adnexal source

- **Biliary disease**
  - Pregnancy alters biliary homeostasis
  - Gallbladder "glozing" seen in 25% of women immediately postpartum

**DOX: OB/GYN Causes Of Abdominal Pain In Pregnancy**

- Large, Fluid
- Adenomatous
- Abruptio
- Uterine Rupture
Clinical Issues
- Delayed diagnosis is main cause of mortality
- If mother's health is compromised, fetus also adversely affected
- If gaseous appendicitis/peritonitis develop, fetal loss rate as high as 70%
- Use ultrasound as first line for imaging
- Use MRI as second line
- CT can be performed safely, but should be used judiciously when other modalities cannot appropriately address clinical situation
- Obtain consent from mother if anticipated radiation dose > 10 mGy
- Use contrast media as required by the clinical situation

Key Facts
- Mutagenic and teratogenic effects have not been described after administration of gadolinium or iodinated contrast media
- Iodinated contrast given to mother has potential to depress fetal/neonatal thyroid function
- Thyroid function should be checked during 1st week of life
- Pregnancy is NOT a contraindication to surgery

Diagnostic Checklist
- Nausea and vomiting beyond first trimester is abnormal
- No single diagnostic procedure results in a radiation dose significant enough to threaten the well-being of the developing embryo and fetus
- Pregnancy should not alter appropriate evaluation of an acutely injured pregnant woman

ACUTE ABDOMEN IN PREGNANCY

PATHOLOGY

General Features
- Epidemiology
  - Incidence of acute abdominal conditions in pregnant population
    - Pyelonephritis 10.25:1,000
    - Appendicitis 0.38:1,000
    - Paracentesis 0.5:7,100
    - Bowel obstruction 0.3:1,000
    - Cholecystitis 0.25:1,000
    - Adnexal masses in pregnancy
- Teratoma 3.7%
- Endometrioma 14%
- Simple cyst 13.1%
- Cystadenoma 12.1%
- Tubal cyst 8.4%
- Fibroid 3.7%
- Carcinoma 0.9%

CLINICAL ISSUES

Presentation
- Most common signs/symptoms: Abdominal pain
- Other signs/symptoms
  - Nausea, vomiting
  - Fever
  - Elevated white cell count
  - Pyuria

- Pain moves with uterus/adnexa when patient changes position
- Pain due to peritoneal irritation does not move with change in patient position

Adnexal torsion
- Maximum risk at end of first trimester, as uterus rises out of pelvis, and postpartum as uterus involutes
- Actually rare, < 1% torsion rate in series of 125 adnexal masses > 4 cm in diameter

- Incidence decreased to 4% in some women by one year post delivery
- Incidental gallstones seen in 2-5% of pregnant women
- Gallbladder contractility decreased

Acute pancreatitis
- Most cases are idiopathic in pregnant population
- Amylase and lipase not altered by pregnancy

Bowel obstruction
- Small bowel obstruction is second most common non-obstetric cause for surgical intervention in pregnancy
- 60-70% due to adhesions, 25% colonic volvulus
- Presents with abdominal pain, nausea, vomiting
- Pregnancy-related nausea and vomiting uncommon after 1st trimester

Renal stones
- Hematuria
- Dilated ureter
- Ureters taper at pelvic brim in physiologic calcification
- Caliber transition proximal or distal to this suggests obstruction

Pyelonephritis
- Pyuria
- Positive urine culture

Bowel perforation
- Free intraperitoneal gas
- Peptic ulcer disease generally improves in pregnancy

Abdominal trauma
- Pregnancy should not alter appropriate evaluation of acutely injured women
- Even minor maternal trauma can have devastating consequences for fetus
- Re-evaluate 10-14 days post event to exclude fetal injury

Fibroid infarction
- May have point tenderness over fibroid
ACUTE ABDOMEN IN PREGNANCY

Natural History & Prognosis
- Delayed diagnosis is main cause of morbidity
- If mother’s health is compromised, fetus also adversely affected
- Appendicitis
  - Greater mortality less effective in “abdominal policies” in pregnancy
  - Delayed diagnosis = increased risk for perforation, especially in third trimester
  - Overall fetal mortality reported at 5-8%
  - Most attributed to preterm delivery
- Ovarian cysts: likely better outcome with modern medical care
- If gangrenous appendicitis or perforation, fetal loss rate may be as high as 70%
- Cholecystitis
  - Premen labor may increase to 20-35% if perforation develops
- Spontaneous abortion
  - Mostly (diagnostic in pregnant populations)
  - Some series report high association with gallstones
  - Up to 70%
- Prognosis used to be poor for mother and fetus but much improved with modern management
- Small bowel obstruction
  - Delayed diagnosis = lower complication rates
  - Premen labor rate increases from 5% to 20-35% with perforation
- Fibroids important if large or retroperitoneal
  - 10-40% of patients with large fibroids in pregnancy will have complications
  - Large > 5 cm in diameter or > 200 cm in volume
  - Pain requiring narcotic analgesia in 20% of women with fibroid > 5 cm diameter
  - 57% urination (in absence of oliguria or other risk factors) if retroperitoneal, with volume > 200 cm
  - 50% fetal demise in this series

Treatment
- Aggressive evaluation of all significant pain
- Use ultrasound as first line for imaging
- Use MRI in second line
- CT can be performed safely, but should be used judiciously when other modalities can appropriately address clinical situation
- Obtain culture from mother if anticipated radiation dose > 10 mgY
- Calculated dosimetry at author's institution is 14 mgY for an abdominal/pelvic CT

Contrast agents
- Use contrast media as required by the clinical situation
- Maternal and anesthetic effects have not been described after administration of gadolinium or iodinated contrast media
- Indicated contrast given to mother has potential to depress fetal/necrotic thyroid function
- Thyroid function should be checked during 1st week of life
- Pregnancy is NOT a contraindication to surgery
- Several series document successful laparoscopic surgery, particularly for gallbladder disease
- No increase in preterm labor or fetal loss

DIAGNOSTIC CHECKLIST

Consider
- Nausea and vomiting beyond first trimester is abnormal
- Mortality of acute abdomen in pregnancy is linked to delay in diagnosis and treatment
- Neither imaging nor surgery are contraindicated because patient is pregnant
- International Council for Radiation Protection standard
  - No single diagnostic procedure results in a radiation dose significant enough to threaten the well-being of the developing embryo and fetus
  - Likelihood that child will NOT develop malignancy due to 2nd/3rd trimester radiation exposure
    - 10 mgY = 99.88%
    - 50 mgY = 99.7%
    - 100 mgY = 99.48%
    - With no diagnostic radiation exposure, likelihood is 99.93%
- Consider formulation of an institutional policy for consent to radiation exposures in pregnancy

Image Interpretation Pearls
- Imaging features of acute abdominal inflammatory conditions are less altered by pregnancy than are clinical features
- Location may be different: appendix rises out of pelvis as uterus enlarges
- Presentation may be different
  - Appendicitis may present with pyrexia
  - Hydrophobia does not necessarily imply obstruction, especially on the right
- Remember that pregnancy can present with abdominal pain
- Pregnancy should NOT alter appropriate evaluation of an acutely ill gravid patient

SELECTED REFERENCES
ACUTE ABDOMEN IN PREGNANCY

IMAGE GALLERY

Typical

[Images showing various abdominal conditions in pregnancy]

Typical

[Left] Axial/lipper and longitudinal/long images show a non-compressible, dilated appendix (curved arrow). Rose fat confirmed a blood-filled tube (arrow). At surgery, the appendix was adherent to the spleen. Proteus subtype revealed. 

[Right] Cervical ultrasound shows a echogenic focus (curved arrow) with distal acoustic shadowing (arrow) in the upper pole of the left kidney. This is the typical appearance of a renal calcuks.

Typical

[Left] Ultrasound shows a thinned-alveolar pattern (arrow) with stone (arrowhead). Packed medullary thrombosis (thrombus) revealed. 

[Right] 2D USK shows an abdominal pregnancy. There is no surrounding amnion and amniotic fluid, and placental tissue is located directly into the abdominal wall (arrow) and tissues (arrow).

Diagnosis made at 26 weeks. The mother presented with acute abdominal pain.

Typical

[Left] Clinical photograph shows extensive eclampsia on the maternal abdomen and thigh (arrows). 

[Right] Axial color Doppler ultrasound in a patient involved in a car accident shows a cord loop (arrow) surrounded by adherent clot (curved arrow). Other images showed a large placental abruption with intramural hematoma.

[Images of various obstetric conditions and their ultrasound findings]
DIABETES

Terminology

Abbreviations and Synonyms
- Diabetic embolopathy
- Infant of diabetic mother (IDM)

Definitions
- Preeclampsia: diabetes (type I or II): Diabetes mellitus diagnosed prenatally
- Gestational diabetes: any degree of glucose intolerance diagnosed during pregnancy
  - Diagnosis by oral glucose tolerance test between 24-28 weeks gestation
  - GDM by definition, resolves following pregnancy, although recurrence is common.
  - Increased risk of ultimately developing overt (type II) diabetes.

Imaging Findings

General Features
- Best diagnostic clue
  - Abnormal growth + structural anomalies in the fetus of a diabetic mother
  - May be macroscopic (>90th percentile), large for gestation age (LGA) or growth restricted (IUGR)

Ultrasoundographic Findings
- Gestational diabetic fetus often macrosomic
  - Accelerated growth apparent by late 2nd trimester
  - Disproportionate increase in abdominal and head circumference
  - Increased skin thickness of trunk, head
  - IUGR more common in long-standing diabetes
  - Cardiac anomalies: right ventricular hypertrophy
  - Decreased femoral diastolic velocity
  - Polyhydramnios
  - Polyhydramnios
  - Cardiac anomalies: right ventricular hypertrophy
  - Cardiac anomalies: left ventricular hypertrophy
  - Cardiac anomalies: septal defects
  - Cardiac anomalies: atrial septal defects

DDx: Aneuploidy And CNS Anomalies

- Social Agnogenesis
- Neoplasia
- Spina Bifida
- Holoprosencephaly

- Holoprosencephaly
DIABETES

Terminology
- Diabetic left colonic atrophy
- Pregnancy diabetes (type 1 or 2): Diabetes mellitus diagnosed prenatally
- Gestational diabetes: Any degree of glucose intolerance diagnosed during pregnancy

Imaging Findings
- Gestational diabetic fetus often macrosomic
- EEG: more common in long-standing diabetics
- Caudal dysplasia/regression sequence
- Central nervous system (CNS) abnormalities: 20-fold increase over non-diabetic
- Congenital anomalies: 5-fold increase over non-diabetic
- Polyhydramnios common
- Oligohydramnios more common in pregnancies of long-standing diabetics

Femoral hypoplasia
- Radial ray abnormalities, hypoplastic thumbs
- Genitourinary (GU)
- Renal agenesis
- Hydrenephrosis
- Duplicated collecting system
- Multi-renal kidneys
- Gastrointestinal (GI)
- Anorectal malformation/atriesin
- Diverticula
- Short colon syndrome
- Single umbilical artery (6%)
- Polyhydramnios common
- Often associated with LGA or macronomic fetuses
- Oligohydramnios more common in pregnancies of long-standing diabetics
- Often associated with intrauterine growth restriction (IUGR)

Imaging Recommendations
- Thorough evaluation of fetal anatomy in every diabetic
- Often obese maternal body habitus makes detection of subtle anomalies difficult
- Use endovaginal ultrasound for better early anatomic evaluation
- Significant malformations often detectable by late 1st trimester
- Holosomnally
- Amnioncephy
- Neural tube defect (NTD)
- Monthly ultrasound to evaluate fetal growth, amniotic fluid volume
- Fetal echocardiography to evaluate heart
- Consider fetal MRI to evaluate intracranial anomalies of when maternal body habitus precludes complete ultrasound examination

Key Facts
- Significant malformations often detectable by late 1st trimester

Top Differential Diagnoses
- Macrosomia
- Aneuploidy

Pathology
- Major malformations in 6-10%
- Poor metabolic control, especially in 1st trimester, increases risk of malformations
- Levels of HbA1C correlate with risk of malformations

Clinical Issues
- Increased spontaneous abortions, 20%
- Perinatal mortality 4-13%
- Preconceptional planning is critical, with goal of euglycemia to minimize malformation risk

DIFFERENTIAL DIAGNOSIS

Macrosonia
- May be seen without diabetes
- Overgrowth syndromes: Beckwith-Wiedemann, Weaver, Soto, Marshall-Safran

Aneuploidy
- Findings vary according to condition
- Trisomy 21, 18, 13
- Older growth restricted, not macrosonic

Congenital heart defects
- Isolated or syndromal

Neural tube defects
- Isolated vs. syndromal

Caudal dysplasia sequence
- Although rare, also found in non-diabetics

PATHOLOGY

General Features
- General path comments
  - Major malformations in 6-10%
  - 2-3x non-diabetics
  - Poor metabolic control, especially in 1st trimester, increases risk of malformations
  - Structural anomalies account for 50% of perinatal deaths
- Glycosylated hemoglobin (HbA1C) provides retrospective index of glycaemic status over preceding 4-8 weeks
- Levels of HbA1C correlate with risk of malformations
- < 6.5% = no increased risk
- 7.0-8.5% = 5% anomalies
- > 10% = 22% anomalies
- Malformation risk not increased in true gestational diabetes
DIABETES

- Great diabetic first recognized during pregnancy, has similar risk for embryopathy as a known pregonnatorial diabetic
- Epidemiology of diabetes in pregnancy
  - 25.3:1.000 pregnant woman
  - Prevalence increasing in United States, paralleling obesity
  - Rate varies with ethnic group (greatest for Native Americans) and age (higher with older mothers)
  - Risk factors: gestational diabetes
  - Older age, multiple gestation, obesity, previous pregnancy with gestational diabetes
  - Etiology of diabetic embryopathy
    - Metabolic derangements associated with hyperglycemia contribute to teratogenesis
    - Exact mechanism uncertain
    - Many theories center on role of hyperglycemia in increasing oxidative stress
    - Generates reactive oxygen species by accelerating rate of O2 consumption
    - Hyperglycemia may trigger apoptotic signaling pathways
    - Inhibit cell survival pathways embryonic malformations
    - Experimental studies suggest deficient expression of Pax6, a gene required for normal tube closure
  - Microscopic Features
    - Abnormal placentas
      - Thickened basal membrane, decreased vascular surface of villous villi
    - Fibrinoid necrosis, villous infarct, chorangiosis
  - Staging, Grading or Classification Criteria
    - White's classification based on age at diagnosis and years of duration
      - Class A = pregestational diabetes
      - Class B = age 20, > 10 years duration
      - Class C = under age 20, > 10 years duration
      - Class D = < age 10, > 20 years duration
      - Class E = nephropathy
      - Class F = proliferative retinopathy
      - Class G = macrovascular complications, including cardiomyopathy
      - Class H = prior renal transplant
      - Longer duration or earlier onset = risk of vascular disease, including placenta

CLINICAL ISSUES

- Presentation
  - Major malformation in known diabetic
  - Macronovas and polyhydramnios in unsuspected gestational diabetic, parenting for late care

Natural History & Prognosis

- Increased incidence of stillbirth
- Higher if mother has fasting hyperglycemia
- Perinatal mortality 4.1%
- Increased birth trauma and cesarean section rate
- Newborn complications
- Hypoglycemia, hypothyroidism, hypothyroidism
- Long-term prognosis dependent upon presence, type of structural malformations
- Some, like atheroemboliopoecephaly and caudal dysplasia, are lethal or life-limiting
- LGI infant exposed to diabetic milieu in utero: increased risk for development of metabolic syndrome
- Obesity, hypertension, dyslipidemia, glucose intolerance

Treatment

- Preconceptional planning is critical, with goal of euglycemia to minimize malformations risk
- Strict metabolic control throughout pregnancy
- Assess for evidence of maternal diabetic and organ disease or dysfunction
- Renal, hypertension, cardiac, ophthalmologic
- Close fetal surveillance
- Nonstress testing, biophysical profiles, serial ultrasounds fetogrowth
- Delivery prior to term, with evidence of fetal lung maturity, to decrease risk of stillbirth
- Consider steroid administration for enhancement of fetal lung maturity, as HDM at risk for delayed pubertal development
- Delivery at a tertiary care facility
- Pregnancy termination an option with multiple or severe malformations
- Preconceptional folic acid, while recommended for all women of reproductive age, is of uncertain efficacy in preventing diabetes associated NTD

SELECTED REFERENCES

(Left) Axial ultrasound of the pelvis shows absence of the sacrum, with fusion of the iliac wings medially (arrow). The mother was an uncontrolled diabetic.

(Right) Clinical photograph shows a macromeric twin at an uncontrolled gestational diabetic. The infant weighed 3,900 g at 32 weeks gestation. Note the increased fat distribution (arrow).

(Left) Coronal T2 WI MRI of a fetus of a diabetic mother shows lack of adrenal differentiation and a monoventricle (arrow), diagnostic of alobar holoprosencephaly. (Right) Gross pathology shows the brain in the same fetus, stillborn at 35 weeks gestation. The monoventricle (arrow) and fused thalami (open arrow) correlate with the MRI findings.

(Left) Clinical photograph shows an infant of a diabetic mother with bilateral renal hypoplasia (open arrow). Postaxial polydactyly is also noted (curved arrow), as well as symmetrical (arrow).

(Right) Color Doppler echocardiogram along the right ventricle in the same newborn shows two parallel vessels exiting the chamber (arrows), consistent with a double outlet right ventricle, a common lesion in diabetes.
**TERMINOLOGY**

**Definitions**
- Dilatation of renal collecting system in a pregnant woman

**IMAGING FINDINGS**

**General features**
- Best diagnostic clue: 'Unilateral', dilated collecting system with absent ureteric jet = high probability of obstruction

**Ultrasonographic Findings**
- Gray-scale Ultrasound
  - Dilated intrarenal collecting system
  - Pelvis dilated to variable degree
  - Calyces mildly dilated in physiologic caliectasis
  - "Clubbed" calyces suggest obstruction
  - Dilated ureters
  - If seen, try to determine level of obstruction
  - Dilation below ilium suggests obstruction
- Color Doppler
  - Very useful to look for ureteric jets
  - Scan in axial plane over bladder trigone
  - Color Doppler displays moving echoes in color
  - Ureteric 'jet' streams into bladder

- Displayed as color or background of arborizing ureteric jets in bladder
- Twinkle artifact
- Rapidly changing color complex seen persistently behind stones, like a comet's tail
- Pulsed Doppler
  - Intrarenal resistive index (RI)
  - RI = systolic velocity - end diastolic velocity/systolic velocity
  - Physiologic caliectasis does not alter renal hemodynamics
  - Acute obstruction = increased vascular resistance within 6 hours of onset
  - Increased vascular resistance = increased RI
  - Measure RI in both kidneys
  - RI difference between kidneys should be < 0.1
  - Mean RI in non-obstructed kidneys 0.59 +/- 0.04
  - Mean RI in obstructed kidneys 0.71 +/- 0.04

**Imaging Recommendations**
- Start with ultrasound
  - If collecting system dilated
  - Rescan after patient empties bladder
  - Rescan after change in patient's position, elevate side of dilated collecting system
  - Collecting system will empty if dilatation secondary to extrinsic-ureteric compression
  - Look for dilated ureters

**DDx: Abnormal Maternal Kidneys**

- Pyelectasis
- Oligohydramnios
- Duplicity
- Renal Stones
MATERIAL HYDRONEPHROSIS

**Imaging Findings**
- Best diagnostic clue: Unilateral, dilated collecting system with absent ureteric jet → high probability of obstruction
- Physiologic hydronephrosis does not alter renal hemodynamics
- RI difference between kidneys should be < 0.1
- Stones seen as filling defects within columns of high signal urine

**Top Differential Diagnoses**
- Physiologic hydronephrosis
- Renal obstruction
- Vescoureteric reflux
- Duplicated collecting system
- Pyelonephritis
- Renal cysts

**Key Facts**
- Use both TA and EV approaches
- Urates seen as fluid-filled tubes posterior to bladder
- May visualize peristalsis
- May see obstructing stone
- Use color Doppler to differentiate dilated ureter from vessels
- Normal ureter should taper before crossing iliac vessels
- If dilated beyond this point → obstruction more likely
- Look for ureteral jets
- Compression of ureter by pregnant uterus may cause false positive diagnosis of ureteric obstruction if patient supine
- Scan with patient in lateral decubitus position, symptomatic side up
- If presenting fetal parts obscure bladder trigone, use EV sonography
- Technique for EV sonography to evaluate ureteric jets
- Do not have patient empty bladder completely
- Important to see movement of urine (ureteric jet) within bladder
- Scan patient in lateral decubitus position with symptomatic side uppermost
- Magnetic resonance urography (MRU)
  - MRU: Utilizes T2 weighted sequences
  - Fluid (ureter) is high signal on T2WI
  - Easy to see length of ureters on coronal MR scans
  - Stones seen as filling defects within columns of high signal urine
- Tailored intravenous pyelogram
  - Full length scout view
  - 1 min, 15 min films coned to renal area
  - If 1 min film shows dense nephrogram, do full length film at one hour
  - If 1 min film shows faint nephrogram and 15 min shows little excretion, do full length film at two hours
- Computed tomography
  - Best modality to see stones

**Pathology**
- Collecting system dilatation seen in 90% of pregnant women by third trimester

**Clinical Issues**
- Physiologic hydronephrosis of no functional significance
- Obstructed, infected kidney requires urgent decompression

**Diagnostic Checklist**
- Appendicitis in pregnancy may cause flank pain, pyuria
- Significant hydronephrosis in early gestation likely to be pathologic
- Dilated ureter secondary to physiologic hydronephrosis tapers at iliac crest on coronal MR images or before crossing iliac vessels on ultrasound

**Differential Diagnosis**

**Physiologic hydronephrosis**
- Non-obstructive dilatation of collecting system attributed to compression of ureters at pelvic brim by gravid uterus
- Asymptomatic
- Right only or R > L
- No inter-kidney difference in RI

**Renal obstruction**
- Ureteropelvic junction (UPJ) obstruction
  - Patient may be aware of diagnosis
  - Pelvis dilated but ureter normal in caliber
  - History of pain precipitated by fluid challenge
  - Long standing UPJ obstruction associated with marked cortical thinning
- Ureteric filling defect
  - Calculus is most common ureteric filling defect in pregnant population
  - Look for echogenic focus with distal acoustic shadow
  - Twinkle artifact may be helpful to identify stones
  - Usually associated with microscopic hematuria

**Vescoureteric reflux**
- Patient may be aware of diagnosis
- Usually not symptomatic unless infection coexists
- Look for parenchymal scarring from previous episodes of infection that caused parenchymal damage
- Indicates long-standing condition
MATERNAL HYDROEUPHISIS

Duplicated collecting system
- Upper and lower pole collecting system drain into separate urters
- Ureters may unite to be separate at level of bladder
- Ureteric pole ureters insert lower in bladder and more medially than normal
  - Upper ureter: risk of obstruction
  - Lower ureter: risk of reflux
- Most likely diagnosis if only part of renal collecting system is dilated

Pyelonephritis
- May or may not be associated with collecting system dilatation in pregnancy
  - Pelvis normal in 34.7%
  - Pelvis mildly dilated (6-10 mm) 33.3%
  - Pelvis moderately dilated (11-15 mm) 21.3%
  - Pelvis severely dilated (>16 mm) 10.7%
- Patient febrile with elevated white cell count
- Sputum, UTI urine with positive urine culture

Renal cysts
- Diabetic cysts may be mistaken for hydromephrosis
  - Cysts are not dilated
- Autosomal dominant polycystic kidney disease (ADPKD)
  - Bilateral, often large cysts

PATHOLOGY

General Features
- Epidemiology
  - Collecting system dilatation seen in 90% of pregnant women by third trimester
    - 2.6 > 1.4
- Renal stone disease
  - Seen in 1:1,500 pregnancies
- Most common painless conditions precipitating admission of the pregnant patient
  - Pyelonephritis
  - 2-5% of pregnancies

CLINICAL ISSUES

Presentation
- Most common signs/symptoms
  - Flank pain
  - Fever, if associated with infection
- Microscopic hematuria, if associated with stones

Natural History & Prognosis
- Physiologic colicctasis: no functional significance
- Mild degree of cal icctasis may persist after delivery, particularly in multiparous patient
- Twenty weeks gestation: marks threshold for development of significant dilatation

Treatment
- Renal stones
  - Standard treatment not altered in pregnancy
  - Hydration
  - Antigens
- 20-30% may require intervention for renal stone disease
  - Percutaneous nephrolithotomy
  - Ureteroscopy, basket retrieval, laser lithotripsy
- May require stent placement: Ultrasoned may be used as guidance rather than fluoroscopy
- Pyelonephritis
  - Treated aggressively with intravenous fluid and antibiotics
  - Septic increases risk of preterm labor
  - If inadequate response to appropriate antibiotic therapy, urine or CPT to evacuate complications
  - Obstructed, infected kidney requires urgent decompression
  - Reftters deployed on renal pelvis
  - May require antibiotic coverage throughout pregnancy
- UTI obstruction
  - Symptomatic treatment until delivery

DIAGNOSTIC CHECKLIST

Consider
- Infected, obstructed collecting system requires urgent decompression
- Physiologic calicctasis + pyria may mimic contralateral pyelonephritis
- Appendicitis in pregnancy may cause flank pain, pyuria
  - Appendicitis relates up out of pelvis, irritates ureter

Image Interpretation Pearls
- Physiologic calicctasis
  - Starts at 6-10 weeks gestation, rarely marked before 20 weeks
  - Significant calicctasis in early gestation likely to be pathologic
- Physiologic calicctasis does not delay renal function
  - Rs will be similar in dilated and non-dilated kidney
- Dilated ureters secondary to physiologic calicctasis taper at iliac vessels around MR image or before crossing iliac vessels on ultrasound
  - More distal dilatation suggests obstruction

SELECTED REFERENCES
MATERNAL HYDRONEPHROSIS

IMAGE GALLERY

Typical

(Left) Pulsed Doppler ultrasound shows the typical low-resistance waveform seen in the interstitial arteries. The resistive index is increased in obstructed kidneys but is decreased in unobstructed kidneys. (Right) Transverse pelvic sonogram produces a “jet” from the ureteral orifice which is easily detected with color Doppler. The curved arrow shows the typical appearance of the jet. If jets are seen, complete ureteral obstruction can be excluded.

Typical

(Left) Axial T2WI MRI shows normal left collecting system (arrow) and mild physiologic dilatation of the right collecting system (curved arrow). MRI was performed for evaluation of fetal pelvic mass. Open arrow denotes the posterior meniscus. (Right) Sagittal ultrasound through the maternal right kidney shows multiple dilated calyces (arrows) in a patient with severe obstruction. Physiologic caliectasis does not usually cause the degree of collecting system dilatation.

Typical

(Left) Axial CECT shows an excreted, dilated right kidney with standing uric stones (white arrow) and a dilated pelvis (arrow). CT should be used judiciously in pregnancy, being reserved for cases in which other modalities can not adequately address the clinical question. (Right) Axial T2WI in a case of pyelonephritis shows edematous kidneys with dilated calyces (arrow). This is a serious complication of obstruction, requiring urgent decompression.
HELLP SYNDROME

TERMINOLOGY

Abbreviations and Synonyms
- Acute, Elevated Liver enzymes, Low Platelets (AcELLP)

Definitions
- HELLP syndrome is a serious variant of preeclampsia seen primarily in young primigravidas
  - Usually preeclampsia, occasionally eclampsia
  - Usually presents in 3rd trimester
  - Up to 20% may present postpartum
  - Rarely seen in multiparous patients

- American College of Obstetricians & Gynecologists laboratory criteria
  - Hemoglobin < 11g/dL
  - Bilirubin > 1.2 mg/dL
  - Lactate dehydrogenase > 600 U/L
  - Aspartate aminotransferase > 70 U/L
  - Platelet count < 100,000/mm²

Ultrasoundographic Findings
- Liver hemorrhage or infarction
  - Usually peripheral
  - Irregular or wedge-shaped
  - Heterogeneous echogenicity
  - Increased echogenicity scotely
  - May become more hypoechoic over time

- Peripancreatic fluid
  - Hyperechoic thickening of peripancreatic area

- Subcapsular hematoma
  - Lenticular shape with compression of liver parenchyma
  - Complex, echogenic fluid
  - May see fluid-fluid level
  - Enlarged liver
  - Predominantly right lobe

- Occasionally anterior/dependent

MR Findings
- T1WI & T2WI
  - Signal intensity varies according to several factors
  - Degree & age of hemorrhage or infarct
  - Degree of necrosis & steatosis
  - Degree of necrosis & cellular necrosis
  - TIW, Low signal intensity
  - T2WI: High signal intensity

IMAGING FINDINGS

General Features
- Best diagnostic clue: Intraperitoneal or subcapsular fluid collection (hematoma) on US or CT

ODx: Diffuse or Focal Liver Lesion With Hemorrhage

- Hemorrhagic Adenoma
- Congenital
- Hepatic Trauma
- Post-OB Trauma
**HELLP SYNDROME**

**Terminology**
- Hemolysis, Elevated Liver enzymes, Low Platelets (HELLP)

**Key Facts**
- **Pathology**: 4-12% of patients with preeclampsia have HELLP syndrome

**Imaging Findings**
- Best diagnostic clue: Intraperitoneal or subcapsular fluid collection (trombosis) on US or CT
- Acute: Hypertension (first 24-72 hours)
- Chronic: Decreased attenuation (after 72 hours)

**Top Differential Diagnoses**
- Bleeding hepatic tumor
- Spontaneous bleed (coagulopathy)
- Hepatic trauma
- Acute fatty liver of pregnancy

**CT Findings**
- Liver hematomas
  - Well-defined, hyper- or hypodense
  - Acute: Hypertension (first 24-72 hours)
  - Chronic: Decreased attenuation (after 72 hours)
  - Subcapsular or intraparenchymal
    - Nondisplaced
  - Liver infarction
  - Small or large areas of low attenuation
  - Usually peripheral & wedge-shaped
  - Occasionally acute active extravasation

**Imaging Recommendations**
- Best imaging tool
  - Ultrasonography
  - May see US features before increase in biologic makers (41% of cases)
- Try to avoid CT because of ionizing radiation, can also be used as clinical situation warrants

**Differential Diagnosis**

**Bleeding hepatic tumor**
- Adenoma and hepatocellular carcinoma (HCC) most common liver tumors to spontaneously bleed
- Hematoma may be intraparenchymal or subcapsular
  - Can be indistinguishable from HELLP syndrome
- Look for enhancing, heterogeneous, spherical hepatic mass
- Does not have clinical features of HELLP

**Spontaneous bleed (coagulopathy)**
- History of bleeding disorder
- Lab data important
- Imaging appearance identical to HELLP

**Hepatic trauma**
- History of injury to liver
- Intraparenchymal or subcapsular hematomas
- Lacerations, wedge-shaped areas of infarction
- Areas of active hemorrhage (moderately with vessels)
- Hemoperitoneum

**Clinical Issues**
- Acute epigastric & RUQ pain present in 90% of cases
- Overall maternal mortality rate is 1.5%
- Maternal and fetal mortality approach 50% in cases of liver rupture

**Diagnostic Checklist**
- Rule out bleeding liver tumors (e.g., adenoma, HCC) & other liver pathologies like acute viral hepatitis & acute fatty liver of pregnancy
- Very rarely, can occur without classic preeclampsia triad (hypertension, proteinuria & edema)

**Acute fatty liver of pregnancy**
- Usually diffusely increased liver echogenicity
- Low attenuation by CT
- NC: Intraparenchymal or subcapsular fluid collection

**PATHOLOGY**

**General features**
- General path comments
  - Pathophysiology of HELLP syndrome: begins in placental bed
  - Arteriole vasoconstriction → endothelial damage → fibrin deposition
  - Platelet deposition on fibrin aggregates → decrease number of circulating platelets
  - Red blood cell destruction by fibrin aggregates (hemolytic anemia)
  - Abnormal cells in peripheral smear (burr cells & schistocytes)
  - Elevated indirect bilirubin levels & anemia
  - Hepatocytic destruction: Due to hepatic microemboli (liver function tests)
  - Distention of liver from impeded blood flow
  - Distention causes right upper quadrant (RUQ) pain
  - Severe cases: Liver rupture & subcapsular hematoma
- Pathophysiology of preeclampsia
  - Primary site: InCREASEd size of glomerular endothelial cells
  - Abnormal vasoconstriction & hyperreactive vascular smooth muscle
  - Hypertension → proteinuria → edema
- Etiology
  - Variant of severe preeclampsia & occasionally eclampsia
  - Factors implicated in preeclampsia & eclampsia
    - Coagulation abnormalities
    - Hormonal factors
    - Renoparenchymal ischemia
    - Immune mechanisms
HELLP SYNDROME

- Underlying maternal diseases also implicated
  - Hypertension, diabetes, renal disease
- Epidemiology
  - Prevalence
  - 4-12% of patients with preeclampsia have HELLP syndrome
  - Preeclampsia occurs in 6-8% of pregnancies
- Maternal mortality rate in severe preeclampsia due to HELLP syndrome is 3.5%

Gross Pathologic & Surgical Features
- Enlarged liver
- Posterior hemangioma or infarct
- Subcapsular hematoma

Microscopic Features
- Perivenous necrosis
- Microthrombi
- Fibrin deposits in sinusoids & portal veins

CLINICAL ISSUES

Presentation
- Most common symptom:
  - Acute epigastric & RUQ pain present in 90% of cases
- Abnormal liver function tests, low platelets and hematocrit
- Other symptoms:
  - Malaise, headache, nausea, vomiting
  - Edema, weight gain
  - Headache, visual impairment
  - Preeclampsia: Classic triad
    - Hypertension, proteinuria & edema
  - Eclampsia
    - Classic triad of preeclampsia + seizures
    - Clinical differential diagnosis:
      - Viral hepatitis, gallstones, peptic ulcer
      - Pancreatitis, acute fatty liver
      - Hemolytic urticarial purpura
  - HELLP syndrome:

Demographics
- Age: 2nd & 3rd decades
- Ethnicity: More frequent in African-Americans

Natural History & Prognosis
- Good prognosis if no complications
- Liver enzymes usually normalize within 48 hrs of delivery
- Thrombocytopenia and anemia resolve more slowly
- Complications:
  - Rupture of subcapsular hematoma
  - Hepatic necrosis
  - Deteriorated intravascular coagulation (DIC)
  - Abdominal pain
  - Pulmonary edema, hypoglycemia, renal failure
  - Overall maternal mortality rate is 3.3%
  - Generally cured of liver rupture
  - Maternal and fetal mortality approach 50% in cases of liver rupture

Treatment
- Expedient delivery of fetus
  - Steroids to promote lung maturity
  - Conservative treatment if no complications
  - Hepatic rupture & extra-abdominal bleeding must be treated emergently
  - Surgery, selective embolization

DIAGNOSTIC CHECKLIST

Consider
- Rule out bleeding liver tumors like adenoma, HCC & other liver pathologies like acute viral hepatitis & acute fatty liver of pregnancy
- Preeclampsia & HELLP syndrome
  - Must be thoroughly checked for in all pregnant women with acute abdominal pain
- HELLP syndrome
  - Can clinically mimic cholestasis, biliary colic & hepatic failure
  - Very rarely, can occur without classic preeclampsia triad (hypertension, proteinuria & edema)

Image Interpretation Pearls
- Subcapsular hematoma
- Coalescense, isoechoic fluid collection
- Indistinguishable from fluid collections of bleeding tumors like adenoma & HCC
- Look for heterogeneous, enhancing, spherical liver tumors
- Liver hemangioma or infarct
  - Usually peripheral, irregular or wedge-shaped
  - Increased echogenicity

SELECTED REFERENCES
**HELP SYNDROME**

**IMAGE GALLERY**

**Typical**

*Left:* Sagittal ultrasound of the maternal liver shows a subcapsular hematoma (open arrow). The hemorrhage is located and contains two locules. There is also a pleural effusion (open arrow). *Right:* Axial ultrasound shows the peripheral subcapsular hematoma (arrow). A white fluid-fluid level is seen within the hematoma (open arrow) and is caused by settling of lipid products.

**Typical**

*Left:* Axial CECT shows a small heterogenous subcapsular hematoma (open arrow) deforming the lateral contour of the liver. Free intraperitoneal blood (open arrows) is seen in the left abdomen. *Right:* Axial CECT shows massive hemorrhotremence (arrow) in a patient with HELLP syndrome. The peritoneal fluid is high density and thickens the bowel. A left pericardial shear hematoma (open arrow) is also seen.

**Typical**

*Left:* Axial CECT shows heterogeneous liver parenchyma (open arrow), consistent with bleeding and/or congestion. Free fluid (open arrow) is seen surrounding the liver and spleen. *Right:* Axial CECT shows large areas of necrotizing liver (arrow), consistent with infection or "sick, helpless, hypoxic" infection and microvesicular steatosis complications of HELLP syndrome.
OVARIAN VEIN THROMBOSIS

TERMINOLOGY

Abbreviations and Synonyms
- Postpartum ovarian vein thrombosis (POVT)
- Septic purpuric ovarian vein thrombosis (SPOV)

IMAGING FINDINGS

General Features
- Faint diagnostic clue filling defect within ovarian vein
- Location
  - 90% right-sided
  - Reminder left-sided, or rarely bilateral

Ultrasoundographic Findings
- May be difficult to see entire length of vein secondary to overlying bowel gas
- In one study only 52% of right and 23% of left ovarian veins were identified
- Ovarian enlargement, hypoechogenic adnexal mass
- Ovarian vein: Tubular structure anterior to psoas
- Look for thrombus using color Doppler

MR Findings
- Reported sensitivity 92%, specificity 100%
- Flow arroets may cause difficulties in time-of-flight or phase-contrast studies

Thrombus within the right ovarian vein is seen as an intraluminal filling defect on both side Doppler imaging (top images) and contrast-enhanced MR images (bottom images).

- Gadolinium-enhanced MRA venogram: Improve visualization and accuracy

CT Findings
- Reported sensitivity as high as 100%; specificity 99%
- Accuracy not as high as other studies
- Low-attenuation filling defect within ovarian vein
- Thickened, enhancing vessel wall
- Surrounding inflammatory changes
- Streaky soft tissue density obscuring surrounding fat
- Follow cephalad extent of thrombus to rule out extension into inferior vena cava (IVC)

Imaging Recommendations
- Contrast-enhanced CT is study of choice
- Fast, accurate and able to rule out other pathology
- May potentially use ultrasound in a thin patient
- If either of above are non-diagnostic, consider MRI

DIFFERENTIAL DIAGNOSIS

Endometritis
- Most common cause of postpartum fever
- Icteric fluid and gas in endometrial cavity
- Neither is specific
- Patients develope within 48-72 hrs with antibiotics

DDx: Postpartum Fever

- Endometritis
- Endometritis
- Appendicitis
- Pyelonephritis
OVARIAN VEIN THROMBOSIS

Imaging Findings
- 90% right-sided
- Thickened, enhancing vessel wall
- Surrounding inflammatory changes
- Follow cephalad extent of thrombus to rule out extrinsic intromission
- Ultrasound: cava (IVC)

Top Differential Diagnoses
- Endometritis
- Pyelonephritis

Key Facts
- Appendicitis

Clinical Issues
- Requires treatment with both broad spectrum antibiotics and heparin

Diagnostic Checklist
- Always consider POVT in a postpartum patient with persisting fever and abdominal pain, despite adequate antibiotic coverage

PATHOLOGY

General Features
- Endothelium
- Venous stasis
- Three-fold enlargement of ovarian veins during pregnancy
- Incompetent valves cause pooling
- Venous velocity significantly decreases postpartum, increasing stasis
- Ovarian vein compression
- Inframural enlarged uterus
- Pelvic veins
- Hypercoagulable state

- Pregnancy
- Postpartum: Clotting factors II, VII, IX, and X increased
- Usually occurs secondary to postpartum infection
- Vascular endothelium injured by ascending bacterial infection = thrombosis
- Risk factors
- Cesarean section
- Endometritis
- Obesity
- Epidemiology
- Rare disorder
- Complicates 0.15-0.18% of pregnancies

TREATMENT
- Requires treatment with both broad spectrum antibiotics and heparin

DIAGNOSTIC CHECKLIST

Consider
- Always consider POVT in a postpartum patient with persistent fever and abdominal pain, despite adequate antibiotic coverage

Image Interpretation Pearls
- Do not mistake ovarian veins for artere
- Must follow course back to IVC

SELECTED REFERENCES

CLINICAL ISSUES

Presentation
- Postpartum pelvic/abdominal pain and fever

Natural History & Prognosis
- Generally complete resolution with treatment
- Thrombus may progress to IVC or renal veins
- Rarely, septic pulmonary embolism

IMAGE GALLERY

(Lefl) Axial CECT shows the classic appearance of POVT (arrow) with a thick, enhancing vessel wall and low-density intramural clot. It is important to follow the course of this tubular structure to confirm it is the ovarian vein and evaluate for propagation of clot into the IVC.
(Right) Axial CECT shows similar findings as a left-sided POVT (arrow); left-sided POVT occurs in ≈ 15% of cases.
RH INCOMPATIBILITY

Ultrasonogram of a middle cerebral artery shows a peak systolic value of 49 cm/s. Zone A for a 15 week gestation. Acf/RI was subsequently performed for fetal anemia due to Rh sensitization.

**TERMINOLOGY**

**Abbreviations and Synonyms**
- Rh Rh factor
- Rh (Rh) incompatibility
  - Most commonly Rh D antigen incompatibility

**Definition**
- Maternal antibodies cross placenta and cause lysis of fetal red blood cells, leading to fetal anemia
- Fetal has Rh D (+) erythrocytes and mother has Rh D (-) erythrocytes
- Fetal erythrocytes gain access to maternal circulation
- Maternal immune response generates antibodies against D antigen
- Sensitization can be from prior pregnancy

**IMAGING FINDINGS**

**Ultrasonographic Findings**
- Elevated middle cerebral artery (MCA) peak systolic velocity (PSV)
- Doppler gate should be placed near origin of MCA
- No angle correction allowed
- Several MCA PSV measurements should be obtained
- Best measurement chosen, not average

**DIFFERENTIAL DIAGNOSIS**

**Minor antigen alloimmune syndromes**
- Kell, Duffy, Kidd, E, C, c and many others
  - Most are variably present in different ethnic populations
  - Most sensitizations caused by incompatible blood transfusions
  - Transfusion frequency rising since Rh-immune globulin prophylaxis developed
  - Decreasing incidence of Rh sensitization
  - Management of pregnancy same as for Rh alloimmunization

**DDx: Skin Thickening**

- Maternally Hydrops
- Dermatitis Warts/Cold
- Cystic Hygroma - 3D
- Maculopapular
## RH INCOMPATIBILITY

### Terminology
- Maternal antibodies cross placenta and cause lysis of fetal red blood cells, leading to fetal anemia

### Imaging Findings
- Elevated middle cerebral artery (MCA) peak systolic velocity (PSV)
- Fetal hydrups

### Top Differential Diagnoses
- Minor antigen alloimmune syndromes
- Parovirus infection

### Pathology
- Most cases of Rh alloimmunization causing serious hemolytic disease of fetus/newborn result from maternal-fetal incompatibility to D antigen

### Key Facts

#### Clinical Issues
- Fetal hemolytic disease similar or more severe in subsequent pregnancies
- Hemolysis and hydrops develop at similar gestational age or earlier in subsequent pregnancies
- Few fetuses develop hydrups in a first sensitized pregnancy
- Need for intervention generally based on relationship of MCA PSV to gestational age
- Routine prophylaxis with Rh-immune globulin decreases risk of alloimmunization from 16% to 0.17%

### Diagnostic Checklist
- MCA velocity should be measured with zero degree angle of insonation near origin

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### Parovirus Infection
- Transplacental transmission in about 1/3 of cases
- Parovirus attacks red blood cell precursors → anemia
- Hydrops uncommonly seen
  - Poor prognostic sign 2 occurs
  - May be secondary to anemia or viral myocarditis
- Clinical management variable
  - Weekly ultrasonic follow-up for 8-12 weeks after maternal seroconversion
  - Assessment for hydrups
  - MCA Doppler check

### Nonimmune Hydrops
- Multiple causes including aneuploidy, cardiac, masses

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### PATHOLOGY

#### General Features
- Genetics
  - Genetic locus for Rh antigen complex on short arm of chromosome 1
  - Fisher-Race nomenclature used in obstetrics
  - Assuming presence of three genetic loci, each with two major alleles
  - Antigens produced by these alleles are C, c, D, E, and e
  - Rh gene complex described by three letters: e.g. gene complexes can exist
  - Possible gene complexes: CDe, cDe, CDe, CDe, CDE, DE, and CDE
- Most cases of Rh alloimmunization causing serious hemolytic disease in fetus/newborn result from maternal-fetal incompatibility to D antigen
  - Rh(+) = presence of D antigen
  - Rh(-) = absence of D antigen
  - Rh antigen biochemistry
  - Rh antigens → polypeptides embedded in lipid phase of erythrocyte membrane
  - May be involved in maintaining erythrocyte cell membrane integrity
  - D antigen expressed early in embryonic life

#### Etiology
- Fetomaternial hemorrhage
  - Amount necessary to cause alloimmunization varies
  - Need sufficient volume to cause alloimmunization, most commonly occurs at delivery
  - 16% of Rh- women become alloimmunized by first Rh-incompatible pregnancy, if not treated with Rh-immune globulin
  - 1-2% of Rh- women become alloimmunized due to antenatal hemorrhage, if not treated with Rh-immune globulin
  - Abortion, ectopic pregnancy and amniocentesis can also cause alloimmunization
- Maternal immune response
  - Generates antibodies against Rh- antigen on fetal blood cells
  - Maternal anti-D antibodies cross placenta
  - Lead to fetal erythrocyte destruction
  - 30% of Rh- women do not generate antibodies when exposed to Rh(+) blood
- Epidemiology
  - Rh alloimmunization
    - 10,210,000 live births
  - Other alloimmune syndromes
    - 35,000,000 live births
  - Caucasians
    - 15% Rh(-)
  - African-Americans
    - 5-18% Rh(-)
  - Asians
    - 1-2% Rh(-)

### CLINICAL ISSUES

#### Presentation
- Many fetuses have no sonographic abnormalities
- Fetal hydrups
- High output heart failure
Natural History & Prognosis
• Obstetric history important for management of Rh-antigenized patient
• Fetal hemolytic disease similar or more severe in subsequent pregnancies
• 8% risk of a hydropic Rh-incompatible fetus, if prior history of hydrops due to Rh-incompatibility
• Horrific and hypoglycemia develop at similar gestational age or earlier in subsequent pregnancies
• Few fetuses develop hydrops in a first sensitized pregnancy

Treatment
• Serial MCA Doppler measurement to monitor fetal anemia
  • Need for intervention generally based on relationship of MCA PSV to gestational age
  • Zone A: Trimester
  • Zone B: Repeat measurement 5-7 days
  • Zone C: Repeat measurement 7-10 days
  • Zone D: Repeat measurement 2-3 weeks
• Serial amniocentesis
  • OD450 = amount of shift in optical density (OD) from linearity at 450 am
  • Spectrophotometric analysis of amniotic fluid
  • Correlates with amount of bilirubin in amniotic fluid
  • Estimates degree of fetal red cell hemolysis
  • Need for further intervention (next amniocentesis or cordocentesis) based on measurement
• MCA PSV and OD450 have similar accuracy of diagnosis
• MCA Doppler less invasive
• Decreased risk of complications associated with amniocentesis
• Management of un sensitized Rh(-) pregnant patient
  • Routine prophylaxis with Rh-immune globulin decreases risk of alloimmunization from 16% to 0.17%
  • Given at 28 weeks gestation
  • Also within 72 hours after delivery
• Should also be given for prophylaxis in other clinical scenarios
• After ectopic gestation
• After chorionic villus sampling or amniocentesis
• After abortion (spontaneous or elective)
• Management of a first Rh-sensitized pregnancy
  • No previous affected pregnancy
  • Antibody titer:
    • If anti-D antibody titer > 1:4 → Rh-sensitized
    • Use of anti-D antibody titer determines need for amniocentesis or increased surveillance
  • If anti-D antibody titer ≥ 1:8 → monthly anti-D titers and serial ultrasound
  • If anti-D antibody titer ≥ 1:8 → either serial MCA PSV or serial amniocentesis
• Determine fetal antigen status
  • Can determine paternal Rh antigen status if unknown
• Confirm fetal Rh status from DNA analysis of amniotic fluid
• If fetus Rh-negative or father Rh-negative, may follow with serial ultrasounds

• Management of subsequent Rh-sensitized pregnancy
• History of prior affected pregnancy: Hydrops, in utero transfusion (IUT), neonatal transfusion
• Maternal anti-D antibody titer ≥ 1:8
• Increased surveillance
• Serial MCA Doppler for PSV
• Amniocentesis for measurement of OD450 and to confirm fetal antigen status
• Fetal blood sampling and transfusion
  • Cordocentesis used to check for fetal anemia
  • Gold standard for measuring fetal hemocrit
• Ultrasound guidance used to access fetal circulation
• Typical IUT later
• Umbilical vein
• Intravenous, used if access to the vein limited
• Volume of blood transfused depends on:
  • Fetal gestational age
  • Fetal hematocrit
• Donor hematocrit
• Transfused red blood cells have reduced lifespan
• Fetal hemocrit decreases 1-2% per day (following transfusion)
• Requires IUT to be repeated after 2-3 weeks
• Complication rate of 2-5% reported
• Premature rupture of amniotic membranes
• Infection
• Air embolism
• Emergency cesarean section
• Fetal death

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls
• MCA velocity should be measured with zero degree angle of insonation near origin

SELECTED REFERENCES
**IMAGE GALLERY**

**Typical**
- *Left:* Transabdominal ultrasound during ICT shows the needle traversing the amniotic fluid (arrow), with the tip terminating at the base of the umbilical cord (scattered arrows).
- *Right:* Transabdominal ultrasound during another ICT shows the needle traversing the placenta (arrow) into the base of the cord in a 28 week fetus. Transabdominal needle placement can help stabilize the needle for insertion.

**Typical**
- *Left:* Coronal ultrasound shows bivacunos resulting from amniocentesis. Placental fluid (arrow), amnion (open arrow), and skin thickening (scarred arrow) are present.
- *Right:* Sagittal ultrasound of the same fetus shows marked skin edema, with thickening of the skin over the umbilical area and distorting the fetal profile.

**Typical**
- *Left:* Axial ultrasound of an amnionic fluid following intropositional transfusion shows a collection of blood in the abdomen (arrow). Access to the cord was limited. Intropositional cord cuts are slowly absorbed into fetal circulation.
- *Right:* Axial ultrasound shows a complication following transcervical. As it is seen in the cervix paracervical (arrow) and myometrium (curved arrow). A trial MFD 2 weeks later showed a normal heart and there was an uneventful term delivery.
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