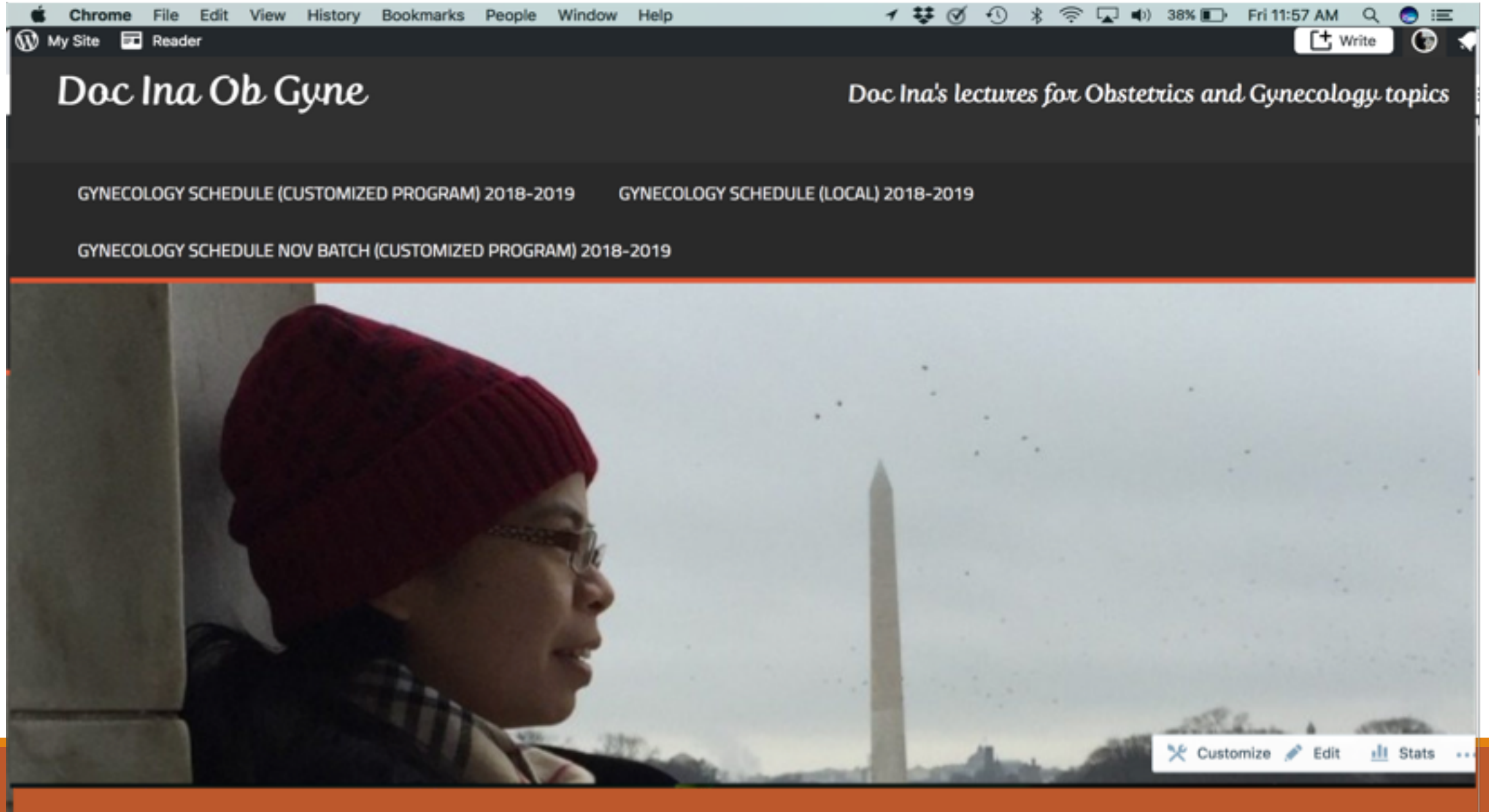
Fetal growth and development

INA S. IRABON, MD, FPOGS, FPSRM, FPSGE

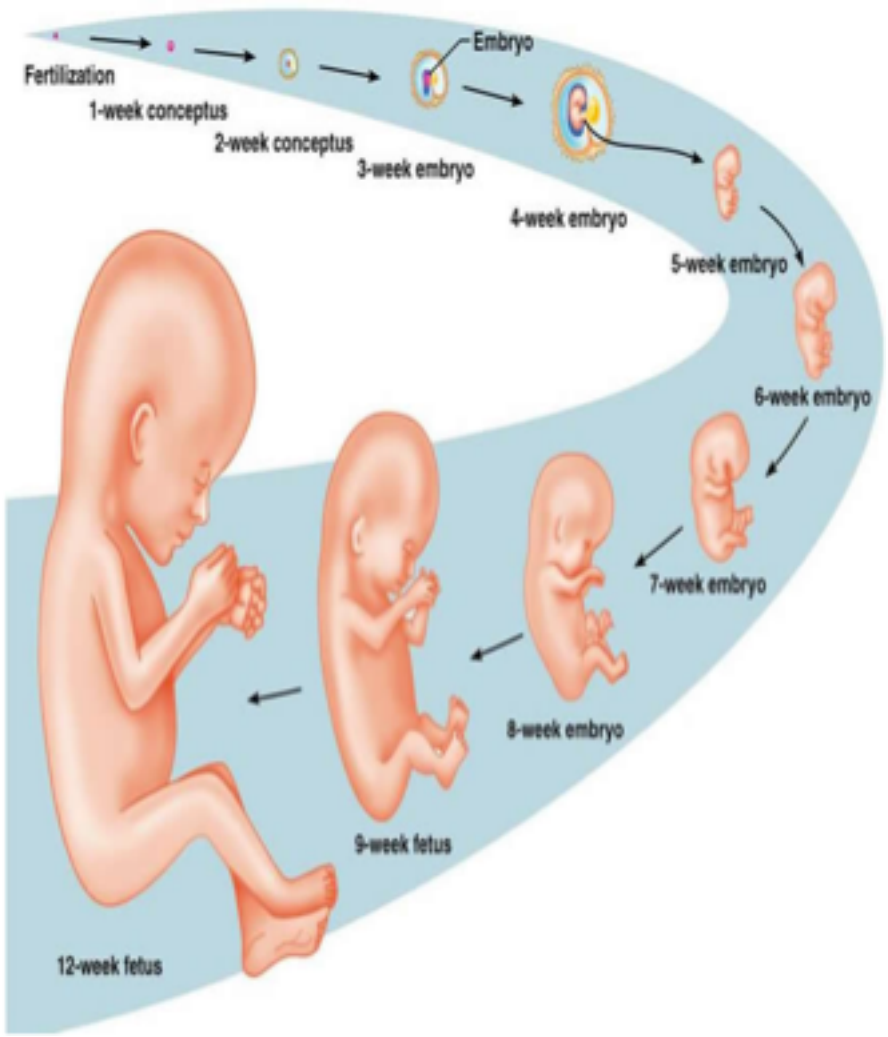
OBSTETRICS AND GYNECOLOGY
REPRODUCTIVE ENDOCRINOLOGY AND INFERTILITY
LAPAROSCOPY AND HYSTEROSCOPY

To download the lecture deck:



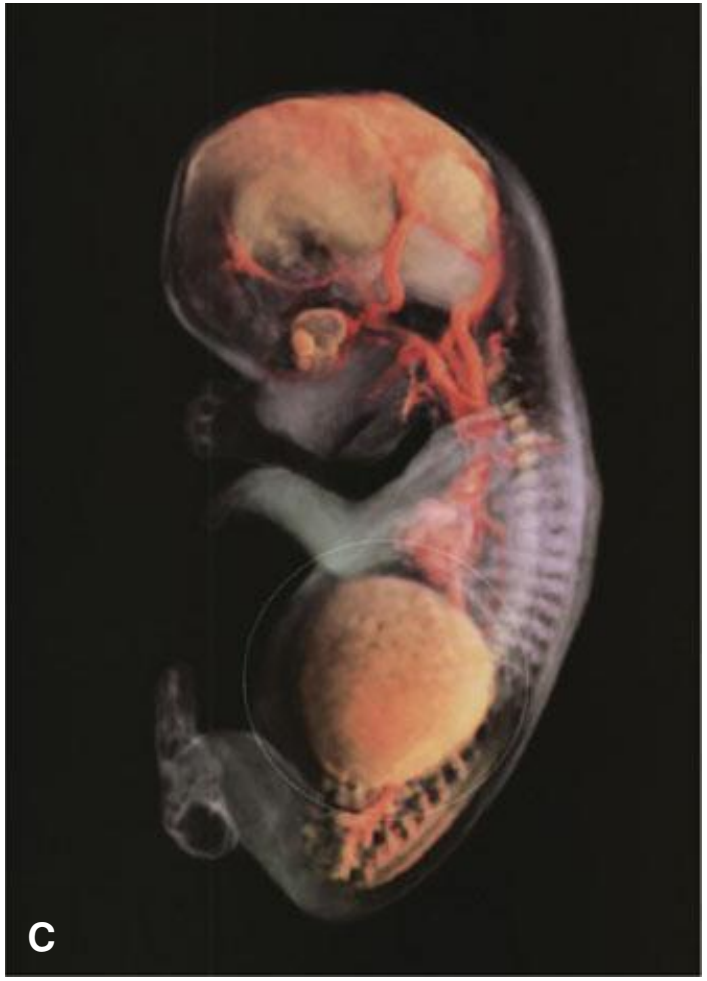
Reference

Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 24th edition; 2014; chapter 7



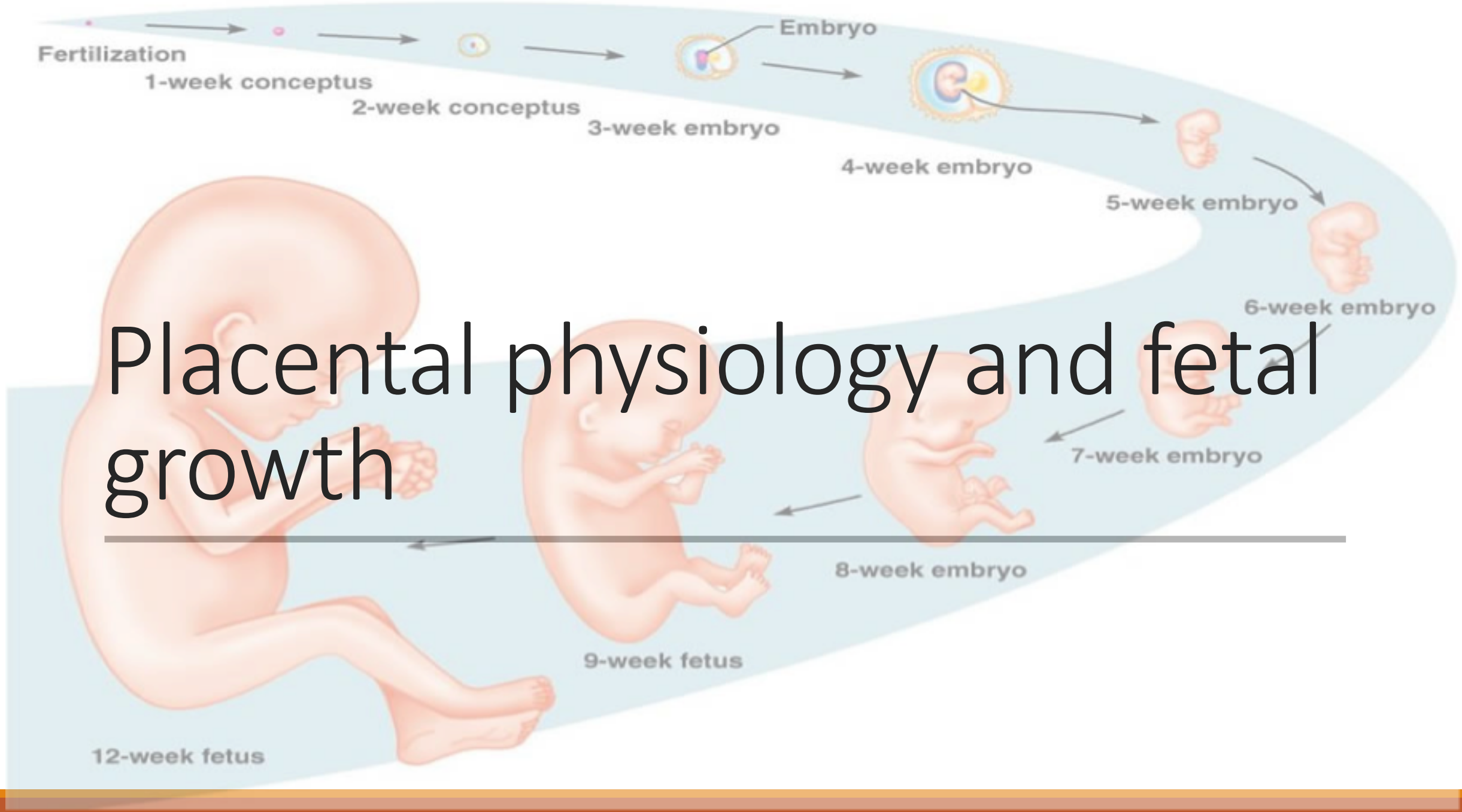
Outline

1. FETAL GROWTH AND DEVELOPMENT
2. PLACENTAL PHYSIOLOGY AND FETAL GROWTH
3. FETAL NUTRITION
4. FETAL ORGAN SYSTEM DEVELOPMENT
5. DEVELOPMENT OF GENITALIA
6. DISORDERS OF SEXUAL DEVELOPMENT



Fetal period

- Transition from the embryonic period to the fetal period begins **8 weeks after fertilization**—or 10 weeks after onset of last menses.
- Development during the fetal period consists of growth and maturation of structures that were formed during the embryonic period.
- Crown-to-rump measurements, which correspond to the sitting height, are most accurate for dating



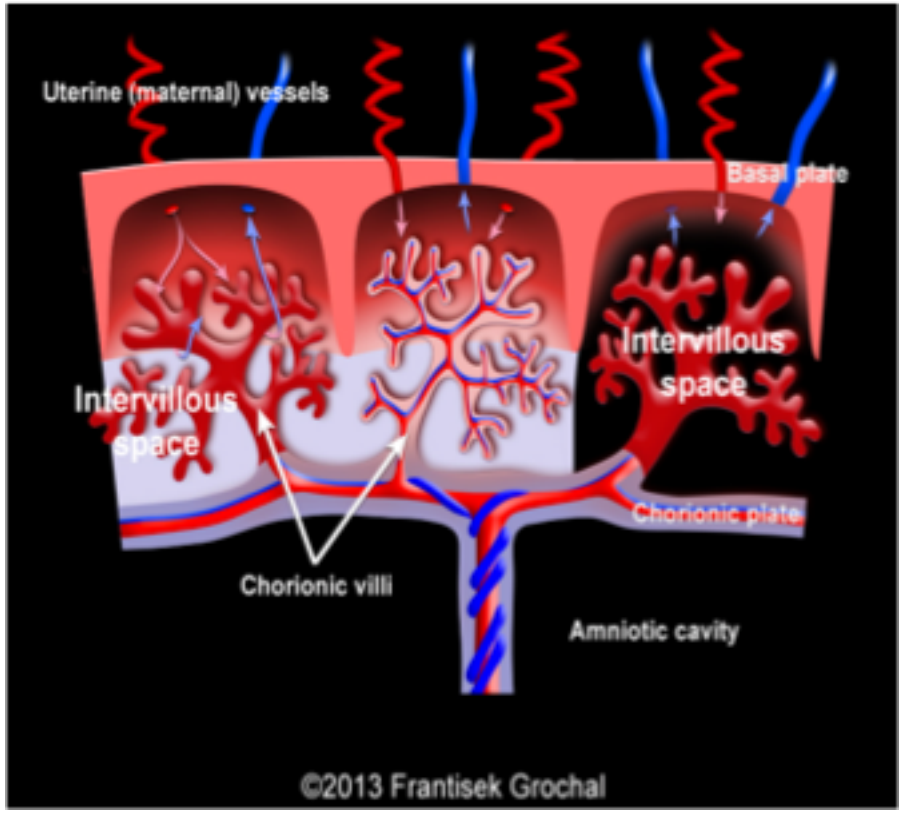
Placental physiology and fetal growth

Placenta

- organ of transfer between mother and fetus →transfer of oxygen and nutrients from the mother to the fetus and carbon dioxide and metabolic wastes from fetus to mother.
- There are no direct communications between fetal blood (contained in the fetal capillaries of the chorionic villi) and maternal blood (intervillous space).
- Bidirectional transfer depends on the processes that permit or aid the transport through the syncytiotrophoblast that line chorionic villi.

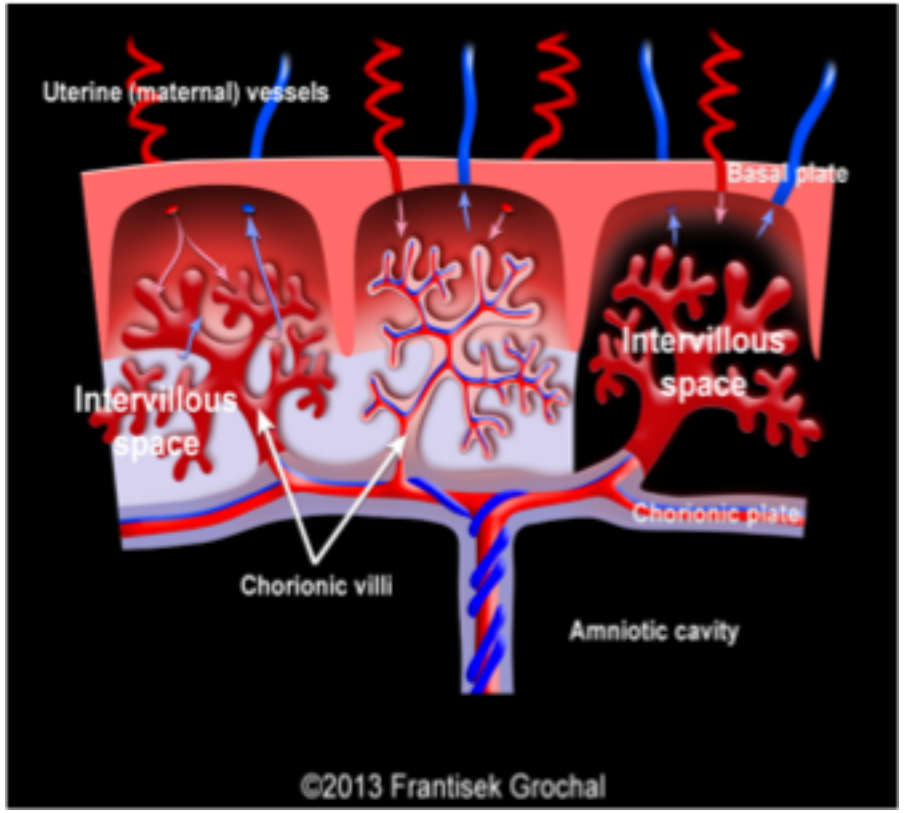
Intervillous space

- Maternal blood within the intervillous space is the **primary unit of maternal–fetal transfer.**
- Blood from the maternal spiral arteries directly bathes the trophoblasts.
- Substances transferred from mother to fetus first enter the intervillous space and are then transported to the syncytiotrophoblast.
- Thus, the chorionic villi and intervillous space function together as the fetal lung, gastrointestinal tract, and kidney.



Intervillous space

- Active labor contractions reduce blood flow into the intervillous space → degree of reduction depends on the contraction intensity.
- Blood pressure within the intervillous space is significantly less than uterine arterial pressure, but somewhat greater than venous pressure.



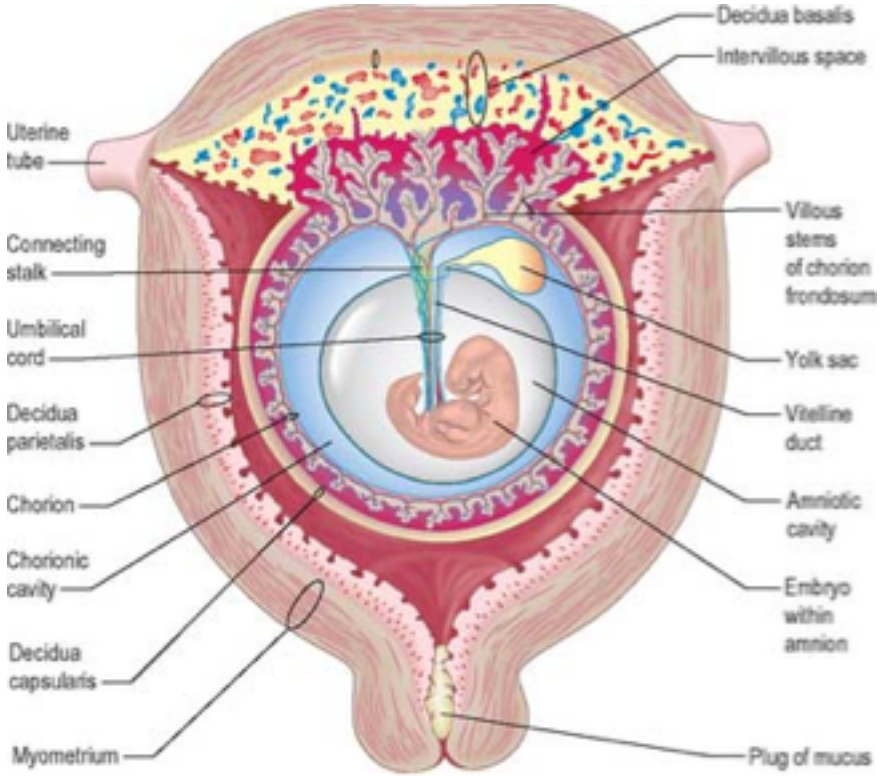
Placental transfer

Mechanism of transfer

- Most substances with a molecular mass less than 500 Da pass readily through placental tissue by **simple diffusion** → oxygen, carbon dioxide, water, most electrolytes, and anesthetic gases
- Some low-molecular-weight compounds undergo transfer facilitated by syncytiotrophoblast.
  - usually those that have low concentrations in maternal plasma but are essential for normal fetal development.
- Insulin, steroid hormones, and thyroid hormones cross the placenta, but very slowly.

Mechanism of transfer

- hormones synthesized in situ in the trophoblasts enter both the maternal and fetal circulations, but not equally
  - Ex: human chorionic gonadotropin (HCG) and placental lactogen are much lower in fetal plasma than in maternal circulation
- Substances of high molecular weight usually do not traverse the placenta
  - Exception: immunoglobulin G—molecular weight 160,000 Da—which is transferred by way of a specific trophoblast receptor-mediated mechanism.

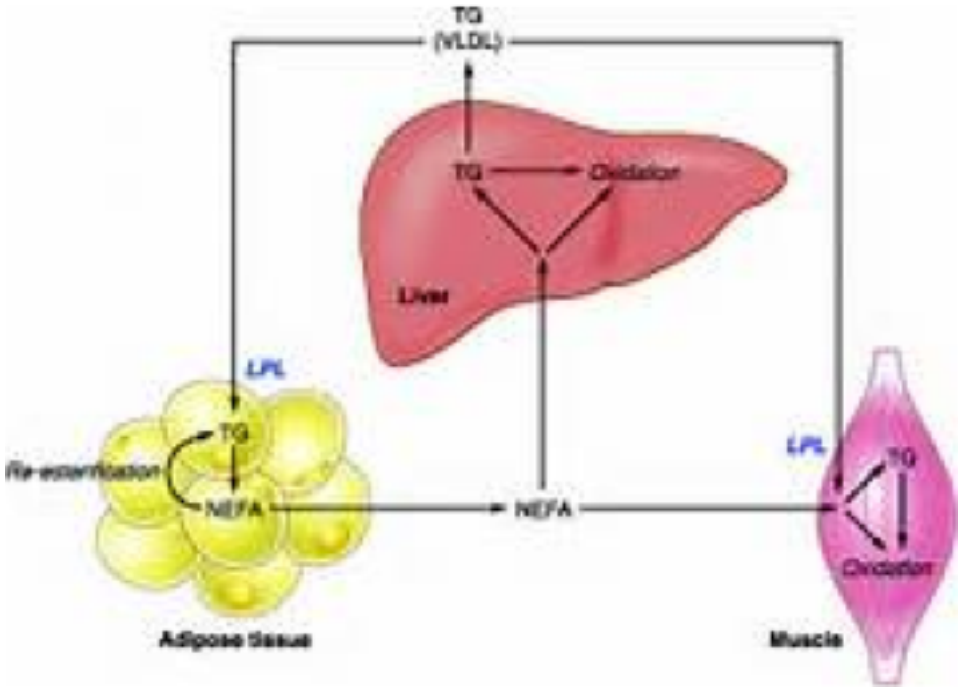


Fetal Nutrition

3 major maternal storage depot:

1. Liver
2. Muscle
3. Adipose tissue

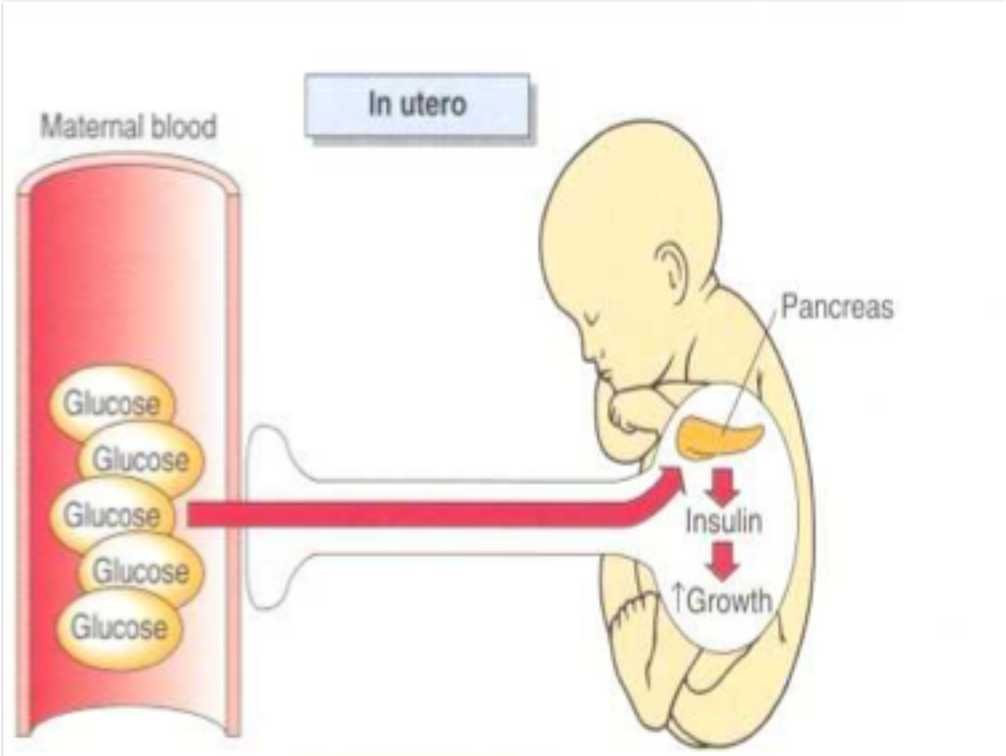
Insulin – storage hormone



Glucose and Fetal Growth: **Glucose and Insulin** Role in Fetal Macrosomia

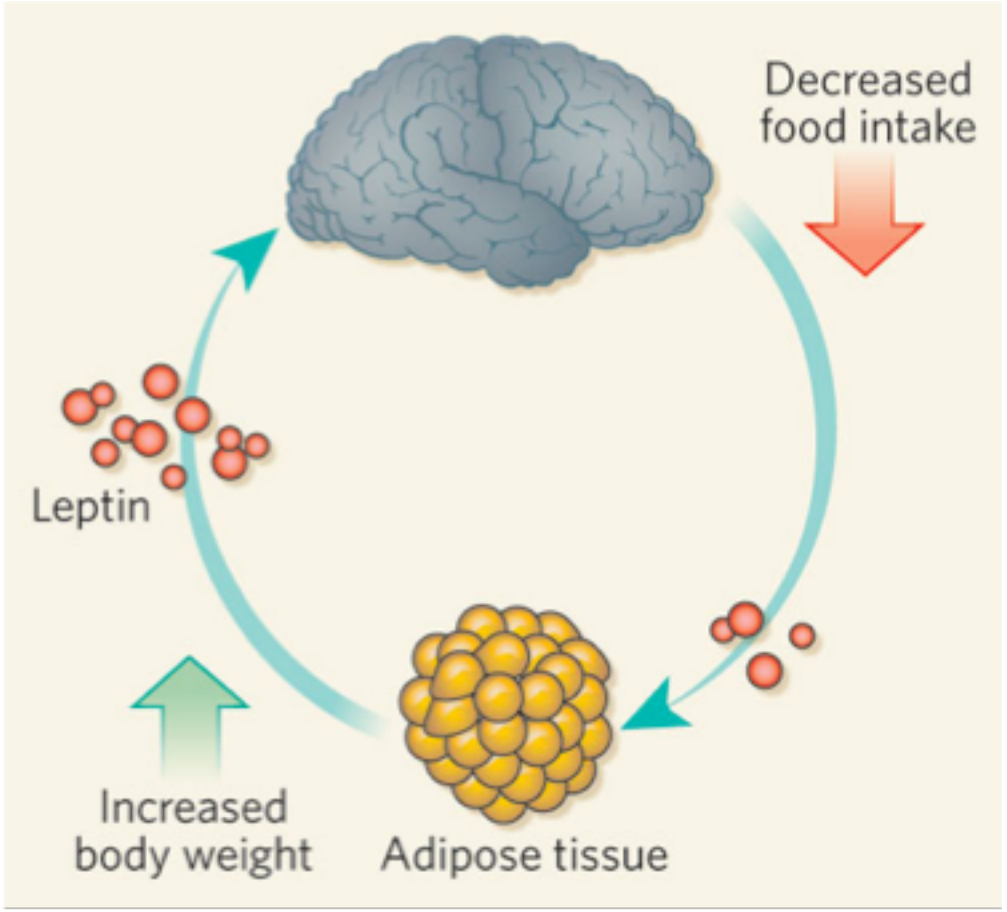
- fetal hyperinsulinemia is one driving force for fetal macrosomia

- insulin-like growth factor and fibroblast growth factor are important regulators of placental development and function



Glucose and Fetal Growth: **Leptin**

- This polypeptide hormone was originally identified as a product of adipocytes and a regulator of energy homeostasis.
- contributes to angiogenesis, hemopoiesis, osteogenesis, pulmonary maturation, and neuroendocrine, immune, and reproductive functions
- Leptin is produced by the mother, fetus, and placenta.
- It is expressed in syncytiotrophoblast and fetal vascular endothelial cells.



Glucose and Fetal Growth: Proteins

Placental transfer of larger proteins is limited, but there are exceptions:

- Immunoglobulin G (IgG) crosses the placenta in large amounts via endocytosis and trophoblast Fc receptors.
- IgG transfer depends on maternal levels of total IgG, gestational age, placental integrity, IgG subclass, and antigen nature
- **IgA and IgM** of maternal origin are effectively excluded from the fetus

FETAL ORGAN SYSTEM DEVELOPMENT

Amnionic Fluid Formation

Early pregnancy: amnionic fluid is an ultrafiltrate of maternal plasma.

2nd trimester: consists largely of extracellular fluid that diffuses through the fetal skin → reflects the composition of fetal plasma

After 20 weeks: amnionic fluid is composed largely of fetal urine.

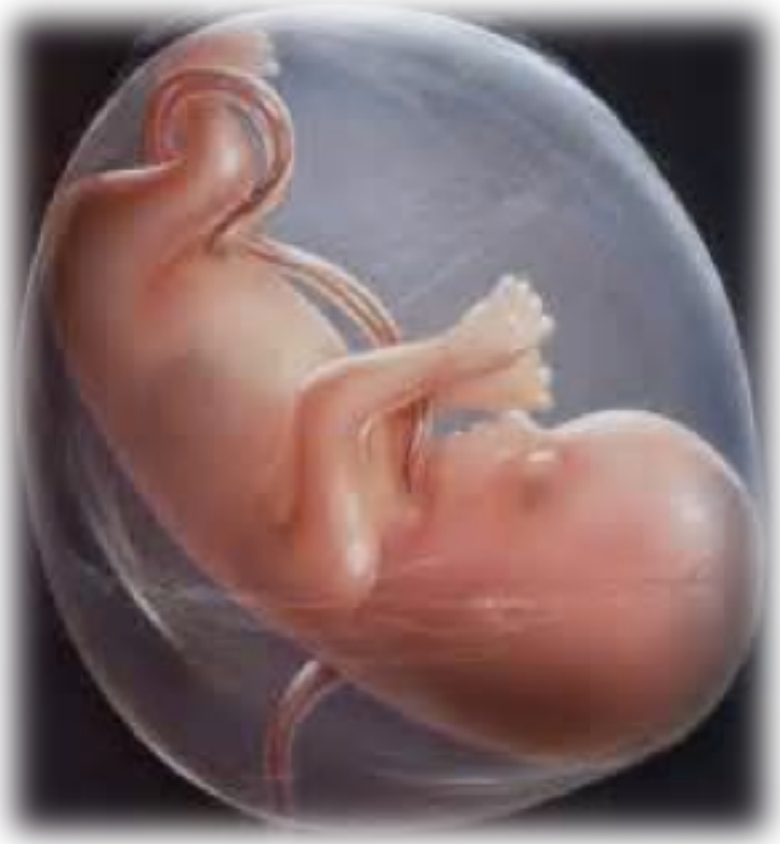
Amnionic Fluid Formation

- Fetal kidneys start producing urine at 12 weeks, and by 18 weeks, they are producing 7 to 14 mL per day.

- In general, the volume increases by 10 mL per week at 8 weeks and increases to 60 mL per week at 21 weeks, then **peaks at 34 weeks.**

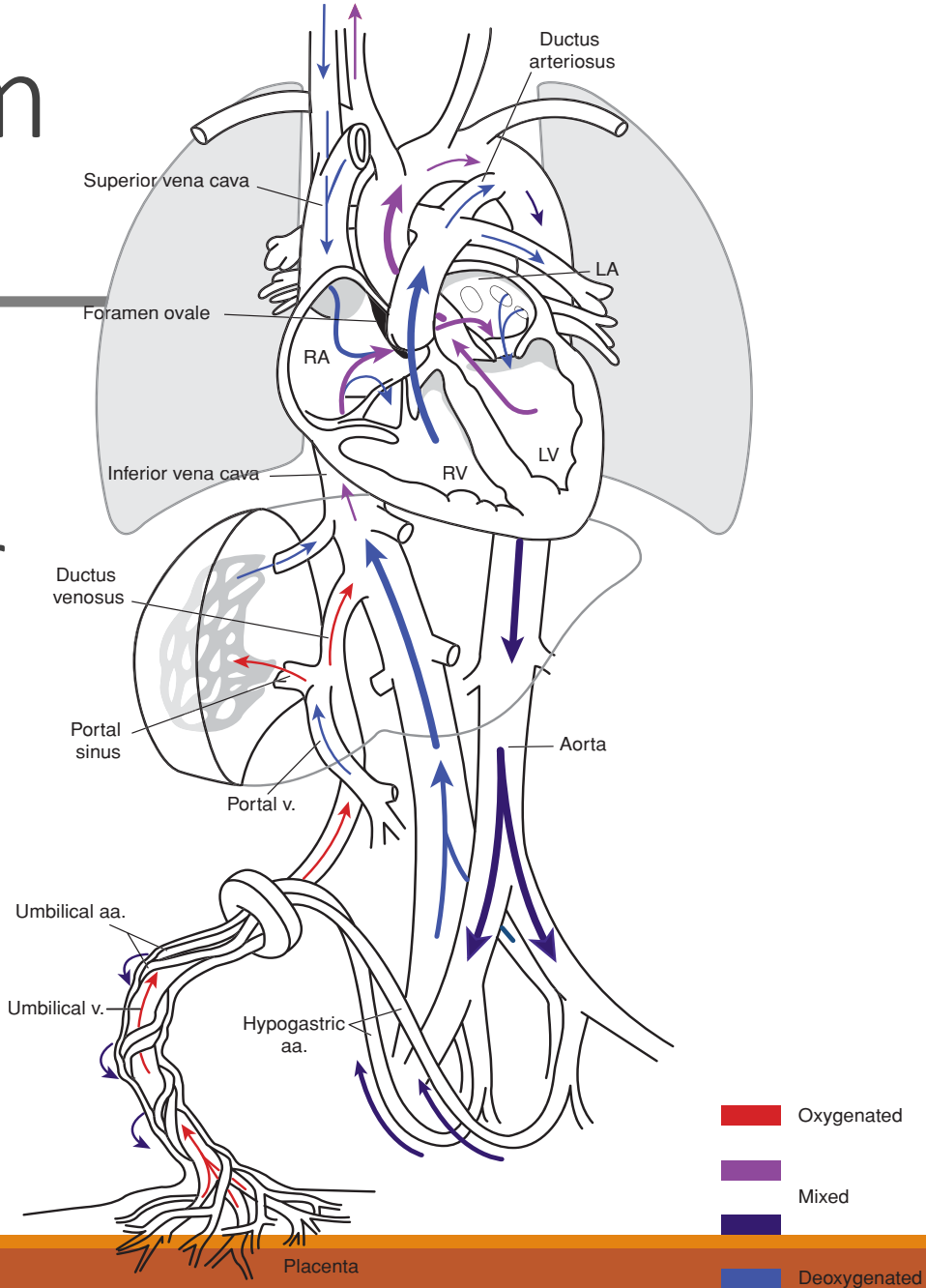
Amnionic Fluid Formation

1. Amnionic fluid serves to cushion the fetus, allowing musculoskeletal development and protecting it from trauma.
2. Maintains temperature and has a minimal nutritive function.
3. Ingestion of fluid into the gastrointestinal tract and inhalation into the lung may promote growth and differentiation of these tissues.
4. Intrapulmonary fluid formation and the alternating egress and retention of fluid in the lungs by breathing movements are essential to normal pulmonary development.



Fetal Cardiovascular System

- substantially different from that of the adult;
- because fetal blood does not need to enter the pulmonary vasculature to be oxygenated, most of the right ventricular output bypasses the lungs.
- fetal heart chambers work in **parallel** (**adult: series**) →effectively supplies the brain and heart with more highly oxygenated blood than the rest of the body.

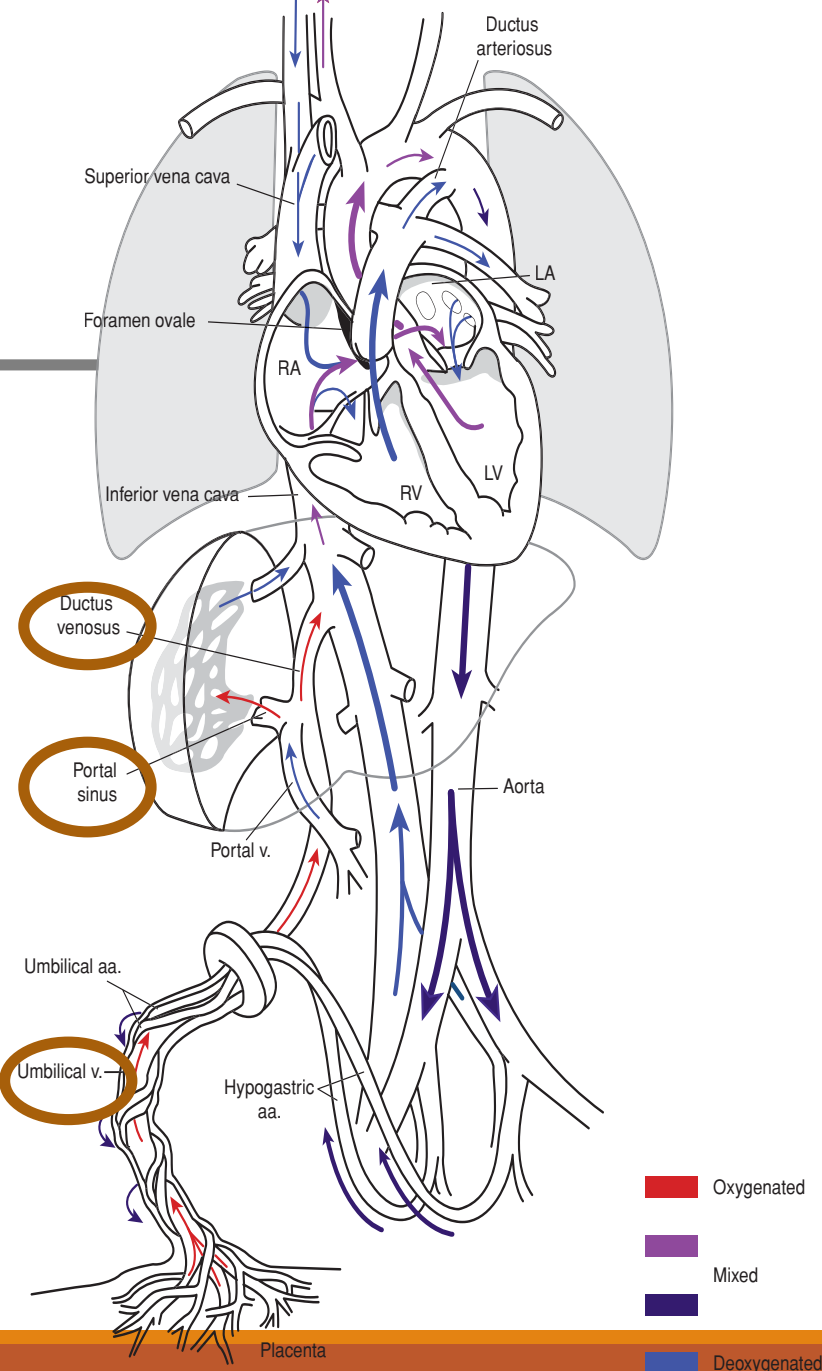


Fetal Cardiovascular System

Oxygen and nutrient materials required for fetal growth and maturation are delivered from the placenta by the **single umbilical vein** → divides into the *ductus venosus and the portal sinus.*

Ductus venosus: is the major branch of the umbilical vein and traverses the liver to enter the inferior vena cava directly; *carries well-oxygenated blood directly to the heart.*

Portal sinus carries blood to the hepatic veins primarily on the left side of the liver, and oxygen is extracted.



Fetal Cardiovascular System

- In contrast to postnatal life, the ventricles of the **fetal heart work in parallel, not in series**.
- Well-oxygenated blood enters the left ventricle, which supplies the heart and brain, and less oxygenated blood enters the right ventricle, which supplies the rest of the body.

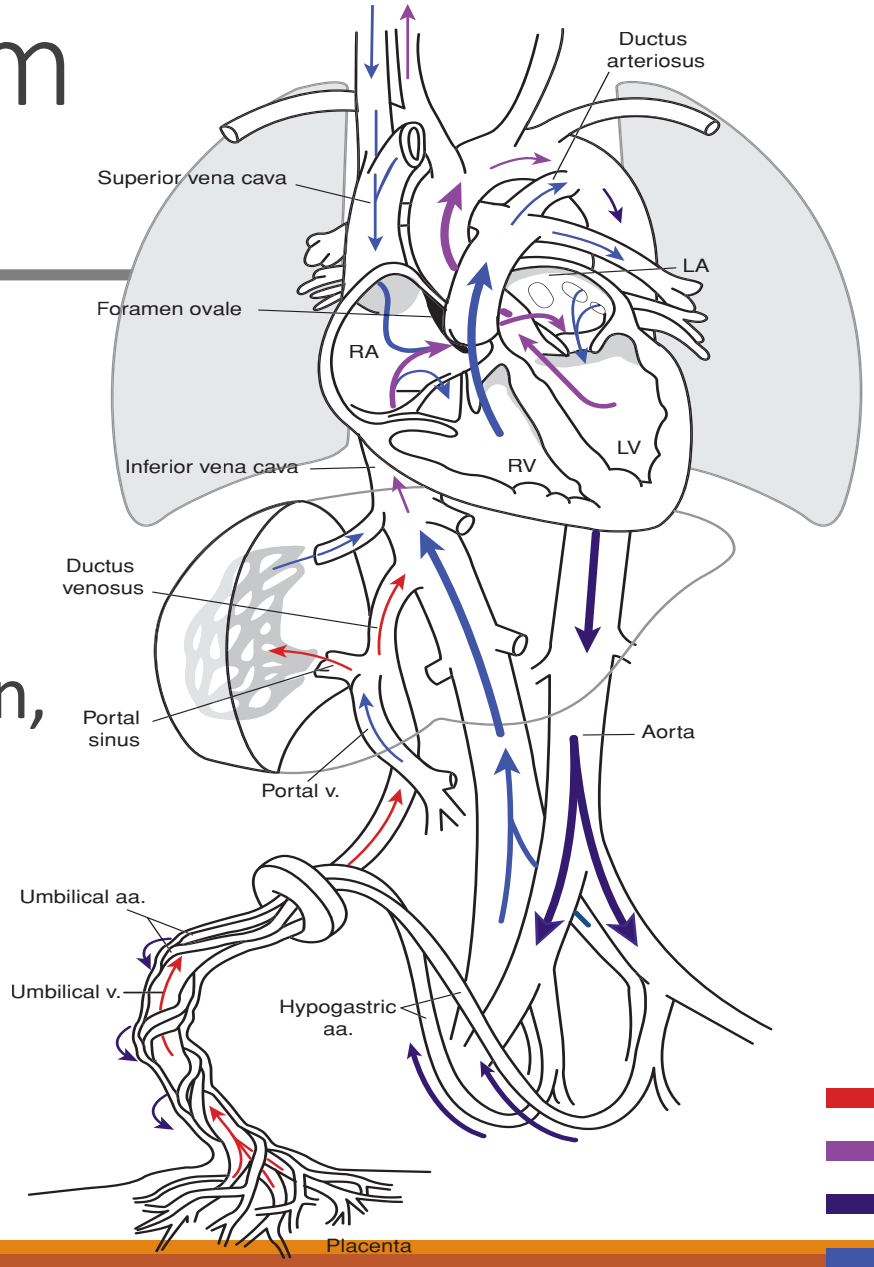


FIGURE 7-8 The intricate nature of the fetal circulation is evident. The degree of blood oxygenation in various ves from that in the postnatal state. aa = arteries; LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ve

Fetal Cardiovascular System

- The **well-oxygenated blood tends to course along the medial aspect of the inferior vena cava** and the **less oxygenated blood flows along the lateral vessel wall** →aids their shunting into opposite sides of the heart.
- Once this blood enters the right atrium, the **crista dividens** preferentially shunts the **well-oxygenated blood** from the medial side of the inferior vena cava through the foramen ovale into the left heart and then to the heart and brain.

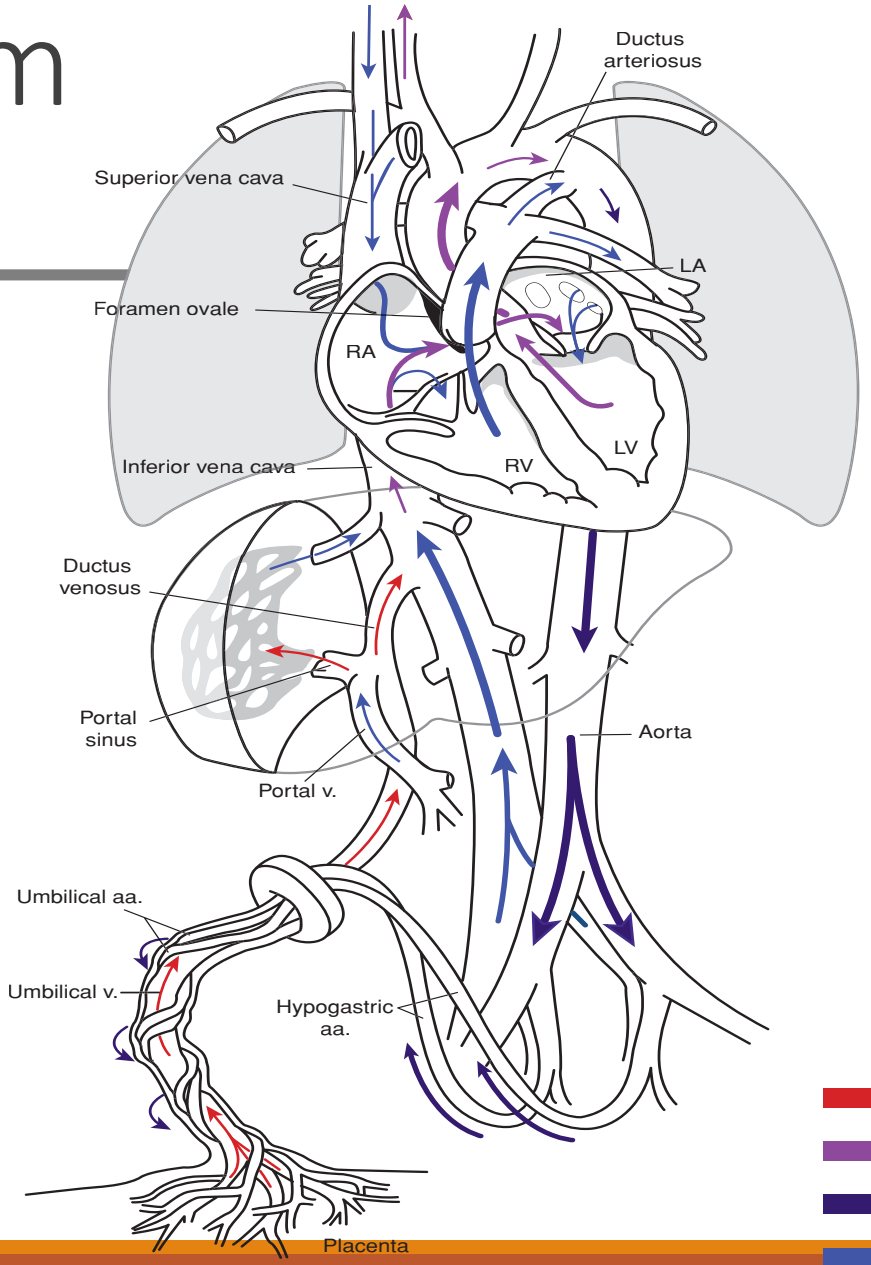


FIGURE 7-8 The intricate nature of the fetal circulation is evident. The degree of blood oxygenation in various ves from that in the postnatal state. aa = arteries; LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ve

Fetal Cardiovascular System

- After these tissues have extracted needed oxygen, the resulting less oxygenated blood returns to the right atrium through the **superior vena cava.**
- The less oxygenated blood coursing along the lateral wall of the inferior vena cava enters the right atrium and is deflected through the tricuspid valve to the right ventricle.

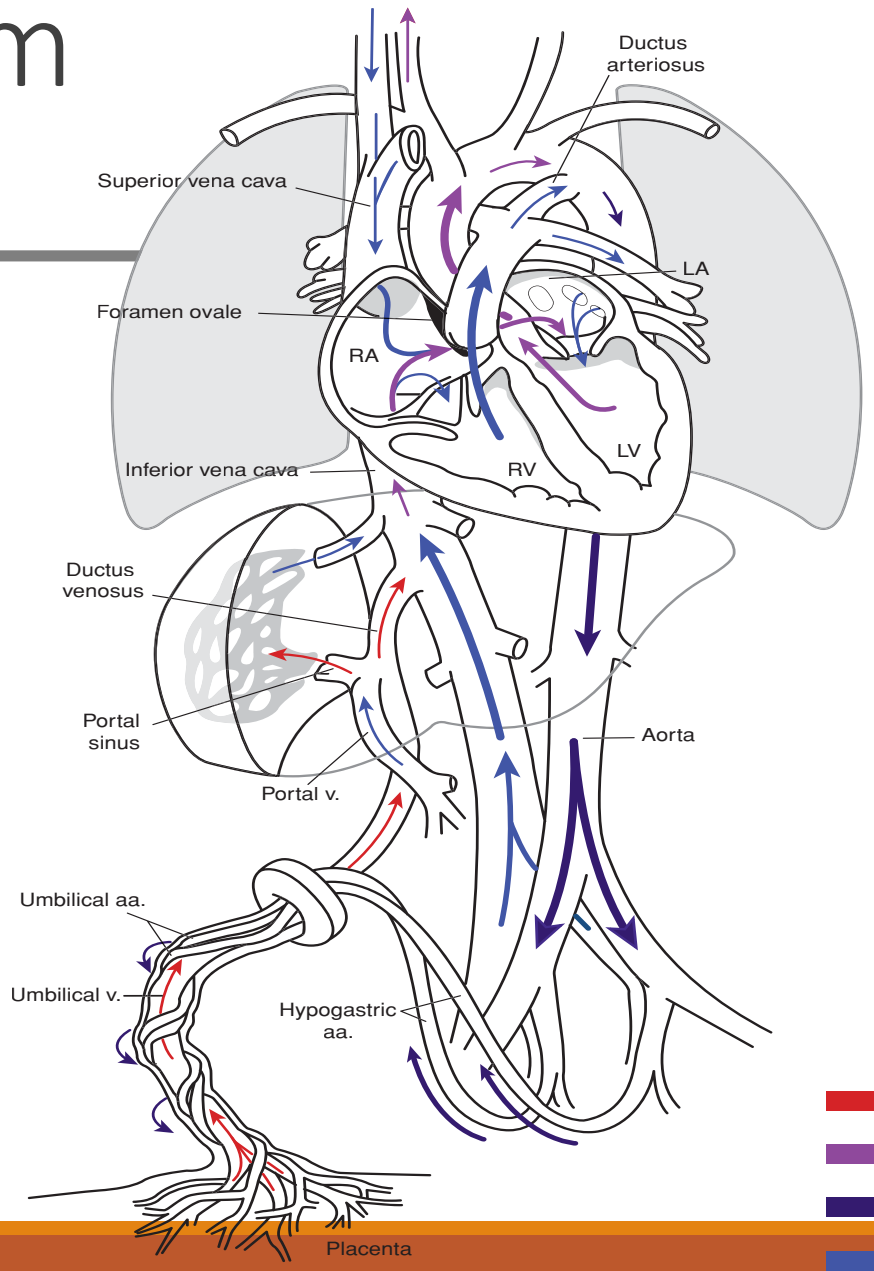


FIGURE 7-8 The intricate nature of the fetal circulation is evident. The degree of blood oxygenation in various ves
from that in the postnatal state. aa = arteries; LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ve

Fetal Cardiovascular System

- Almost 90 % of blood exiting the right ventricle is shunted through the ductus arteriosus to the descending aorta.
- right ventricular output returns to the placenta through the two hypogastric arteries, which distally become the umbilical arteries.
- In the placenta, this blood picks up oxygen and other nutrients and is recirculated through the umbilical vein.

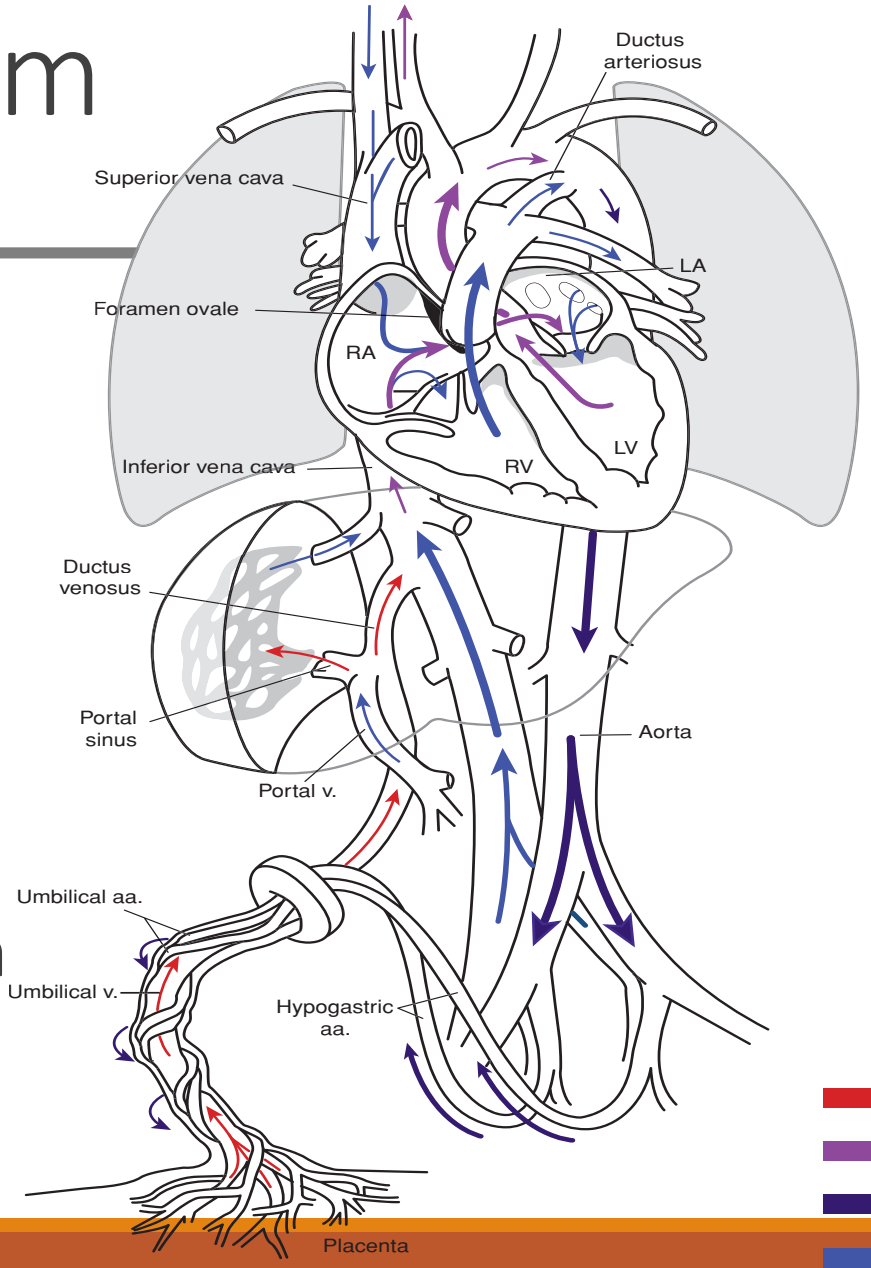


FIGURE 7-8 The intricate nature of the fetal circulation is evident. The degree of blood oxygenation in various ves from that in the postnatal state. aa = arteries; LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ve

Circulatory Changes at Birth

- After birth, the *umbilical vessels, ductus arteriosus, foramen ovale, and ductus venosus* normally constrict or collapse.
- With the functional closure of the ductus arteriosus and the expansion of the lungs, blood leaving the right ventricle preferentially enters the pulmonary vasculature to become oxygenated before it returns to the left heart → the ventricles, now effectively work in series.

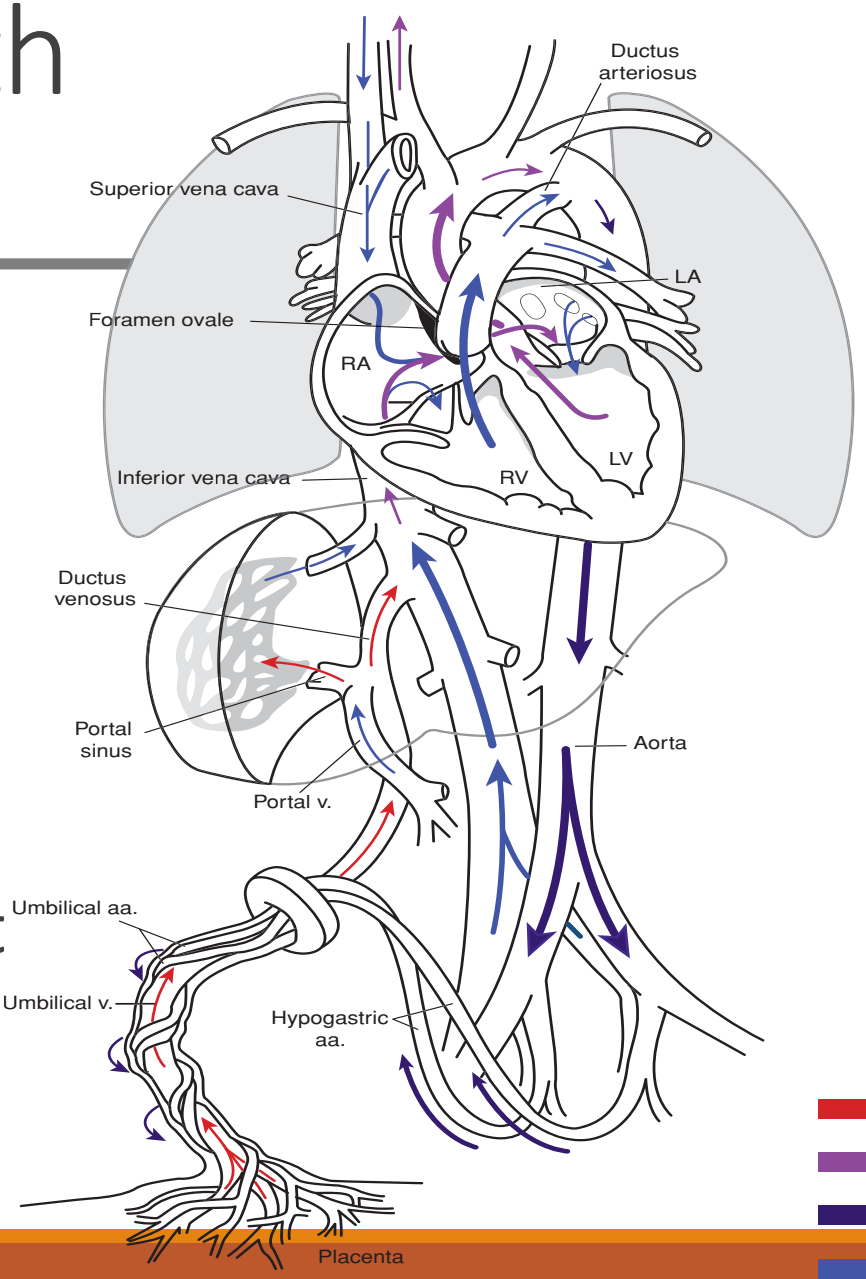


FIGURE 7-8 The intricate nature of the fetal circulation is evident. The degree of blood oxygenation in various ves
from that in the postnatal state. aa = arteries; LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ve

Circulatory Changes at Birth

- the more distal portions of the hypogastric arteries, undergo atrophy and obliteration within 3 to 4 days after birth → these become the **umbilical ligaments**
- intraabdominal remnants of the umbilical vein form the **ligamentum teres**.
- Ductus venosus constricts by 10 to 96 hours after birth and is anatomically closed by 2 to 3 weeks, resulting in formation of the **ligamentum venosum**

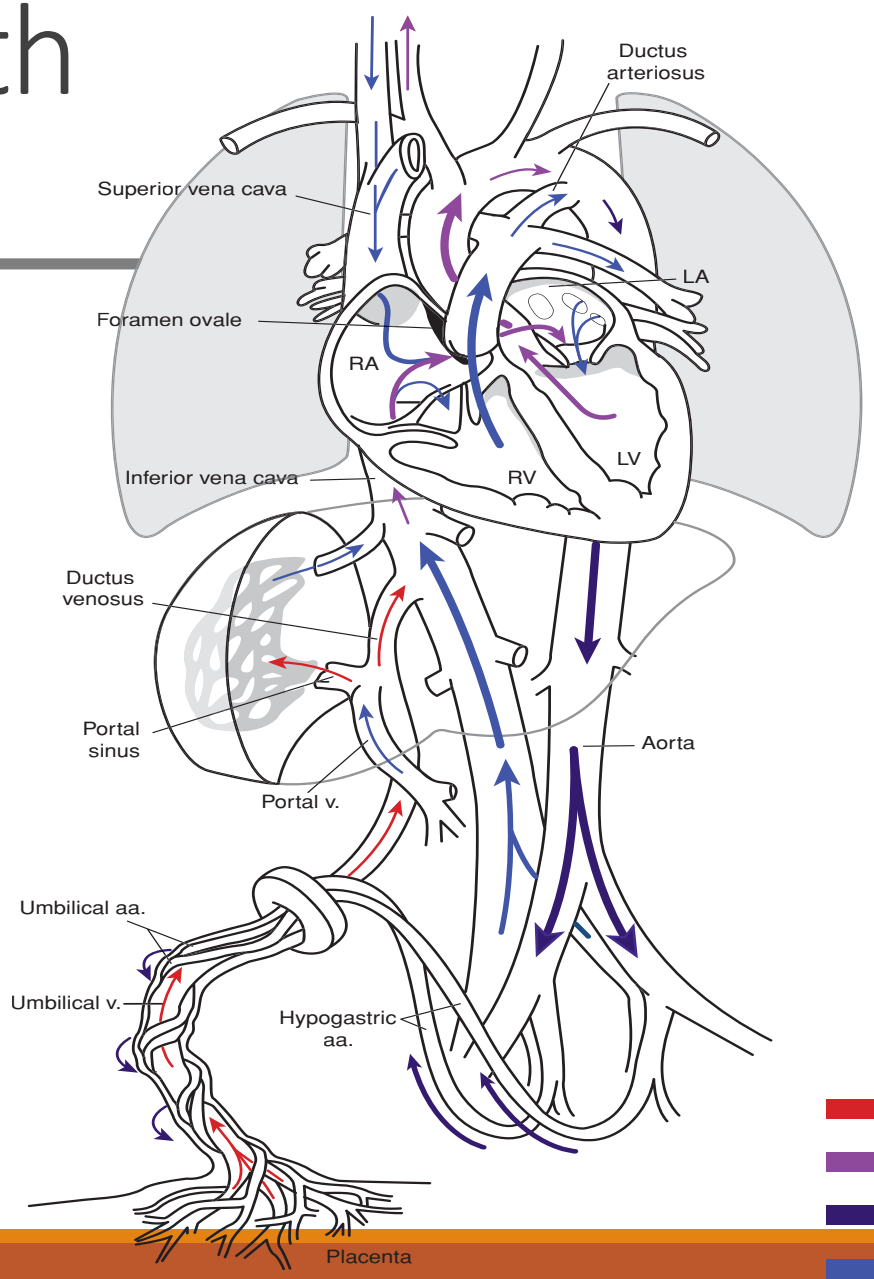
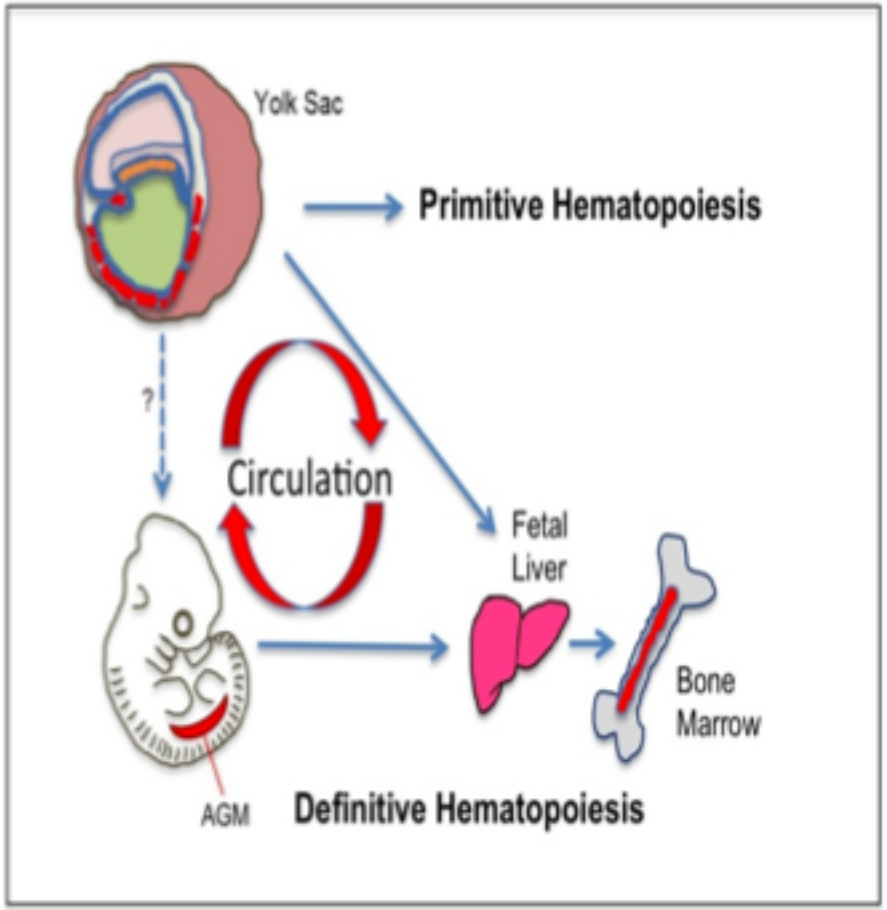


FIGURE 7-8 The intricate nature of the fetal circulation is evident. The degree of blood oxygenation in various ves from that in the postnatal state. aa = arteries; LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ve

HEMATOLOGICAL DEVELOPMENT

Hemopoiesis

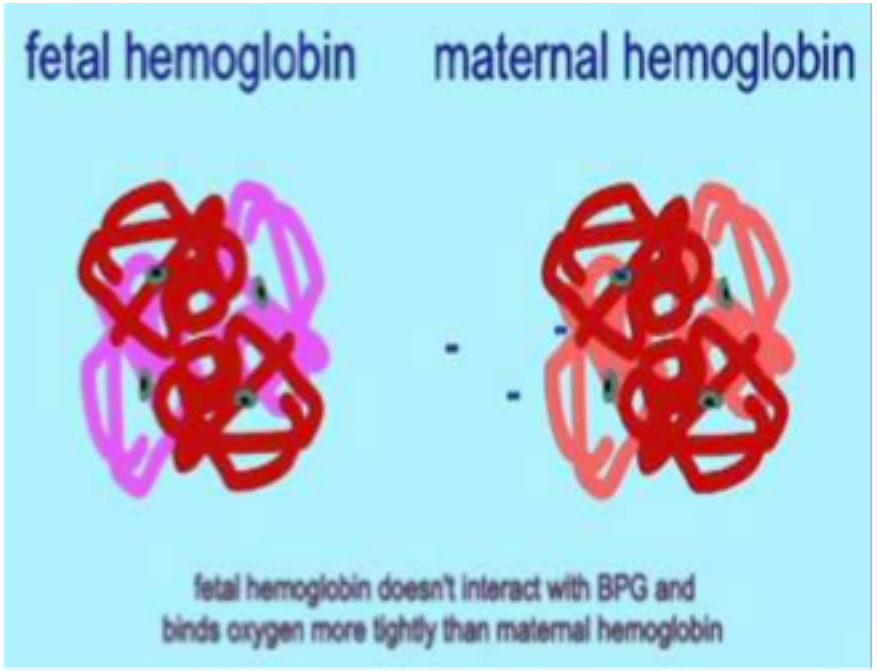
- hemopoiesis is demonstrable first in the yolk sac, followed by the liver and finally bone marrow.
- the *first erythrocytes* released into the fetal circulation are nucleated and macrocytic.
- As fetal development progresses, circulating erythrocytes become smaller and nonnucleated.
- Because of their large size, fetal erythrocytes have a short life span, which progressively lengthens to approximately 90 days at term.



Fetal Hemoglobin

tetrameric protein composed of 2copies of 2 different peptide chains, which determine the type of hemoglobin produced.

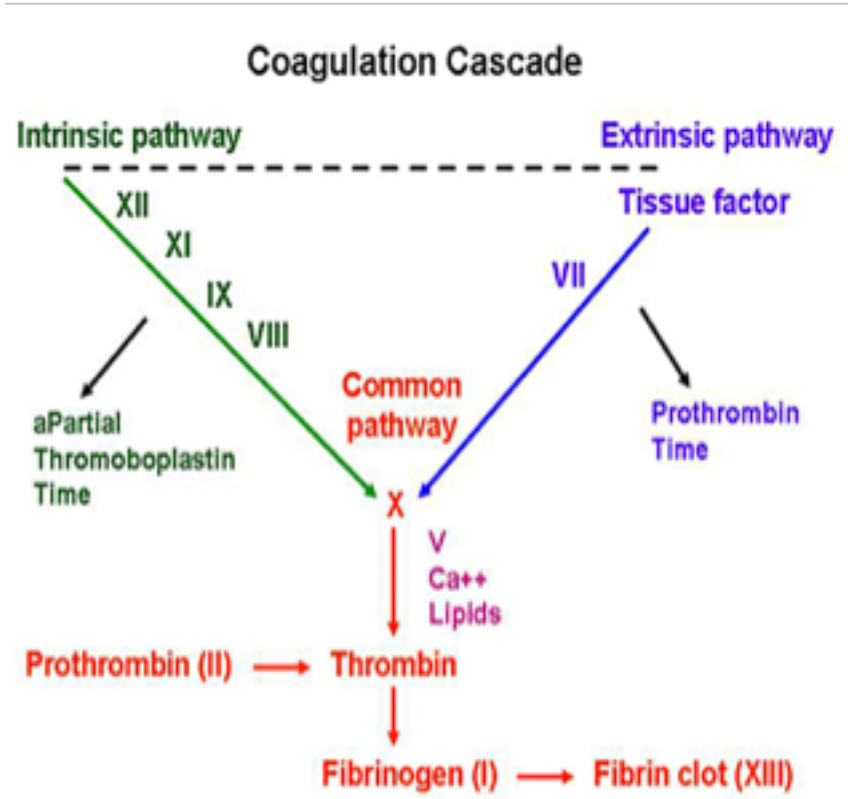
1. Fetal blood is first produced in the yolk sac, where hemoglobins Gower 1, Gower 2, and Portland are made.
2. Erythropoiesis then moves to the liver, where **fetal hemoglobin F** is produced.
3. When hemopoiesis finally moves to the bone marrow, **adult-type hemoglobin A** appears in fetal red blood cells and is present in progressively greater amounts as the fetus matures



Coagulation factors

Coagulation Factors

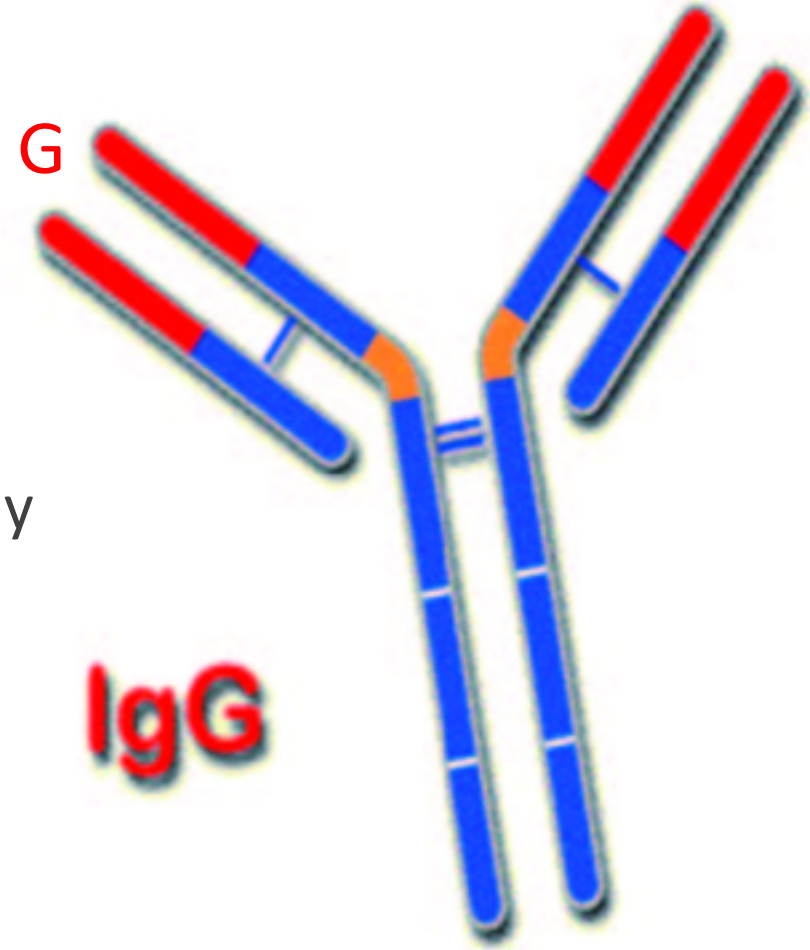
- There are no embryonic forms of the various hemostatic proteins.
- In normal neonates, the levels of factors II, VII, IX, X, XI, prekallikrein, protein S, protein C, antithrombin, and plasminogen, are all approximately 50 percent of adult levels.
  - Without prophylactic treatment, the vitamin K-dependent coagulation factors usually decrease even further during the first few days after birth.
  - this decline is amplified in breastfed infants and may lead to newborn hemorrhage



Immunology

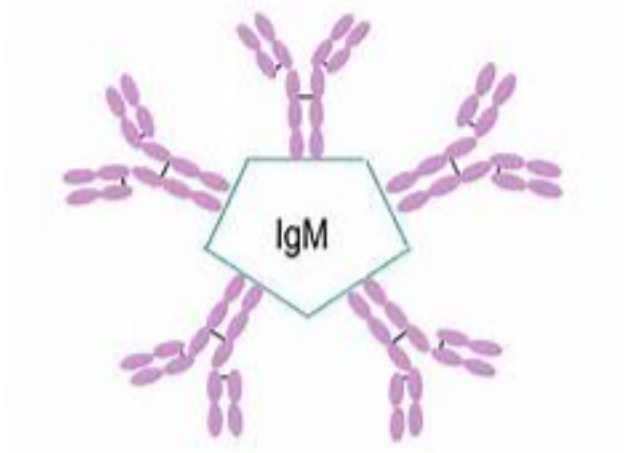
Immunoglobulin G

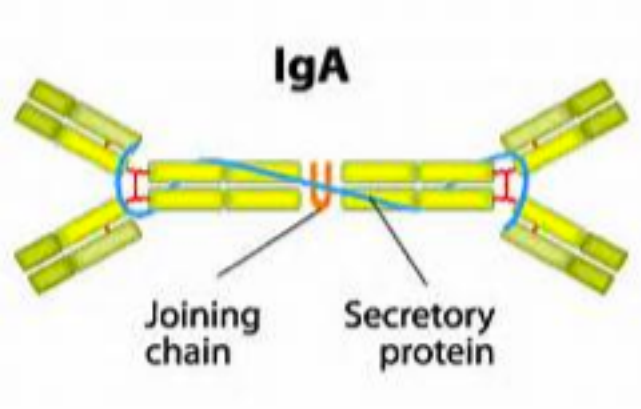
- Fetal plasma immunoglobulins consist almost totally of transferred maternal immunoglobulin G (IgG).
- The bulk of IgG is acquired during the last 4 weeks of pregnancy
  - Accordingly, preterm neonates are endowed relatively poorly with protective maternal antibodies.
  - Newborns begin to slowly produce IgG, and adult values are not attained until 3 years of age.



Immunoglobulins M and A

- Because IgM is not transported from the mother, any IgM in the fetus or newborn is that which it produced.
- Increased levels of IgM are found in newborns with congenital infection such as rubella, cytomegalovirus infection, or toxoplasmosis.
- Immunoglobulin A (IgA) ingested in colostrum provides mucosal protection against enteric infections.





Skull

Skull

- the most important sutures are the frontal, sagittal, two coronal, and the two lambdoid.
- **Fontanel**: irregular space enclosed by a membrane at the junction of several sutures
  - **Greater, or anterior, fontanel** is a lozenge-shaped space situated at the junction of the sagittal and the coronal sutures.
  - **Lesser, or posterior, fontanel** is a small triangular area at the intersection of the sagittal and lambdoid sutures.

**localization of these fontanels gives important information concerning the presentation and position of the fetus during labor*.

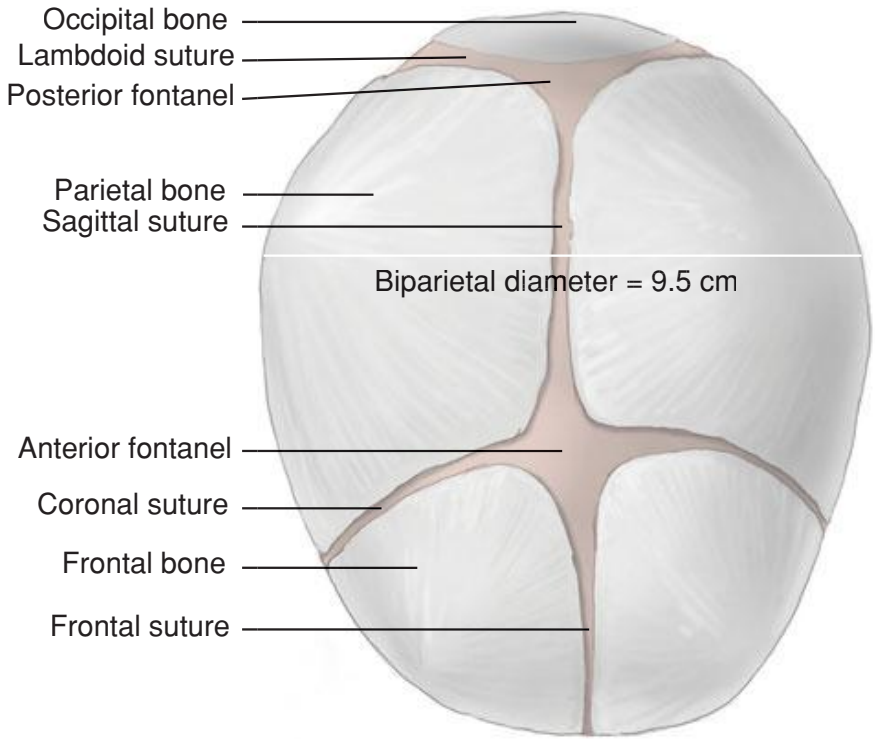


FIGURE 7-11 Fetal head at term showing fontanels and sutures.

Skull: diameters and circumferences

1. **Occipitofrontal** (11.5 cm): line extending from a point just above the root of the nose to the most prominent portion of the occipital bone.
2. **Biparietal** (9.5 cm): greatest transverse diameter of the head, which extends from one parietal bone to the other.
3. **Bitemporal** (8.0 cm): the greatest distance between the two temporal sutures.
4. **Occipitomental** (12.5 cm): from the chin to the most prominent portion of the occiput.
5. **Suboccipitobregmatic** (9.5 cm): from the middle of the large fontanel to the undersurface of the occipital bone where it joins the neck.

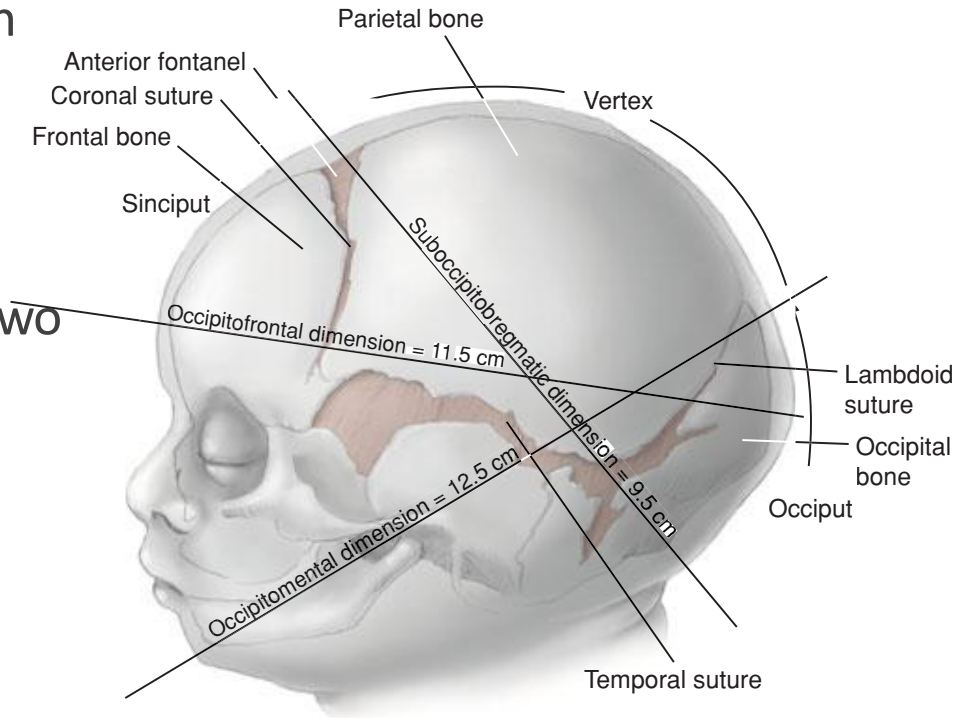


FIGURE 7-12

Skull: diameters and circumferences

- greatest circumference of the head: corresponds to the plane of the occipitofrontal diameter, averages 34.5 cm
- smallest circumference: corresponds to the plane of the suboccipitobregmatic diameter, is 32 cm.
- Cranial bones are connected by a thin fibrous tissue layer → allows considerable shifting or sliding of each bone to accommodate the size and shape of the maternal pelvis ("molding").

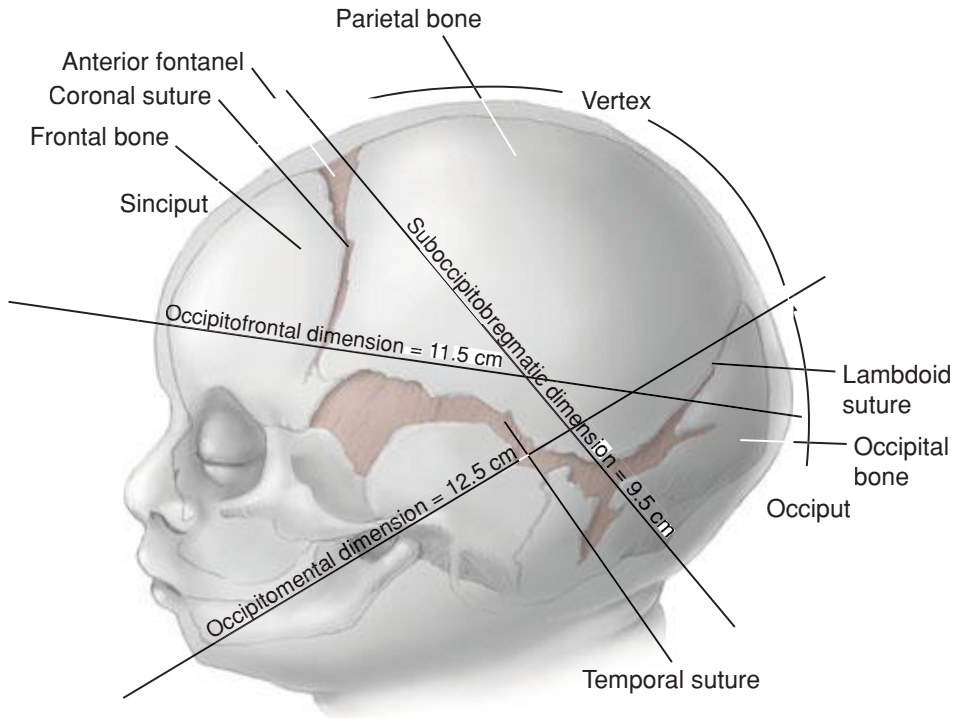
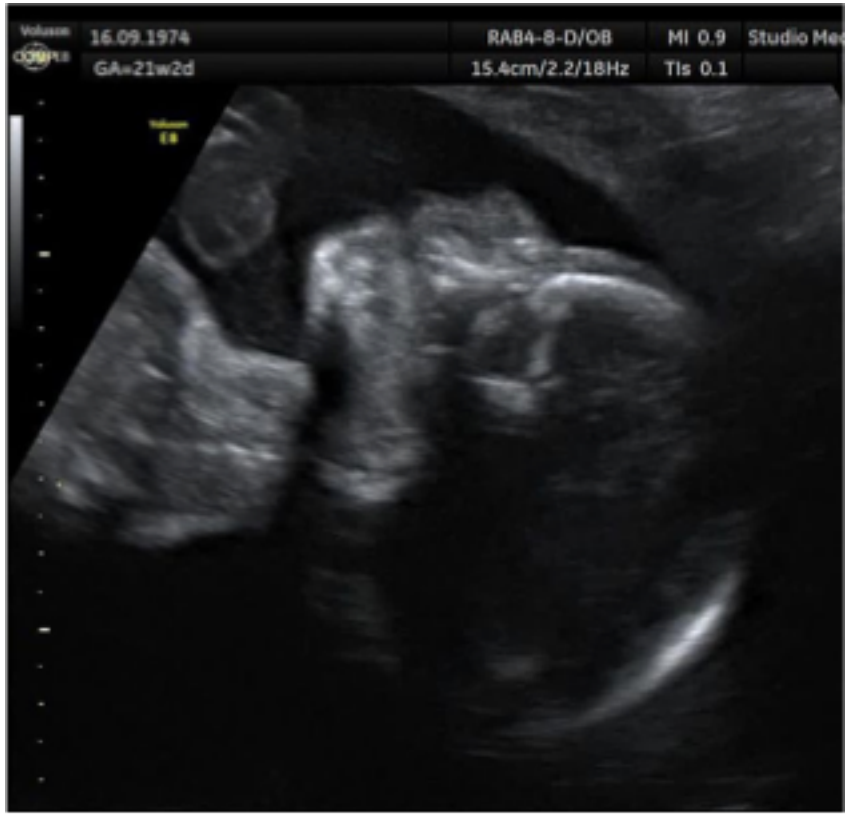


FIGURE 7-12

Gastrointestinal system

Gastrointestinal System

- Swallowing begins at 10 to 12 weeks, coincident with the ability of the small intestine to undergo peristalsis and transport glucose actively
- It is not clear what stimulates swallowing, but the fetal neural analogue of thirst, gastric emptying, and change in the amnionic fluid composition are potential factors



Gastrointestinal System

Several anomalies can affect normal fetal gastrointestinal function.

1. Hirschsprung disease—"congenital aganglionic megacolon", prevents the bowel from undergoing parasympathetic-mediated relaxation and thus from emptying normally; recognized prenatally by grossly enlarged bowel during sonography.
2. Obstructions such as duodenal atresia, megacystis-microcolon syndrome, or imperforate anus can also prevent normal bowel emptying.
3. Meconium ileus → (commonly found with fetal cystic fibrosis) is bowel obstruction caused by thick, viscid meconium that blocks the distal ileum.

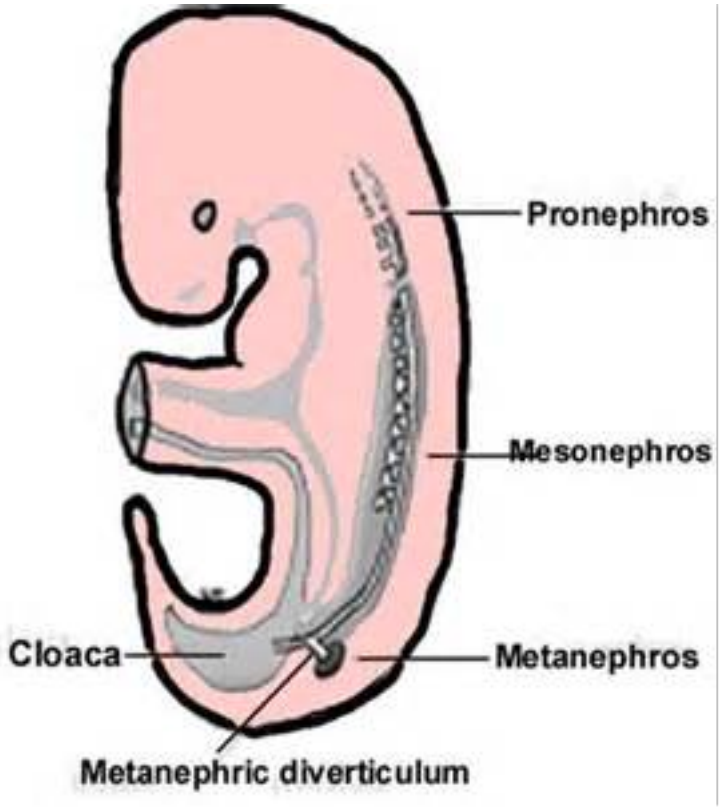
Meconium

- Fetal bowel contents consist of various products of secretion, such as glycerophospholipids from the lun desquamated fetal cells, lanugo, scalp hair, and verni
- It also contains undigested debris from swallowed amnionic fluid.
- the dark greenish-black is caused by pigments, especially biliverdin.
- AVP stimulates colonic smooth muscle to contract, resulting in intraamnionic defecation

Urinary system

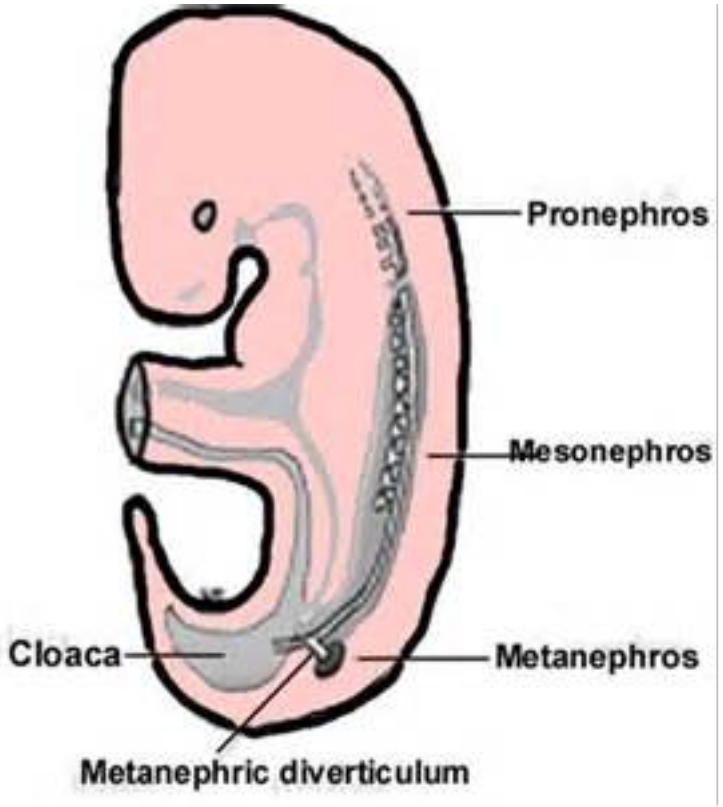
Urinary System

- Two primitive urinary systems—the pronephros and the mesonephros—precede the development of the **metanephros**, which forms the final kidney
- the pronephros has involuted by 2 weeks, and the mesonephros is producing urine at 5 weeks and degenerates by 11 to 12 weeks.
- Failure of these two structures either to form or to regress may result in anomalous urinary system development.



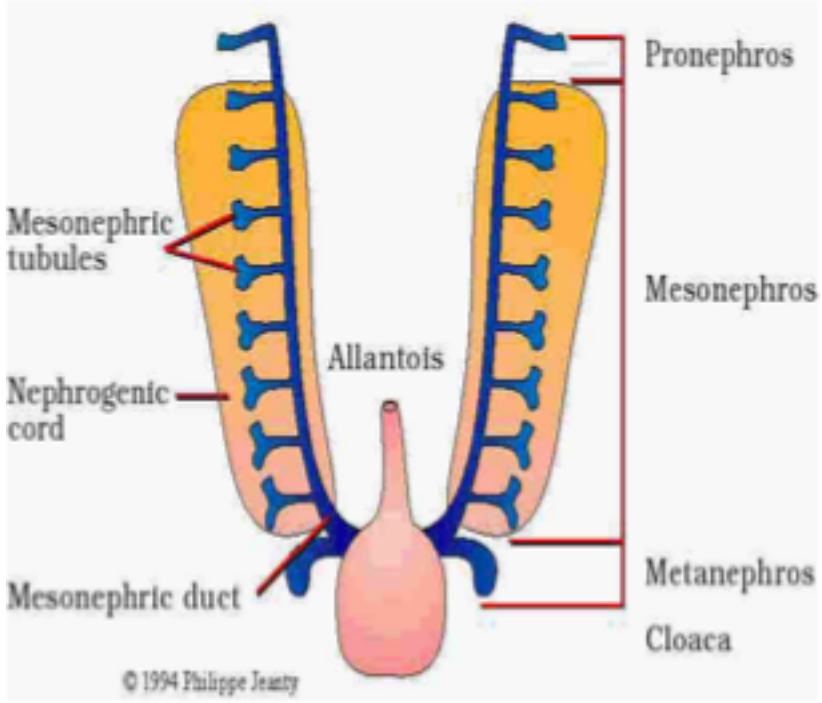
Urinary System

- Between 9 and 12 weeks, the ureteric bud and the nephrogenic blastema interact to produce the metanephros.
- the kidney and ureter develop from intermediate mesoderm.
- the bladder and urethra develop from the urogenital sinus.
- the bladder also develops in part from the allantois.



Urinary System

- Urine usually is found in the bladder even in small fetuses.
- the fetal kidneys start producing urine at 12 weeks.
- By 18 weeks, they are producing 7 to 14 mL/day, and at term, this increases to 27 mL/hr or 650 mL/day

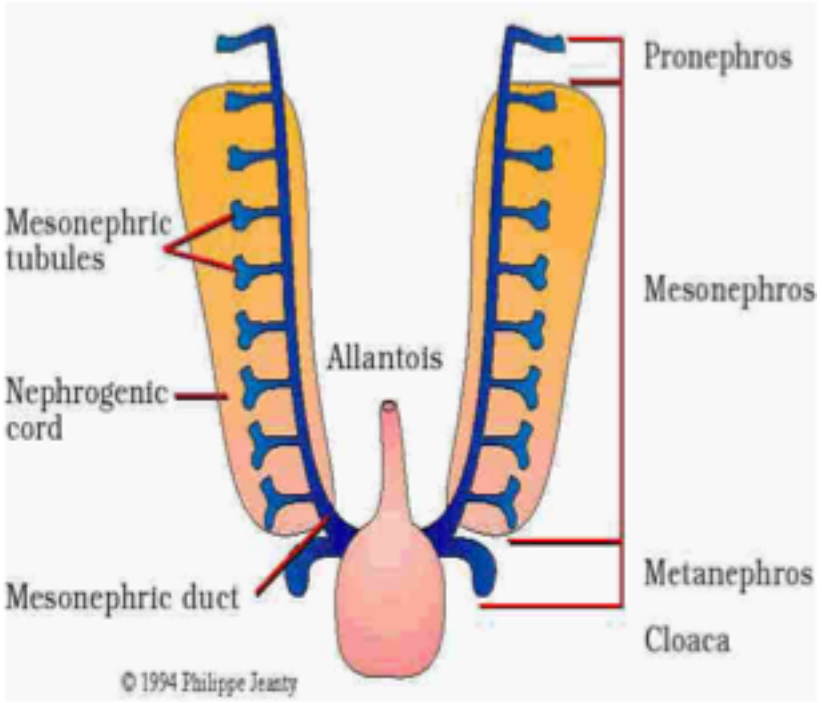


Urinary System

Maternally administered furosemide increases fetal urine formation, whereas uteroplacental insufficiency, fetal-growth restriction, and other types of fetal disorders decrease it.

Kidneys are not essential for survival in utero, but are important in the control of amnionic fluid composition and volume.

- *thus, abnormalities that cause chronic anuria are usually accompanied by oligohydramnios and pulmonary hypoplasia.*



Lung development

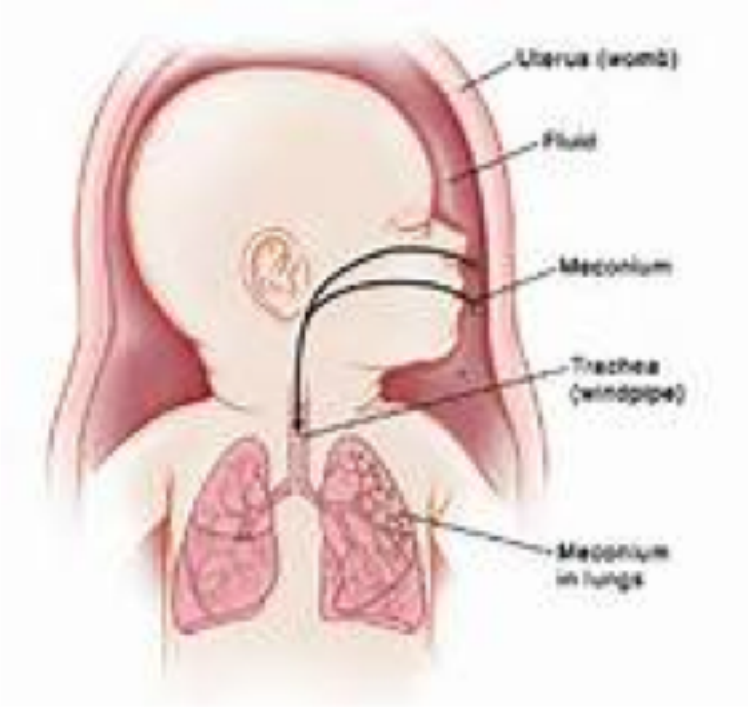
Lung Development

4 essential lung development stages:

1. **pseudoglandular stage:** growth of the intrasegmental bronchial tree between 6 and 16 weeks. During this period, the lung looks microscopically like a gland.
2. during the **canalicular stage**, from 16 to 26 weeks, the bronchial cartilage plates extend peripherally. Each terminal bronchiole gives rise to several respiratory bronchioles, and each of these in turn divides into multiple saccular ducts.
3. the **terminal sac stage** begins at 26 weeks. During this stage, respiratory bronchioles give rise to primitive pulmonary alveoli—the terminal sacs.
4. the **alveolar stage** begins at 32 weeks, the alveolar epithelial lining thins to improve gas exchange; the lymph system forms, and type II pneumonocytes begin to produce surfactant.

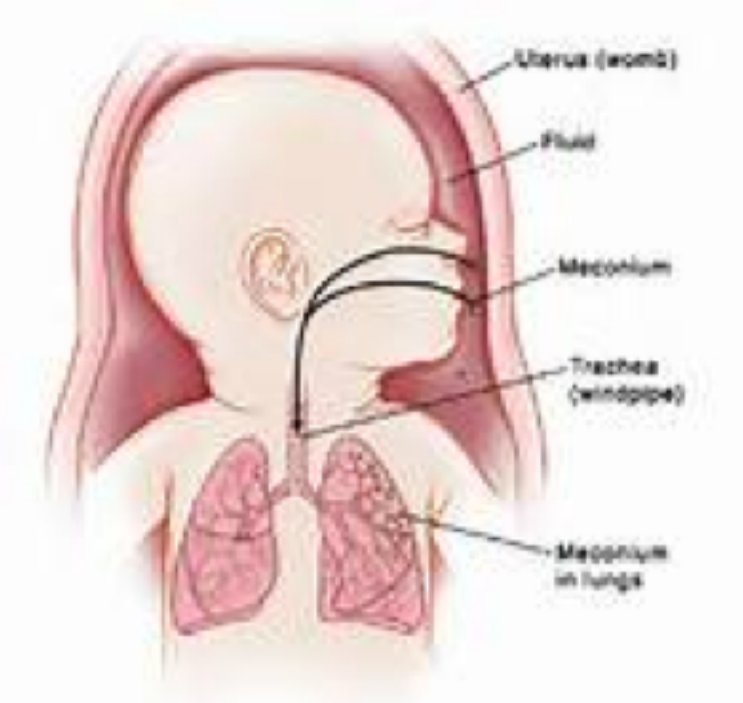
Lung Development: Pulmonary Surfactant

- After the first breath, the terminal sacs must remain expanded despite the pressure imparted by the tissue-to-air interface, and surfactant keeps them from collapsing.
- **Surfactant** is formed in **type II pneumonocytes** that line the alveoli.
- Surfactant uncoils from the lamellar bodies, and it then spreads to line the alveolus to prevent alveolar collapse during expiration.



Lung Development: Pulmonary Surfactant

- the principal active component of surfactant is a specific **lecithin—dipalmitoylphosphatidylcholine (DPPC or PC)**—which accounts for nearly 50 percent.
- Biosynthesis takes place in the type II pneumocytes.
- Phospholipid is the primary surface tension-lowering component of surfactant, whereas the apoproteins aid the forming and reforming of a surface film.



Endocrine gland development

Pituitary Gland

Anterior and Intermediate Lobes. the adenohypophysis, or anterior pituitary, differentiates into five cell types that secrete six protein hormones:

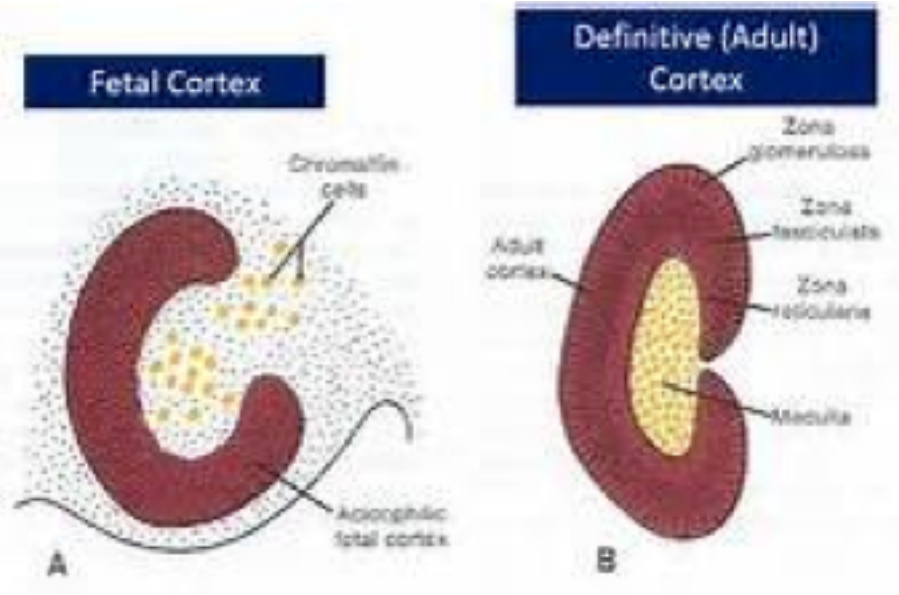
1. **lactotropes** produce prolactin—PRL;
2. **somatotropes** produce growth hormone—GH;
3. **corticotropes** produce corticotropin—ACTH;
4. **thyrotropes** produce thyrotropin or thyroid-stimulating hormone—TSH;
5. **gonadotropes** produce luteinizing hormone—LH and follicle-stimulating hormone—FSH.

Thyroid Gland

- the thyroid gland is able to synthesize hormones by 10 to 12 weeks
- by 12 weeks and throughout pregnancy, the fetal thyroid concentrates iodide more avidly than does the maternal thyroid. thus, maternal administration of either radioiodide or appreciable amounts of ordinary iodide is hazardous after this time.
- Fetal thyroid hormone plays a role in the normal development of virtually all fetal tissues, especially the brain.
  - Its influence is illustrated by congenital hyperthyroidism, which occurs when maternal thyroid-stimulating antibody crosses the placenta to stimulate the fetal thyroid.
  - these fetuses develop tachycardia, hepatosplenomegaly, hematological abnormalities, craniosynostosis, and growth restriction.
  - As children, they have perceptual motor difficulties, hyperactivity, and reduced growth

Adrenal Glands

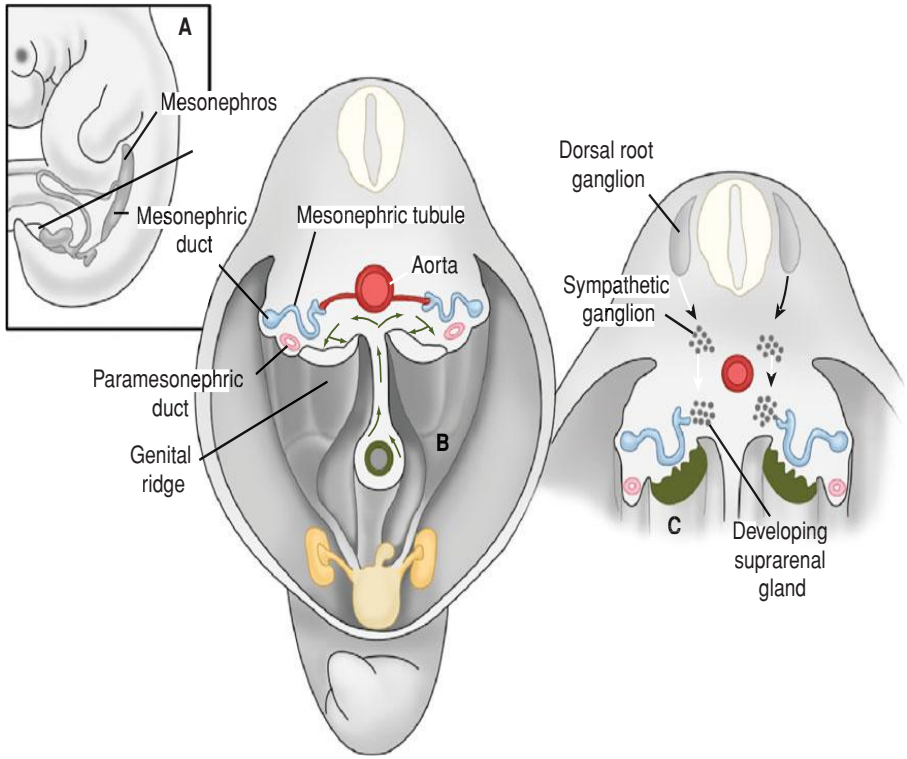
- the fetal adrenal glands are much larger in relation to total body size than in adults.
- the bulk is made up of the inner or fetal zone of the adrenal cortex and involutes rapidly after birth.
- this zone is scant to absent in rare instances in which the fetal pituitary gland is congenitally absent.



Development of genitalia

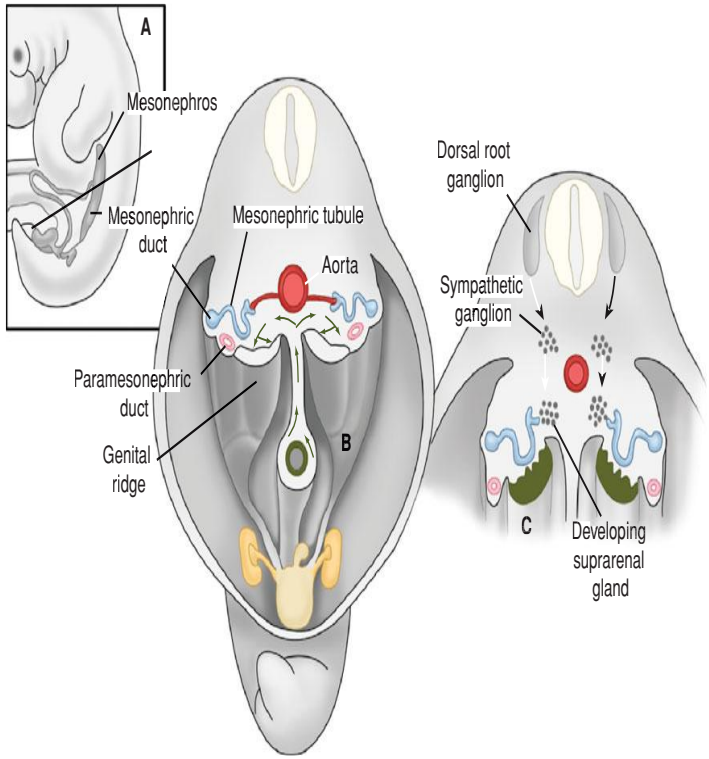
Embryology of Uterus and Oviducts

- the uterus and tubes arise from the müllerian ducts, which first appear near the upper pole of the urogenital ridge in the fifth week of embryonic development
- this ridge is composed of the mesonephros, gonad, and associated ducts.
  - the first indication of müllerian duct development is a thickening of the coelomic epithelium at approximately the level of the fourth thoracic segment.



Embryology of Uterus and Oviducts

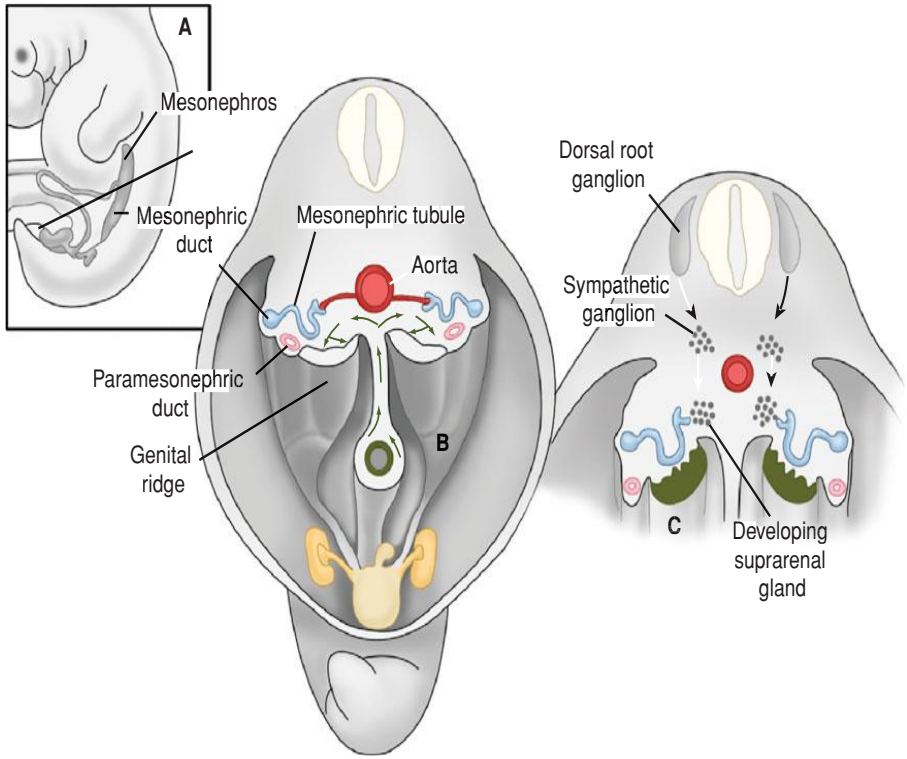
- In the 6th wk, the growing tips of the two müllerian ducts approach each other in the midline. One week later, they reach the urogenital sinus.
- the two müllerian ducts then fuse to form a single canal at the level of the inguinal crest.
  - *this crest gives rise to the **gubernaculum**, which is the primordium of the round ligament.*
- thus, the upper ends of the müllerian ducts produce the fallopian tubes, and the fused parts give rise to the uterus.
- the vaginal canal is not patent throughout its entire length until the sixth month



Embryology of the Ovaries

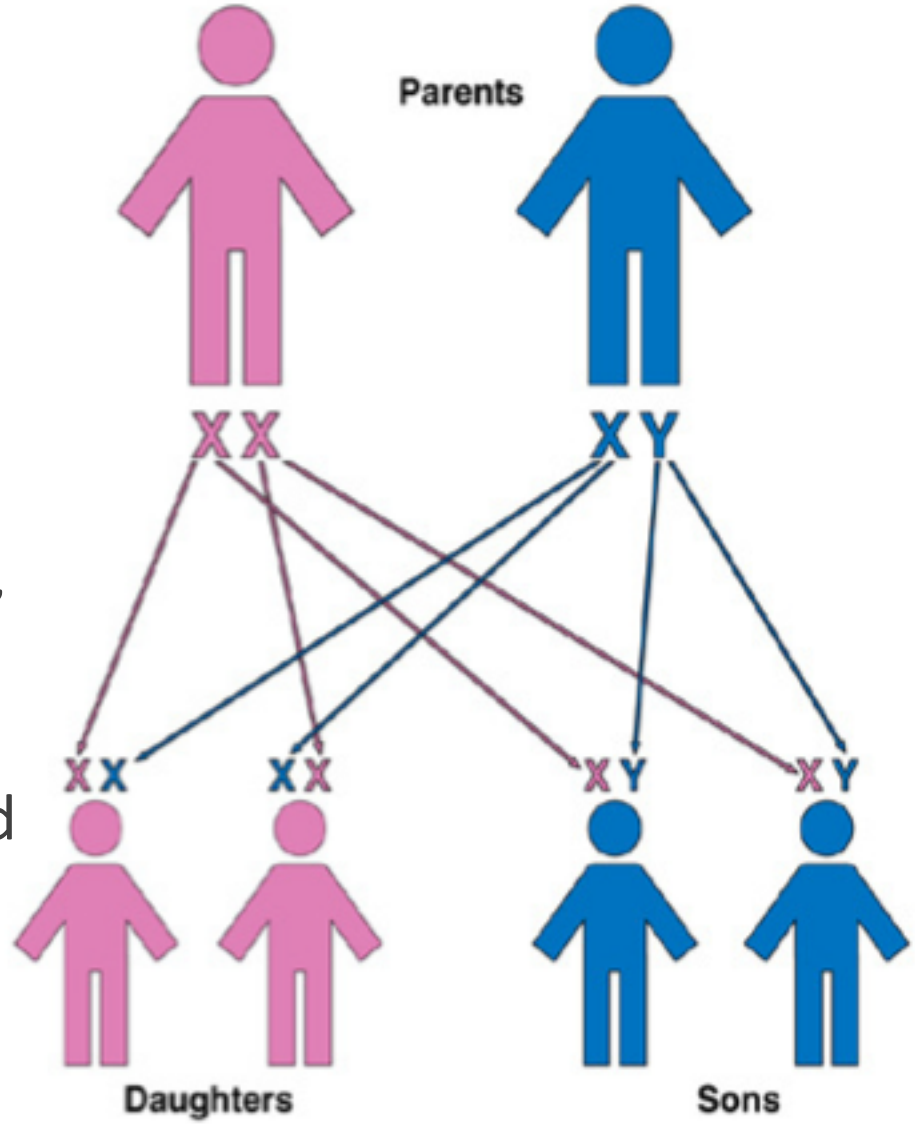
At approximately 4 weeks, gonads form on the ventral surface of the embryonic kidney at a site between the eighth thoracic and fourth lumbar segments.

- the coelomic epithelium thickens, and clumps of cells bud off into the underlying mesenchyme. this circumscribed area is called the **germinal epithelium.**



Sexual Differentiation

- **Chromosomal Gender:** genetic gender—XX or XY—is established at fertilization, but for the first 6 weeks, development of male and female embryos is morphologically indistinguishable.
- **Gonadal Gender** : If a Y chromosome is present, at about 6 weeks after conception, the gonad begins developing into a testis
- Testis development is directed by a gene located on the short arm of Y—testis- determining factor (TDF), also called sex-determining region (SRY).



Sexual Differentiation

Phenotypic Gender

Urogenital tract development in both sexes is indistinguishable before 8 weeks.

thereafter, development and differentiation of the internal and external genitalia to the male phenotype is dependent on testicular function.

In the absence of a testis, female differentiation ensues irrespective of genetic gender.

Specifically, the fetal ovary is not required for female sexual differentiation.

- *Jost and associates (1973) found that if castration of rabbit fetuses was conducted before di erentiation of the genital anlagen, all newborns were phenotypic females with female external and internal genitalia. thus, the müllerian ducts developed into uterus, fallopian tubes, and upper vagina.*

Fetal Testicles and Male Sexual Differentiation

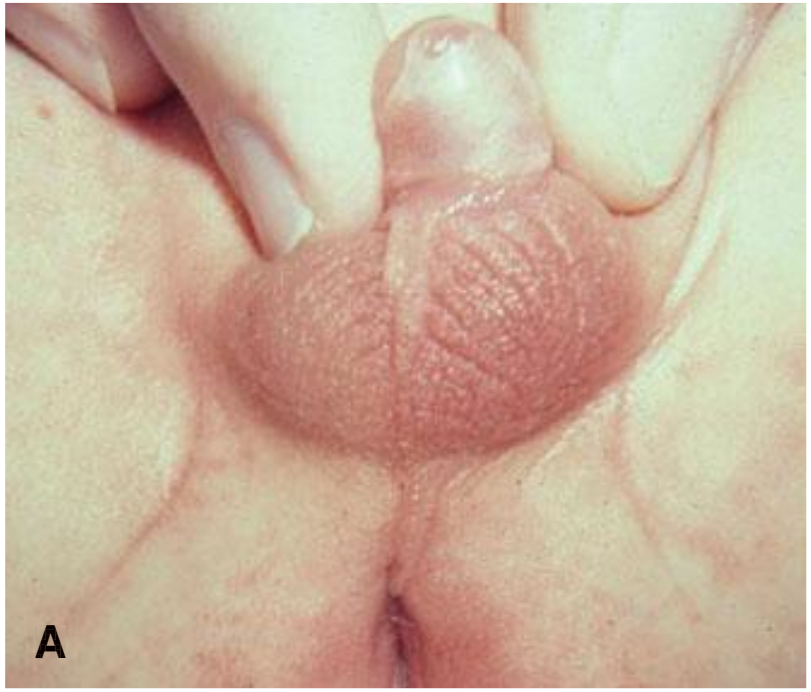
the fetal testis secretes a proteinaceous substance called **Müllerian-inhibiting substance/MIS (or Antimullerian Hormone/AMH)**.

- Causes müllerian duct regression: prevents the development of uterus, fallopian tube, and upper vagina.
- produced by the Sertoli cells of the seminiferous tubules.
- Because it acts locally near its site of formation, if a testis were absent on one side, the müllerian duct on that side would persist, and the uterus and fallopian tube would develop on that side.
- Female external genital differentiation is complete by 11 weeks, whereas male external genital differentiation is complete by 14 weeks

Genital Ambiguity of the Newborn

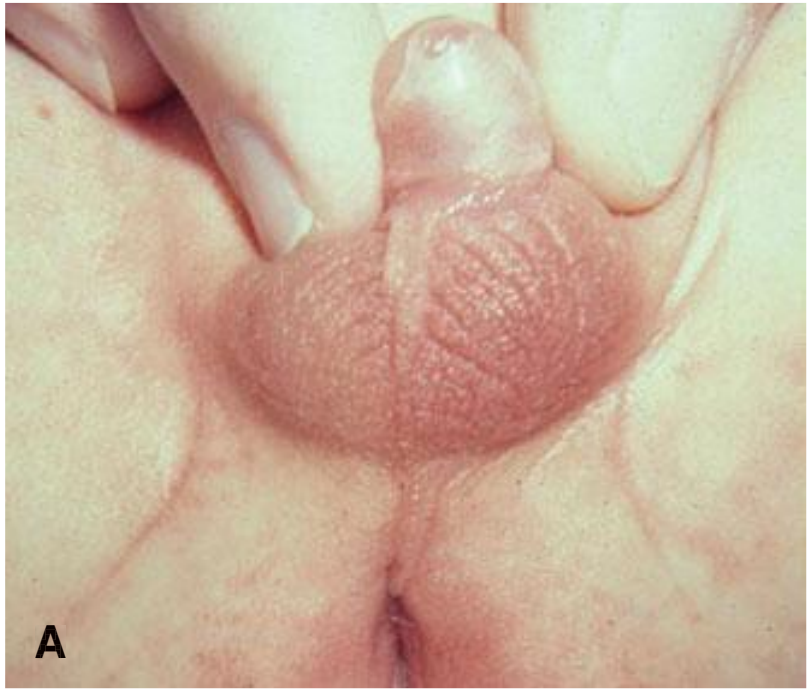
Category 1: Female Pseudohermaphroditism

- MIS is not produced
- Androgen exposure is excessive, but variable, for a fetus genetically predestined to be female.
- karyotype is 46,XX and ovaries are present.
- by genetic and gonadal gender, all are predestined to be female, and the basic abnormality is androgen excess.
- Because MIS is not produced, the uterus, fallopian tubes, and upper vagina develop.



Category 1: Female Pseudohermaphroditism

- If affected fetuses were exposed to a small amount of excess androgen late in fetal development, the only genital abnormality will be **slight to modest clitoral hypertrophy**, with an otherwise normal female phenotype.
- If with greater androgen exposure, clitoral hypertrophy will be more pronounced, and the posterior labia will fuse.
- If androgen levels increase earlier in embryonic development, then more severe virilization can be seen.



Examples of Category 1

Congenital Adrenal Hyperplasia.

- most common cause of androgenic excess in fetuses with female pseudohermaphroditism.
- the hyperplastic glands synthesize defective enzymes that cause impaired cortisol synthesis.
- excessive pituitary ACTH stimulation of the fetal adrenal glands with secretion of large amounts of cortisol precursors, including androgenic prehormones.
- most common hormones involved are steroid 21-hydroxylase, 11β-hydroxylase, and 3β-hydroxysteroid dehydrogenase.
- Deficiency of the last prevents synthesis of virtually all steroid hormones.
- Defficiency of either 17β- or 11β-hydroxylase results in increased deoxycorticosterone production to cause hypertension and hypokalemic acidosis. these forms of congenital adrenal hyperplasia thus constitute medical emergencies in the newborn

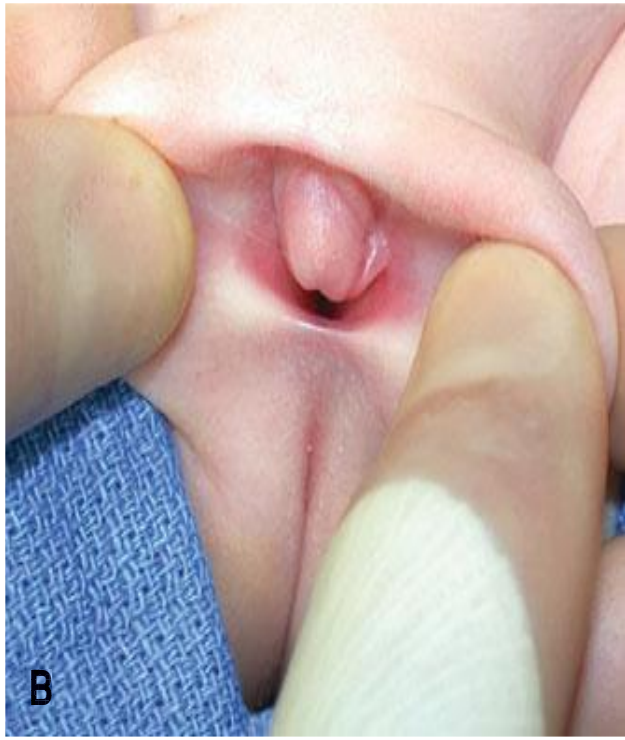
Examples of Category 1

Excessive Androgen from Maternal Sources.

- Transfer of androgen from the maternal compartment may arise from the ovaries with hyperreactio luteinalis or theca-lutein cysts or from Leydig cell and Sertoli-Leydig cell ovarian tumors
- In most of these conditions, the female fetus does not become virilized.
- this is because during most of pregnancy, the fetus is protected from excess maternal androgen by the extraordinary capacity of the syncytiotrophoblast to convert most C19-steroids, including testosterone, to estradiol-17β.
- the only exception to this generalization is fetal aromatase deficiency, which produces both maternal and fetal virilization
- Some drugs also can cause female fetal androgen excess. Most commonly, the drugs implicated are synthetic progestins or anabolic steroids

Category 2: Male Pseudohermaphroditism

- characterized by incomplete and variable androgenic exposure of a fetus predestined to be male.
- the karyotype is 46,XY, and there are either testes or no gonads.
- In some cases, incomplete masculinization follows inadequate production of testosterone by the fetal testis.
- Because testes were present for at least some time in embryonic life, MIS is produced. thus, the uterus, fallopian tubes, and upper vagina do not develop.
- Fetal testicular testosterone production may fail if there is an enzymatic defect of steroidogenesis that involves any one of four enzymes in the biosynthetic pathway for testosterone synthesis.



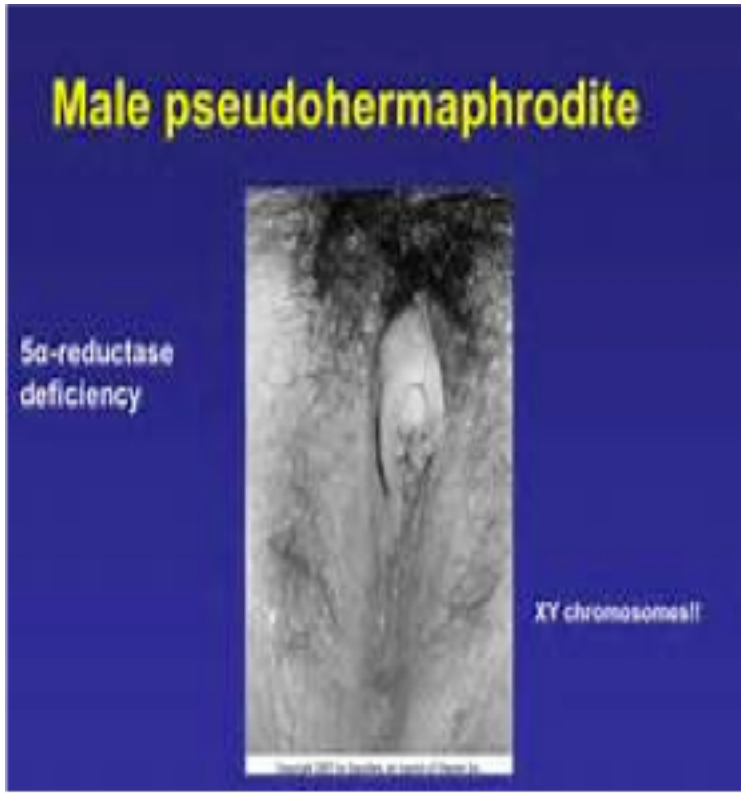
Category 2: Male Pseudohermaphroditism

Androgen resistance or deficiencies in androgen responsiveness are caused by an abnormal or absent androgen receptor protein or by enzymatic failure of conversion of testosterone to 5α-DHT in appropriate tissues

Example of Category 2

Androgen Insensitivity Syndrome/ testicular feminization syndrome

- is the most extreme form of the androgen resistance syndrome
- no tissue responsiveness to androgen → virilization does not occur, and even pubic and axillary hair does not develop because of end-organ resistance.
- female phenotype with a short, blind-ending vagina, no uterus or fallopian tubes, and no wolffian duct structures.
- Increased estrogen secretion (In response to high concentrations of LH, there is increased testicular secretion of estradiol-17β) and absence of androgen responsiveness act in concert to cause feminization in the form of breast development.



Example of Category 2

Familial male pseudohermaphroditism, type I (Reifenstein syndrome):

it constitutes a spectrum of incomplete genital virilization.

Phenotypes can vary from a phenotype similar to that of individuals with incomplete androgen insensitivity to that of a male phenotype with only a bifid scrotum, infertility, and gynecomastia.

Example of Category 2

5α-reductase deficiency in androgen-responsive tissues.

external genitalia that are female but with modest clitoral hypertrophy.

But because androgen action in the wolffian duct is mediated directly by testosterone, there are well-developed epididymides, seminal vesicles, and vas deferens, and the male ejaculatory ducts empty into the vagina.

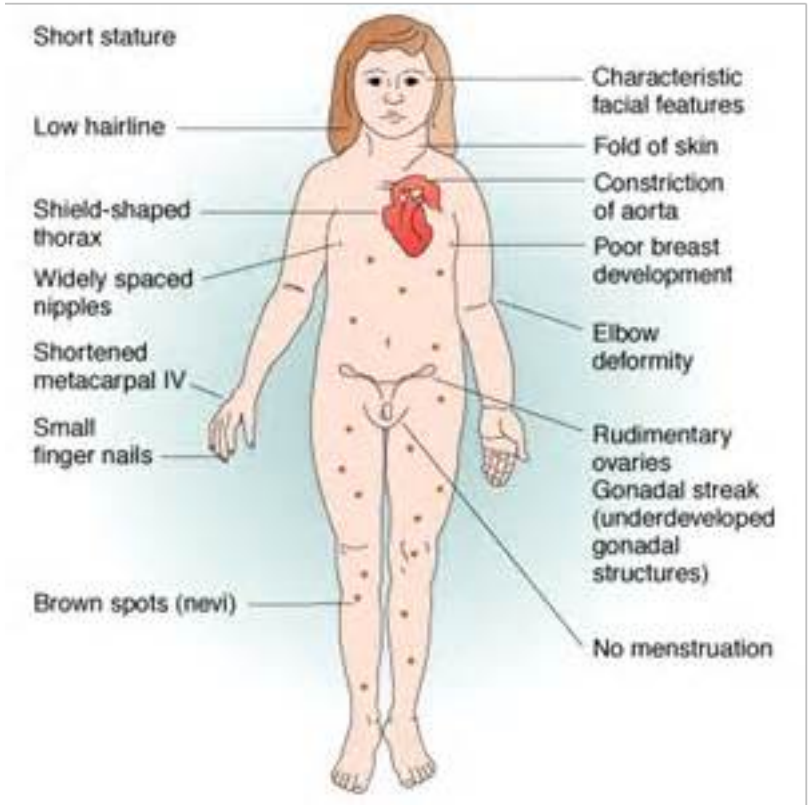
Category 3: Dysgenetic Gonads

- most have abnormally developed gonads, and streak gonads are typically found.
- As a result, MIS is not produced and fetal androgen exposure is variable. the uterus, fallopian tubes, and upper vagina are present.

Example of category 3

Turner syndrome (46,X).

phenotype is female, but secondary gender characteristics do not develop at the time of expected puberty, and genital infantilism persists.



Mixed gonadal dysgenesis

example is a dysgenetic gonad on one side and an abnormal testis or dysontogenetic tumor on the other.

Category 4: True Hermaphroditism

true hermaphrodites have both ovarian and testicular tissues with germ cells for both ova and sperm in the abnormal gonads.

Outline

1. FETAL GROWTH AND DEVELOPMENT
2. PLACENTAL PHYSIOLOGY AND FETAL GROWTH
3. FETAL NUTRITION
4. FETAL ORGAN SYSTEM DEVELOPMENT
5. DEVELOPMENT OF GENITALIA
6. DISORDERS OF SEXUAL DEVELOPMENT

Thank you!

youtube channel: Ina Irabon

www.wordpress.com: Doc Ina OB Gyne