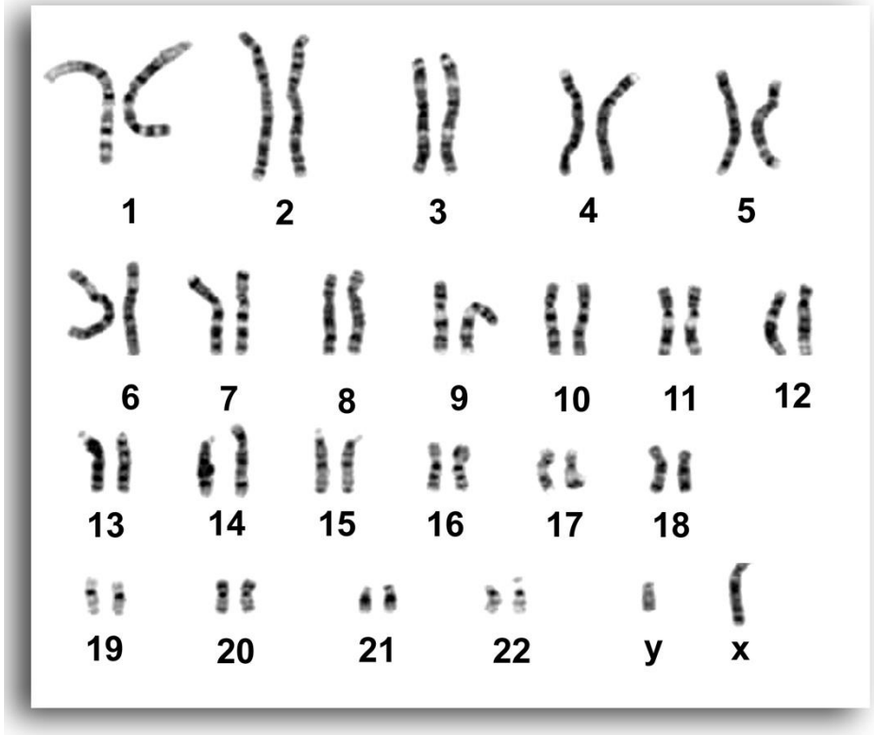
OB GYN SONOGRAPHY REVIEW

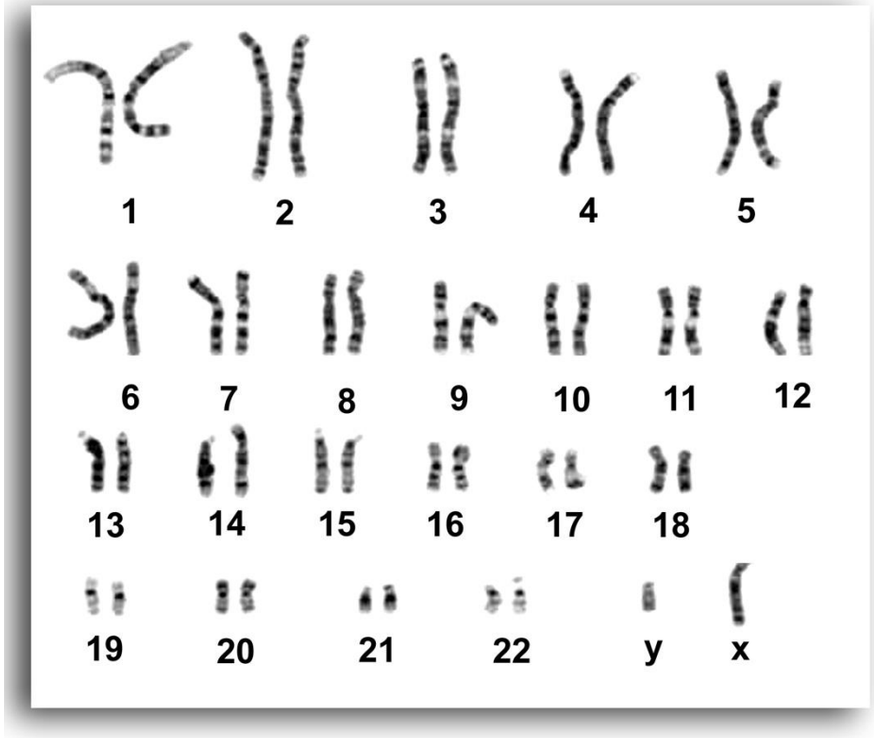
Prenatal Genetic Workup



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Course Outline

- Indications for genetic testing
- Maternal serum testing
- Invasive procedures
- Genetic anatomical survey
- Genetic abnormalities
- Syndromes, associations, sequences



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Indications for Genetic Testing

Standard Practice

- "Screening" sonogram at 18 – 20 weeks:
  - Establish fetal number
  - Establish fetal viability
  - Obtain baseline fetal biometric measurements
  - Provide high-resolution, detailed anatomic survey of all fetal organ systems
  - Assess integrity of placenta, cervix, amount of amniotic fluid present

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Increased Risk of Fetal Disorders

- Maternal age ≥ 35 years at delivery
- Family history of congenital anomalies
- Prior pregnancy with congenital abnormality
- Prenatal exposure to noxious substance (teratogen)
- Maternal diabetes

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Maternal Serum Testing

Standard Practice

- Identify variations of levels of pregnancy-produced substance associated with congenital abnormalities
- *Triple screen* consists of:
  - Maternal serum alpha-fetoprotein (MSAFP)
  - Human chorionic gonadotropin, beta subunit (beta-hCG)
  - Estriol (µE3)
- *Quad screen* adds:
  - The hormone inhibin A (inhA)

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Maternal Serum AFP (MSAFP)

- Protein produced by fetal liver, yolk sac, and GI tract
- In normal pregnancies, levels rise predictably with progressing gestational age
- Peaks at ≈ 14 weeks, begins to decline ≈ 30 weeks
- Levels dependent on gestational age (GA)
- Important to accurately determine GA before interpreting results

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Maternal Serum AFP (MSAFP)

- *Reduced* levels may indicate:
  - Trisomy 13
  - Trisomy 18
  - Trisomy 21
  - Turner syndrome
- *Elevated* levels may indicate:
  - Open neural tube defects
  - Gastroschisis

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Human Chorionic Gonadotropin (hCG)

- Glycoprotein produced trophoblastic tissue
- Not very sensitive as an isolated indicator of nonchromosomal congenital anomalies
- In combination with “soft sonographic markers, elevated levels are associated with high incidence of chromosomal abnornmalities
- Important to accurately determine GA before interpreting results

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Estriol (μE3)

- One of three primary types of estrogen
- Produced by placenta, fetal liver and adrenal glands
- Present in maternal serum in significant amounts during pregnancy
- Useful in assessing risk of fetal anomalies, genetic abnormalities, poor outcomes
- ⬇ amounts associated with adverse outcomes
- ⬇ amounts associated with trisomies 18 and 21

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PRENATAL GENETIC WORKUP

Maternal Serum Markers				
Anomaly	**MSAFP**	**βhCG**	**μE3**	**inhA**
Trisomy 13	Low	n/a	Low	n/a
Trisomy 18	Low	Low	Low	Low/normal
Trisomy 21	Low	High	Low	High
Neural tube defects	High	Normal	Low	Normal
Turner syndrome	Low	Low	Low	Low/normal
Cardiac defects	High	Low	Low	n/a
Abdominal wall defects	High	n/a	n/a	n/a

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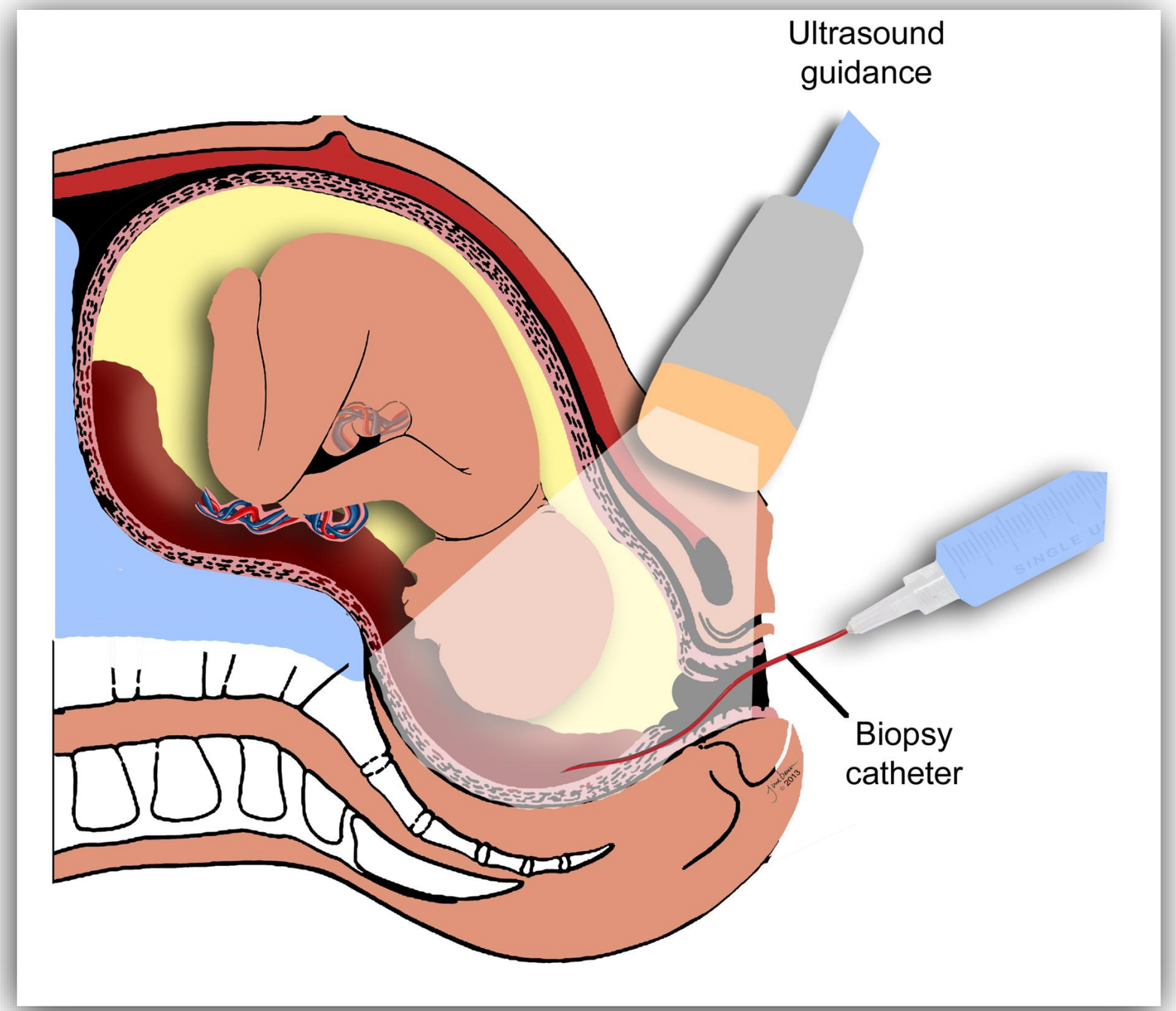
Invasive Procedures

Chorionic Villus Sampling

- Needle or catheter is advanced into chorion frondosum under US guidance
- May be performed transabdominally or transcervically
- Potential risks may include:
  - Spontaneous abortion
  - Maternal sepsis
  - Perforation of amniotic sac
  - Unexplained mid-trimester oligohydramnios
  - Limb reduction defects

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CHORIONIC VILLUS SAMPLING



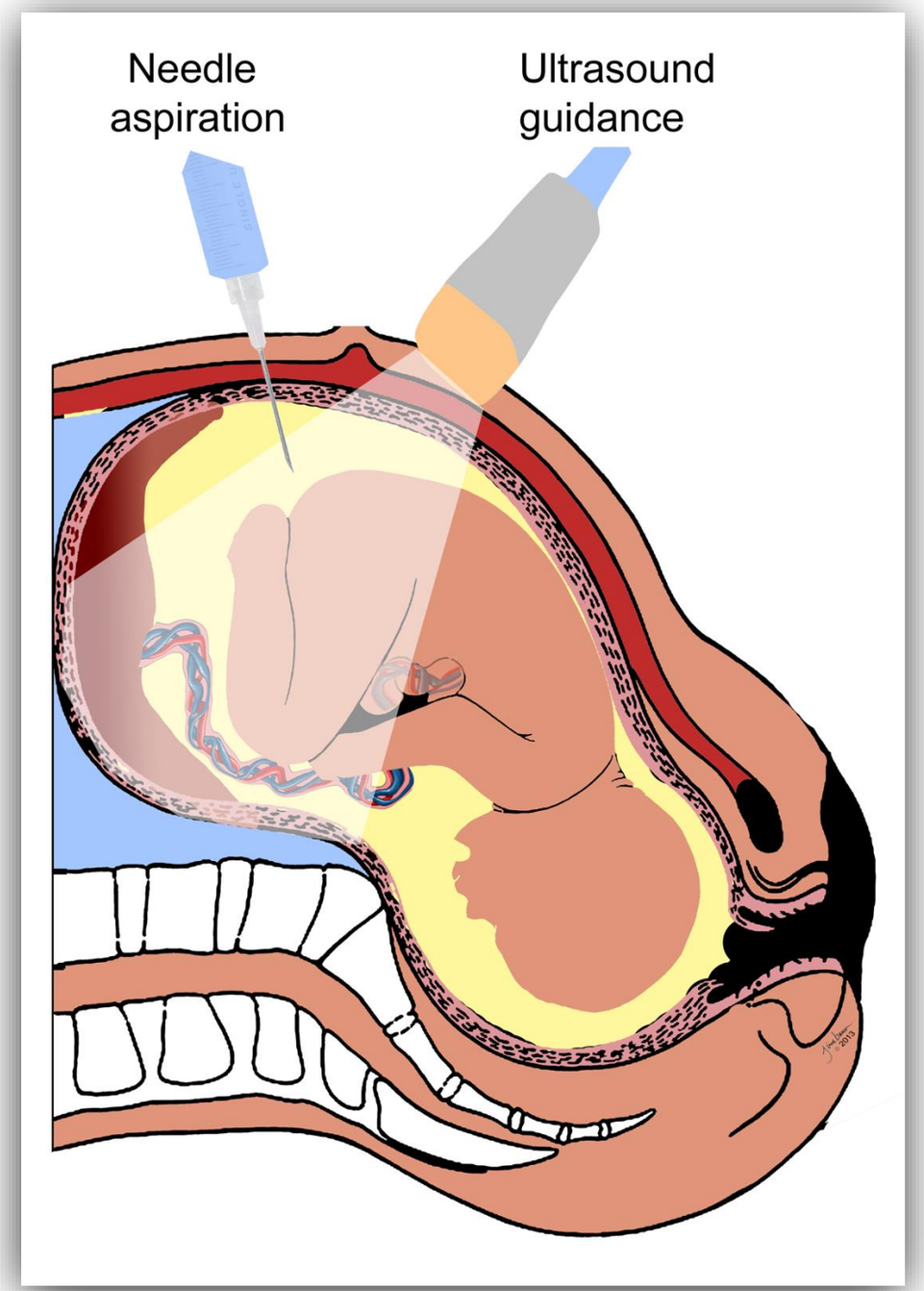
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Amniocentesis

- Needle is advanced transabdominally into amniotic cavity and small amount of fluid is withdrawn
- Fluid may be analyzed for genetic testing (early) or fetal lung maturity (later)
- Biochemical assays for genetic testing include:
  - Amniotic fluid alpha-fetoprotein (AFAFP)
  - Acetylcholinesterase
  - Gamma-glutamyl transpeptidase (GGPT)
  - Bilirubin

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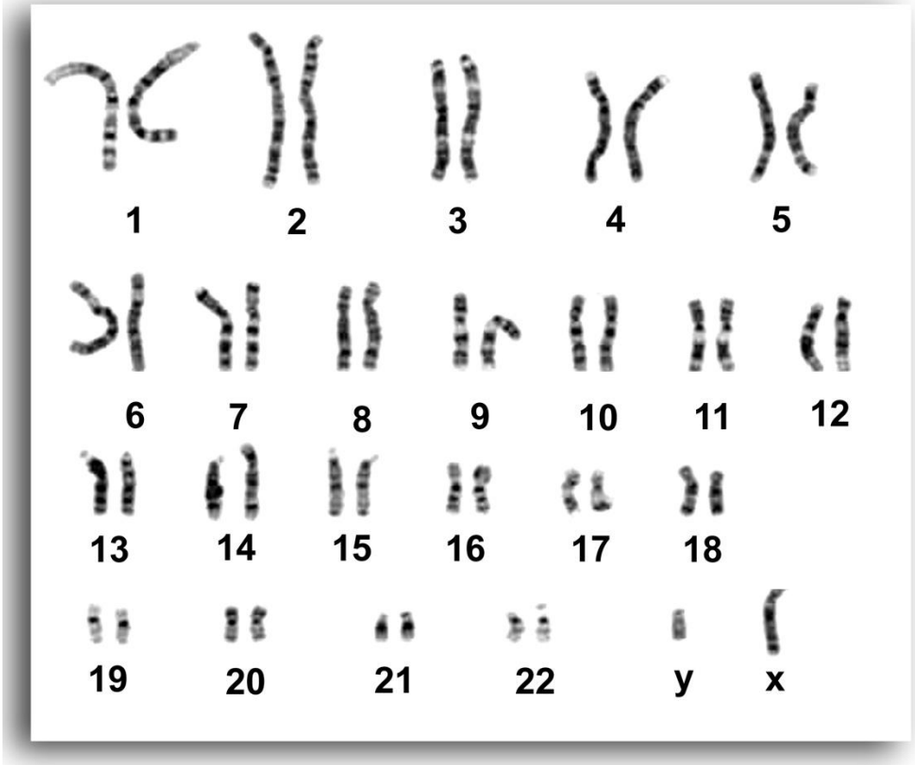
AMNIOCENTESIS



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Amniocentesis

- Chromosomal analysis possible through direct analysis of fetal DNA
- DNA present in free-floating fetal cells from skin, bladder, GI tract, and amnion
- Karyotyping: mapping of fetal chromosomes



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Amniocentesis

- Indications (genetic) include:
  - Advanced maternal age (≥ 35 years)
  - Previous fetus with aneuploidy
  - Parental balanced translocation
  - X-linked recessive disorder
  - Other genetic disorders
  - Fetal anomaly
  - Fetal sex identification
  - Paternity testing

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Amniocentesis

- Indications (MFM) include:
  - Confirmation of lung maturity
  - Evaluation of intrauterine infection
  - Rh isoimmunization
  - Polyhydramnios

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Amniocentesis

- Risks and complications include:
  - Miscarriage (0.06 - 0.5%)
  - Cramping
  - Bleeding
  - Amniotic fluid leakage (1 -2%)
  - Needle injuries (rare)
  - Rh sensitization

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Genetic Anatomical Survey

Rationale

- Provides useful adjunct in earlier detection of some fetal conditions
- Best estimate of risk achieved by integrating:
  - Genetic sonogram
  - Maternal serum screening
  - Maternal age
- *Soft sonographic markers*: minor US abnormalities, considered variants of normal, that do not constitute frank structural defects

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Rationale

- Soft sonographic markers include:
  - Nuchal translucency
  - Nuchal thickening
  - Hyperechogenic bowel
  - Echogenic intracardiac focus
  - Choroid plexus cysts
  - Pyelectasis

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Nuchal Translucency

- Hypoechoic area located between skin and posterior cervical soft tissue (lymphatic fluid)
- Small amount of fluid is normal up to 14 weeks
- Increase in amount of fluid can indicate
  - Specific congenital abnormalities
  - Increase in perinatal morbidity and mortality

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Nuchal Translucency

- Increased translucency value associated with:
  - Trisomies (80-90% detection rate)
  - Diaphragmatic hernia
  - Turner syndrome
  - Congenital heart disease
  - Omphalocele
  - Skeletal dysplasias
  - VACTERL association

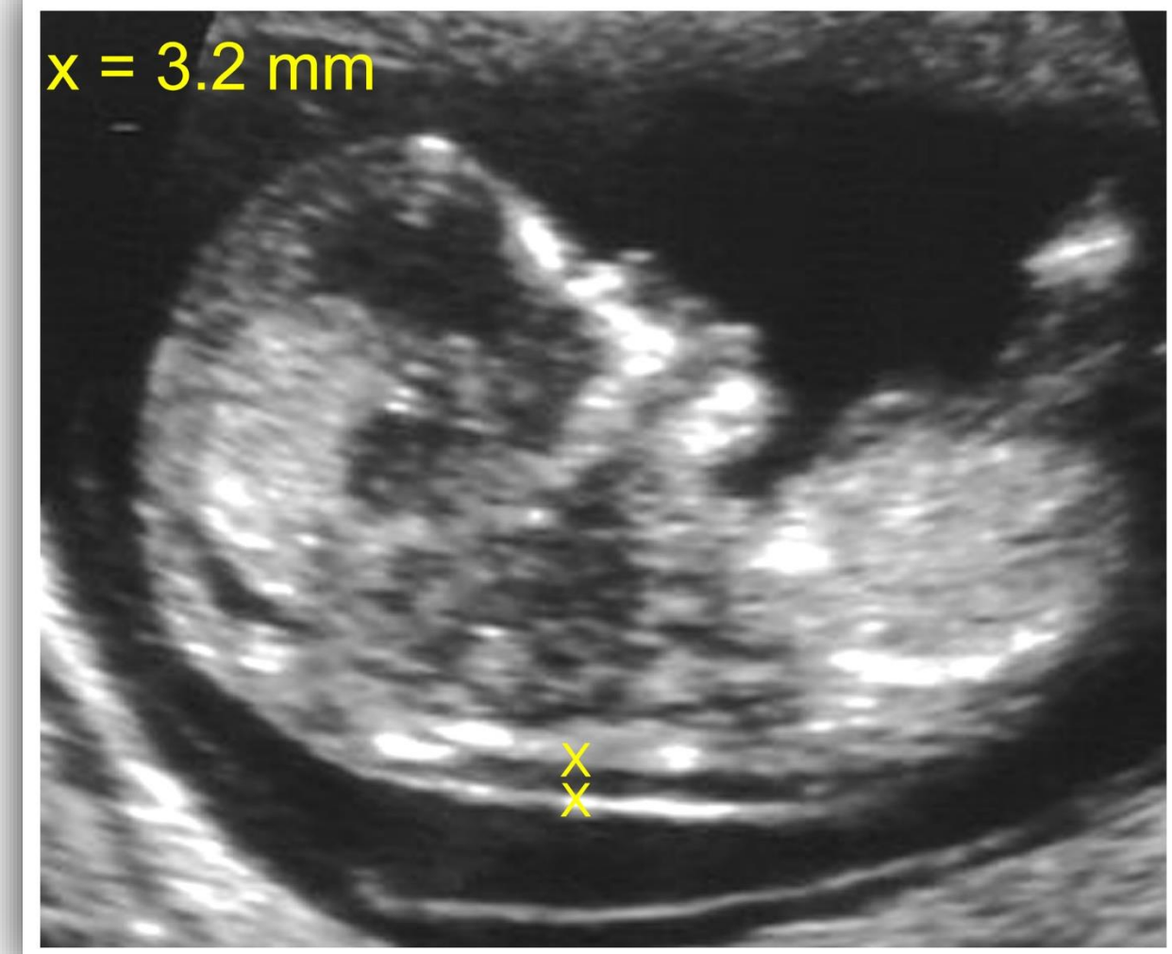
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Nuchal Translucency

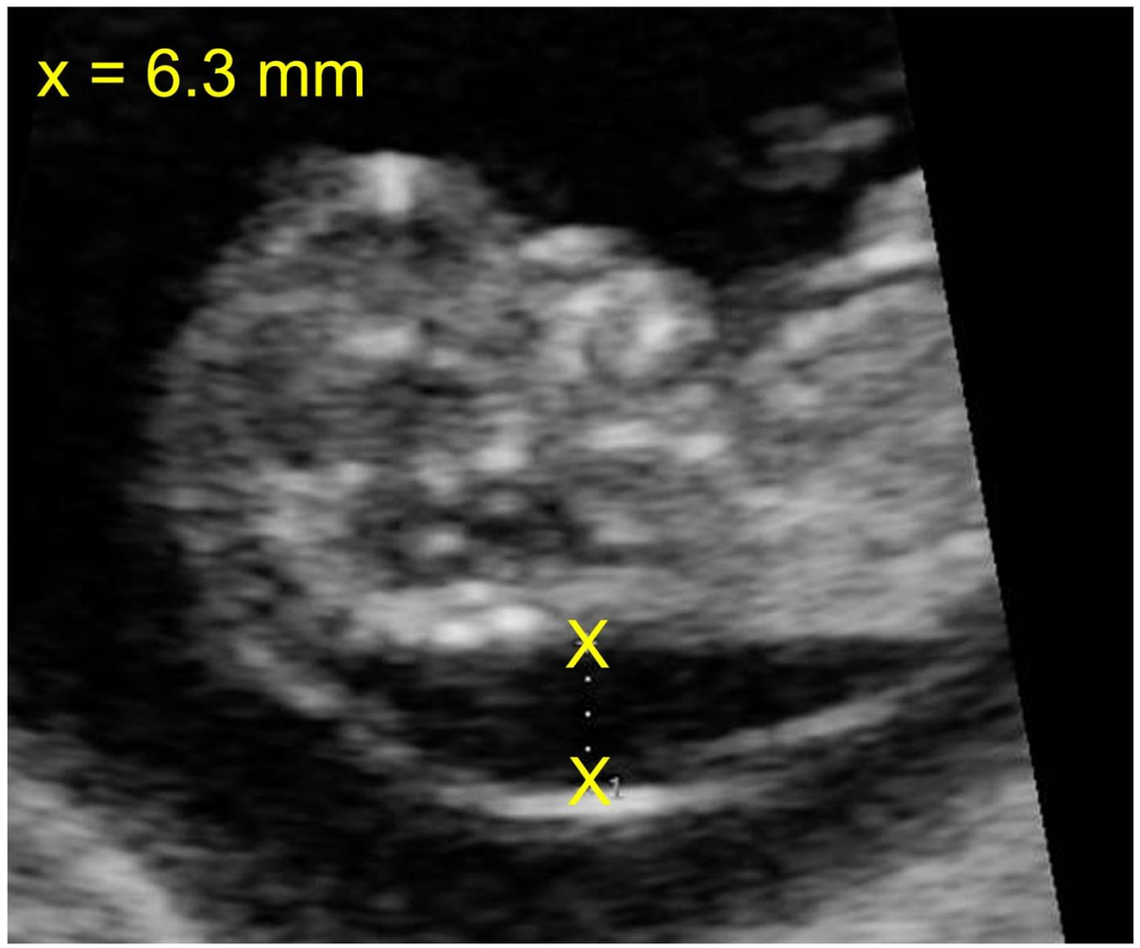
- Sonographic signs:
  - Measured when CRL is 45 – 84 mm
  - Normal value is < 2.5 mm (matched to maternal age and CRL)
  - There should be no septations within the translucent region
  - Abnormal values are ≥ 6 mm

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NUCHAL TRANSLUCENCY



12 weeks
Normal



10 weeks
Abnormal

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Nuchal Thickening

- Increased thickness of soft tissue in posterior fetal cervical region
- Differentiated from nuchal translucency
  - (1^{st} vs. 2^{nd} trimester)
- Measured between 15 – 20 weeks
- Most sensitive and specific 2^{nd} trimester marker for Down syndrome (trisomy 21):
- False positive rates ≈ 1%

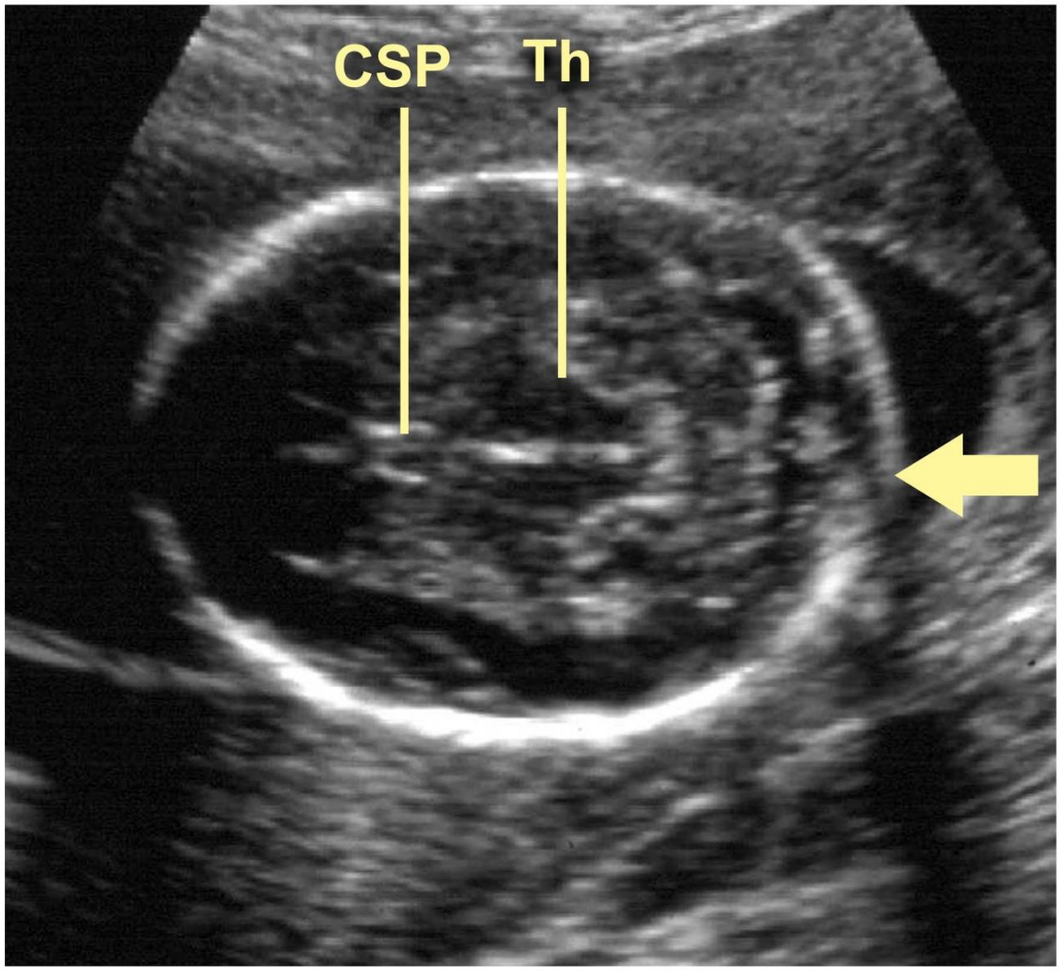
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Nuchal Thickening

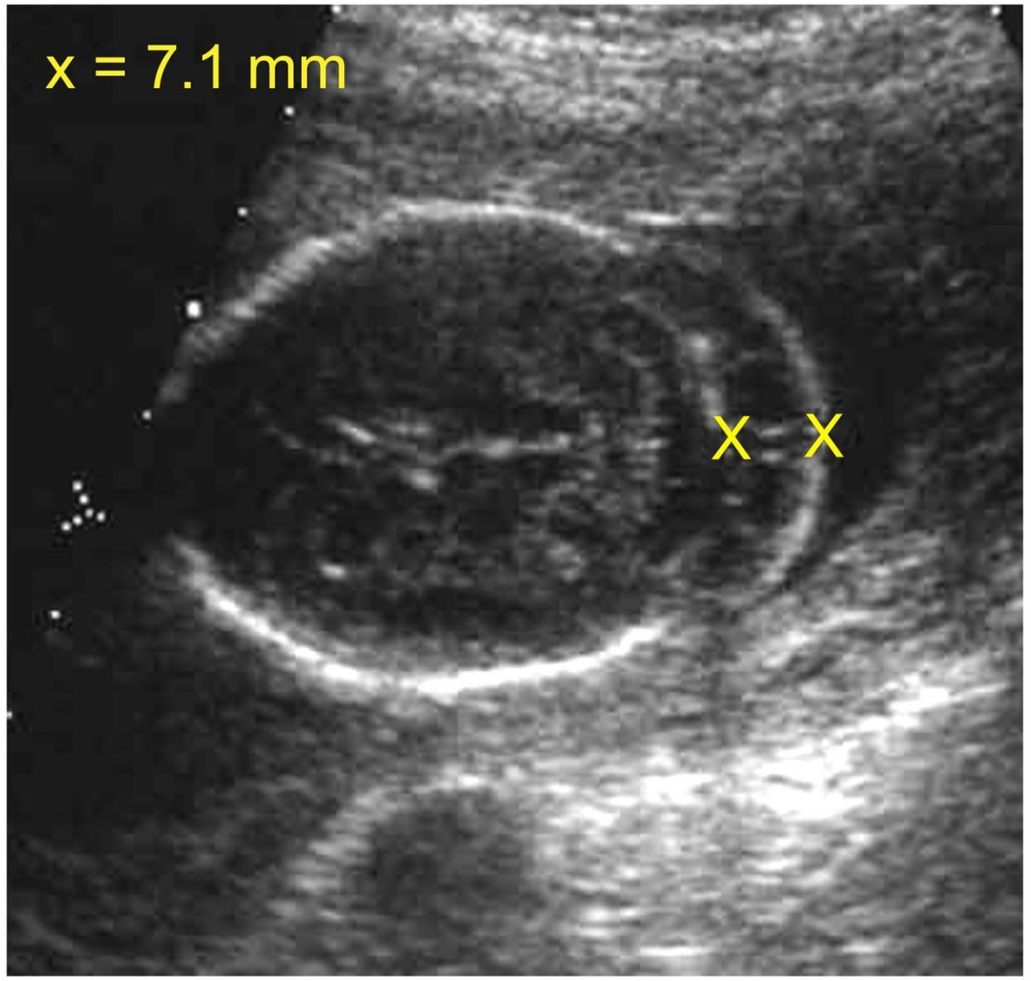
- Sonographic signs:
  - Measured in an axial oblique section at level of posterior fossa
  - Normal value < 6 mm
  - Some authors use 5 mm as cutoff for normal

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NUCHAL THICKENING



Normal



Thickened

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Hyperechogenic Bowel

- Echogenicity of fetal bowel in 2nd trimester is variable
- Normal bowel echogenicity:
- ⇧ adjacent parenchymal organs
- ⇩ adjacent bone

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Hypoechogenic Bowel

- Has been associated with increased risk for :
  - Aneuploidy (trisomies 13, 18, and 21)
  - Cystic fibrosis
  - Congenital infections (TORCH)
  - Congenital bowel malformations
  - Intra-amniotic hemorrhage
  - Meconium ileus
  - Perinatal complications (IUGR)

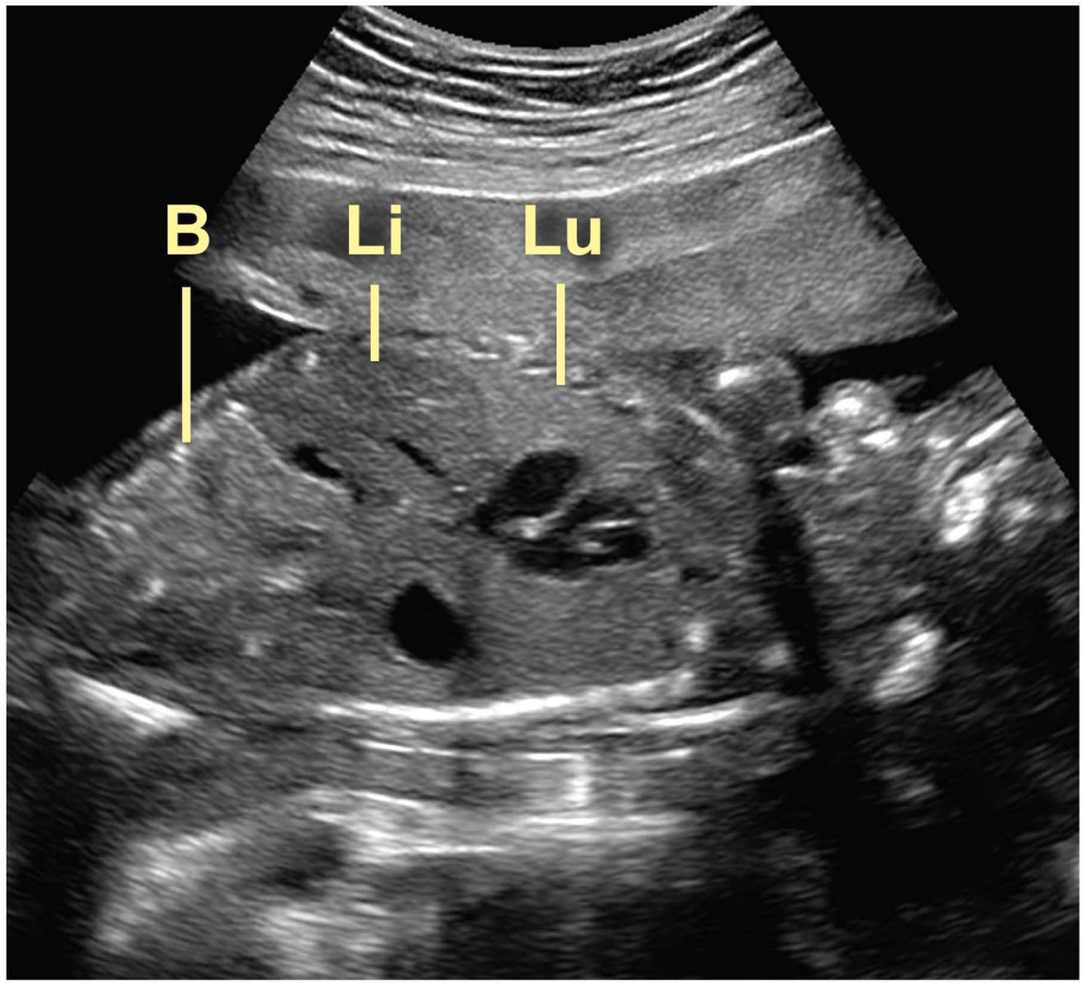
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Hypoechogenic Bowel

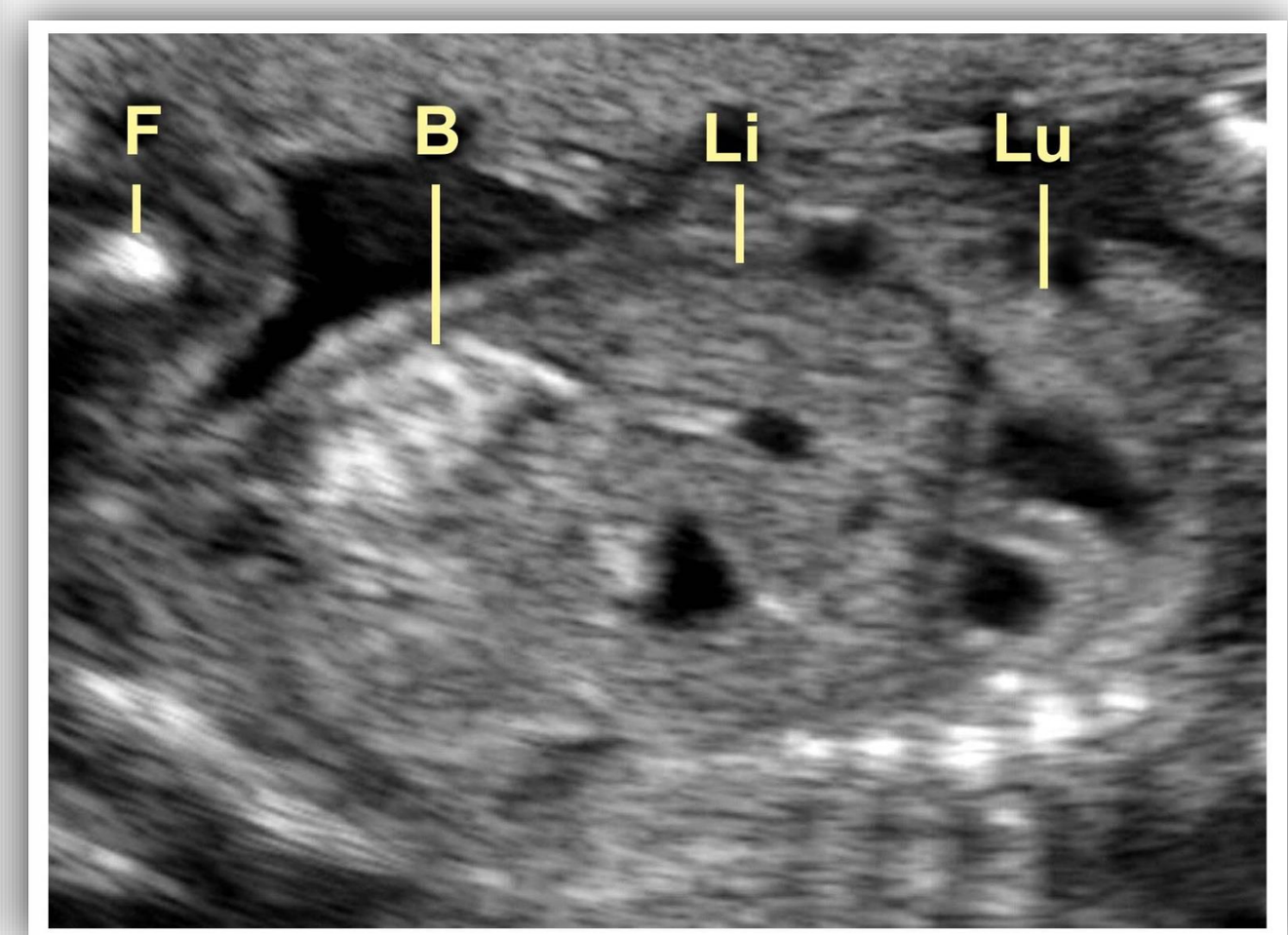
- Sonographic signs:
  - Echogenicity ≥ echogenicity of bone

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HYPOECHOGENIC BOWEL



Normal bowel



Echogenic bowel

B = bowel Lu = lung
Li = liver F = femur

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Echogenic Intracardiac Focus

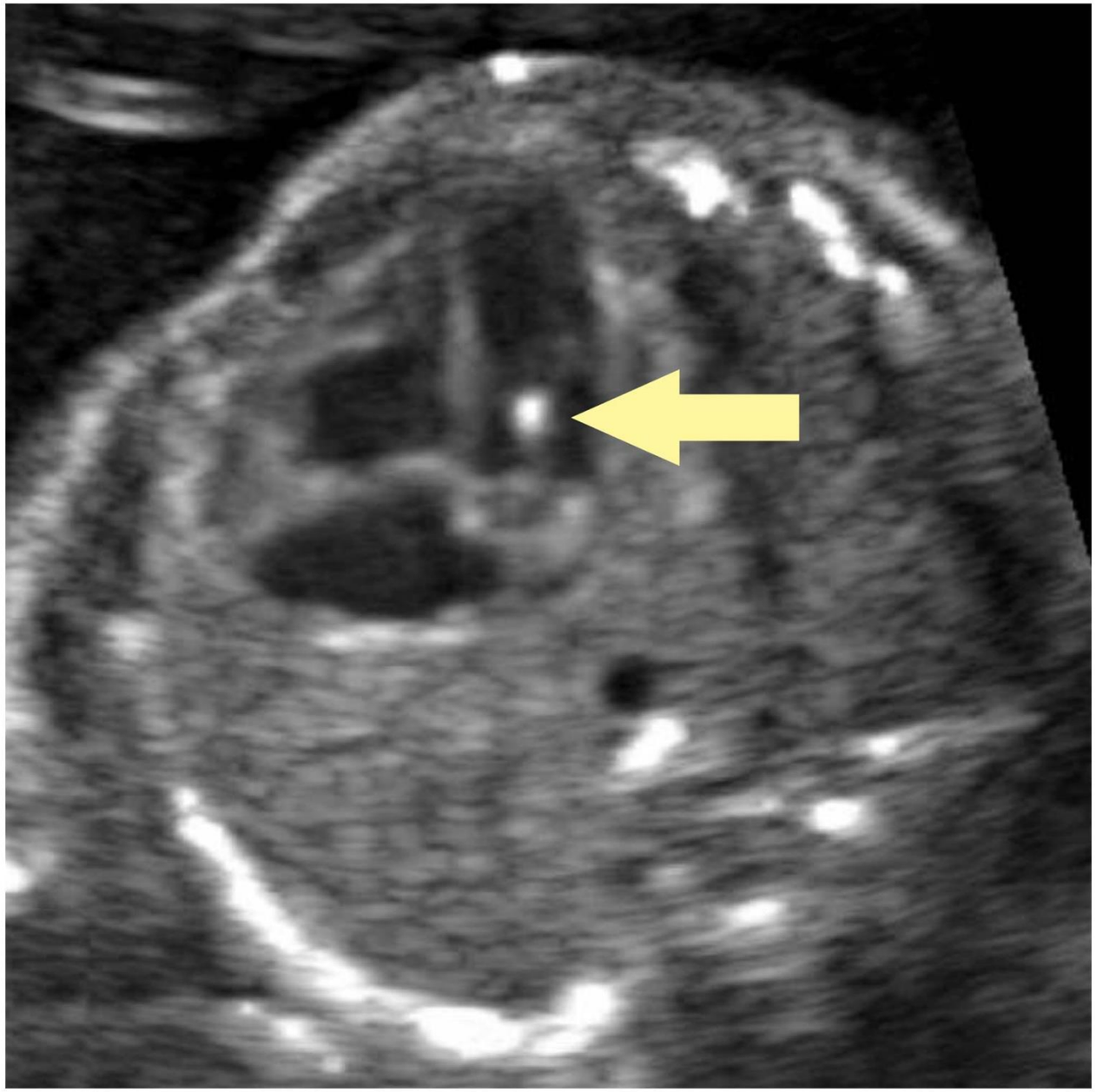
- Seen in about 6% of ALL fetuses
- 90% of time, no concomitant abnormalities
- In low-risk fetuses, generally disappear on subsequent US studies
- In fetus *at risk* for aneuploidy, may represent calcification of papillary muscle
  - Increases probability of trisomy 13 or 21

Echogenic Intracardiac Focus

- Sonographic signs:
  - Punctate, brightly echogenic focus in heart
  - Most commonly in left ventricle

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ECHOGENIC INTRACARDIAC FOCUS



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Choroid Plexus Cysts

- Discrete, well-circumscribed fluid collections within the echogenic choroid plexus
- Located in lateral cerebral ventricle
- Seen in 1– 2 % of all fetuses and almost always regress by 26 weeks
- However, there is a small but statistically significant association with trisomy 18
- Identification warrants follow-up genetic testing in high-risk patients and when other anatomic anomalies are demonstrated

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Choroid Plexus Cysts

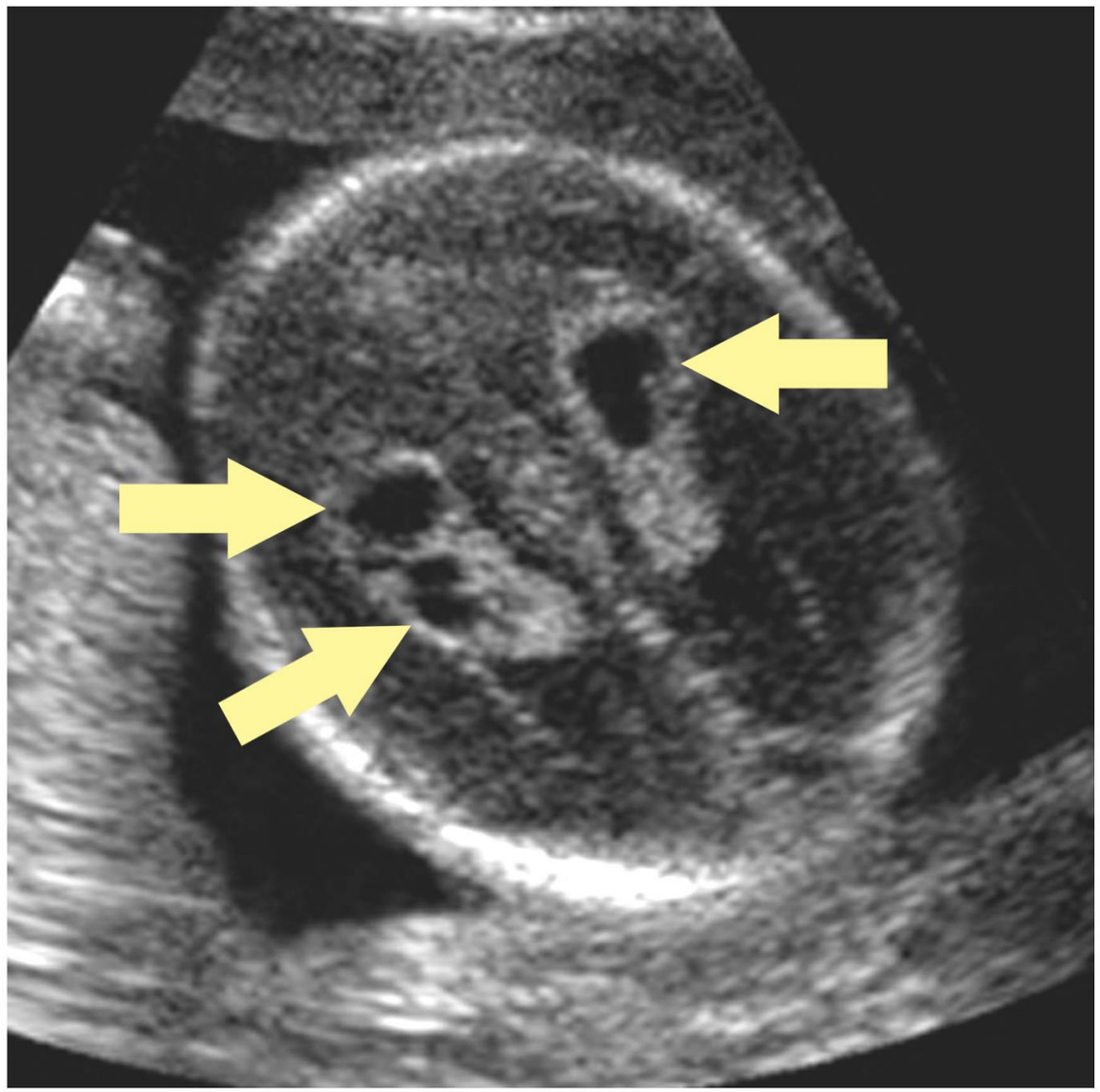
- Sonographic signs:
  - Single or multiple cysts
  - Surrounded by echogenic choroid plexus
  - Located in lateral cerebral ventricle
  - May be uni- or bilateral

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CHOROID PLEXUS CYST



Single, unilateral



Multiple, bilateral

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Pyelectasis

- Dilatation of renal pelvis 5 – 10 mm with urine *without* calyceal involvement
  - > 10 mm dilatation and calyceal involvement more likely obstructive uropathy
- Seen in 2% of normal fetuses
- Seen in 17 – 25% of fetuses with trisomy 21
- As isolated finding, associated with 3.3% risk of Down syndrome

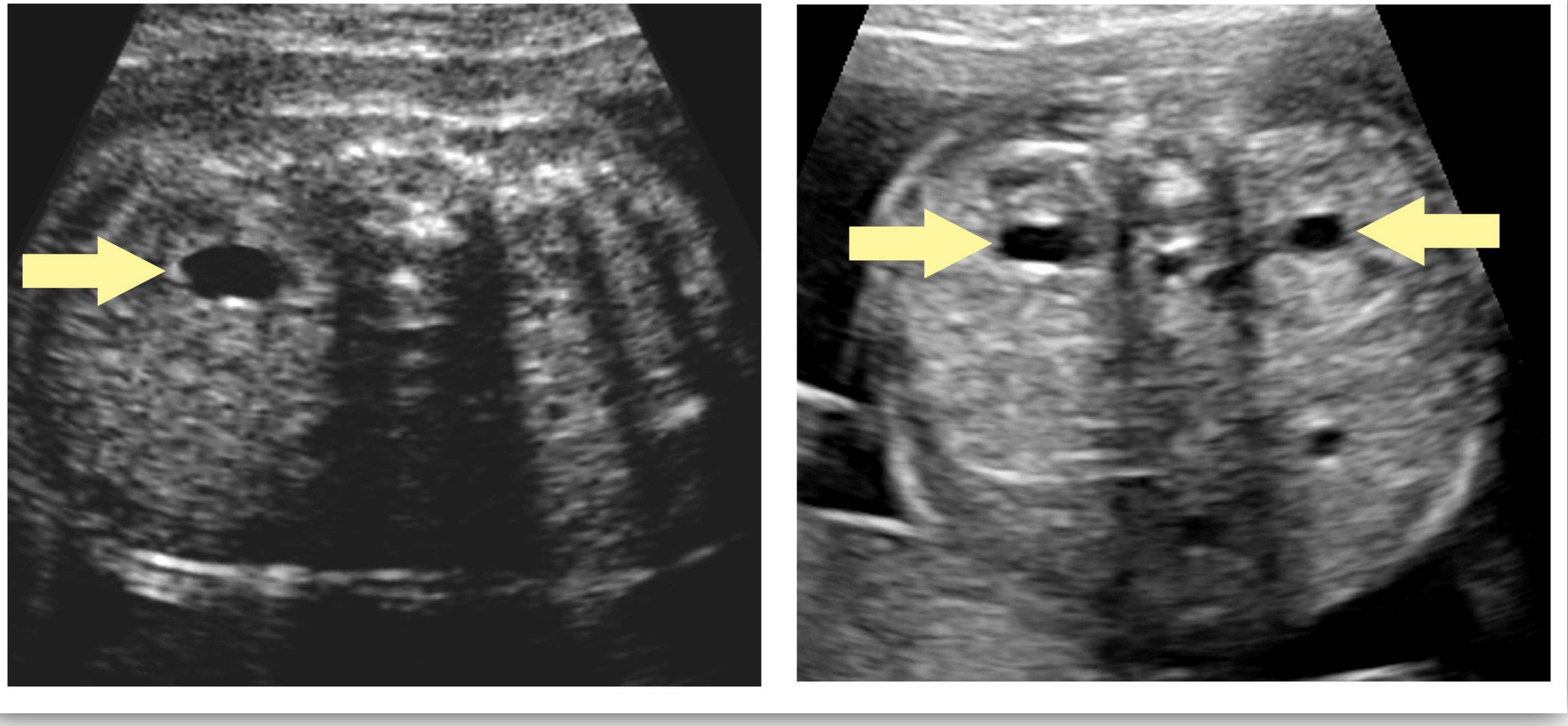
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Pyelectasis

- Sonographic signs:
  - Measurement taken in axial plane at level of renal hilum
  - Uni- or bilateral renal pelvis dilatation
  - Resolves by 26 weeks
  - No associated caliectasis or ureteral dilatation

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PYELECTASIS



Unilateral **Bilateral**

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Genetic Abnormalities

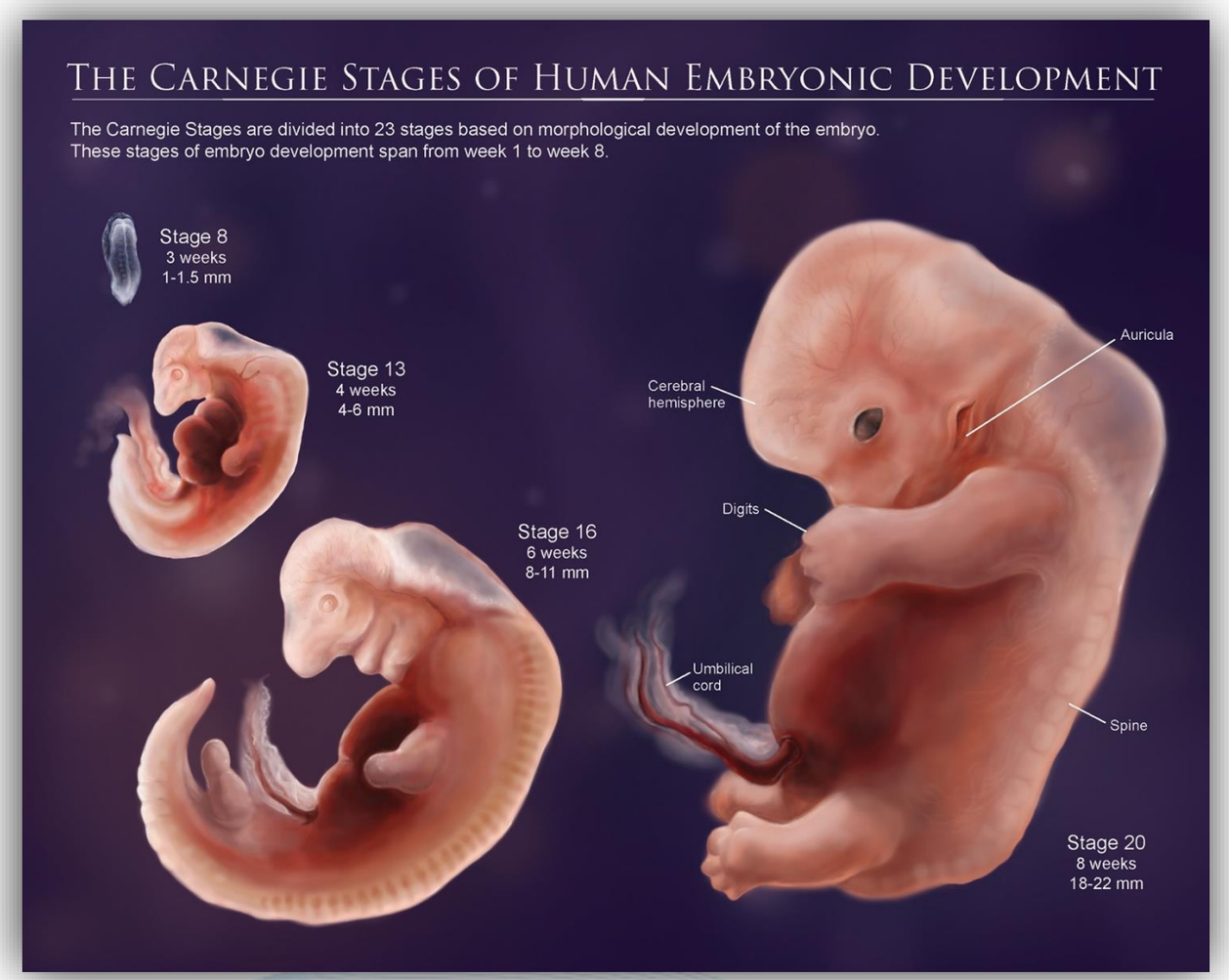
Teratogenesis

- Creation of a deformed organism
- *Terato* = monster; *genesis* = creation
- Teratogen: any substance that causes abnormal structural development in an embryo
- Causes include:
  - Genetic factors
  - Environmental factors
  - Multifactorial inheritance

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Sensitive Period Concept

- Individual embryonic structures are sensitive to specific teratogens at given times in early gestation and ONLY at those given times



Categories of Teratogens

- Physical agents such as:
  - Radiation
  - Heat
  - Mechanical factors (amniotic bands)
  - Drugs and chemical agents
- Maternal factors:
  - Alcohol
  - Coumadin
- Maternal factors:
  - Diabetes
  - Infections (TORCH)

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Terminology

- Karyotype: complete set of chromosomes that a species contains in its genetic makeup (genotype)
- Single-gene disease: medical condition arising from single defective gene
- Aneuploidy: condition characterized by abnormal number of chromosomes (excess or deficient)
- Autosomal recessive disorder: defective recessive genes contributed by each parent
- Autosomal dominant disorder: defective dominant gene contributed by a single parent
- X-linked disease: characteristics or traits influence by genes on the X chromosome

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Aneuploidy

- Types of anomalies characterized by excessive or deficient number of chromosomes include:
  - Triploidy: presence of 3 chromosome across the karyotype
  - Trisomy: presence of 3 chromosomes in a specific location, i.e., trisomy 13, 18, 21 21
  - Disomy: presence fo 2 copies of a chromosome
  - Monosomy: lack of one of the normally paired chromosomes
  - Tetrasomy: presence of 4 copies of a numbered chromosome
  - Pentasomy: presence of 5 copies of a numbered chromosome

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Triploidy

- Lethal genetic syndrome in which conceptus receives an entire extra set of chromosomes
- 80% of pregnancies end in early pregnancy failure
- Frequently associated with:
  - Placental abnormalities particularly partial hydatidiform mole
  - Resulting from excessive paternal genetic material

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Triploidy

- Associated anatomic abnormalities include:
  - Central nervous system anomalies
  - Cardiac anomalies
  - Genitourinary anomalies
  - Hand and foot anomalies
  - Craniofacial anomalies

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Triploidy

- Sonographic markers include:
  - Molar placenta changes
  - Gross and extensive fetal anatomic anomalies as listed above

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Trisomy 21 (Down Syndrome)

- Most common congenital syndrome observed in livebirths
- 1 : 600 – 800 newborns
- Incidence increases with advancing maternal age
  - > 35 years - 1 : 275 pregnancies
  - > 40 years – 1 : 75 pregnancies
- Soft sonographic markers play role in overall risk assessment

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Trisomy 21 (Down Syndrome)

- Associated anatomic abnormalities include:
  - Cardiac anomalies
  - Gastrointestinal anomalies
  - Craniofacial anomalies
  - Skeletal anomalies

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Trisomy 21 (Down Syndrome)

- Sonographic markers include:
  - Nuchal fold thickening
  - Hyperechoic/echogenic bowel
  - Mildly shortened femur and/or humerus
  - Echogenic intracardiac foci
  - Renal pyelectasis
  - Heart defects including: VSDs, ASDs, mild ventriculomegaly

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Trisomy 21 (Down Syndrome)

- Sonographic markers include:
  - Mild brachycephaly
  - Under-ossification of nasal bone
  - Duodenal atresia
  - Cystic hygroma
  - Diaphragmatic hernia

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Trisomy 18 (Edwards Syndrome)

- 2nd most common autosomal trisomy condition
- 1 : 6,000 live births
- Major structural anomalies more common that in trisomies 13, 21
- > 130 anatomic aberrations reported
- Cardiac defects most common

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Trisomy 18 (Edwards Syndrome)

- Associated anatomic abnormalities include:
  - Cardiac anomalies
  - Central nervous system anomalies
  - Face and neck anomalies
  - Skeletal anomalies
  - Gastrointestinal anomalies
  - Genitourinary anomalies
  - Others

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Trisomy 18 (Edwards Syndrome)

- Sonographic markers include:
  - Choroid plexus cysts (present in 1/3 of fetuses)
  - Brachycephaly
  - Single umbilical artery

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Trisomy 13 (Patau Syndrome)

- 3rd most common autosomal trisomy condition
- Only 13% are born live or survive more than several postnatal days
- Extensive structural anomalies
- Most common are cardiac and CNS anomalies

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Trisomy 13 (Patau Syndrome)

- Associated anatomic abnormalities include:
  - Cardiac anomalies (50– 80%)
  - Central nervous system anomalies (70%)
  - Face and neck anomalies
  - Skeletal anomalies
  - Gastrointestinal anomalies
  - Others

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Trisomy 13 (Patau Syndrome)

- Sonographic markers include:
  - Echogenic intracardiac foci
  - Renal pyelectasis
  - Echogenic bowel
  - Mild ventriculomegaly
  - Increase nuchal thickness
  - Hydrops fetalis

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Syndromes, Associations & Sequences

Terminology

- Syndrome: recognizable appearance of several clinical features, often occurring together, that serve as a harbinger of the presence of other, less apparent, abnormalities
- Association: presence of two or more congenital traits, one of known genetic origin, occurring together more often than possible by chance
- Sequence: series of clinical features that arise sequentially from a single cause
  - Potter sequence: constellation of abnormal facies, IUGR, limb anomalies resulting from chronic oligohydramnios (*See GU module*)

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Common Congenital Syndromes

- Amniotic band syndrome
- Beckwith-Wiedemann syndrome
- Caudal regression syndrome
- Sirenomelia
- Ellis-van Creveld syndrome
- Meckel-Gruber syndrome
- Pentalogy of Cantrell

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Amniotic Band Syndrome

- Collection of multiple, bizarre anomalies cause by constricting bands of amniotic tissue
- Early rupture of amnion may result in bands that adhere to fetus and restrict tissue growth
- Multiple, severe, syndromal findings include:
  - Limb defects
  - Craniofacial defects
  - Visceral defects

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Amniotic Band Syndrome

- Limb defects:
  - Amputations
  - Clubfeet
  - Constriction rings
  - Pseudosyndactyly
- Craniofacial defects:
  - Anencephaly
  - Encephalocele
  - Facial clefting
  - Severe facial dysmorphia
- Visceral defects:
  - Gastroschisis
  - Omphalocele

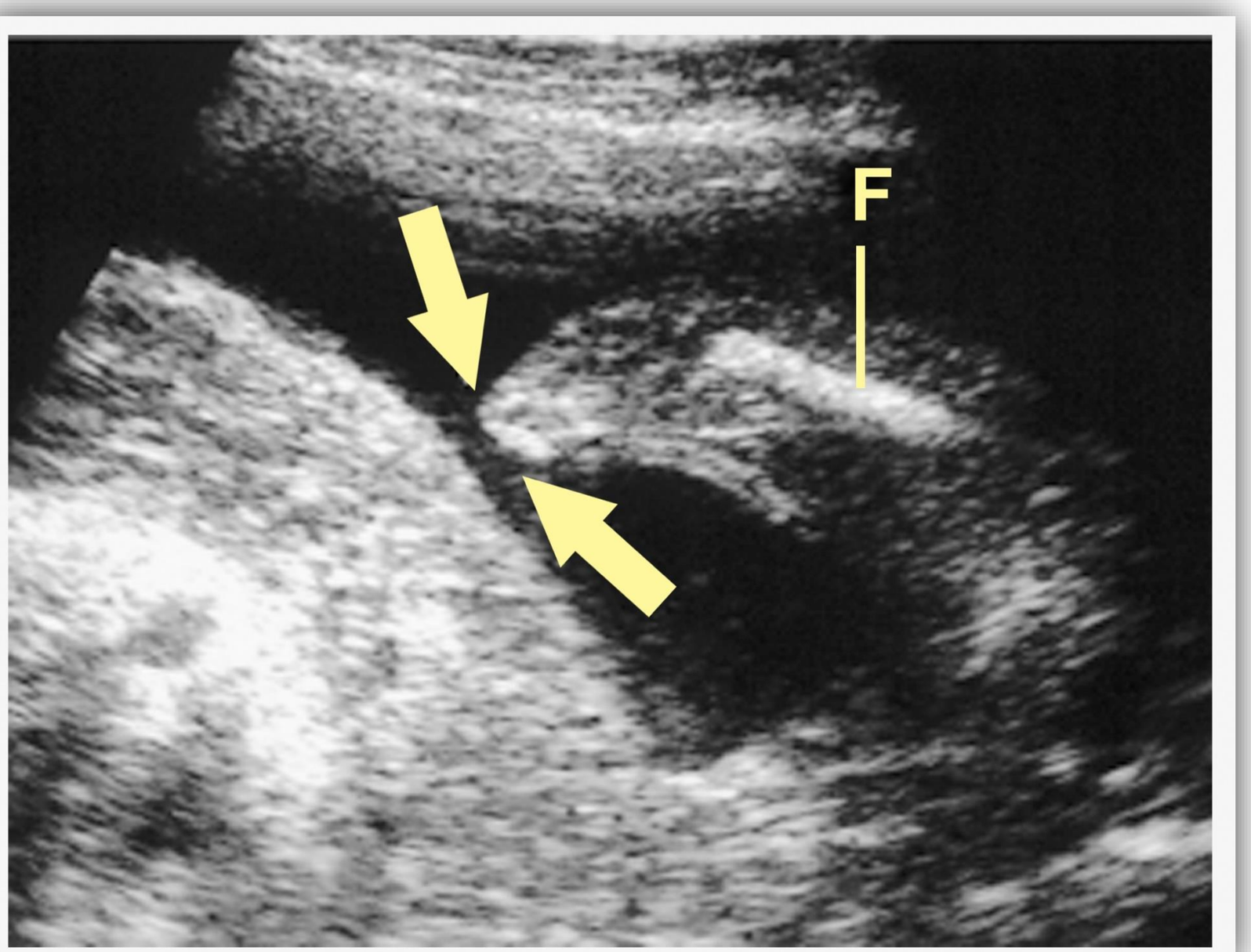
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Amniotic Band Syndrome

- Sonographic signs include:
  - Presence of two or more of mentioned defects
  - Identification of an echogenic, linear structure attached to fetus
  - Fetal postural deformities

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AMNIOTIC BAND SYNDROME



Hand amputation (arrows)
F = forearm

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Beckwith-Wiedemann Syndrome

- A congenital overgrowth syndrome caused by genetic overproduction of growth hormone and insulin-like growth factor
- Multiple organ systems may be affected, i.e., GU, GI, cardiac, genitalia
- Classic syndromal findings include:
  - Omphalocele
  - Macroglossia
  - Visceromegaly (liver, kidneys)

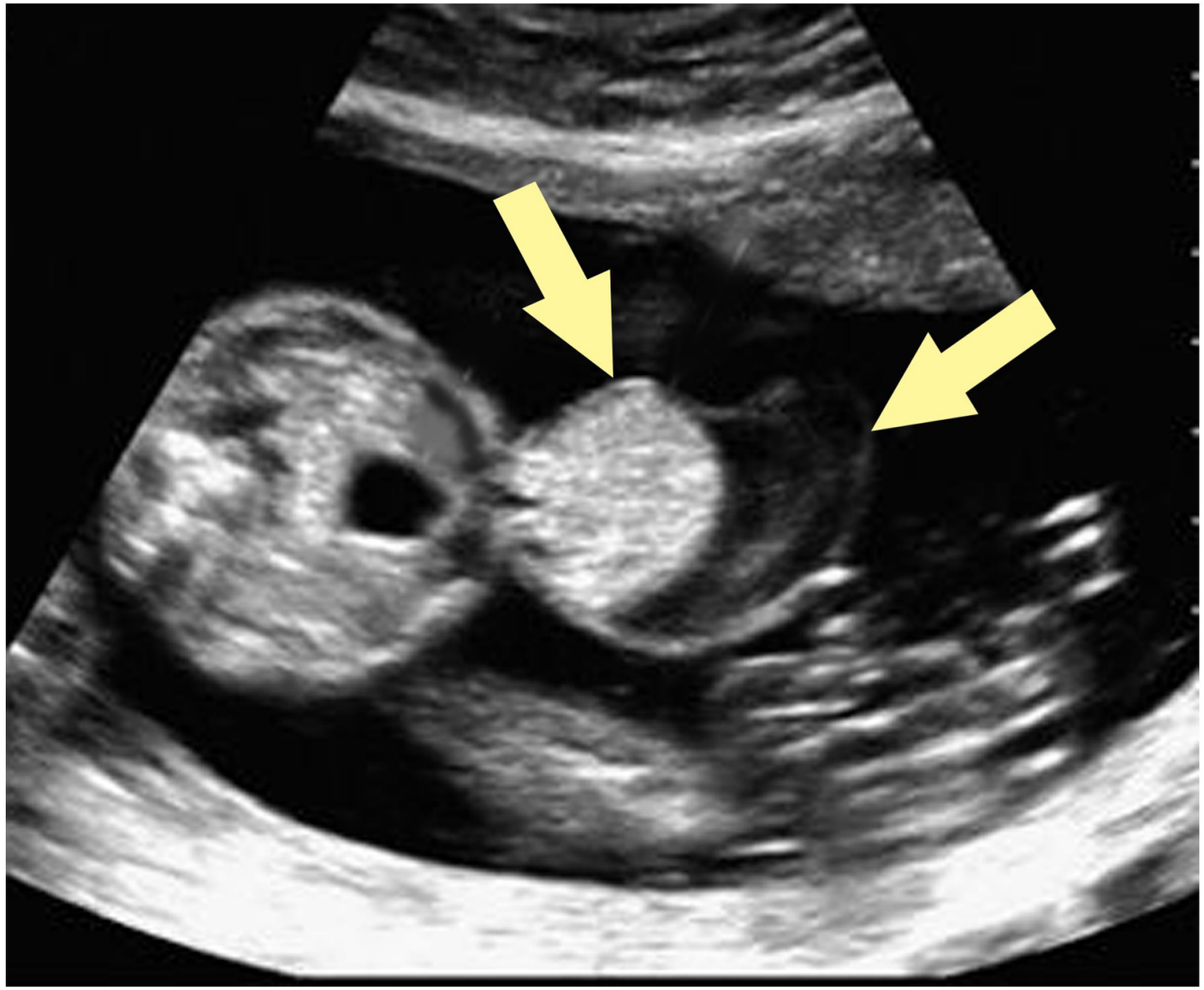


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Beckwith-Wiedemann Syndrome

- Sonographic signs include:
  - Omphalocele
  - Macroglossia
  - Hepatomegaly
  - Nephromegaly
  - Polyhydramnios
  - Placentomegaly

BECKWITH-WIEDEMANN SYNDROME



Omphalocele (arrows)

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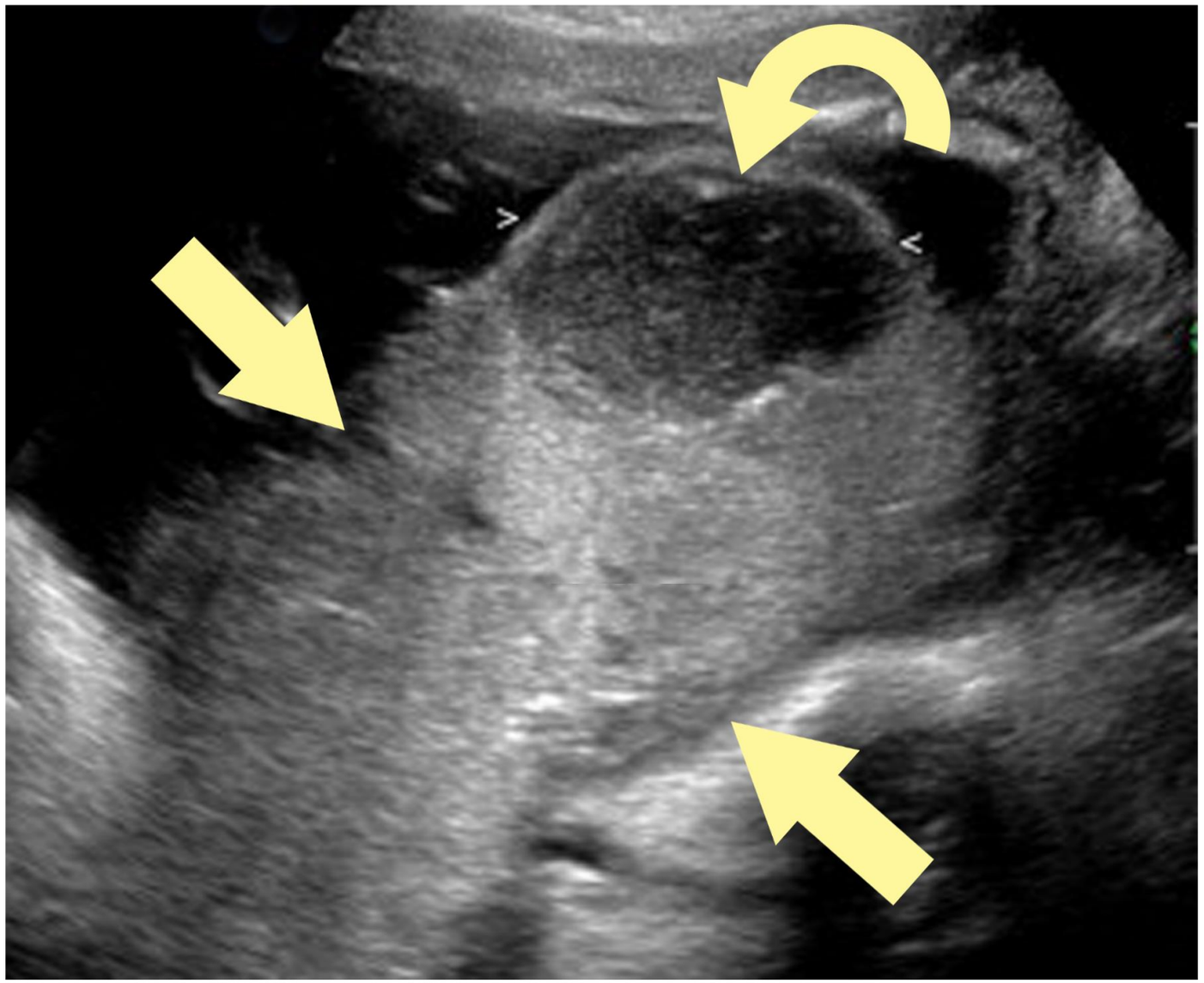
BECKWITH-WIEDEMANN SYNDROME



Macroglossia

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BECKWITH-WIEDEMANN SYNDROME



Placentomegaly (arrows)
Chorioangioma (curved arrow)

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Caudal Regression Syndrome

- Constellation of finding related to developmental disruption of caudal region of the embryo
- Results in underdevelopment and dysplasia of LS vertebrae, posterior gluteal fascia, and distal spinal cord
- Associated abnormalities include:
  - Limb defects
  - Craniofacial defects
  - Visceral defects

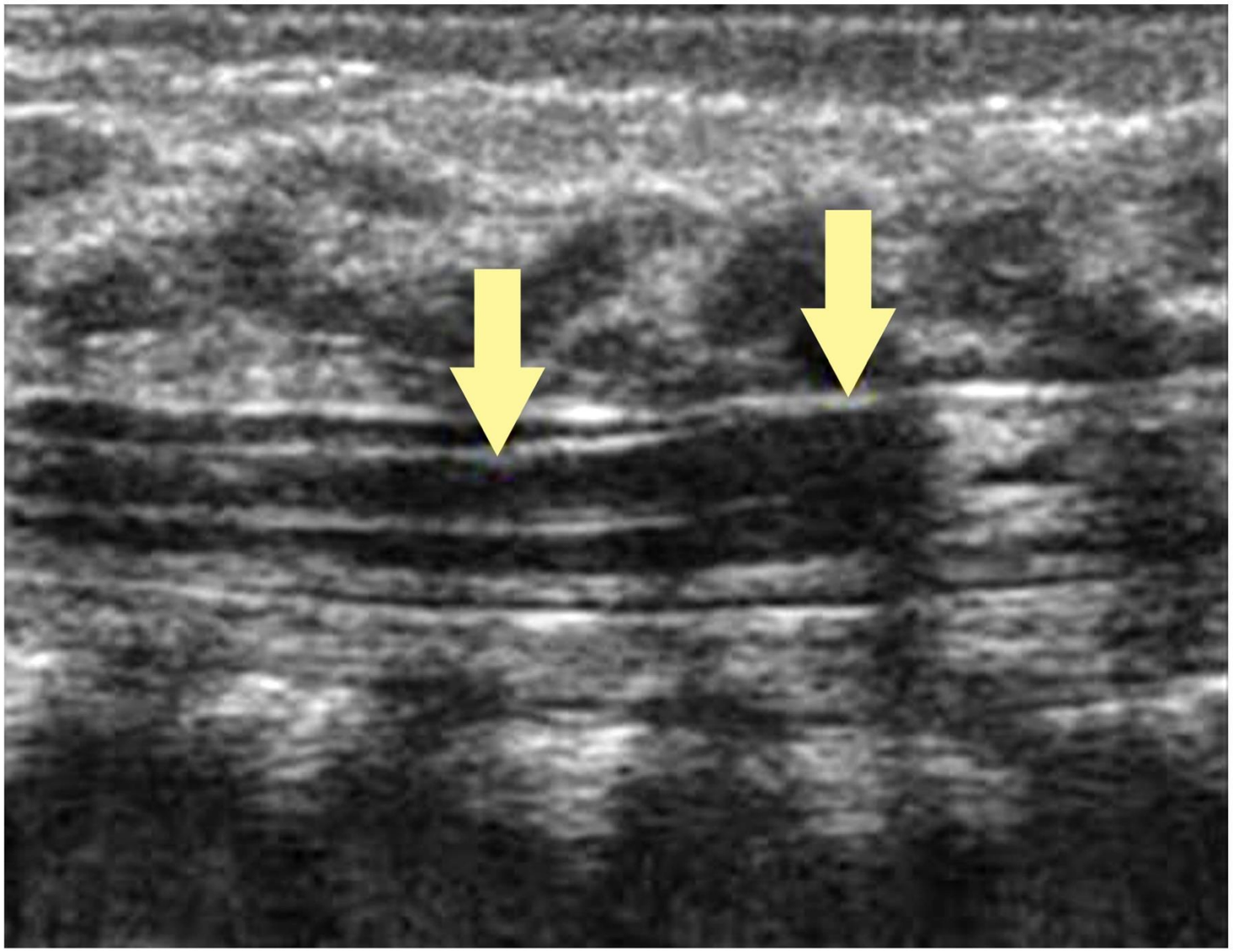
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Caudal Regression Syndrome

- Sonographic signs include:
  - Conus medularis ending above expected level
  - Blunted distal spinal cord
  - Absent or hypoplastic sacrum
  - Lower extremities hyperextended or in a “cross-legged” position

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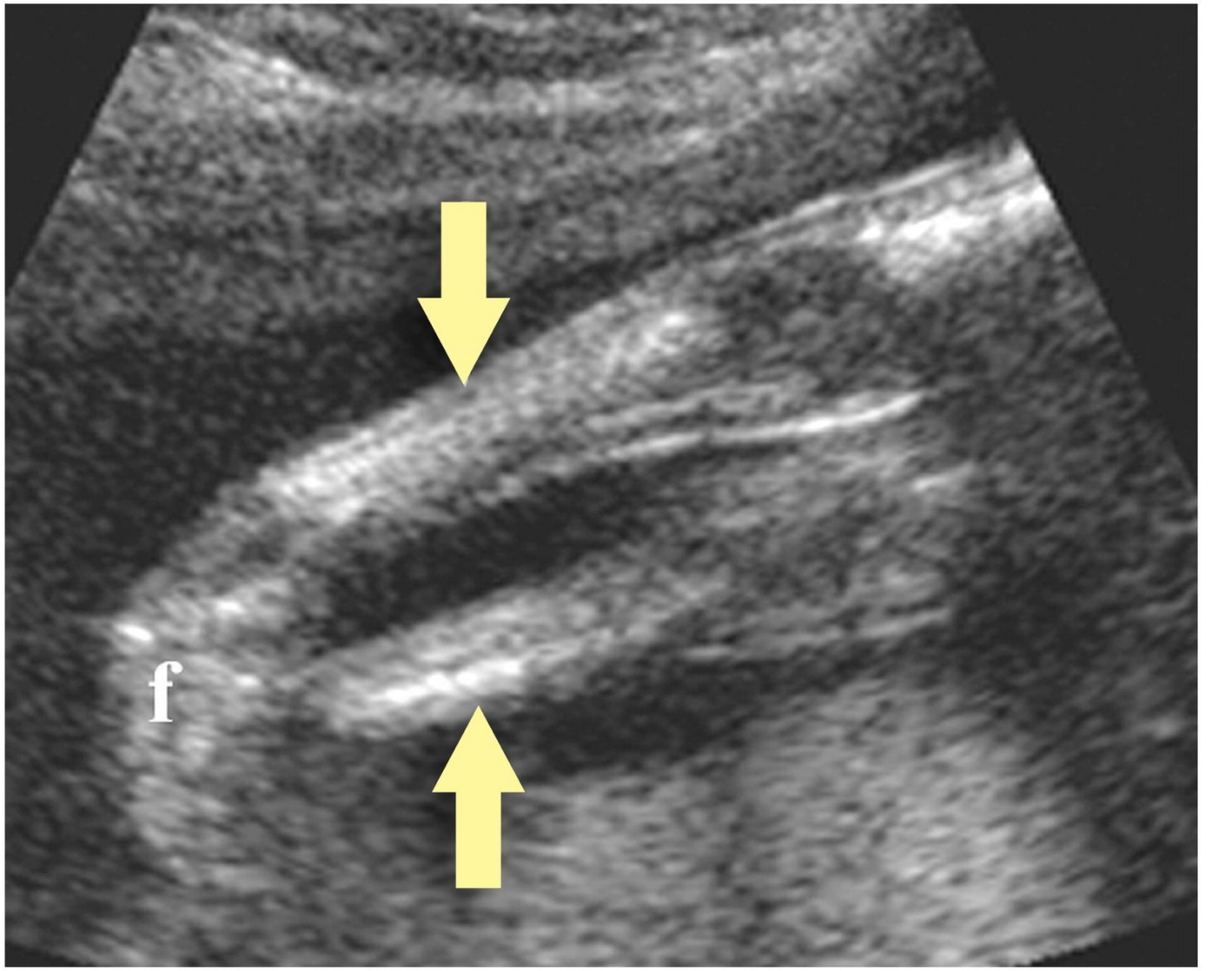
CAUDAL REGRESSION SYNDROME



Conus medularis (arrows) ending above expected level

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CAUDAL REGRESSION SYNDROME



Hyperextended lower extremities (arrows)

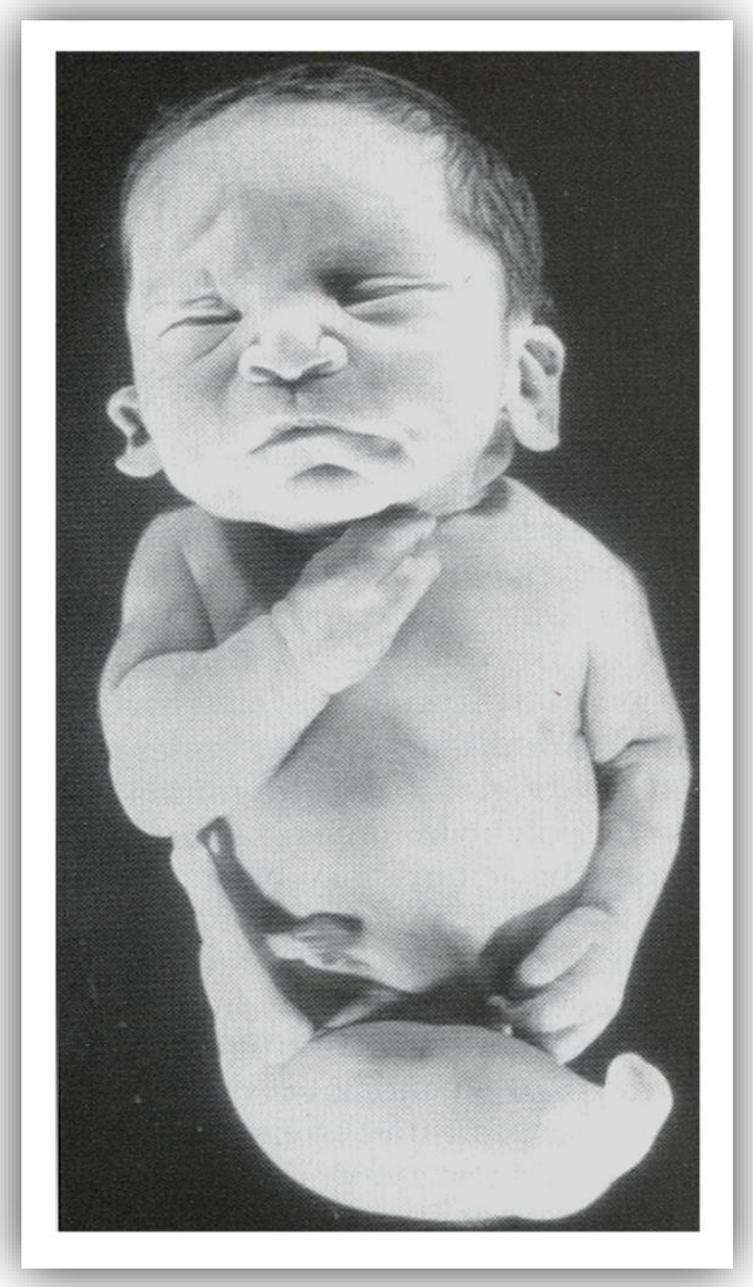
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Sirenomelia

- Similar in appearance to caudal regression commonly called *mermaid syndrome*
- Hypoplastic, anomalously developed lower extremities are encased in a single mass of soft tissue
- Associated abnormalities include:
  - Renal agenesis
  - Single umbilical artery
  - Imperforate anus
  - Cardiac anomalies
  - Abdominal wall defects

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SIRENOMELIA



Single lower extremity

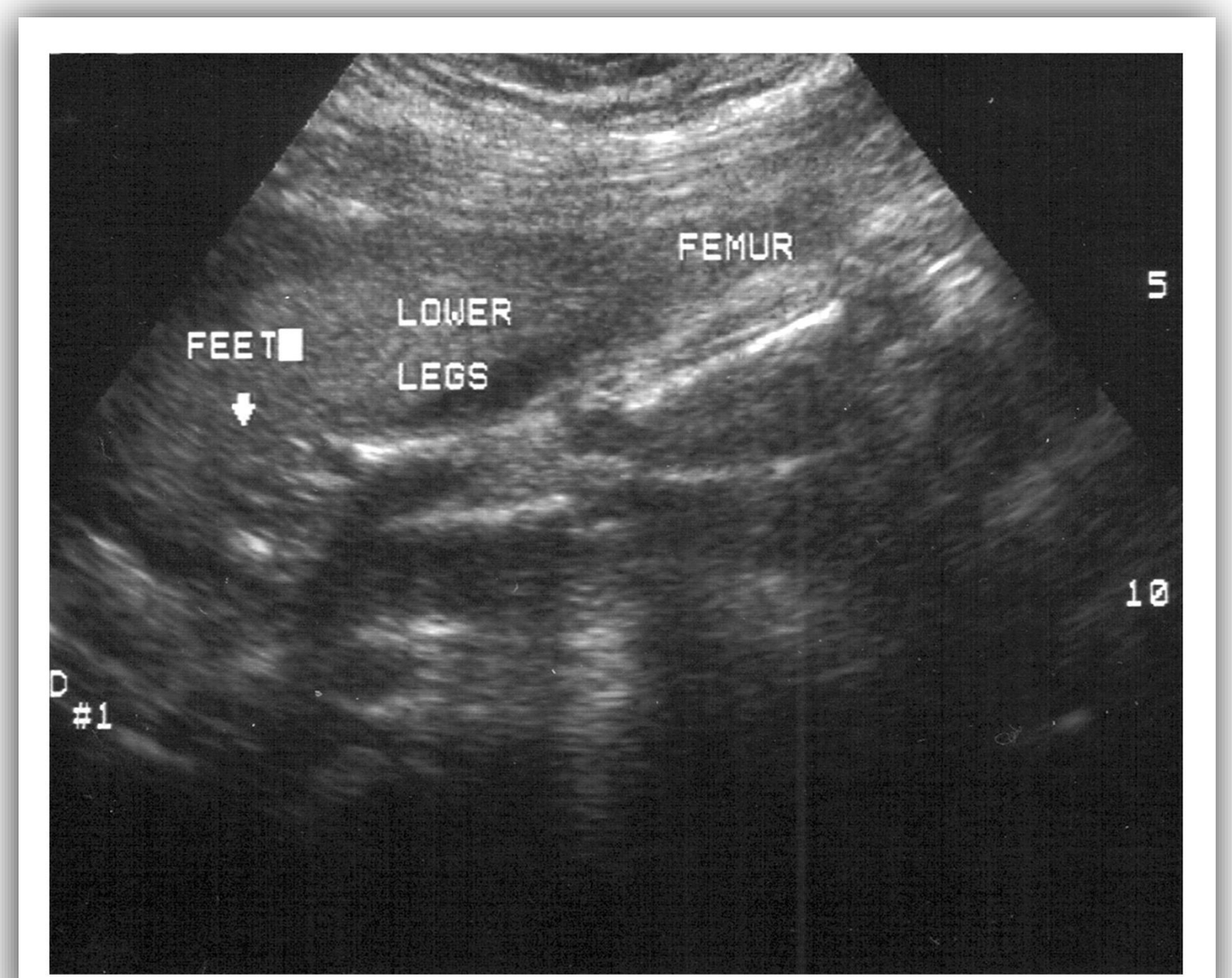
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Sirenomelia

- Sonographic signs include:
  - Appearance of a single lower extremity
  - Absent or fused feet
  - Single umbilical artery
  - Oligohydramnios

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SIRENOMELIA



Single, fused soft tissue mass

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Other Syndromes

- Extensive list of possible syndromes include:
  - Turner's syndrome
  - Kleeblattschadel syndrome
  - Holt-Oram syndrome
  - Fetal alcohol syndrome
  - Pentalogy of Cantrell
  - Meckel-Grube syndrome
  - Treacher-Collins syndrome
  - Ellis-van Creveld syndrome

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Terminology

- Syndrome: recognizable appearance of several clinical features, often occurring together, that serve as a harbinger of the presence of other, less apparent, abnormalities
- Association: presence of two or more congenital traits, one of known genetic origin, occurring together more often than possible by chance
- Sequence: series of clinical features that arise sequentially from a single cause
  - Potter sequence: constellation of abnormal facies, IUGR, limb anomalies resulting from chronic oligohydramnios

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Common Associations

- VACTERL association
- CHARGE association

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COMMON ASSOCIATIONS

VACTERL Association

V ertebral anomalies — hemivertebrae, caudal regression, spina bifida

A norectal anomalies — anal atresia

C ardiac anomalies/cleft lip

TE fistula — tracheoesophageal fistula

R adial ray/renal anomalies

L limb anomalies

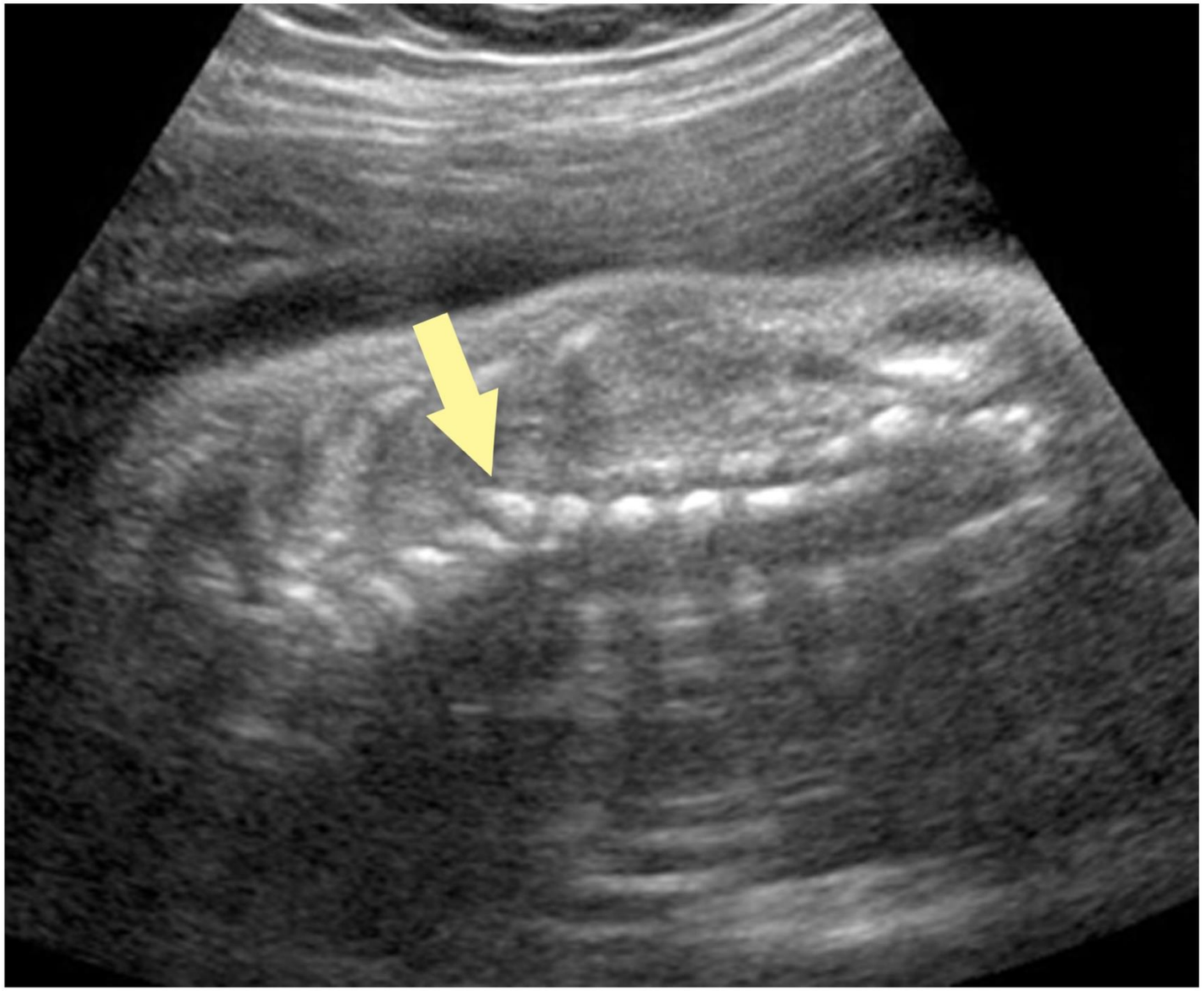
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VACTERL Association

- Sonographic signs include:
  - Polyhydramnios
  - Lumbosacral hemivertebrae
  - Radial ray anomaly
  - ID other anomalies listed above

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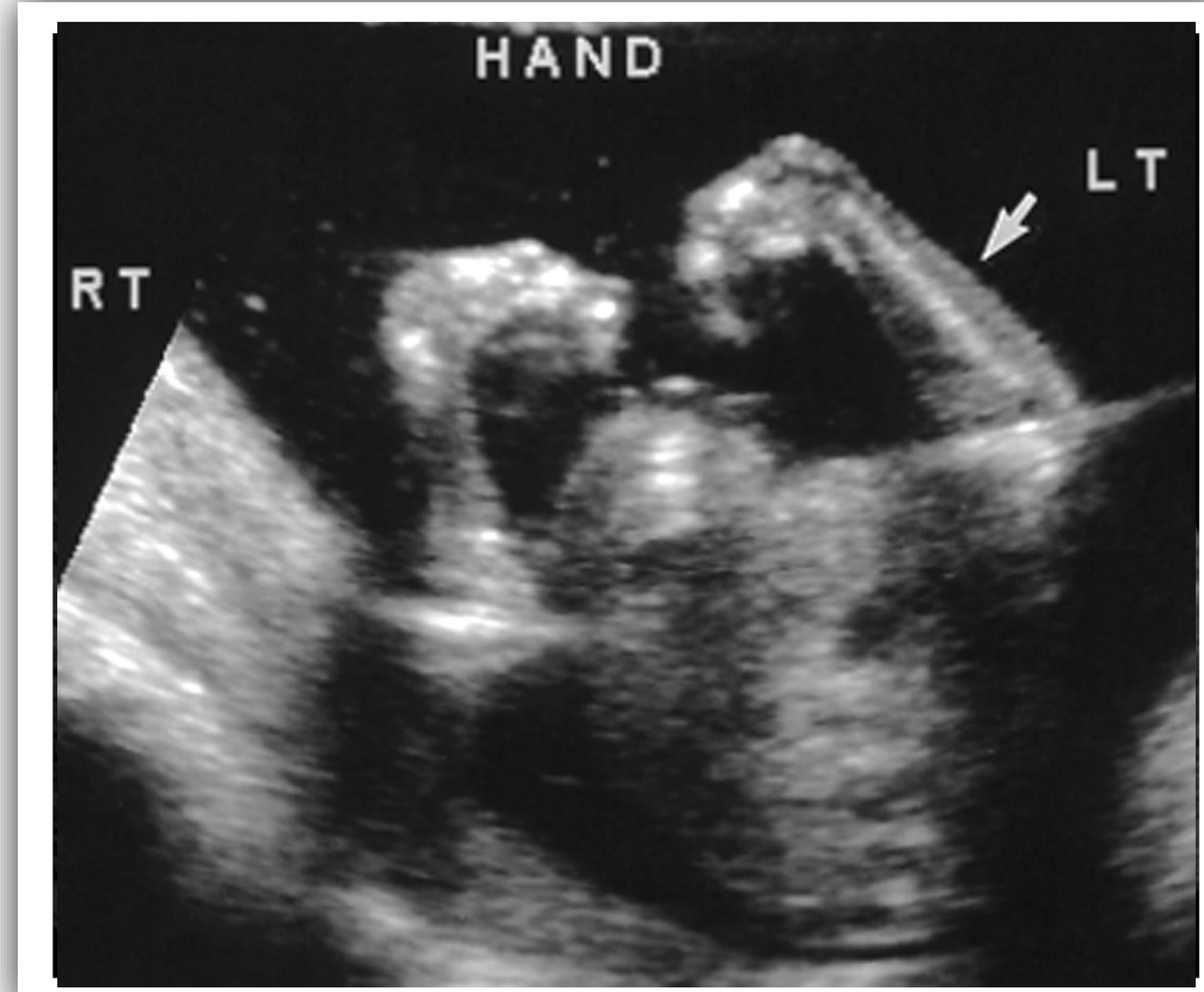
VACTERL ASSOCIATION



Lumbosacral hemivertebrae

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VACTERL ASSOCIATION



Radial ray anomaly

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COMMON ASSOCIATIONS

CHARGE Association

C oloboma — Focal discontinuity in the structure of the eye

H eart defects

A tresia — Choanal: narrowing or blocking of nasal cavity

R etardation (mental)

G enital hypoplasia

E ar abnormalities/deafness

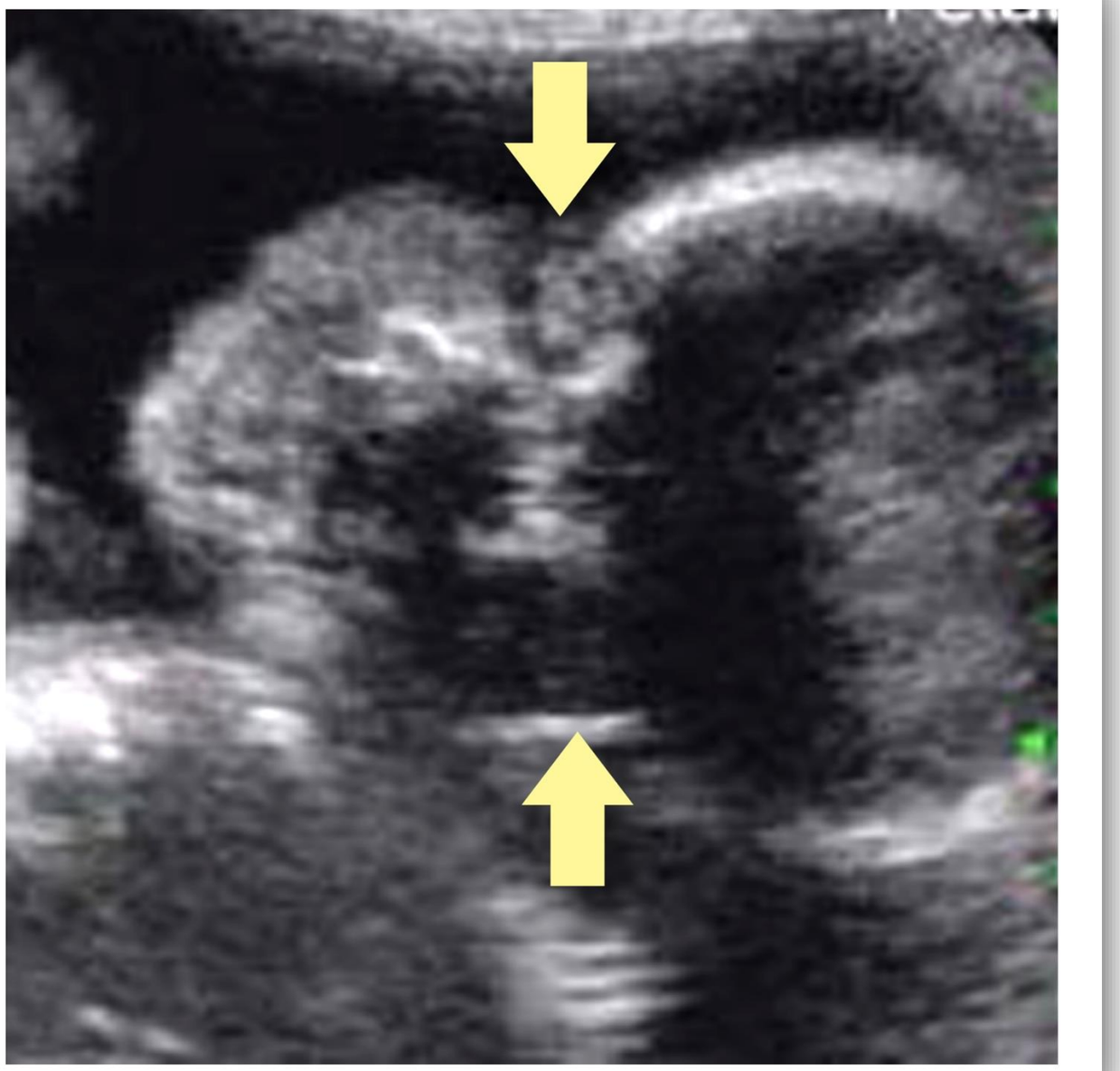
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CHARGE Association

- Sonographic signs include:
  - Microphthalmia
  - Hypotelorism
  - Facial cleft
  - Renal anomalies

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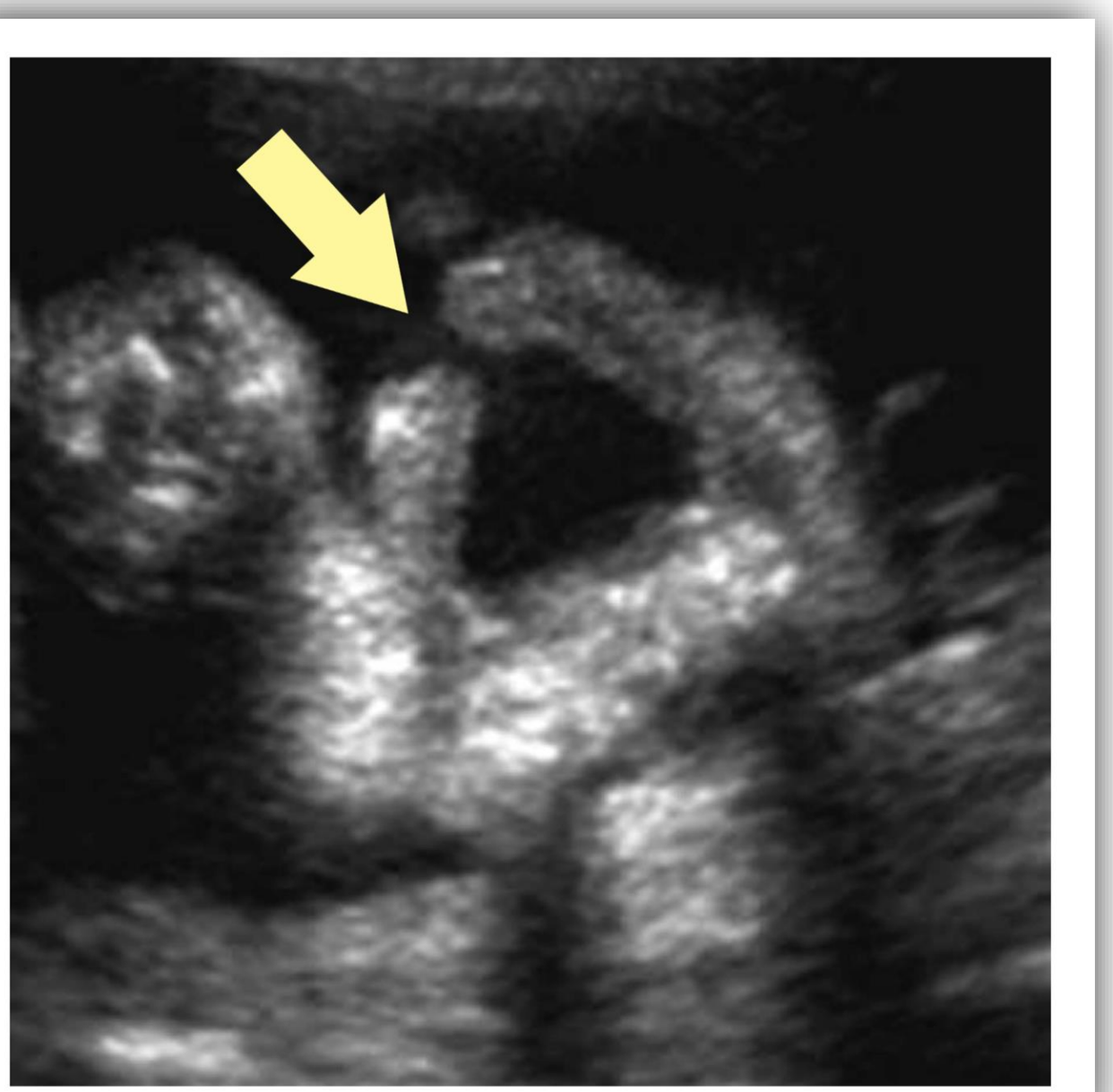
CHARGE ASSOCIATION



Hypotelorism (arrows)

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CHARGE ASSOCIATION



Cleft upper lip

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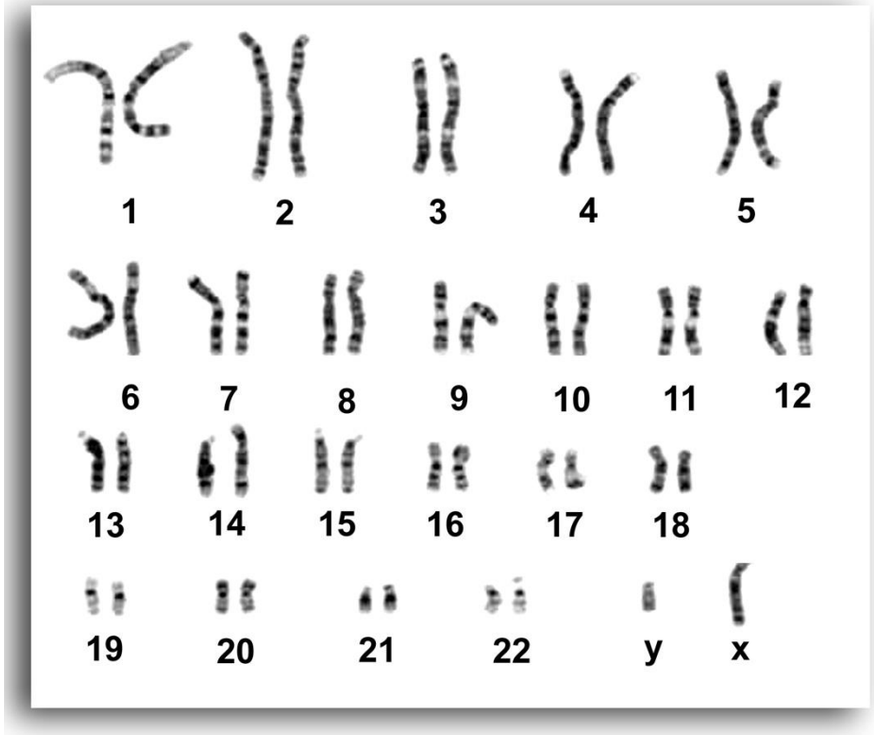
Potter Sequence

- Collection of multiple, bizarre anomalies cause by constricting bands of amniotic tissue
- Early rupture of amnion may result in bands that adhere to fetus and restrict tissue growth
- Multiple, sever, syndromal findings include:
  - Limb defects
  - Craniofacial defects
  - Visceral defects

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OB GYN SONOGRAPHY REVIEW

Prenatal Genetic Workup



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