Approach to Fetal Anomalies

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Introduction

Congenital Anomalies:

Is a term that describe structural, behavioral, functional, and metabolic disorders ,birth defects, congenital anomalies or congenital malformations; these conditions develop prenatally and may be identified before or at birth, or later in life

Epidemiology

- Congenital malformations are a major cause of infant morbidity and mortality in the world.
- Major congenital abnormality occurs in 2 - 3% of live births.
- Minor congenital abnormality occurs in 15% of live born infants.
- This incidence increases in pre-term and small for gestational age infants.
- Congenital anomalies may be single, multiple, and of minor or major clinical significance.
- Birth defects are the leading cause of infant mortality, accounting for approximately 21% of the infant deaths.

Definitions

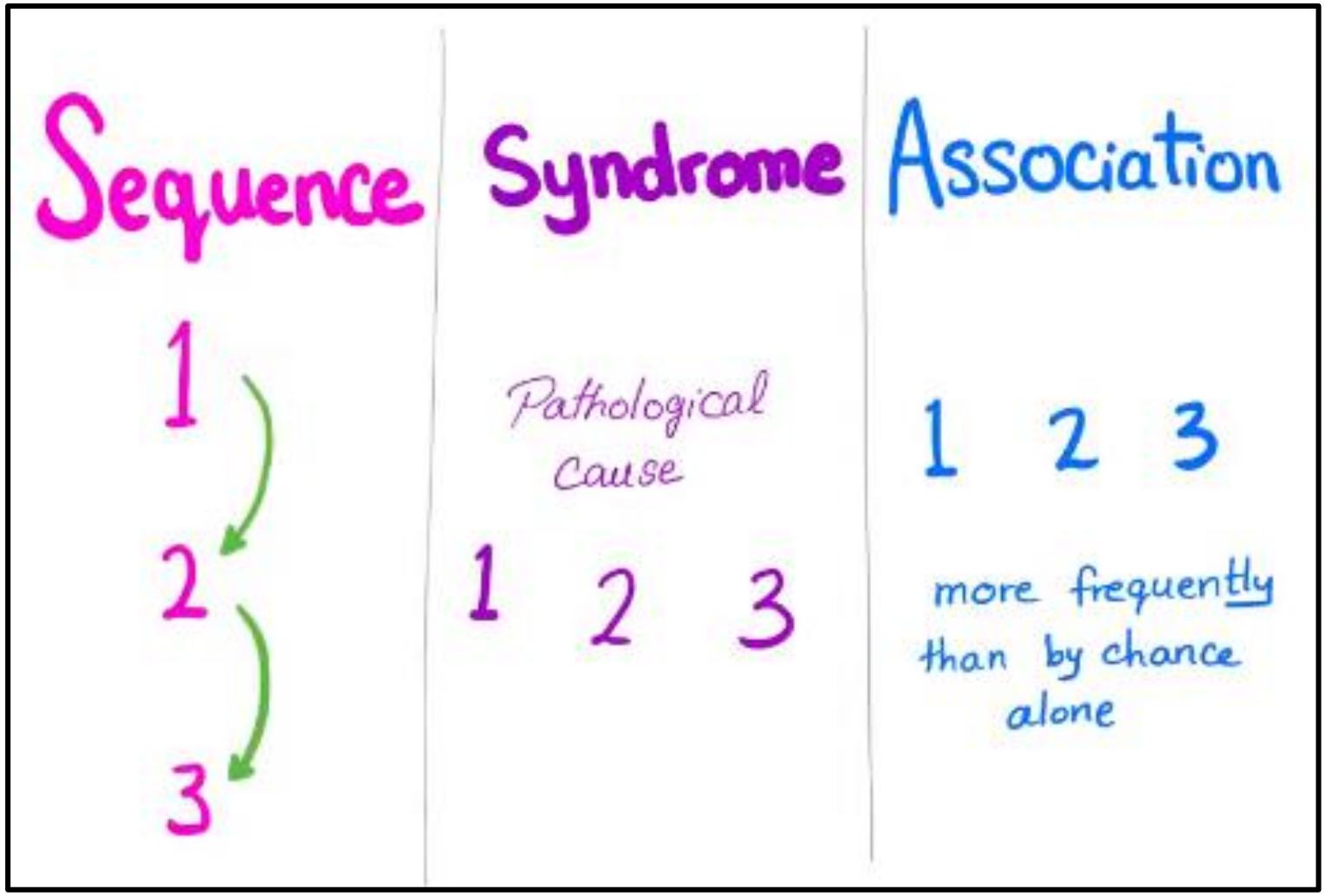
Major anomalies:

defined as anomalies or malformations that create significant medical problems for the patient or that require specific surgical or medical management.

Minor anomalies:

described as features that vary from those that are most commonly seen in the normal population but they not cause increased morbidity.

Definitions



Definitions

Malformation:

It`s a primary error results in partial or complete absence of a structure or alterations of its normal configuration.

- Occur during organogenesis.
- Mostly during the first 8 weeks of gestation.

Definitions

Deformation:

Late change in previously normal structure.

It results from mechanical forces on the fetus which is either extrinsic or intrinsic causes.

- Examples:

Extrinsic causes > small maternal stature, oligohydramnios, uterine malformation.

Intrinsic factors > neuromuscular disease. (club-feet)

Why prenatal diagnosis is important?

- May treat in utero
- To transfer certain cases in utero to deliver in a tertiary care center
- The option of termination
- To anticipate mechanical obstruction in labor
- To avoid unnecessary operative delivery
- To prevent maternal psychological trauma

Etiology of Congenital Malformations

Unknown - 60%

Multifactorial - 20%

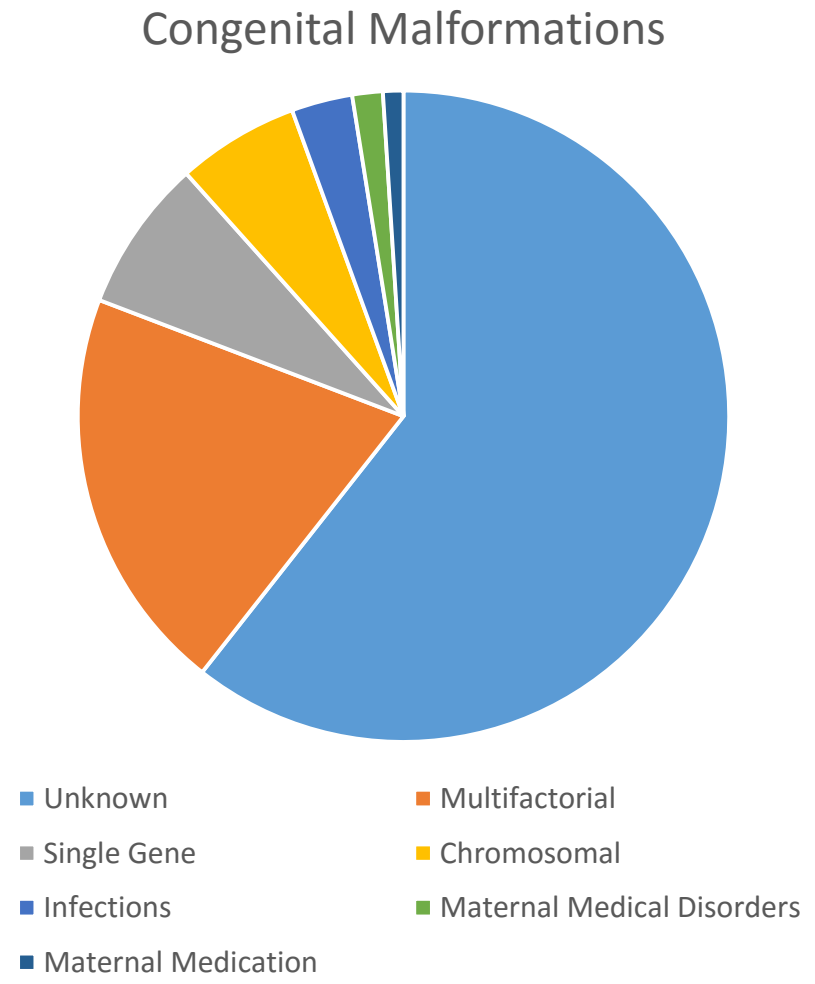
Single-gene - 7.5%

Chromosomal - 6%

Infections - 2-3%

Maternal medical disorders - 1.5%

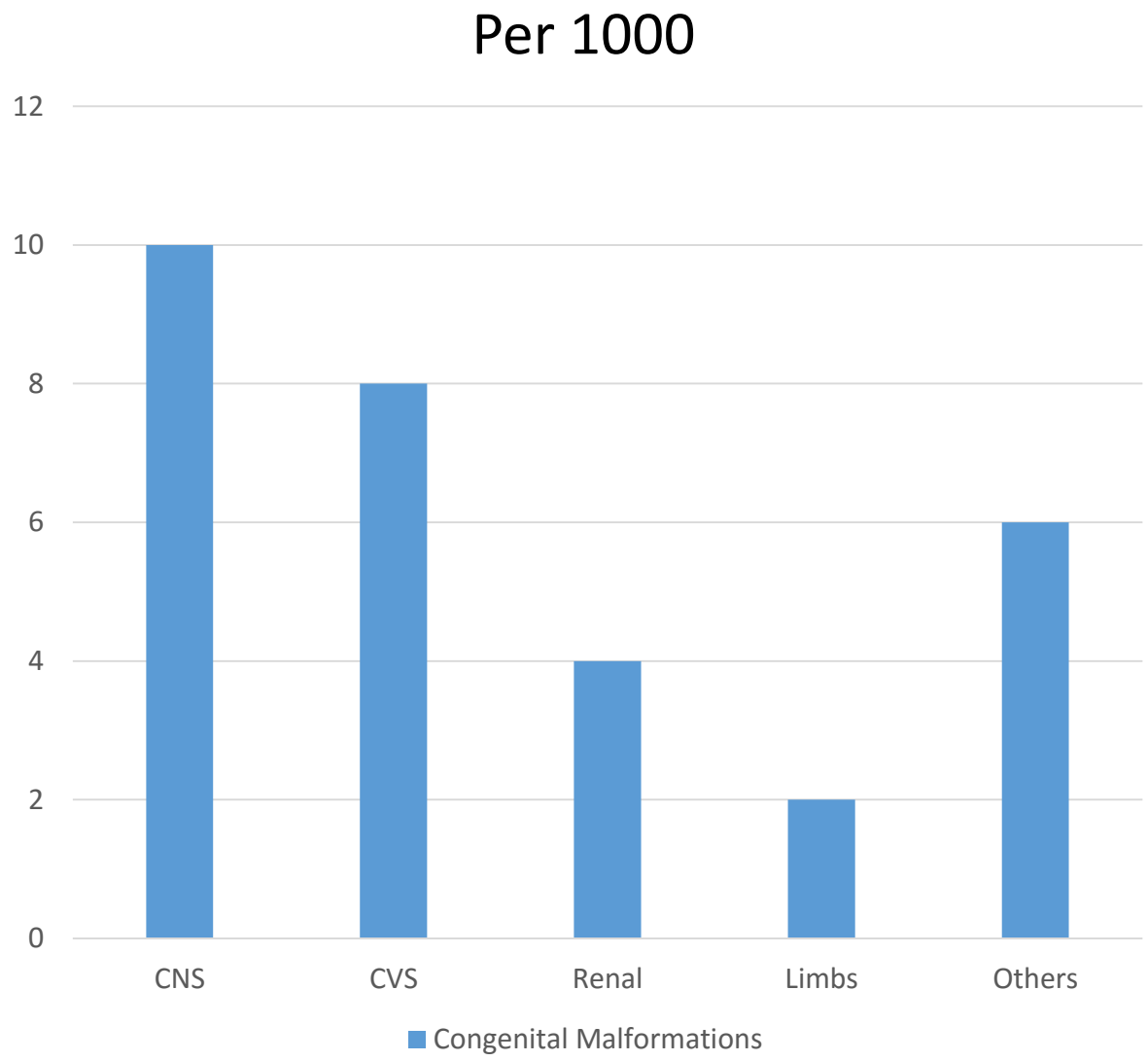
Maternal medication - 1-2%



Etiology

Systems commonly involved
"over all: 30/1000"

- CNS => 10/1000
- CVS => 8/1000
- Renal => 4/1000
- Limbs => 2/1000
- Others => 6/1000



Etiology

Multifactorial

- Neural tube defects
- Abdominal wall defect
- Uropathy
- Cleft lip and palate
- Congenital heart disease

Etiology

Single gene disorders

Autosomal Dominant

- Only one abnormal gene is necessary for disease manifestation.
- **Ex:**
  Neurofibromatosis, tuberous sclerosis, Marfan syndrome, Achondroplasia.

Autosomal Recessive

- Two affected genes must be present for the disease to manifest.
- **Consanguinity** increases the chance.
- **Ex:**
  sickle cell anemia, cystic fibrosis, congenital adrenal hyperplasia, wilson disease, Tay-Sachs disease.

X - linked Recessive

- Carried on X chromosomes
- Inherited through the mother.
- Cannot have male to male transmission.
- **Ex:**
  fragile X (the 2nd most common form of mental retardation after Down syndrome) also G6PD, Duchenne muscular dystrophy.

Etiology

Chromosomal Disorders

Defect is either in;

- Number: non disjunction
- Structure: translocation

Down syndrome is the most common of the chromosomal disorders and the commonest cause of mental retardation in children.

Clinical approach

When to suspect congenital abnormalities?

History

- **Patient's profile:**
  - age of mother (if above 35 years)
  - Ethnicity
  - occupation
- **Past obstetric history**
  - previous history of child died in the neonatal period
  - Recurrent miscarriage in the first trimester
  - Previous history of child died in the neonatal period
  - Previous history of child with birth defect or mental retardation
- **Past medical history**
  - Medical disorders, such as DM, hypertension, thyroid disorders and autoimmune diseases.
  - Exposure to infections during pregnancy.

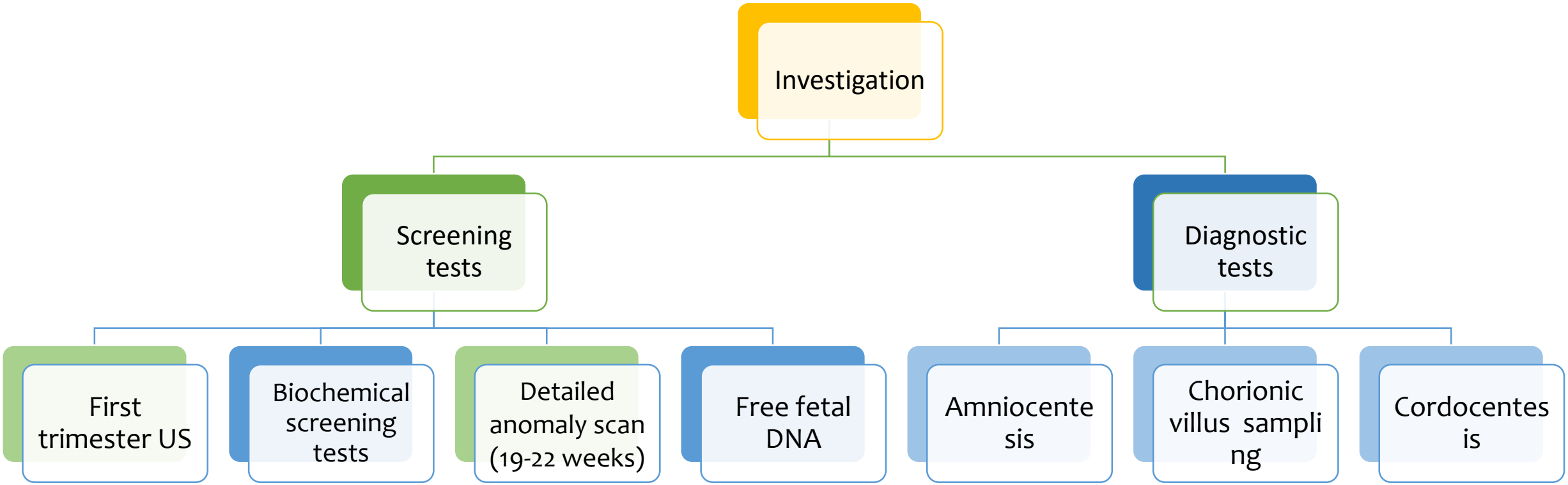
History

- **Drug history**
  - Drugs and herbal supplements
  - Prenatal vitamin or folic acid supplementation
- **Family history**
  - Age of parents
  - Diseases can impact the family's health (multiple cancers, susceptibility to infections, neurodegenerative disorders)
  - Family history of birth defect, chromosomal abnormality, or single gene defect
  - Consanguinity
- **Social history**
  - Smoking, alcohol

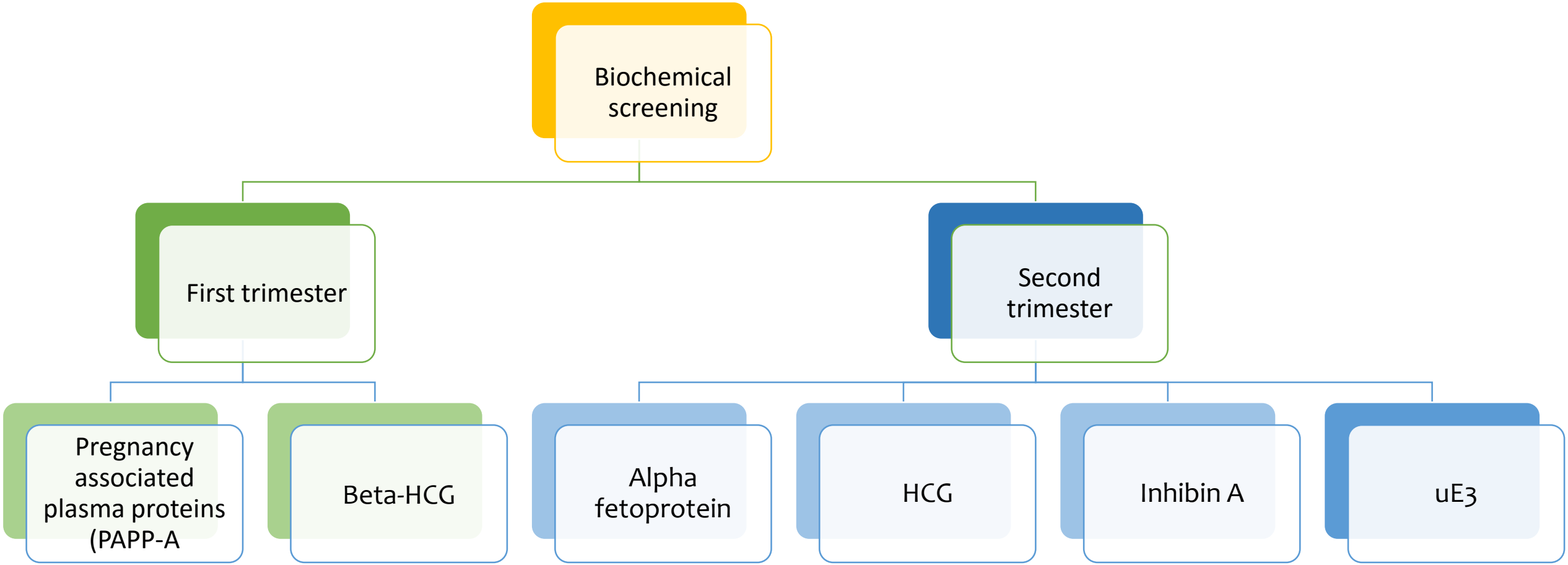
Physical Examination

- Fundal height measurement
- Abdominal masses
- Fetal heart rate
- Fetal movement assessment

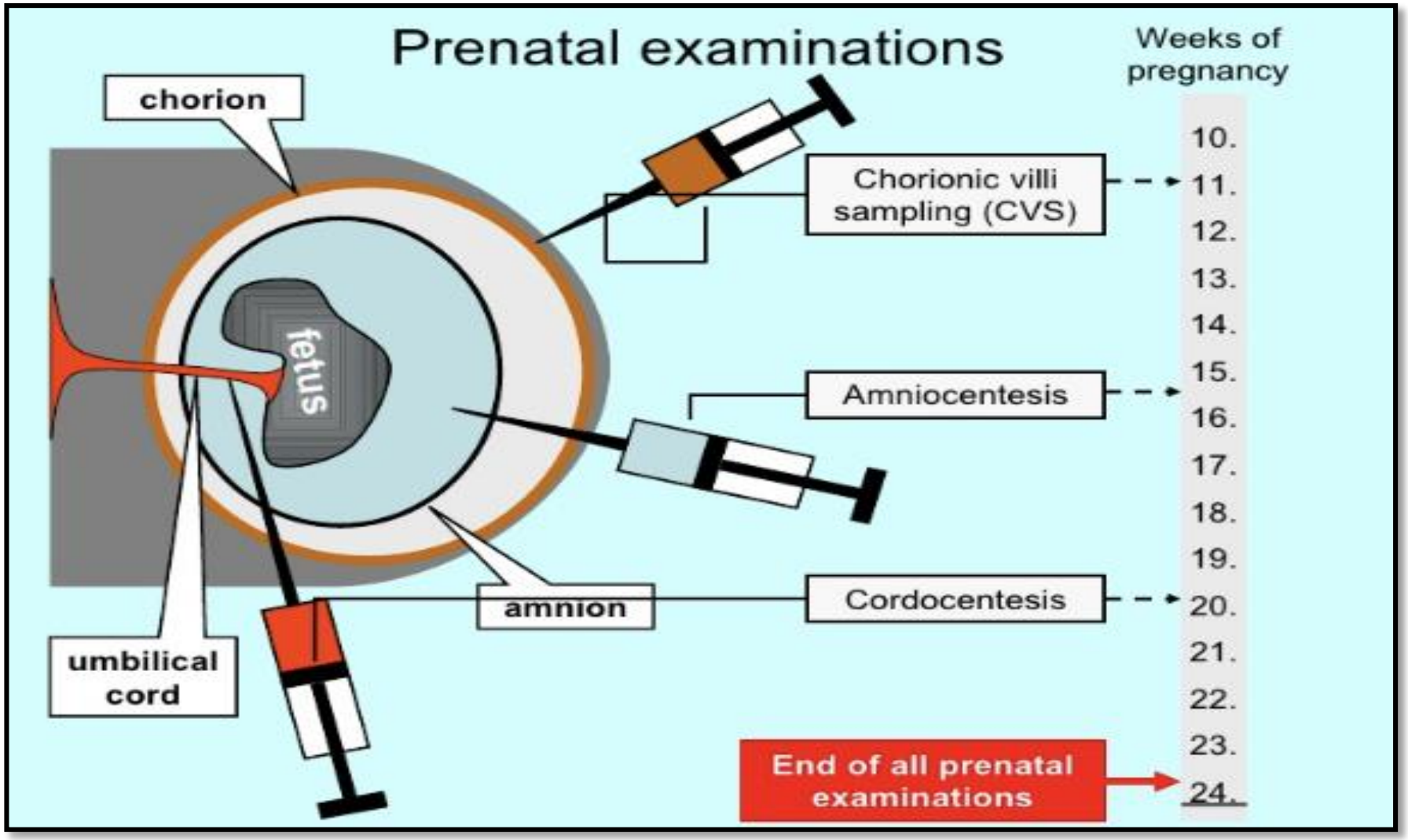
Investigations



Investigations

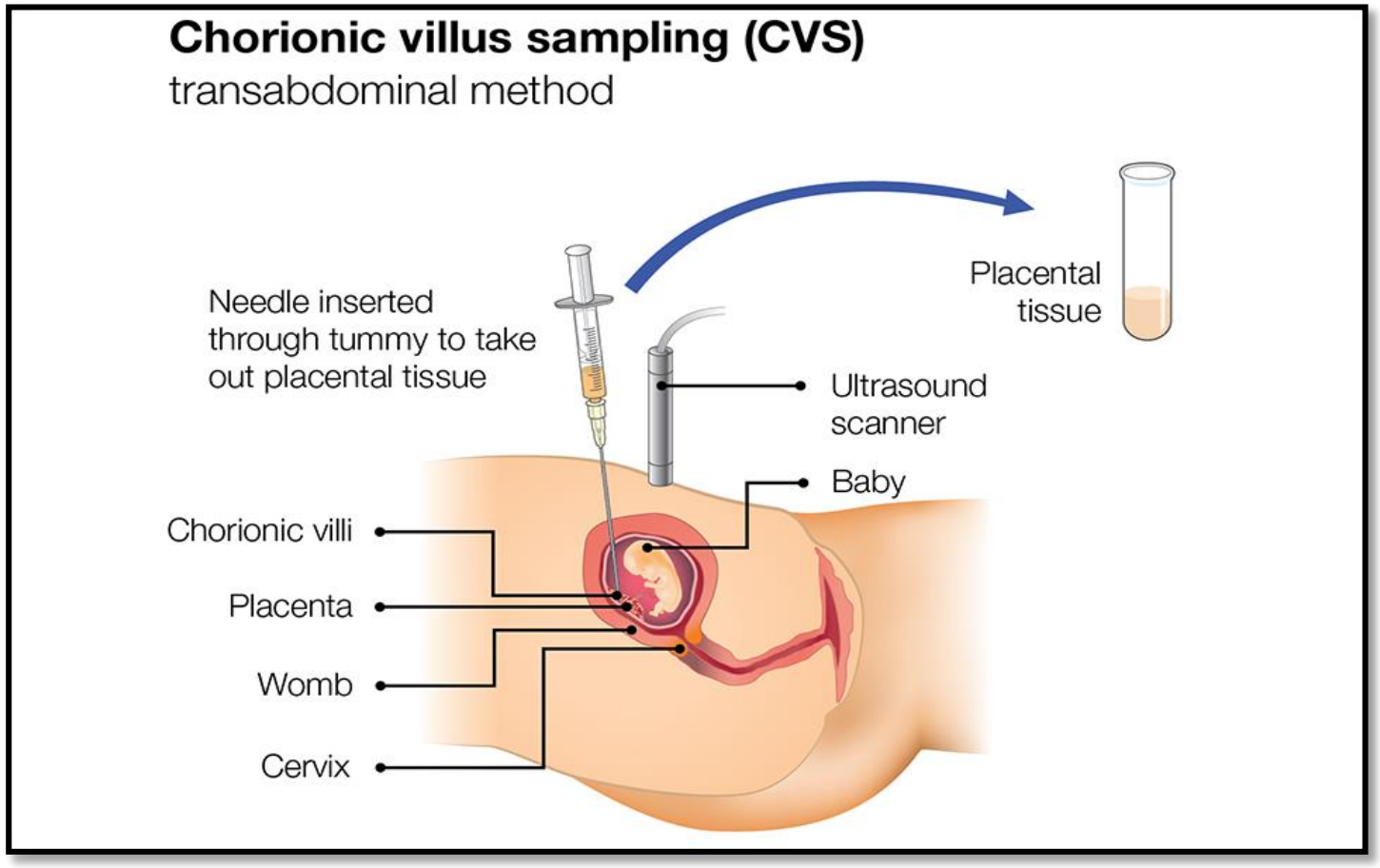


Investigations



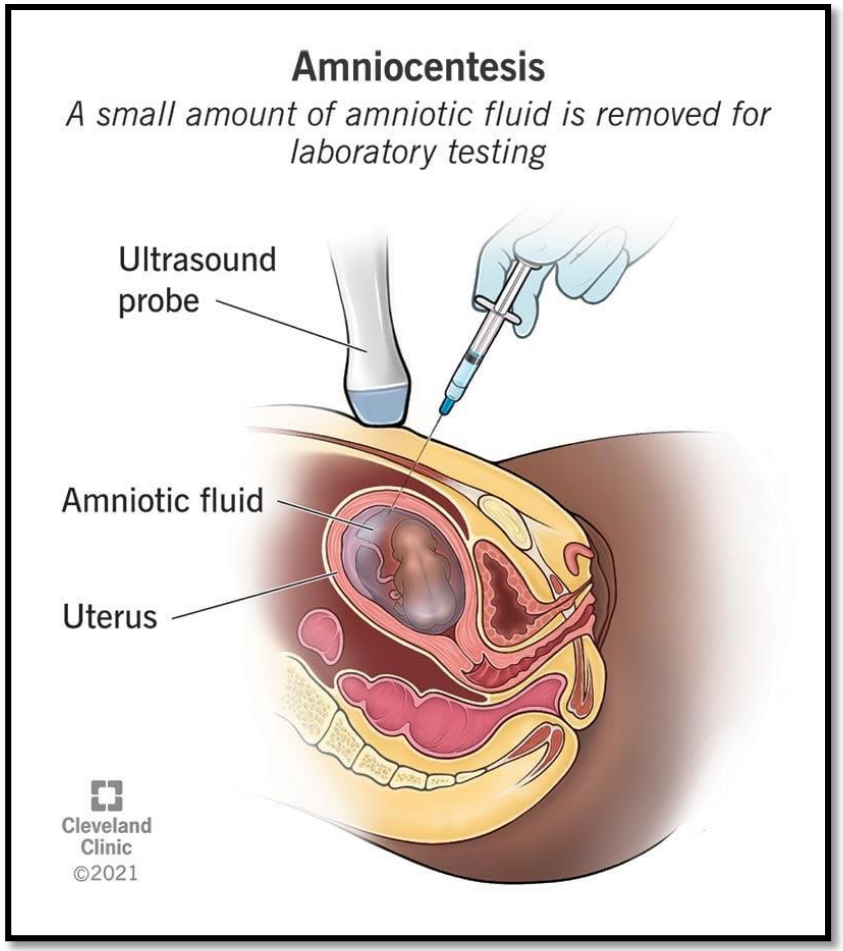
Investigations

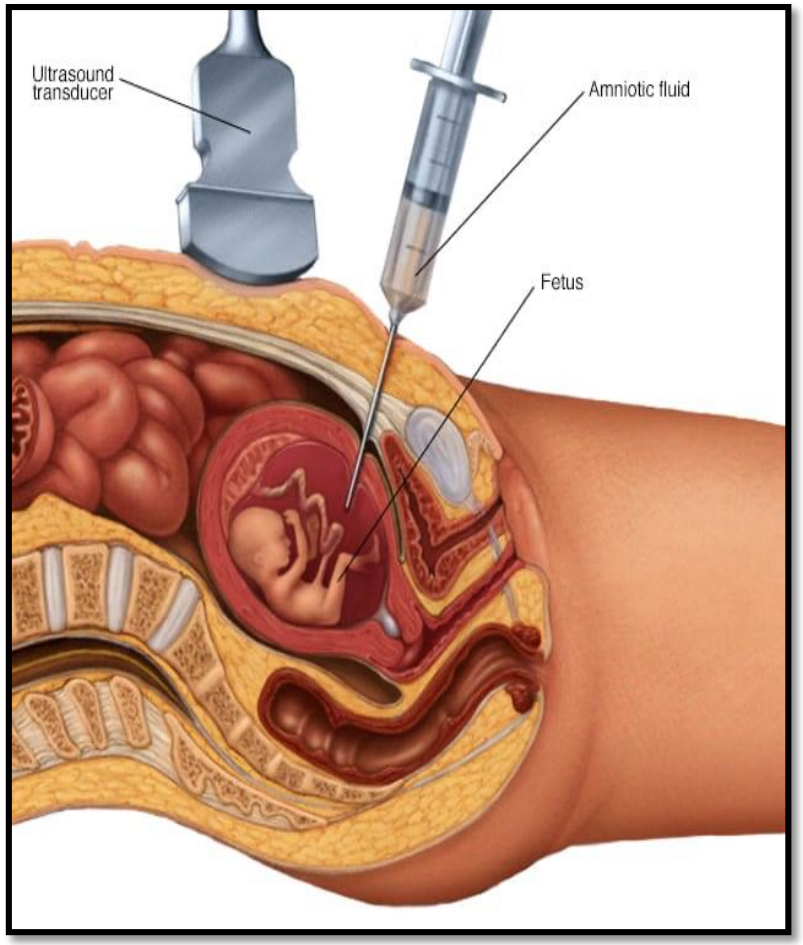
Trans-abdominal chorionic villus sampling



Investigations

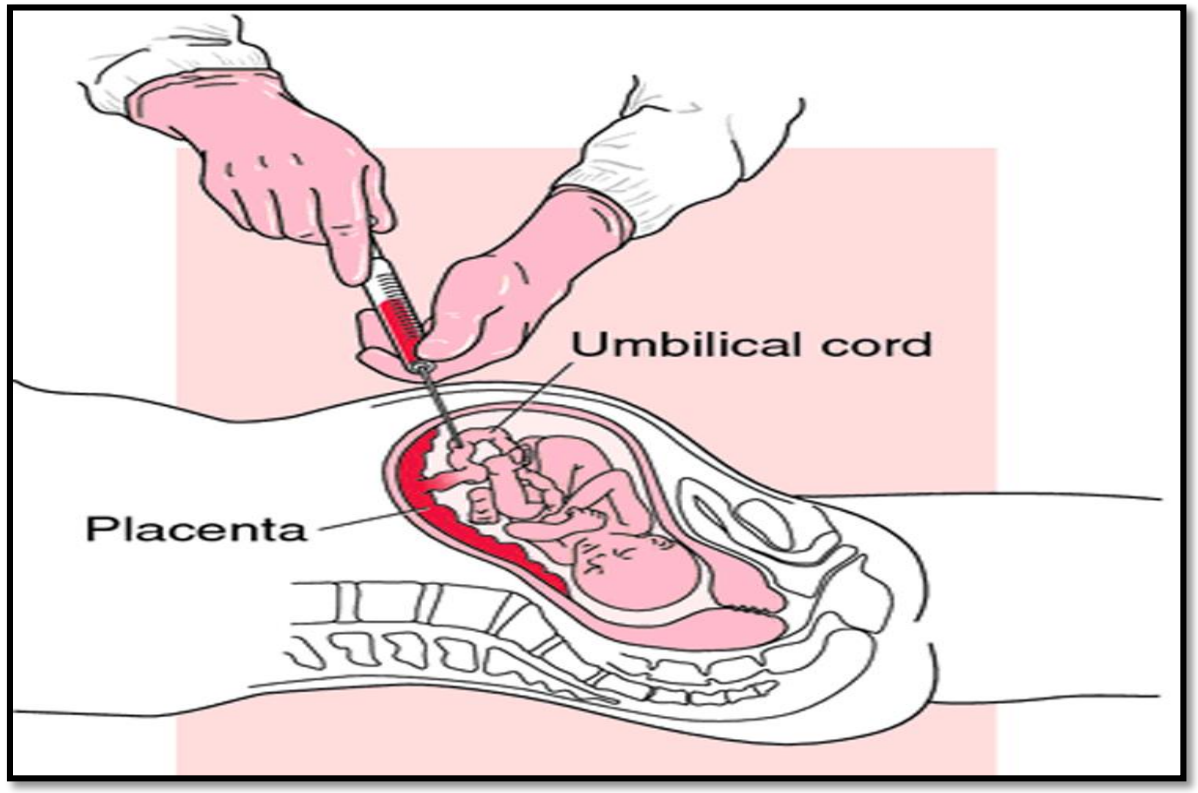
Trans-abdominal amniocentesis





Investigations

Cordocentesis



Down Syndrome

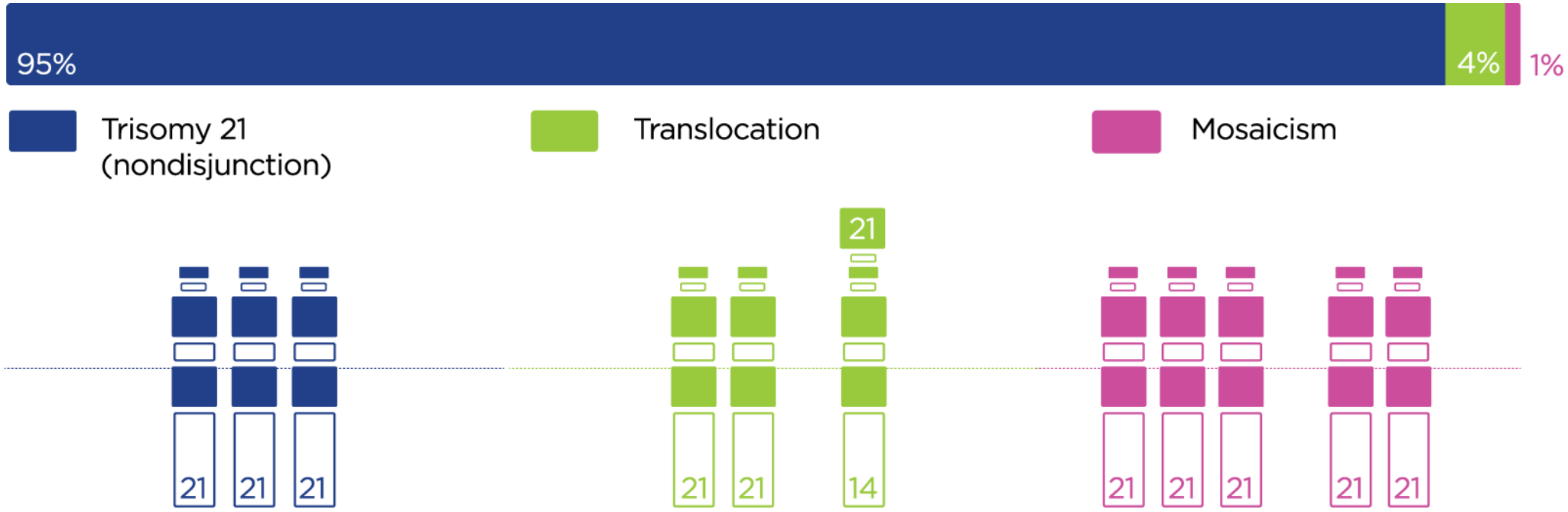
- **the most common autosomal trisomy among live births**

(1 in 500 live births in the absence of termination)

- Prevalence increases with advancing maternal age

Down syndrome risk	Maternal age (years)
1:1475	20
1:1340	25
1:935	30
1:350	35
1:85	40
1:34	45

Down Syndrome Etiology



Baby is born with an extra copy of chromosome 21, meaning there are three copies of chromosome 21 instead of the usual two.

Part of chromosome 21 breaks off during cell division and attaches to another chromosome.

There is a mixture of two types of cells - some containing the usual 46 chromosomes and others containing 47.

A PRIORI RISK FOR DOWN SYNDROME

- A couple with no family or personal history of Down syndrome.
  Risk is based on maternal age at the expected date of delivery .

- A couple with a prior conception with Down syndrome caused by trisomy 21 (three separate chromosome 21s).
  - When the mother is <35 years of age at the time of diagnosis of nondisjunction trisomy 21, the risk of recurrence is approximately 1 percent, which is higher than the maternal age-related risk of Down syndrome for this age group.
  - When the mother is ≥35 years of age at the time of diagnosis of nondisjunction trisomy 21, the risk of recurrence is the maternal age-related risk .

A PRIORI RISK FOR DOWN SYNDROME

- A couple with a prior conception or family member with Down syndrome caused by an unbalanced chromosomal rearrangement or translocation.
  - The parents of an offspring with translocation Down syndrome should undergo peripheral blood chromosome analysis to evaluate for a balanced translocation.
  - Translocations in offspring can be de novo or familial.
    - -When familial, the recurrence risk depends upon the sex of the carrier parent (10 to 15 percent for female carriers and 2 to 5 percent for male carriers).
    - -When de novo, the recurrence risk is based on the mother's age at expected delivery. If <35 years, the recurrence risk is approximately 1 percent. If ≥35 years, it is equal to the age-related risk at expected date of delivery (EDD).
- A couple with a prior conception or family member with mosaic Down syndrome. Family members are not at increased risk.

Prenatal Diagnosis of Down syndrome

- **History :**

-Mother age:

*40 y.o. risk : 1\100

*35 y.o. risk 1\350

-Previous history of down

-Recurrent abortion

-Family history

- **Examination:**

-Small sized fetus

- **Investigation:**

-Abnormal serum markers

-Ultrasound findings

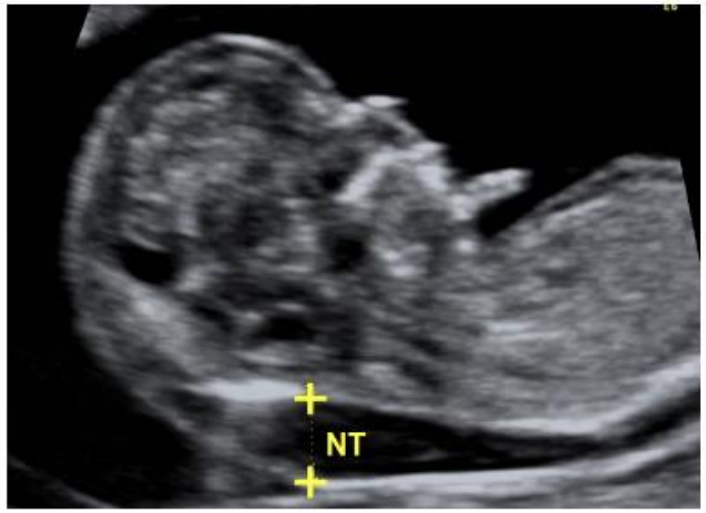
-Amniocenteses, Chorionic villous sampling

First Trimester U.S Assessment

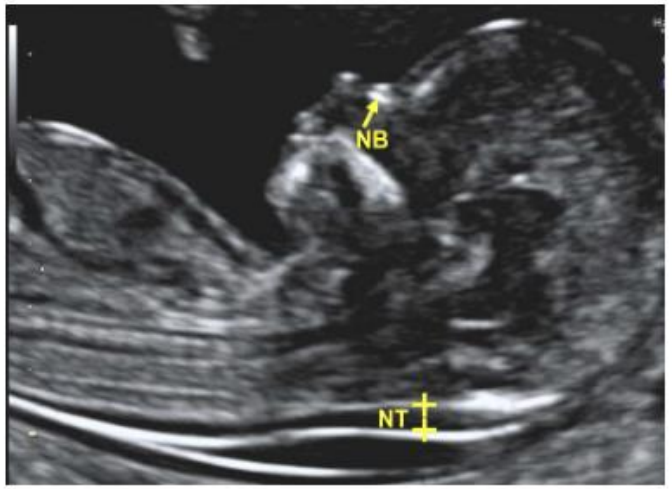
- **Nuchal translucency (NT):**

detection rate for Down Syndrome being 64-70%.

High nuchal translucency

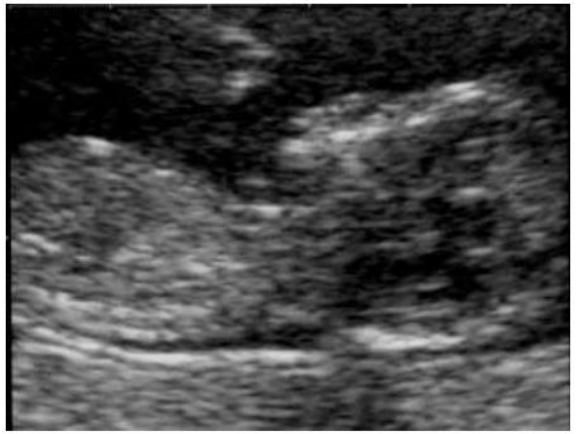


Normal nuchal translucency



- **Absent nasal bone:**

62-70% of fetuses with Down Syndrome

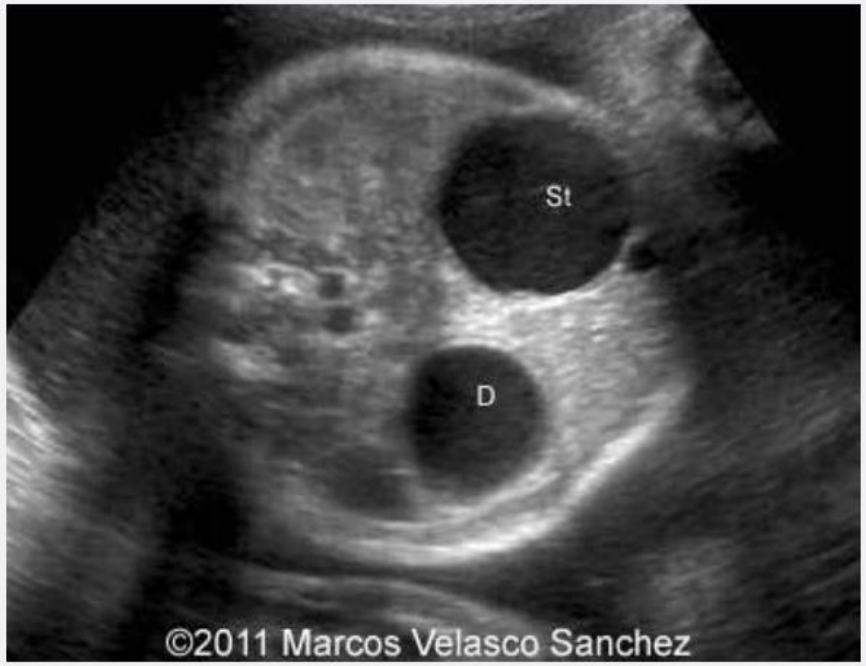


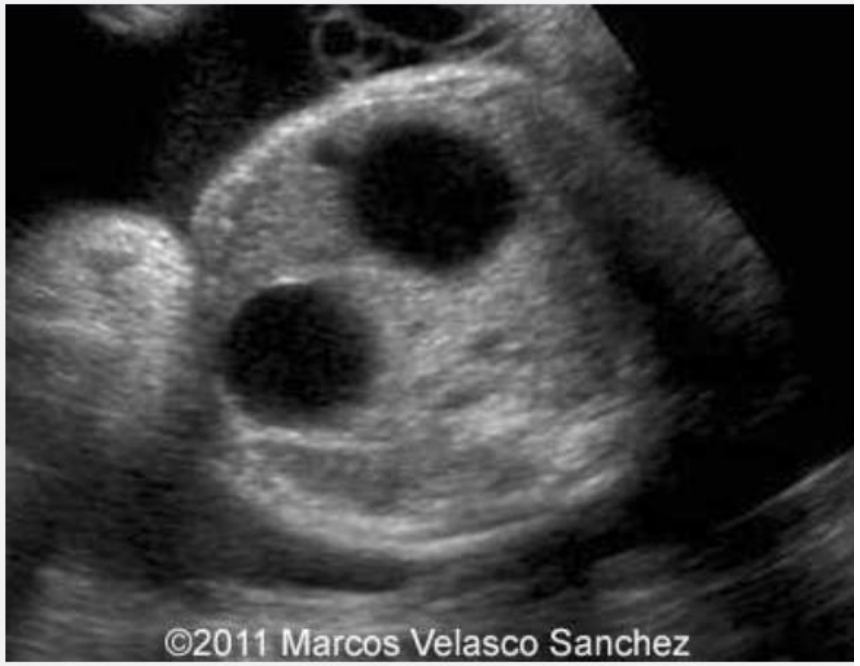
BabyCenter

U.S Assessment

Duodenal atresia (double bubble sign):

- 30% chance that the baby will have Down syndrome.
- U.S scan shows polyhydramnios





Biochemical Screening

1st trimester screening		
Trisomy	β-hCG	PAPP-A
21	↑	↓
18	↓	↓
13	↓	↓

First trimester:

- free beta-HCG : elevated ↑
- PAPP-A (pregnancy associated plasma protein –A) : decreased ↓

Second trimester: (MSAFP ,Hcg ,uE3 ,inhibin)

- B-hcg : elevated ↑
- Inhibin-A : elevated ↑
- uE3(estriol) : decreased ↓
- Maternal aFP : decreased ↓

2nd trimester (quadruple) screening				
Trisomy	hCG	Inhibin A	Estriol	AFP
21	↑	↑	↓	↓
18	↓	— or ↓	↓	↓
13	—	—	—	—

Neural Tube Defects

They are common birth defects of the central nervous system that occur due to a defect in the formation of the neural tube during the first month of pregnancy.

They are thought to have multifactorial etiology, including multigenetic and environmental influences:

- Folate deficiency in the maternal diet
- Chromosomal abnormalities (trisomy 13, 18, 21)
- Maternal diabetes
- Alcohol abuse
- Valproic acid, carbamazepine or opioid use

Neural Tube Defects

The type and severity of malformation varies based on the location of the defect.

This includes both cranial and spinal cord malformations.

- **Cranial:**

  Anencephaly

  Encephalocele

- **Spinal:**

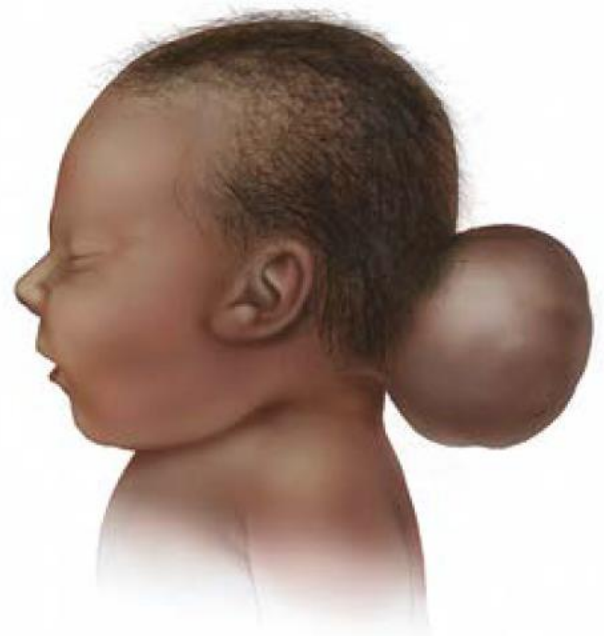
  Spina bifida (Occulta, aperta)

NTD: Anencephaly

- The cerebrum and cerebellum are reduced or absent, but the hindbrain is present.
- It is lethal in all cases because of the severe brain malformation that is present.

NTD: Encephalocele

- there’s an opening in the skull. The fetus's brain and the meninges can protrude through the skull, forming a sac-like bulge.
- It can be corrected surgically



NTD: Spina Bifida

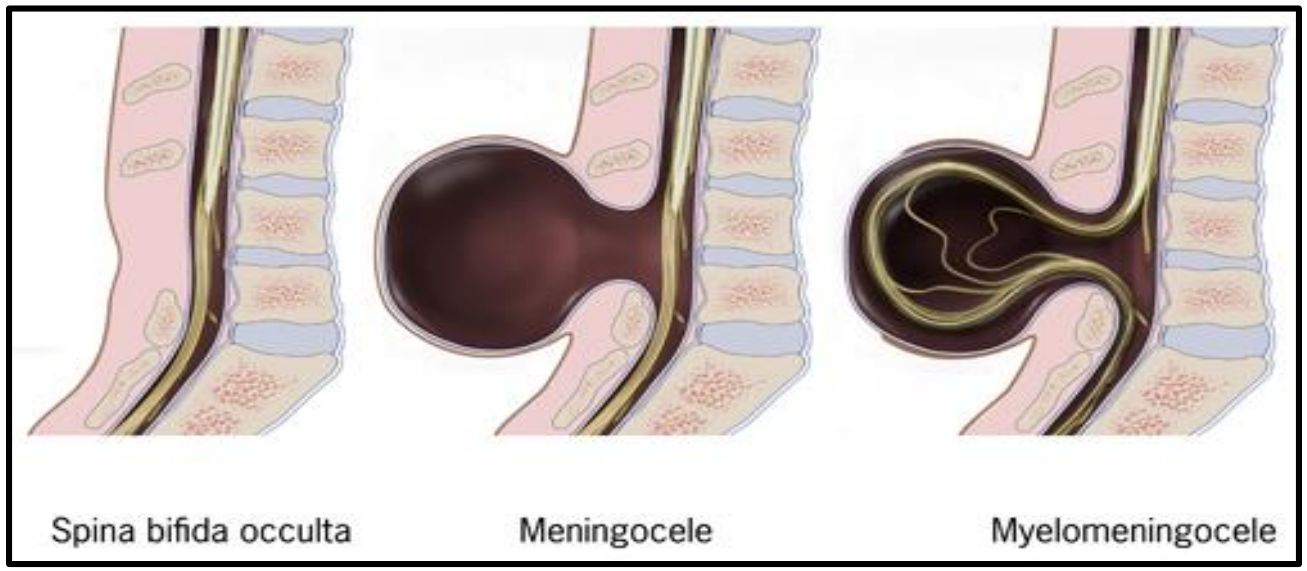
Types:

- Occulta:

Failure of caudal neuropore to close.
The spinal cord, meninges, and overlying skin remain intact, with no herniation.

- Cystica:

Meningocele (herniation of meninges only) and
myelomeningocele (herniation of both meninges and neural tissue).



Spina Bifida Screening

- 80-85% of open neural tube defects can be detected by maternal serum AFP (MSAFP)
- If the MSAFP level is elevated, an ultrasound should be done to rule out multiple gestation, fetal demise, or inaccurate gestational age
- Acetylcholinesterase only present if there is open neural tube defect

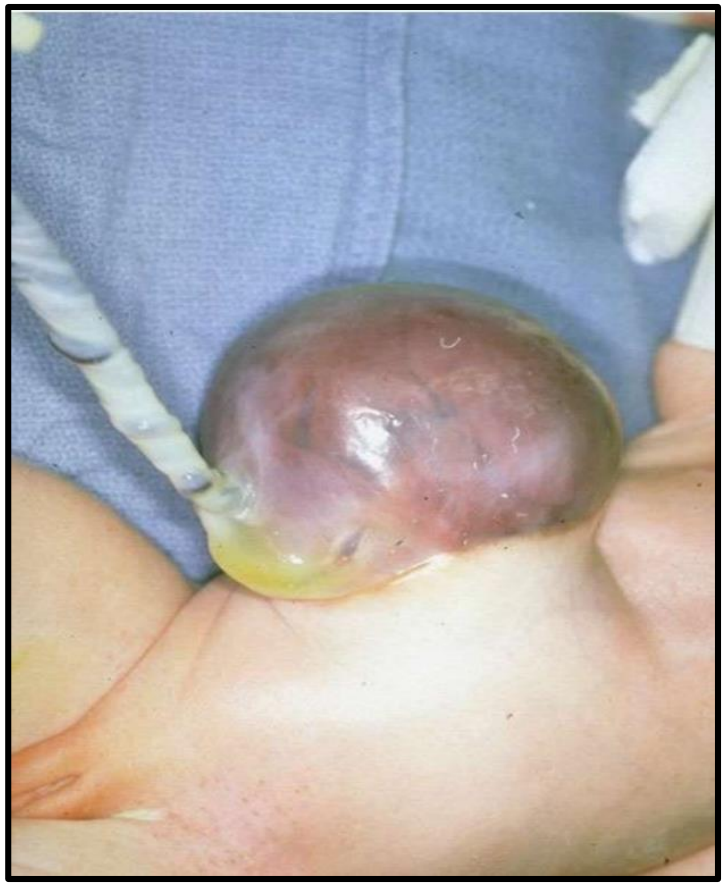
Presentation

- Intra Uterine Growth Restriction
- Malpresentation
- Polyhydroamnios
- Post-term pregnancy
- Decreased fetal movement

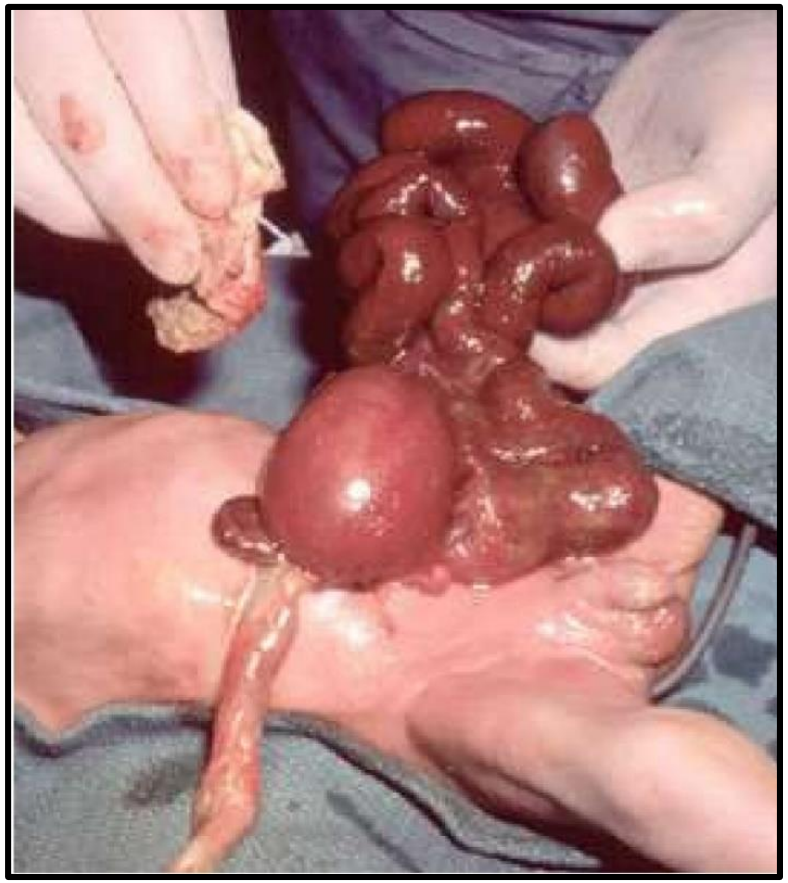
Abdominal wall defects

- Types of ventral wall defects:
  - Gastroschisis
  - Omphalocele
    - With extracorporeal liver
    - With intracorporeal liver
  - Umbilical hernia
  - Ectopia cordis
  - Bladder extrophy
  - Cloacal extrophy
  - Cleft or absent sternum
- Gastroschisis and omphalocele are the two most common types of ventral wall defect

OMPHALOCOELE



GASTROSCHISIS



OMPHALOCOELE GASTROSCHISIS

	OMPHALOCOELE	**Gastroschisis**
Incidence	1 case in 5,386 births	1 case in 2,229 births
Covering sac **Cord location**	Present On the sac	Absent On abdominal wall
Bowel	Normal	Inflammed, edomatous and matted
Size	Exomphalos major (umbilical defect > 5cm) Exomphalos minor (umbilical defect < 5cm)	Small
Pathophysiology	Failure of the midgut to return to abdomen by the 10th week of gestation	Abnormal involution of right umbilical vein/Rupture of a small omphalocoele/Failure of migration and fusion of the lateral folds of the embryonic disc on the 3rd-4th week of gestation

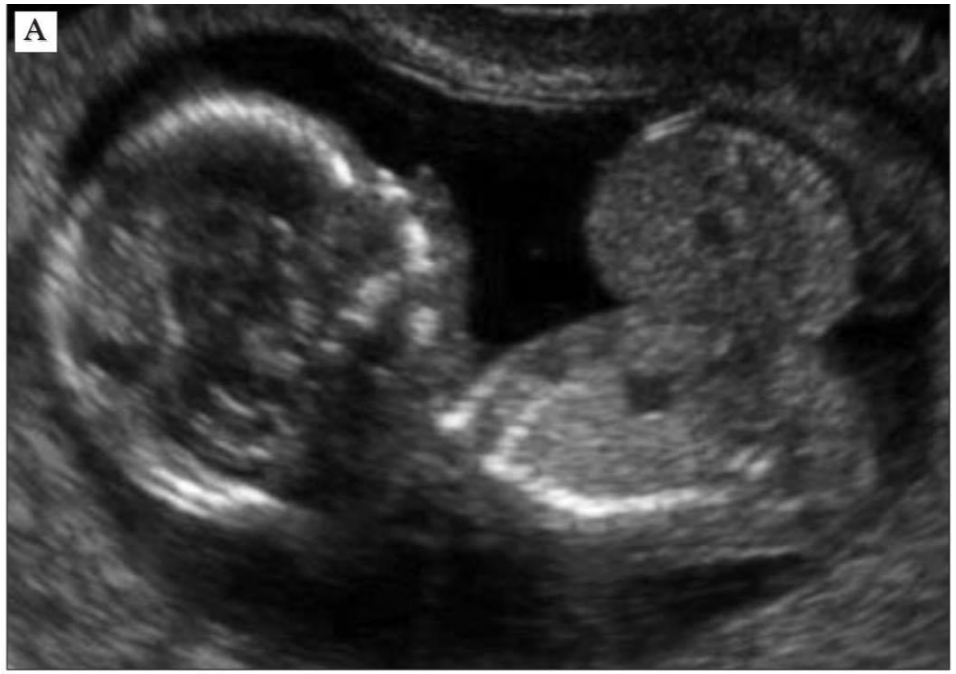
OMPHALOCOELE GASTROSCHISIS

	OMPHALOCOELE	**Gastroschisis**
Other organs **Other anomalies**	Liver often out 50-88%	Rare 10-20%
Prematurity	10-20%	50-60%
IUGR	Less common	Common
Treatment	Often primary	Often staging

Antenatal Diagnosis

- Elevated serum levels of (AFP) alpha-fetoprotein both maternal blood and amniotic fluid
- Ultrasound

-polyhydramnios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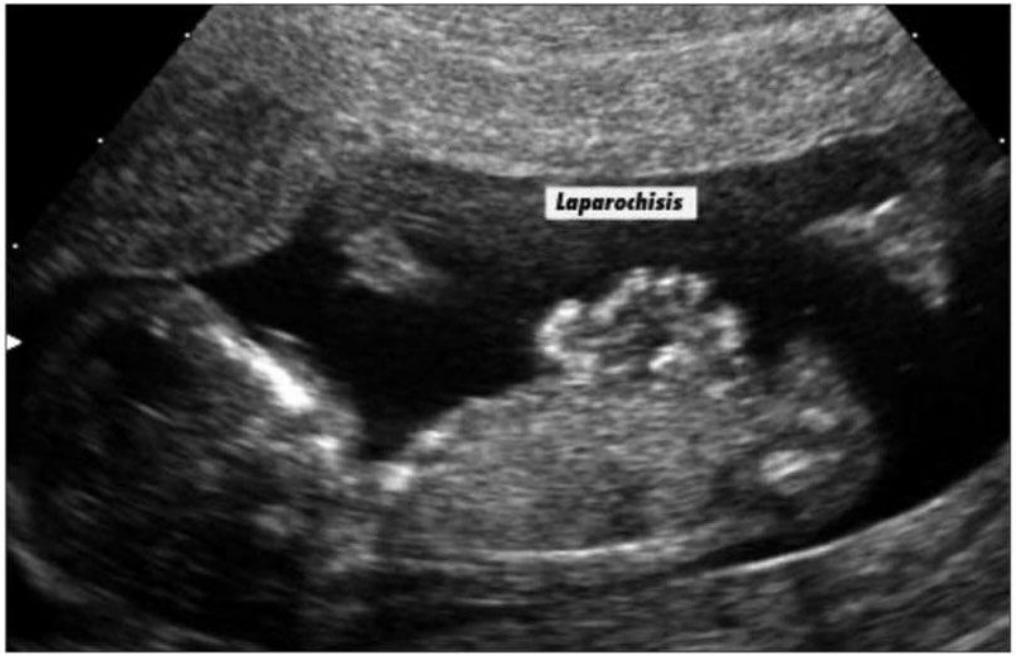
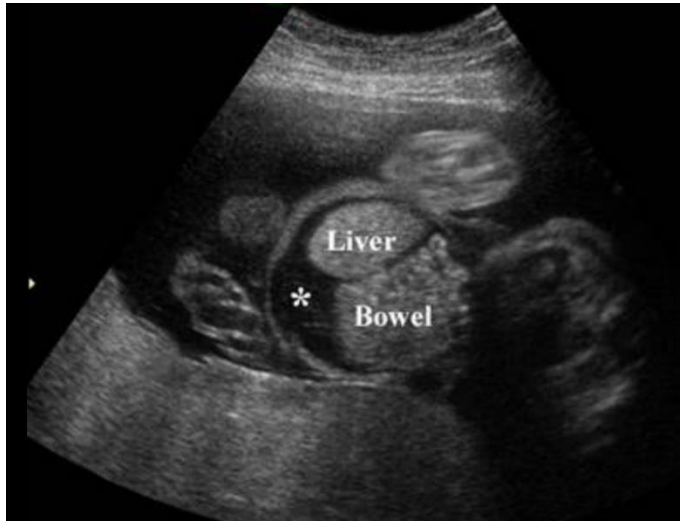
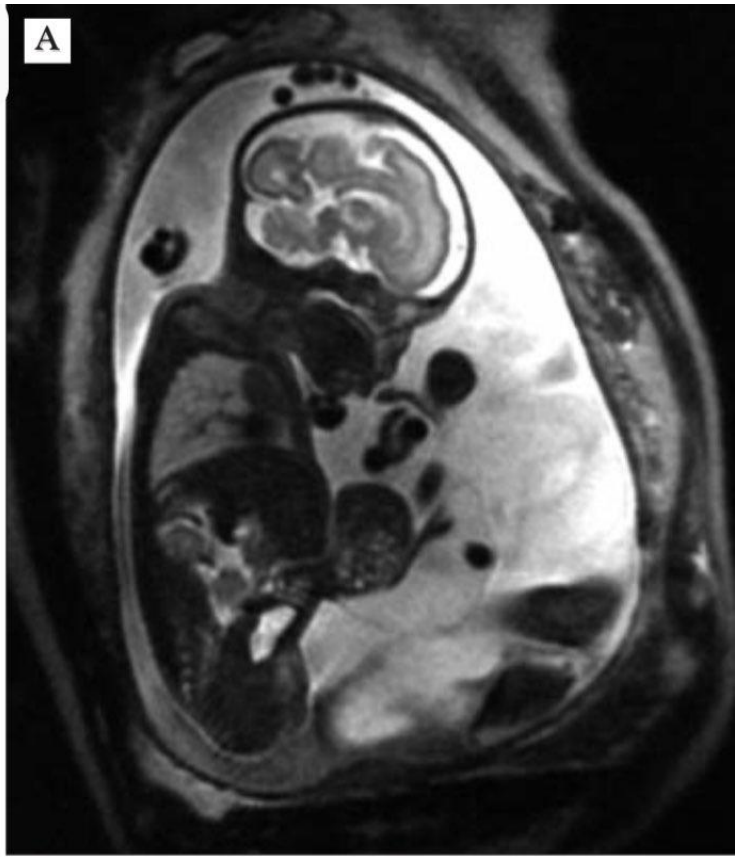
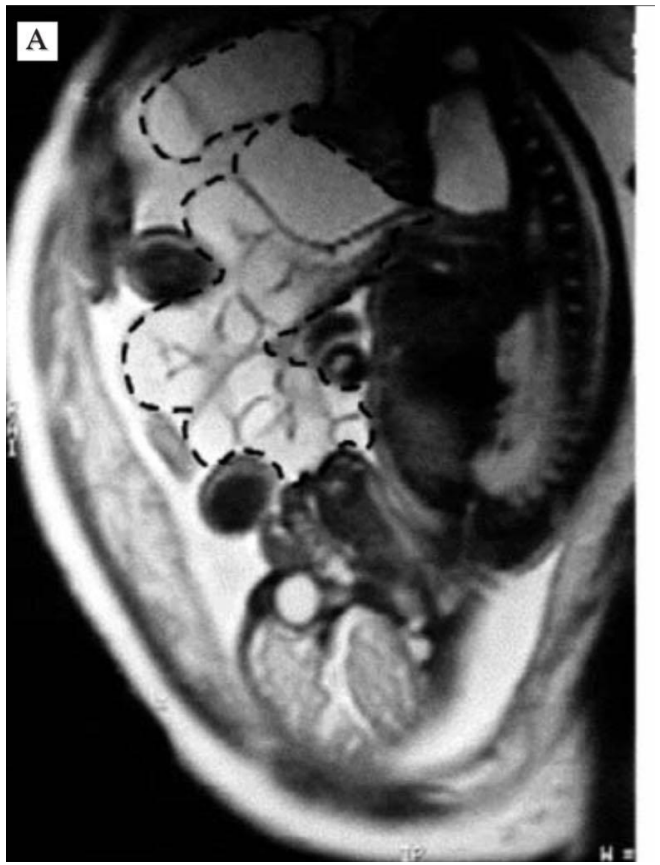

Laparochisis


Liver
*
Bowel

Antenatal Diagnosis

- Nuclear magnetic resonance





Management

- **Delivery**

birth should take place in a tertiary center to provide immediate access to neonatal intensive care and pediatric surgery.

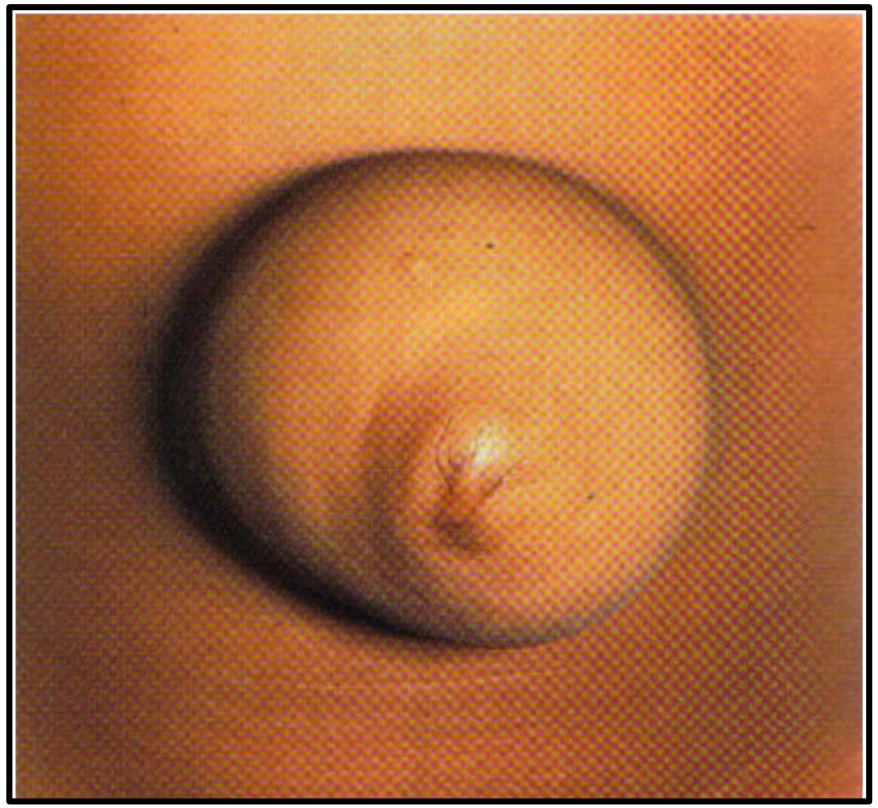
It is essential to reduce the time between birth and reintegration of viscera.

ideal timing of delivery in gastroschisis is controversial

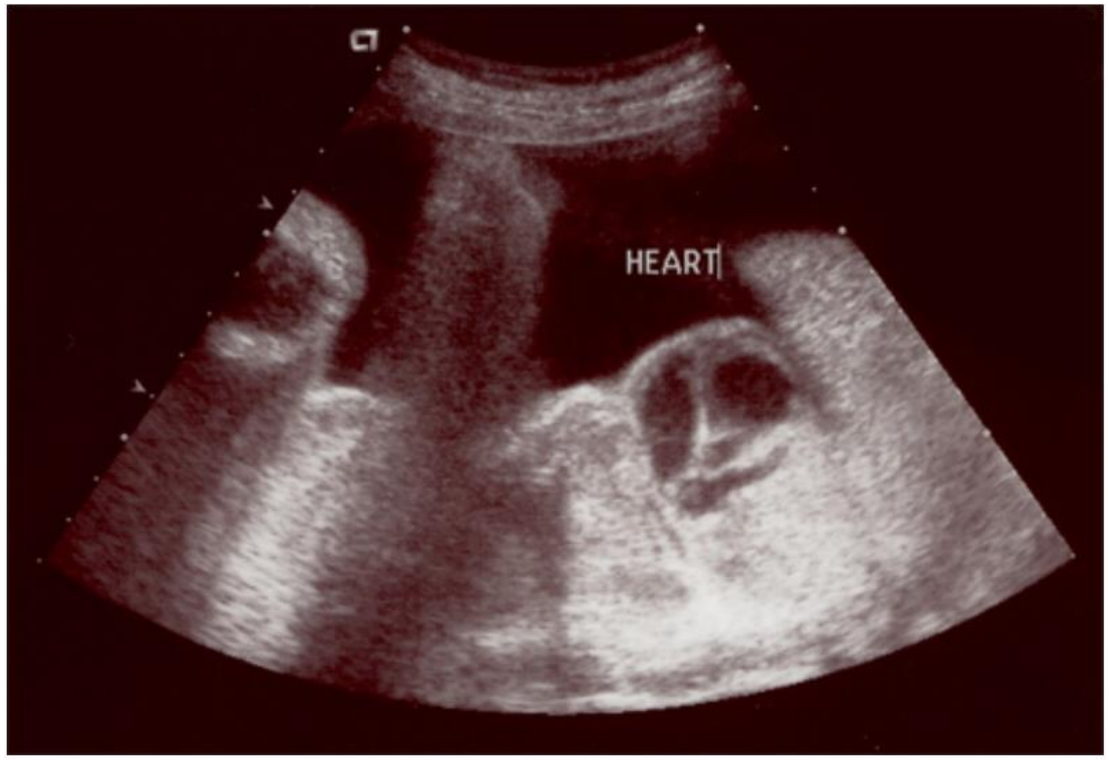
Delivery of babies with omphalocele may be vaginal or cesarean depending on the size and contents of the omphalocele.

In gastroschisis, vaginal delivery unless there is a specific obstetrical indication for a C-section delivery.

Umbilical Hernia

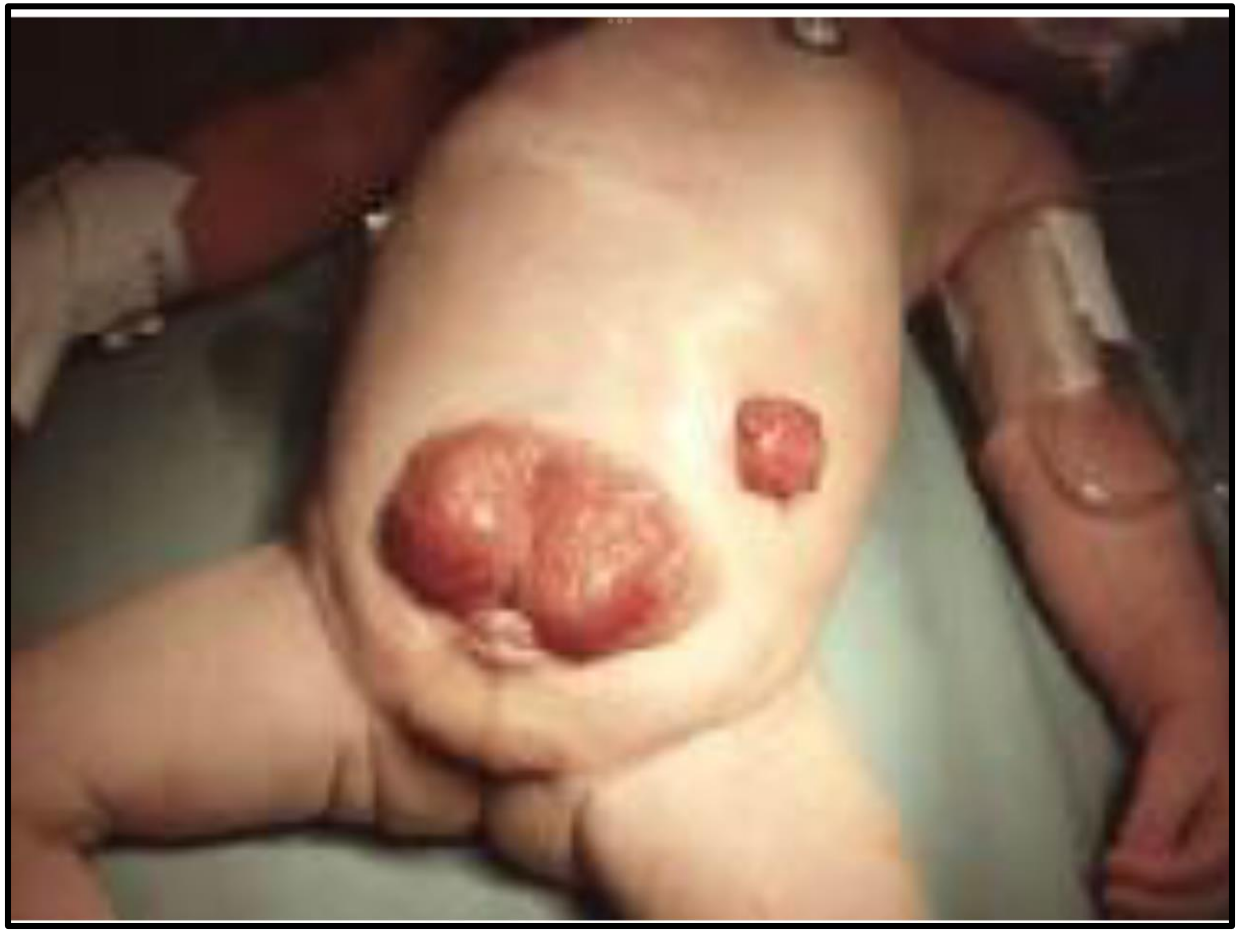


Ectopia Cordis



The heart is protruding through a defect in the chest wall.

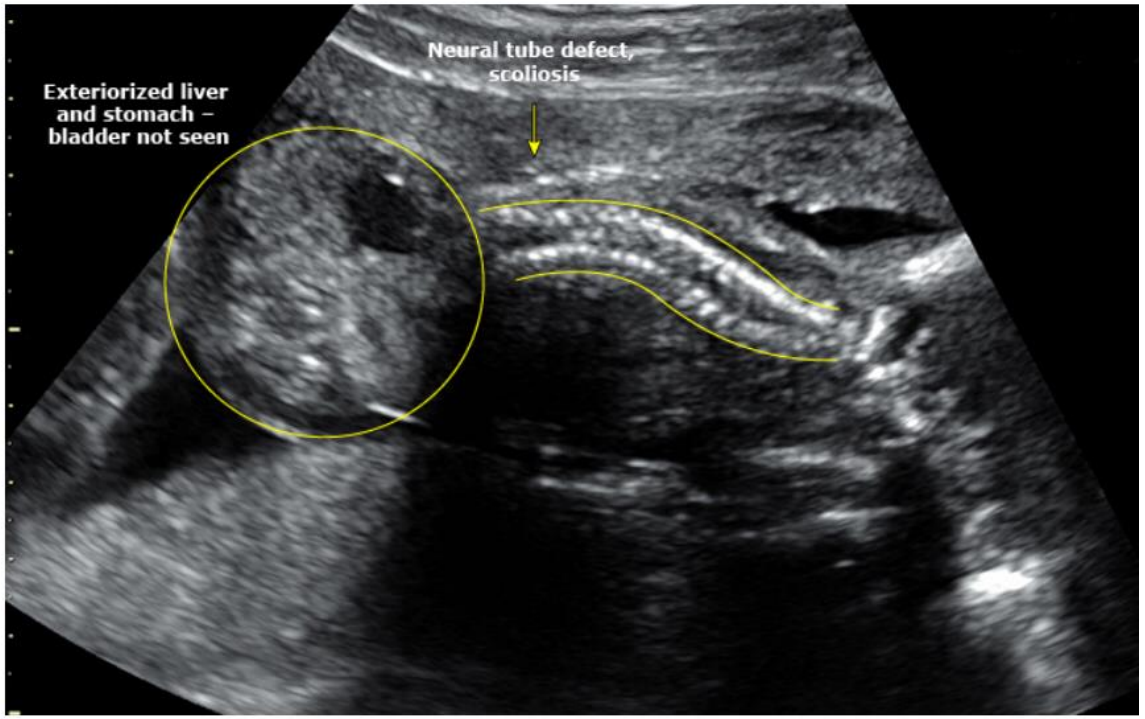
Bladder Exstrophy



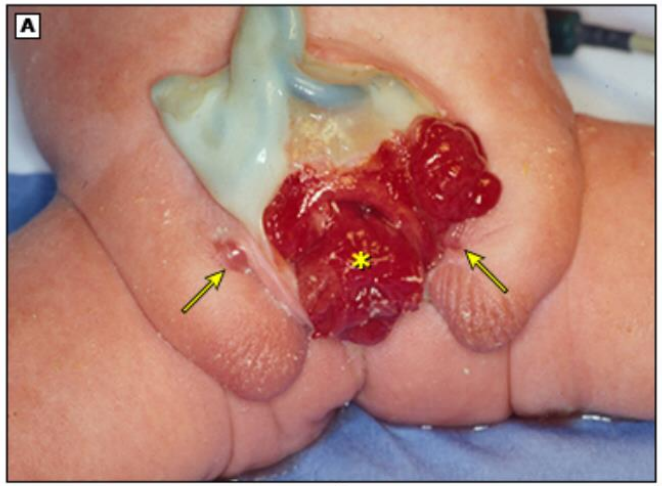
Cloacal Exstrophy

OEIS complex
(omphalocele-exstrophy-imperforate anus-spinal dysraphism)

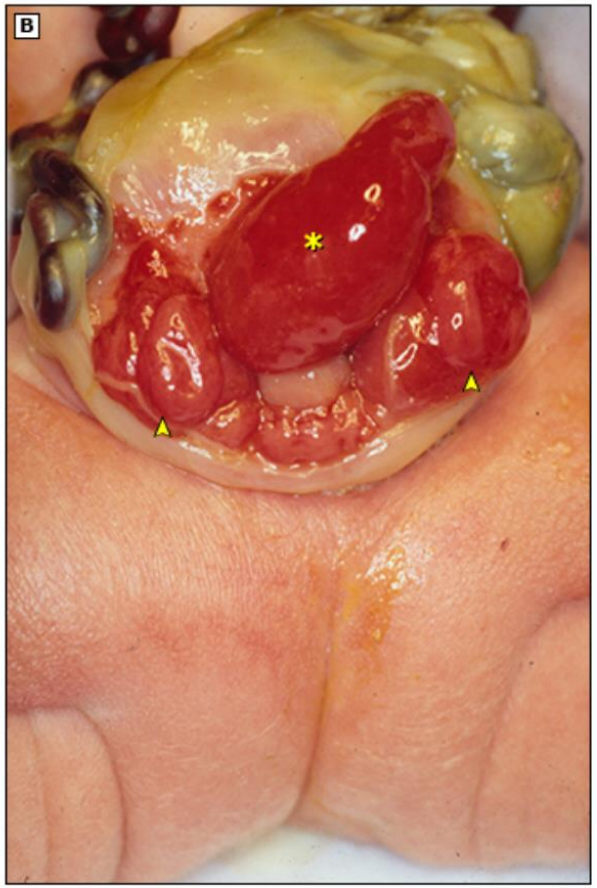
Omphalocele-exstrophy-imperforate anus-spinal dysraphism (OEIS)



OEIS complex (omphalocele-exstrophy-imperforate anus-spinal dysraphism). Imperforate anus cannot be appreciated in this image. The abdominal-pelvic structures are exteriorized.



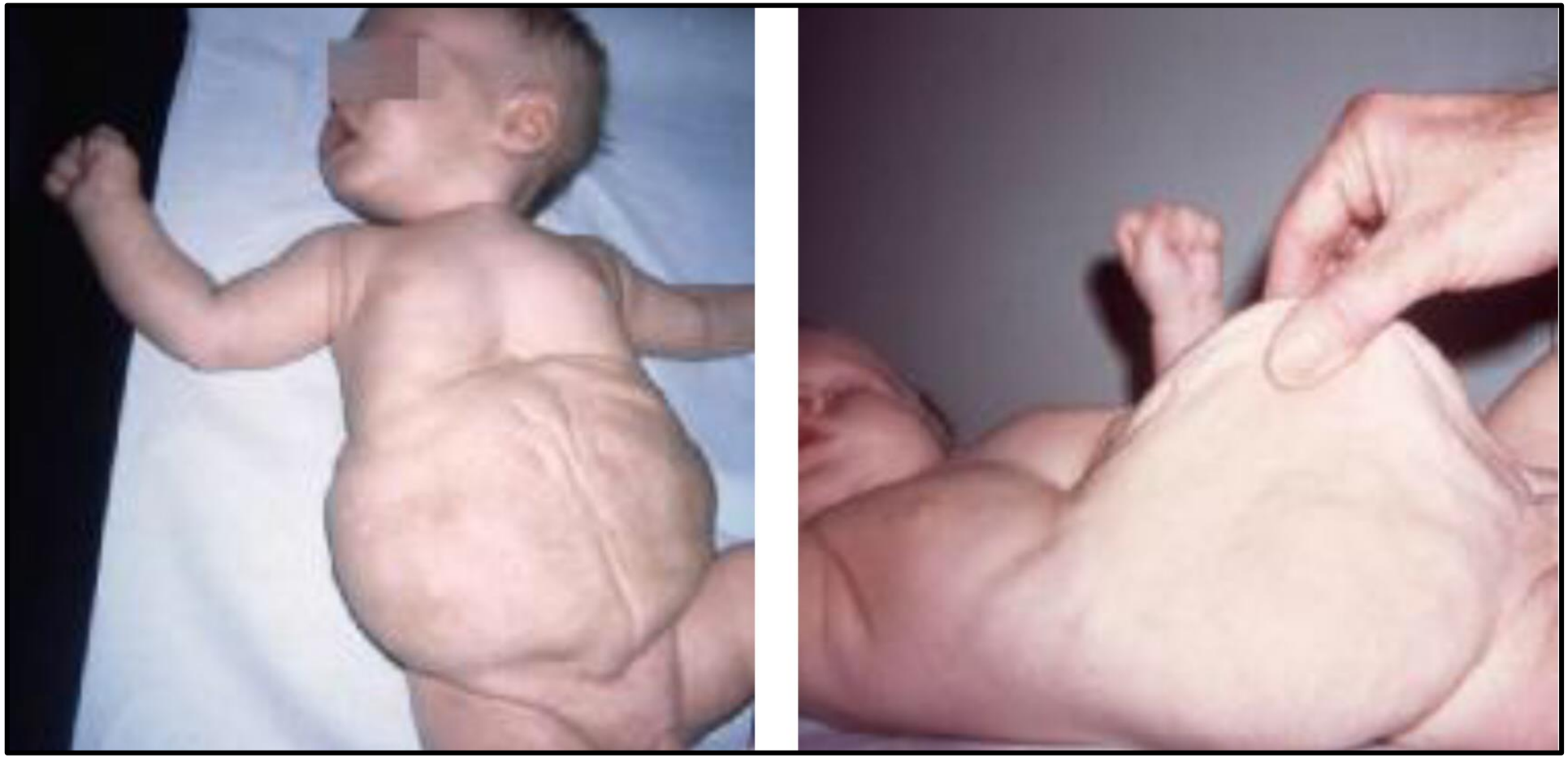
Male



Female

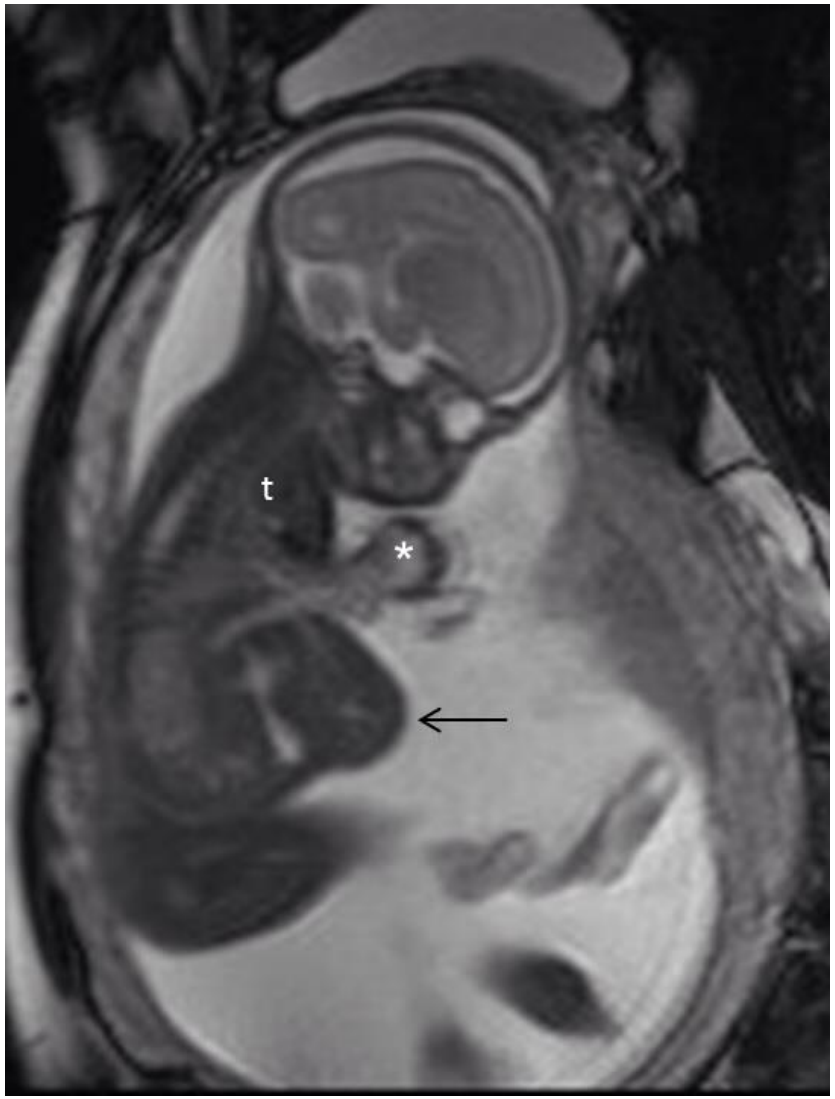
Cloacal exstrophy in a male (A) and female (B) newborn infant. The anus is imperforate, and the hindgut exits from the lower abdominal wall. In both patients, the bladder is split in half (seen best in the female; arrowheads), separated by the hindgut (asterisks). The umbilicus and omphalocele are seen superior to the split bladder and hindgut. The external genitalia are also split; the male has a small hemiphallus (arrows) associated with the scrotum.

Prune Belly Syndrome



Pentalogy Of Cantrell

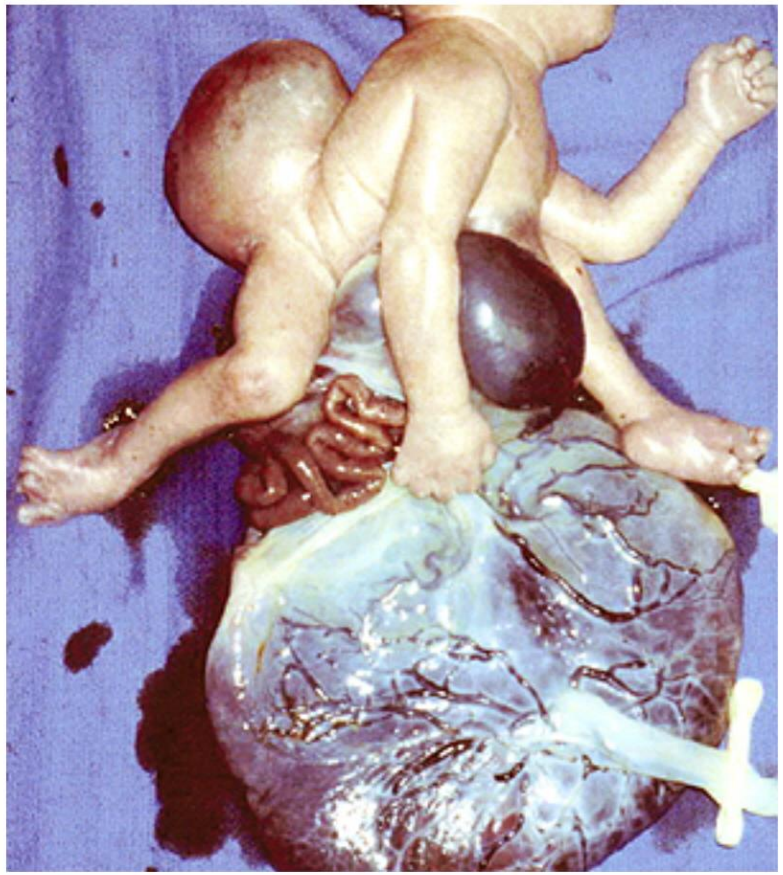
- Omphalocoele
- Anterior diaphragmatic hernia
- Sternal cleft
- Ectopia Cordis
- Intracardiac defect



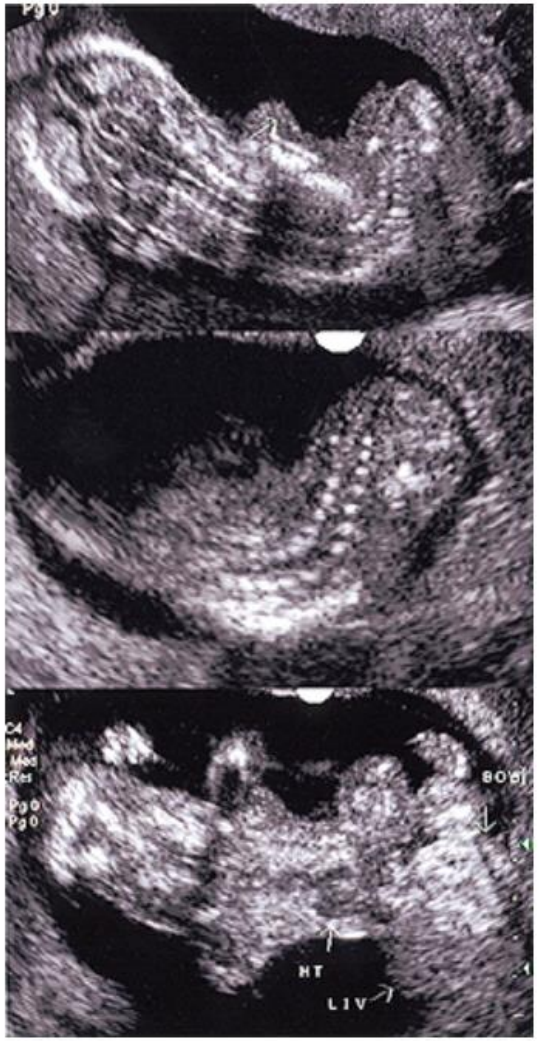
MRI in pregnancy in a case of pentalogy of Cantrell, showing ectopia cordis (*), partial herniation of the liver (arrow), and a small thoracic cavity (t)

Body stalk anomaly

Neonate with body stalk malformation



Body stalk malformation



Multiple defects are evident in this fetus with a body stalk malformation. The upper and middle images show severe kyphoscoliosis. The lower image shows the abdominal wall defect with ectopia cordis (HT) and an omphalocele containing liver and bowel.

Management

Prenatal Diagnosis

Imaging:

- Ultrasound

Alpha-fetoprotein

- The second-trimester maternal serum alpha-fetoprotein (MSAFP)

Obstetric Management

- Counseling
- Delivery

Abdominal Wall Defects

Differential diagnosis of fetal abdominal wall defects

Abnormality	Covering membrane	Site of defect	Findings
Omphalocele	Yes	Cord inserts into the apex of omphalocele membrane.	Full-thickness abdominal wall defect with covering amnion-peritoneal membrane and herniation of viscera. Liver is often herniated; stomach and spleen may also herniate. Associated abnormalities are common and include aneuploidy, additional gastrointestinal abnormalities, cardiac defects, genitourinary anomalies, orofacial clefts, neural tube defects, defects of the diaphragm, polyhydramnios, and growth restriction.
Gastroschisis	No	Cord inserts adjacent to the abdominal wall defect. The defect is usually to the right of the umbilicus.	Full thickness and usually small abdominal wall defect on the right side of the intact and normally inserting umbilical cord with herniation of bowel, which floats in the amniotic fluid. Liver not usually herniated. Associated anatomic defects uncommon.
Umbilical hernia	No	Defect in linea alba. Cord inserts into the hernia sac.	Loops of bowel may be seen within the umbilical cord or bulge from otherwise intact abdominal wall.
Pentalogy of Cantrell	Yes	Cord inserts into omphalocele membrane. The associated abnormalities are cephalad to the umbilical insertion.	Pentalogy consists of: 1. lower sternum defect 2. anterior diaphragm defect 3. parietal pericardium defect 4. omphalocele 5. congenital heart anomalies (classically ectopia cordis)
Body stalk anomaly (also called limb body wall complex)	Yes	Variable	Large body wall defects of the thorax and/or abdomen and limb defects. The intrathoracic and abdominal organs lie outside the cavity and are contained within a sac consisting of amnioperitoneal membrane. The umbilical cord may be extremely short or absent. Severe kyphoscoliosis is often present. Large complex cranial defects and facial clefts may also be present. Renal aplasia/dysplasia and pulmonary hypoplasia are common. Umbilical cord is short. The combination of scoliosis, omphalocele, short cord, and bizarre appearance of the fetal body suggests this diagnosis. Two key features that distinguish this anomaly from omphalocele are that the fetus appears adherent to the placenta and there is no freely floating umbilical cord.
Bladder exstrophy	No	Cord insertion lower than normal on fetal abdomen. Abdominal wall defect is below umbilicus.	Nonvisualization of the bladder is a key finding. Visualization of a normal urinary bladder excludes the diagnosis. Classic bladder exstrophy is not associated with cranial, thoracic, umbilical, spinal, or limb defects.
Cloacal exstrophy (also called OEIS complex: omphalocele, exstrophy of the bladder, imperforate anus, spinal defects)	Yes	Cord insertion lower than normal on fetal abdomen. Abdominal wall defect is below umbilicus.	Full thickness ventral abdominal wall defect with an omphalocele at the superior margin of the defect and exposed bowel and bladder at the inferior margin. The lower abdominal wall defect helps to distinguish cloacal exstrophy from simple omphalocele. The major findings are a solid bulging mass in the lower abdominal wall, non-visualization of the urinary bladder, and normal amniotic fluid volume. Omphalocele, meningomyelocele, lower extremity defects, renal anomalies, widened pubic arches, narrow thorax, hydrocephalus, and single umbilical artery may be observed.
Amniotic band sequence (also called limb body wall complex)	No	Variable	Constriction rings and limb and digital amputation are common findings, but the clinical spectrum is highly variable. Craniofacial abnormalities and nonmidline body wall defects may be present. Shredded amniotic membrane may be seen.

NOTE: If the omphalocele sac ruptures, bowel may be seen floating in the amniotic fluid, as in gastroschisis. In cloacal exstrophy, hydrocolpos can be mistaken for a bladder containing urine.

Adapted from:

1. *Prefumo F, Izzi C. Fetal abdominal wall defects. Best Pract Res Clin Obstet Gynaecol 2014; 28:391.*
2. *Nakagawa M, Hara M, Shibamoto Y. MRI findings in fetuses with an abdominal wall defect: Gastroschisis, omphalocele, and cloacal exstrophy. Jpn J Radiol 2013; 31:153.*
3. *Revels JW, Wang SS, Nasrullah A, et al. An algorithmic approach to complex fetal abdominal wall defects. AJR Am J Roentgenol 2020; 214:213.*

UpToDate®

Congenital Heart Diseases

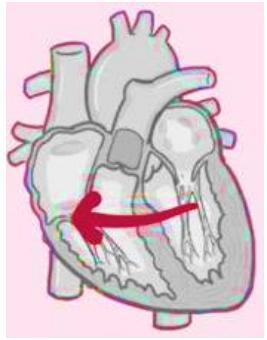
-**10%** associated with other defects or part of a syndrome.

Screening for CHD:
At week 18-22
by Detailed
Anomaly Scan (US)

❑ Acyanotic Defects:

(left to right shunt)

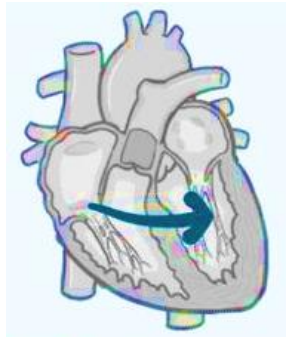
- Ventricular Septal Defect (most common)
- Atrial Septal Defect
- Patent Ductus Arteriosus
- Coarctation of the aorta



❑ Cyanotic Defects:

(right to left shunt)

- Tetralogy of Fallot (most common)
- Transposition of the Great Arteries
- Total Anomalous Pulmonary Venous Return
- Truncus Arteriosus
- Tricuspid Atresia



Congenital diaphragmatic hernia (CDH)

Developmental defect in the diaphragm leading to protrusion of abdominal contents into the thoracic cavity.

Resulting in lung hypoplasia and altered pulmonary vascular development.

Mostly they are left sided as the right hemidiaphragm is relatively protected by liver.

Management:

- Prenatal
- Postnatal

Congenital diaphragmatic hernia (CDH)