PLACENTA, FETAL MEMBRANES AND MULTIPLE GESTATION

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OBJECTIVES OF THE SESSION

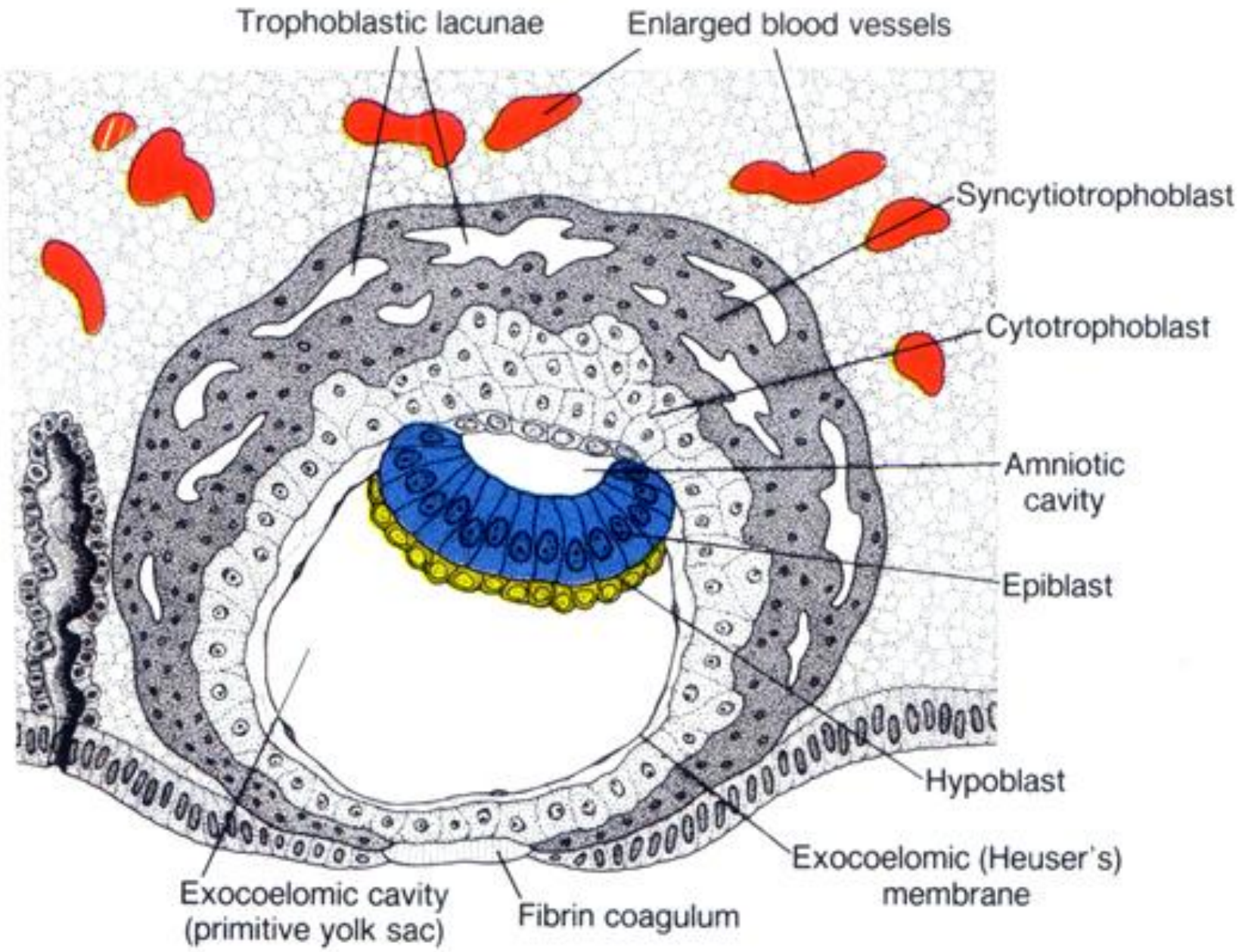
- Understand the components of fetal membranes
- Understand the functions of fetal membranes
- Understand the basis of pathology of fetal membranes.
- Understand the application of this knowledge in clinical practice.
- Understand multiple gestation

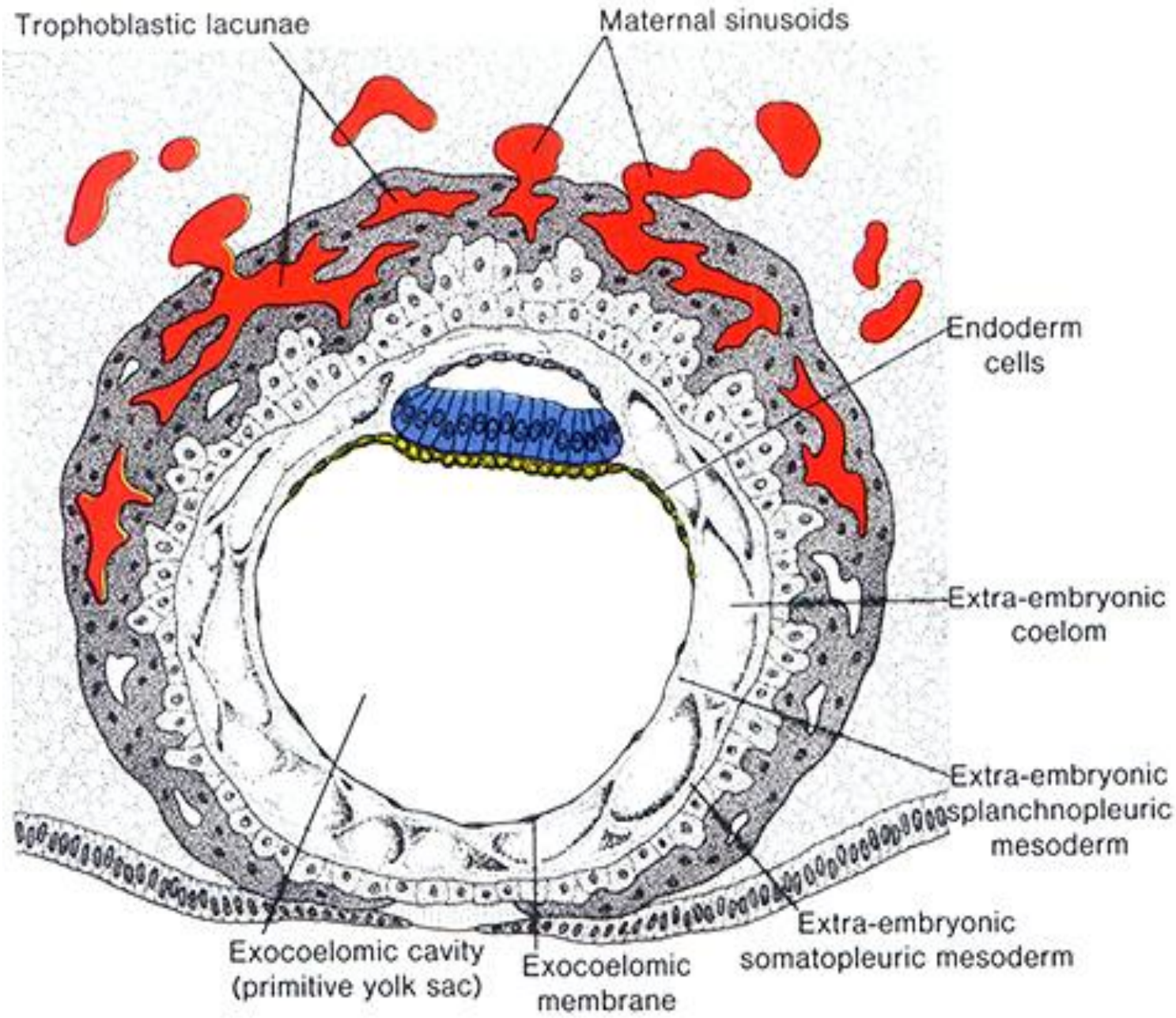
FETAL MEMBRANES

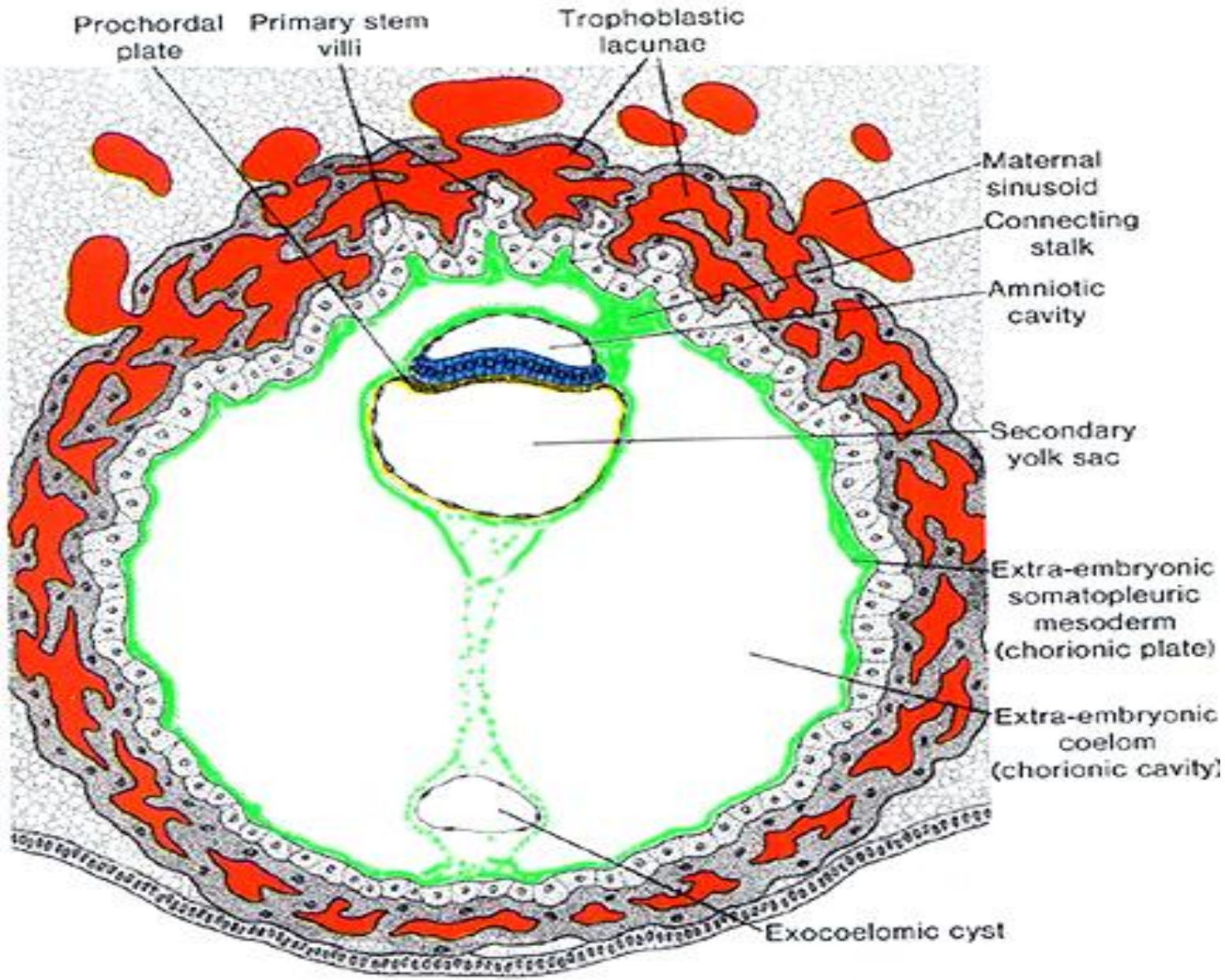
- Include:
  - –Chorion,
  - –Amnion,
  - –Umbilical vesicle (yolk sac),
  - –Allantois

DEVELOPMENT OF THE CHORIONIC SAC

- Trophoblast layer of the blastocyst
- Differentiation into:
  - Cytotrophoblast – inner layer
  - Syncytiotrophoblast – outer layer
- Development of extraembryonic mesoderm
- Formation of isolated lacunae spaces which later coalesce to form one big extraembryonic cavity – renamed chorionic sac
- Chorionic sac surrounds the amniotic cavity and primary umbilical vesicle
- Expansion of chorionic sac reduces the size of umbilical vesicle

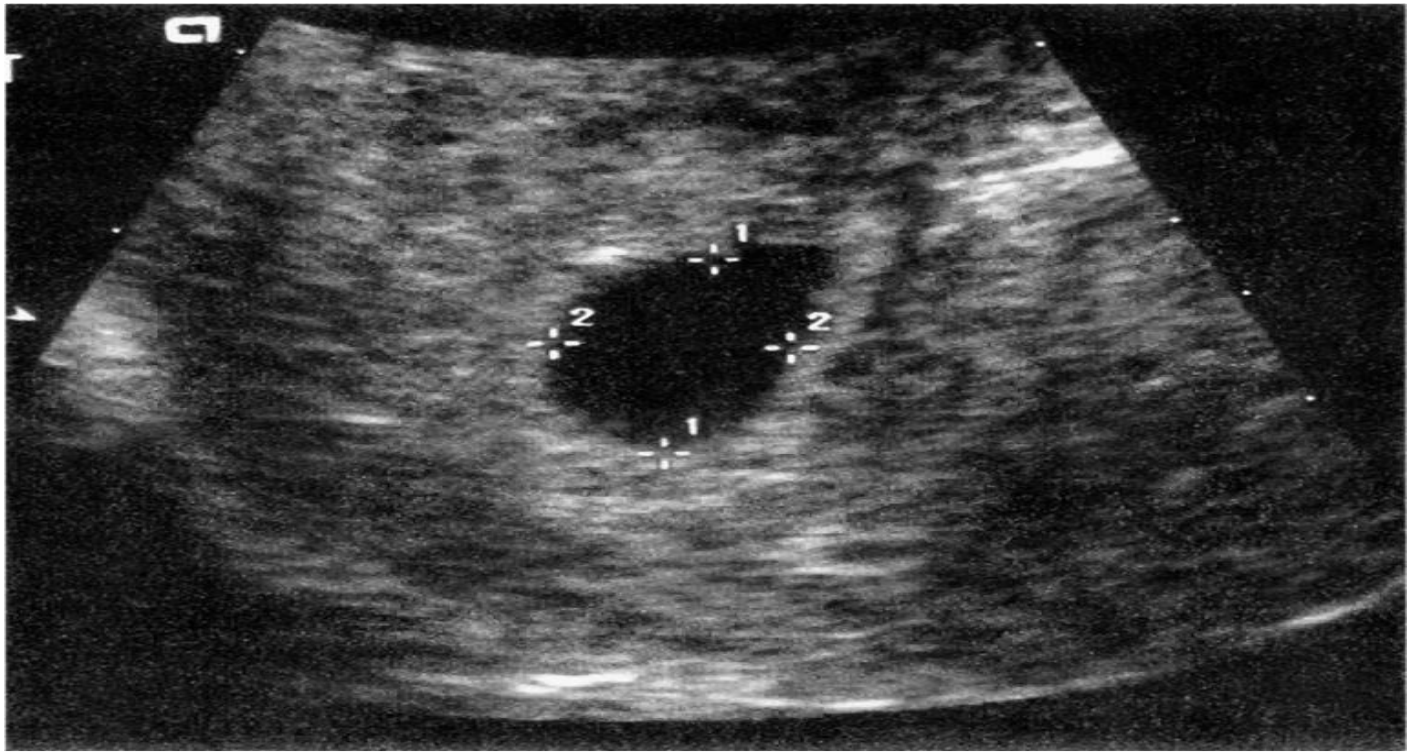

Trophoblastic lacunae
Enlarged blood vessels
Syncytiotrophoblast
Cytotrophoblast
Amniotic cavity
Epiblast
Hypoblast
Exocoelomic (Heuser's) membrane
Exocoelomic cavity (primitive yolk sac)
Fibrin coagulum


Trophoblastic lacunae
Maternal sinusoids
Endoderm cells
Extra-embryonic coelom
Extra-embryonic splanchnopleuric mesoderm
Extra-embryonic somatopleuric mesoderm
Exocoelomic cavity (primitive yolk sac)
Exocoelomic membrane


Prochordal plate
Primary stem villi
Trophoblastic lacunae
Maternal sinusoid
Connecting stalk
Amniotic cavity
Secondary yolk sac
Extra-embryonic somatopleuric mesoderm (chorionic plate)
Extra-embryonic coelom (chorionic cavity)
Exocoelomic cyst

ULTRASONOGRAPHY OF CHORIONIC SAC

- The size of the chorionic (gestational) sac is useful in determining gestational age of embryos using ultrasound in patients with uncertain menstrual histories.

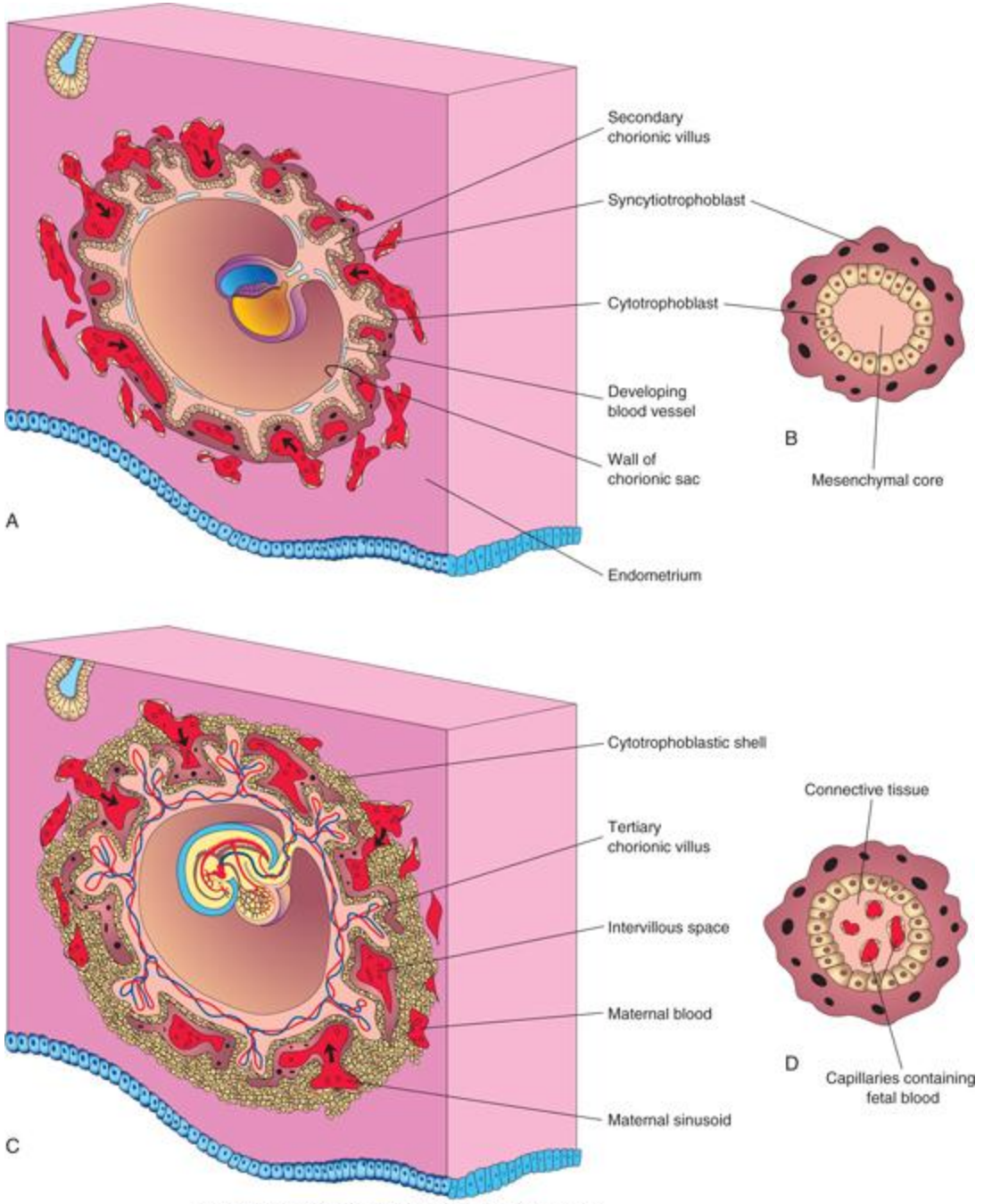


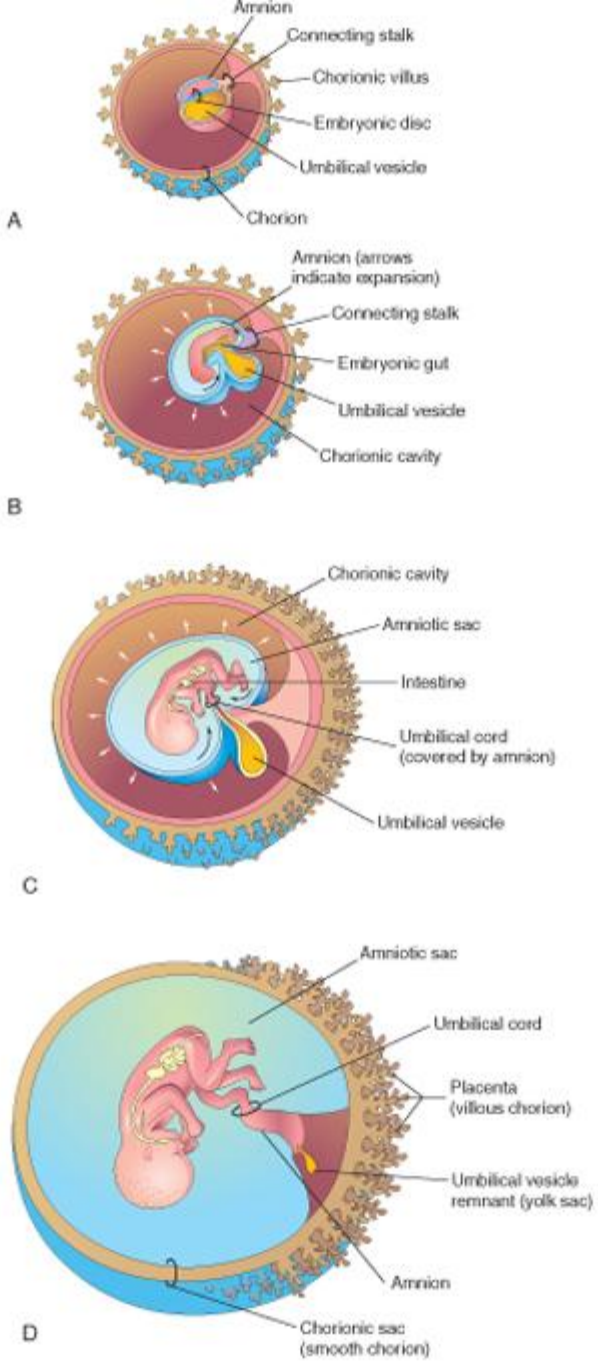
DEVELOPMENT OF CHORIONIC VILLI

- Development of chorionic villi begin with proliferation of cytotrophoblastic cells into the syncytiotrophoblast
- First wave of proliferation produces **primary chorionic villi** at the end of the 2nd week.
- Early in the 3rd week, mesenchyme grows into these primary villi, forming a core of mesenchymal tissue converting primary villi into **secondary chorionic villi** .
- Secondary choriomic villi cover the entire surface of the chorionic sac.
- Some mesenchymal cells in the villi soon differentiate into capillaries and blood cells converting secondary chorionic villi into **tertiary chorionic villi** .

- The capillaries in the chorionic villi fuse to form **arteriocapillary networks**, which soon become connected with the embryonic heart through vessels that differentiate in the mesenchyme of the chorion and connecting stalk.
- By the end of the 3rd week, embryonic blood begins to flow slowly through the capillaries in the chorionic villi.
- Cytotrophoblastic cells of the chorionic villi proliferate and extend through the syncytiotrophoblast to form an extravillous **cytotrophoblastic shell**, which gradually surrounds the chorionic sac and attaches it to the endometrium.

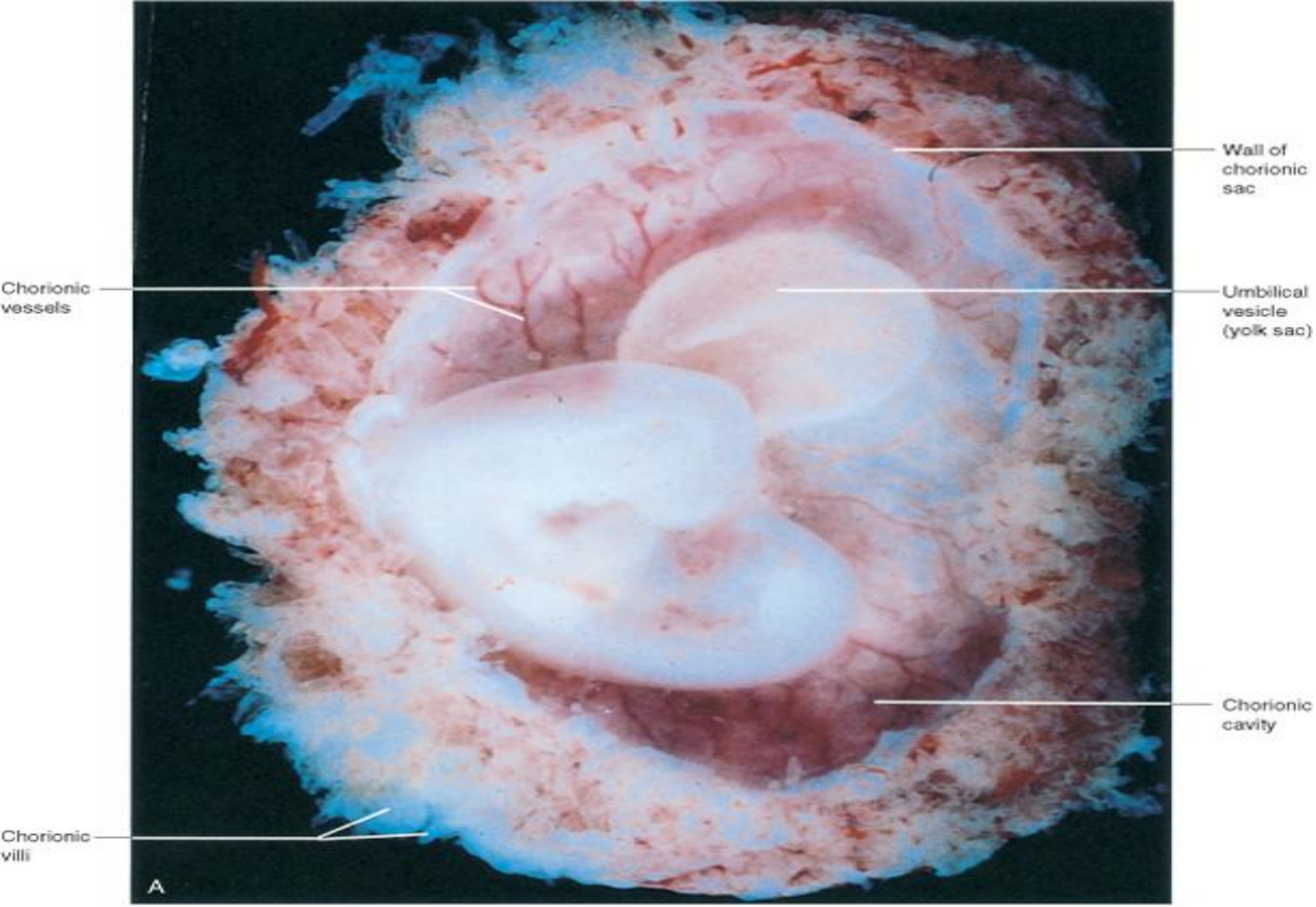
Diagrams illustrating development of secondary chorionic villi into tertiary chorionic villi. **A,** Sagittal section of an embryo (approximately 16 days). **B,** Section of a secondary chorionic villus. **C,** Section of an implanted embryo (approximately 21 days). **D,** Section of a tertiary chorionic villus. The fetal blood in the capillaries is separated from the maternal blood surrounding the villus by the endothelium of the capillary, embryonic connective tissue, cytotrophoblast, and syncytiotrophoblast.

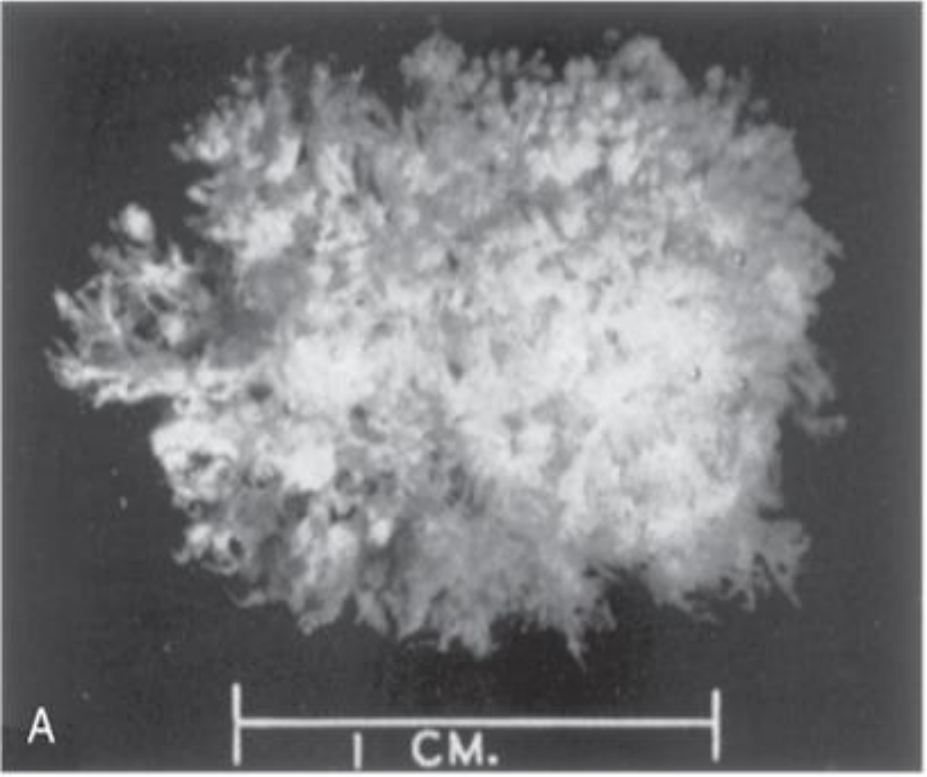


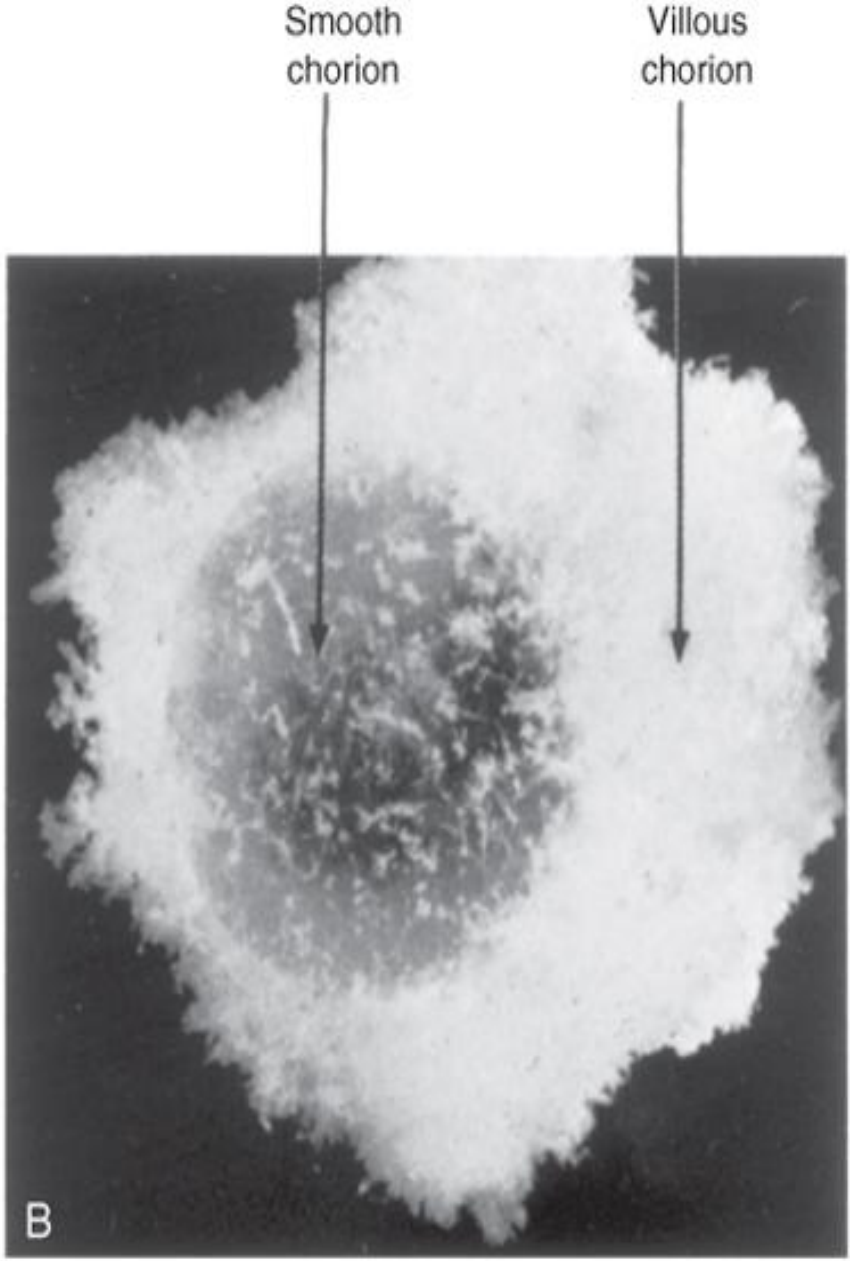


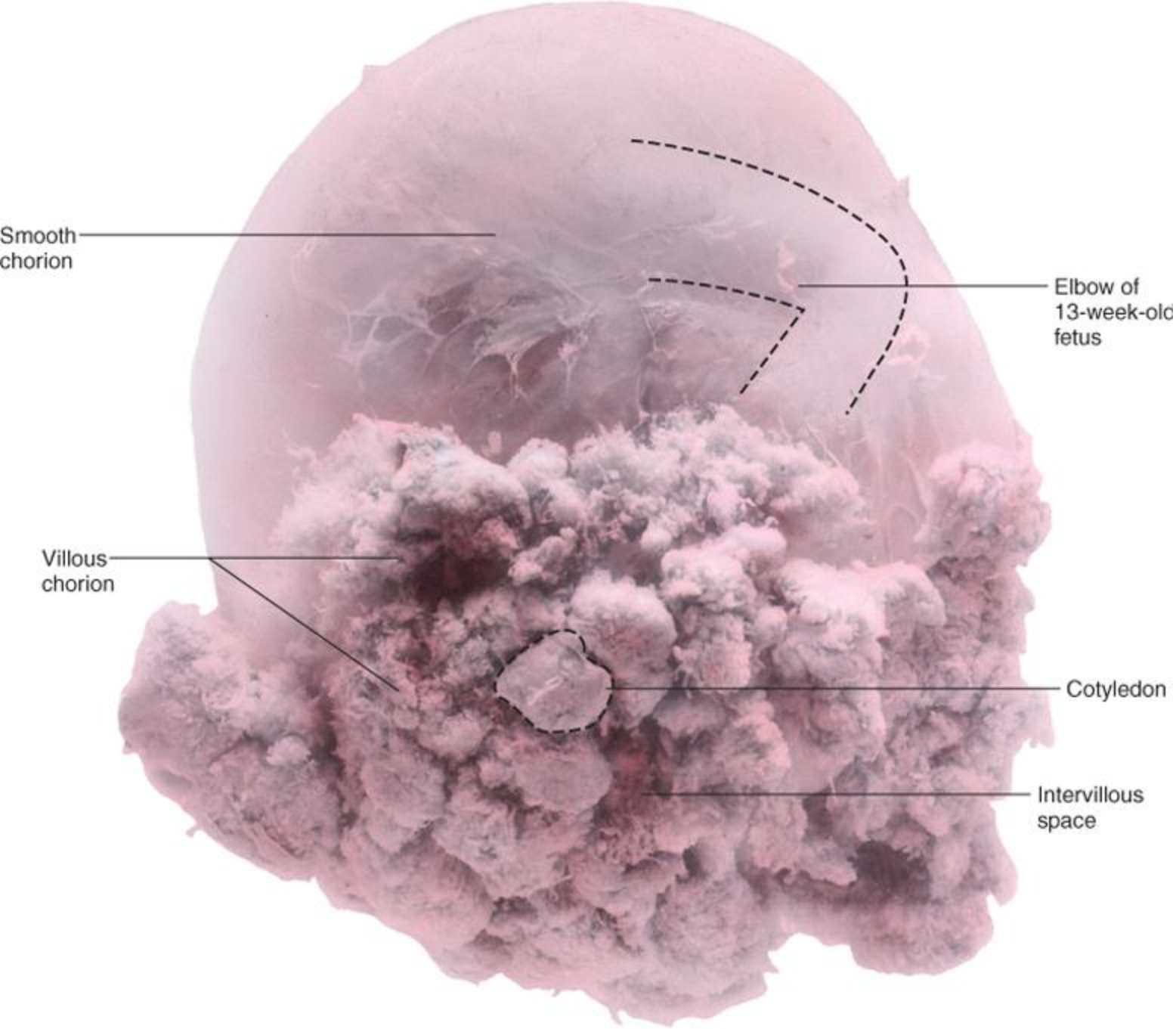
- Cover the entire chorionic sac until the beginning of the 8th week.
- As this sac grows, the villi associated with the decidua capsularis are compressed, reducing the blood supply to them.
- These villi soon degenerate, producing a relatively avascular bare area, the **smooth chorion**.
- Villi associated with the **decidua basalis** rapidly increase in number, branch profusely, and enlarge resulting in a bushy area the **villous chorion - which forms the placenta**.

- The **decidua capsularis**, the layer of decidua overlying the implanted chorionic sac, forms a capsule over the external surface of the sac.
- As the conceptus enlarges, the decidua capsularis bulges into the uterine cavity and becomes greatly attenuated.
- Eventually the decidua capsularis contacts and fuses with the **decidua parietalis**, thereby slowly obliterating the uterine cavity.
- **By 22 to 24 weeks, the reduced blood supply to the decidua capsularis causes it to degenerate and disappear.**
- After disappearance of the decidua capsularis, the smooth part of the chorionic sac fuses with the decidua parietalis.
- **This fusion is not complete , there is a potential space.**







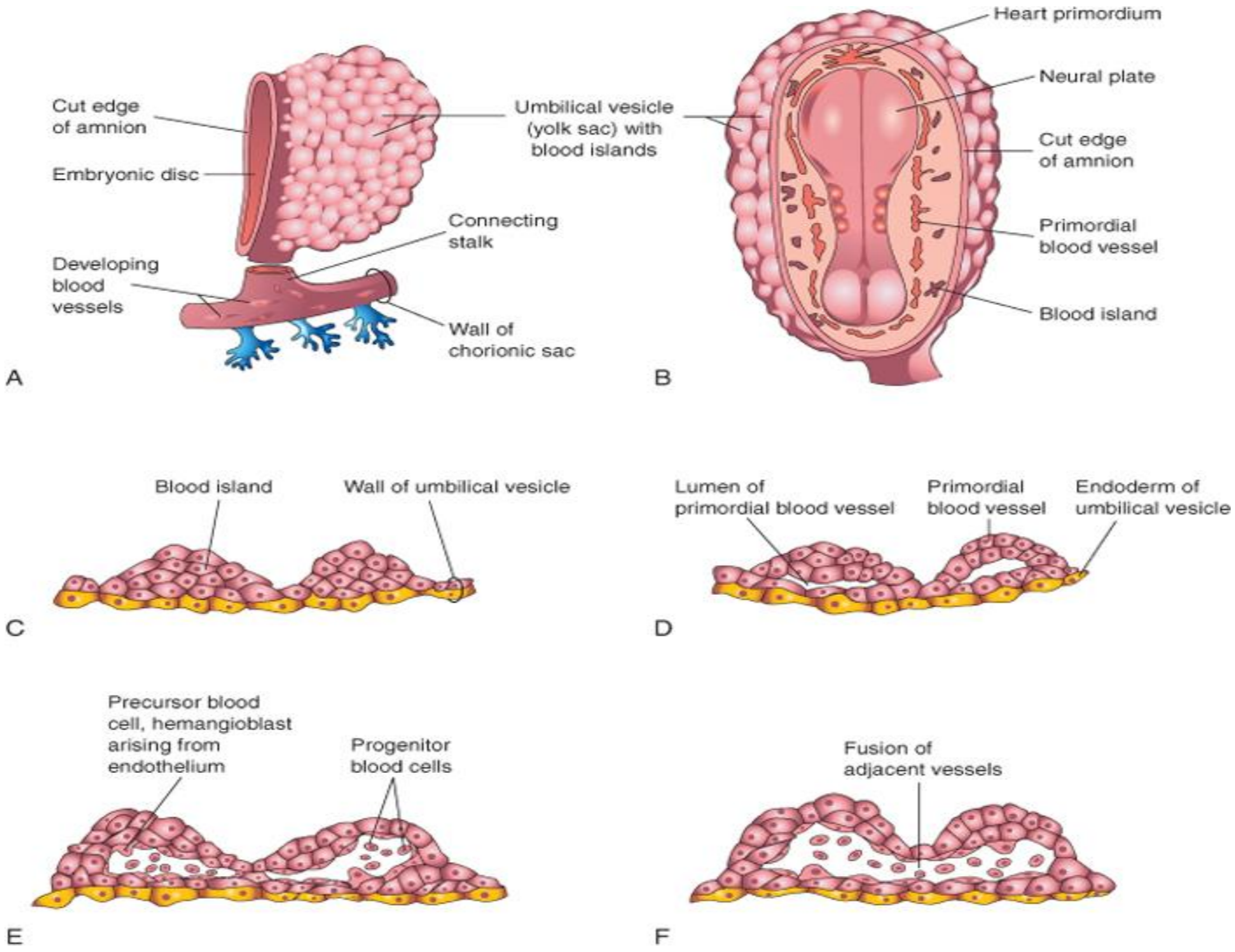


THE UMBILICAL VESICLE (YOLK SAC) (1)

- The blastocystic cavity is renamed umbilical vesicle after formation of amniotic cavity.
- At 32 days, the umbilical vesicle is large.
- By 10 weeks, the umbilical vesicle has shrunk to a pear-shaped remnant approximately 5 mm in diameter and is connected to the midgut by a narrow **omphaloenteric duct (yolk stalk).**
- By 20 weeks, the umbilical vesicle is very small; thereafter, it is usually not visible.

SIGNIFICANCE OF THE UMBILICAL VESICLE (1)

- Nonfunctional in humans but essential for:
  - Transfer of nutrients to the embryo during the **2nd and 3rd** weeks - **NUTRITION**.
  - Blood development beginning in the **3rd** week and continues to form there until hemopoietic activity begins in the liver during the **6th** week - **BLOOD FORMATION**.
  - During the **4th** week, the endoderm of the umbilical vesicle is incorporated into the embryo as the primordial gut - **GUT DEVELOPMENT**.



Successive stages in the development of blood and blood vessels. **A,** Lateral view of the umbilical vesicle and part of the chorionic sac (approximately 18 days). **B,** Dorsal view of the embryo exposed by removing the amnion. **C** to **F,** Sections of blood islands showing progressive stages in the development of blood and blood vessels.

SIGNIFICANCE OF THE UMBILICAL VESICLE (2)

- Endoderm gives rise to the epithelium of the trachea, bronchi, lungs - **RT DEVELOPMENT**.
- Primordial germ cells appear in the endodermal lining of the wall of the umbilical vesicle in the **3rd** week and subsequently migrate to the developing gonads where they differentiate into spermatogonia in males and oogonia in females - **GERM CELLS**.

FATE OF THE UMBILICAL VESICLE

- In very unusual cases, the umbilical vesicle persists throughout pregnancy and appears under the amnion as a small structure on the fetal surface of the placenta near the attachment of the umbilical cord.
- The omphaloenteric duct usually detaches from the midgut loop by the end of the **sixth week.**
- In approximately 2% of adults, the proximal intra-abdominal part of the omphaloenteric duct persists as an **ileal diverticulum (Meckel diverticulum).**

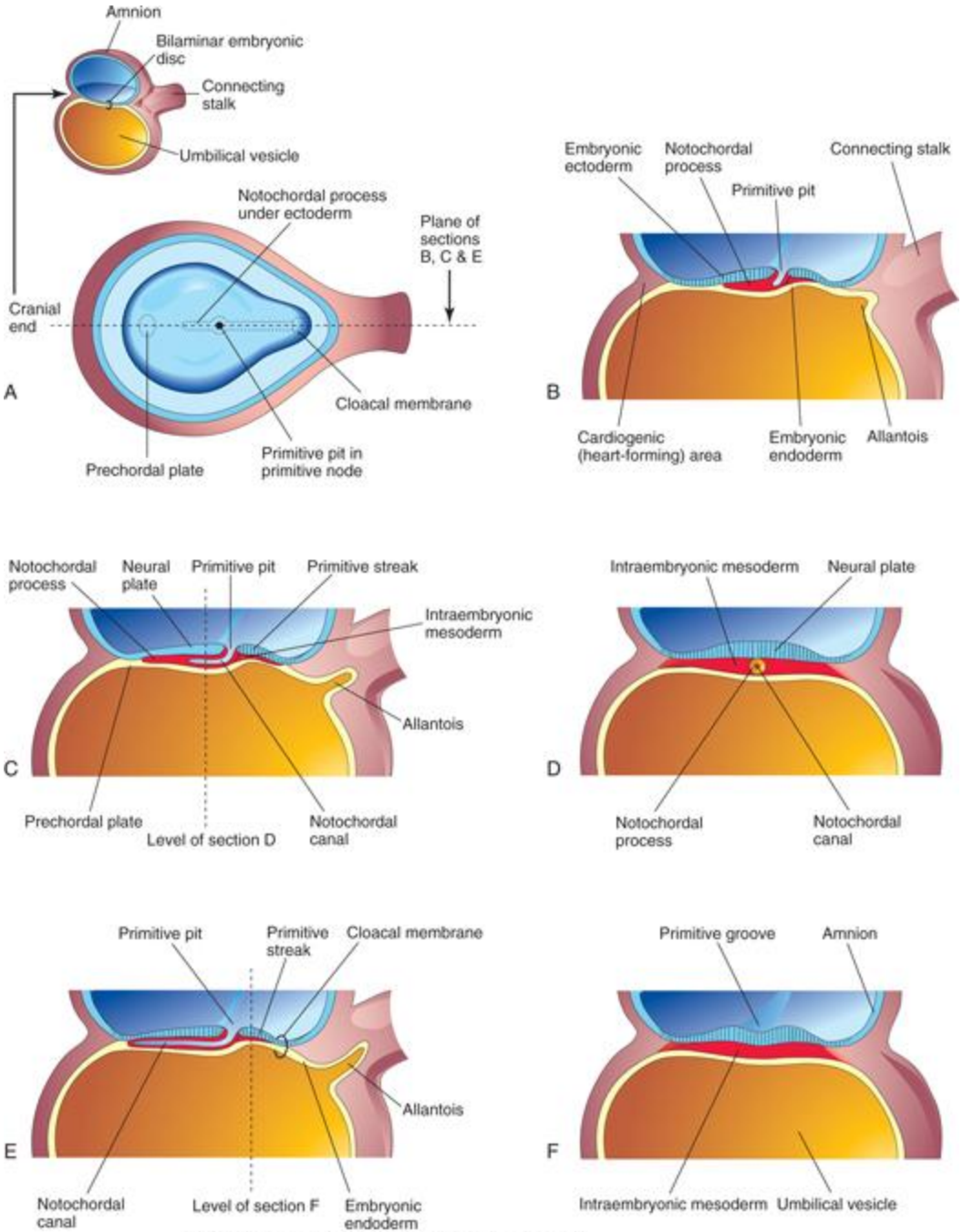
THE ALLANTOIS (1)

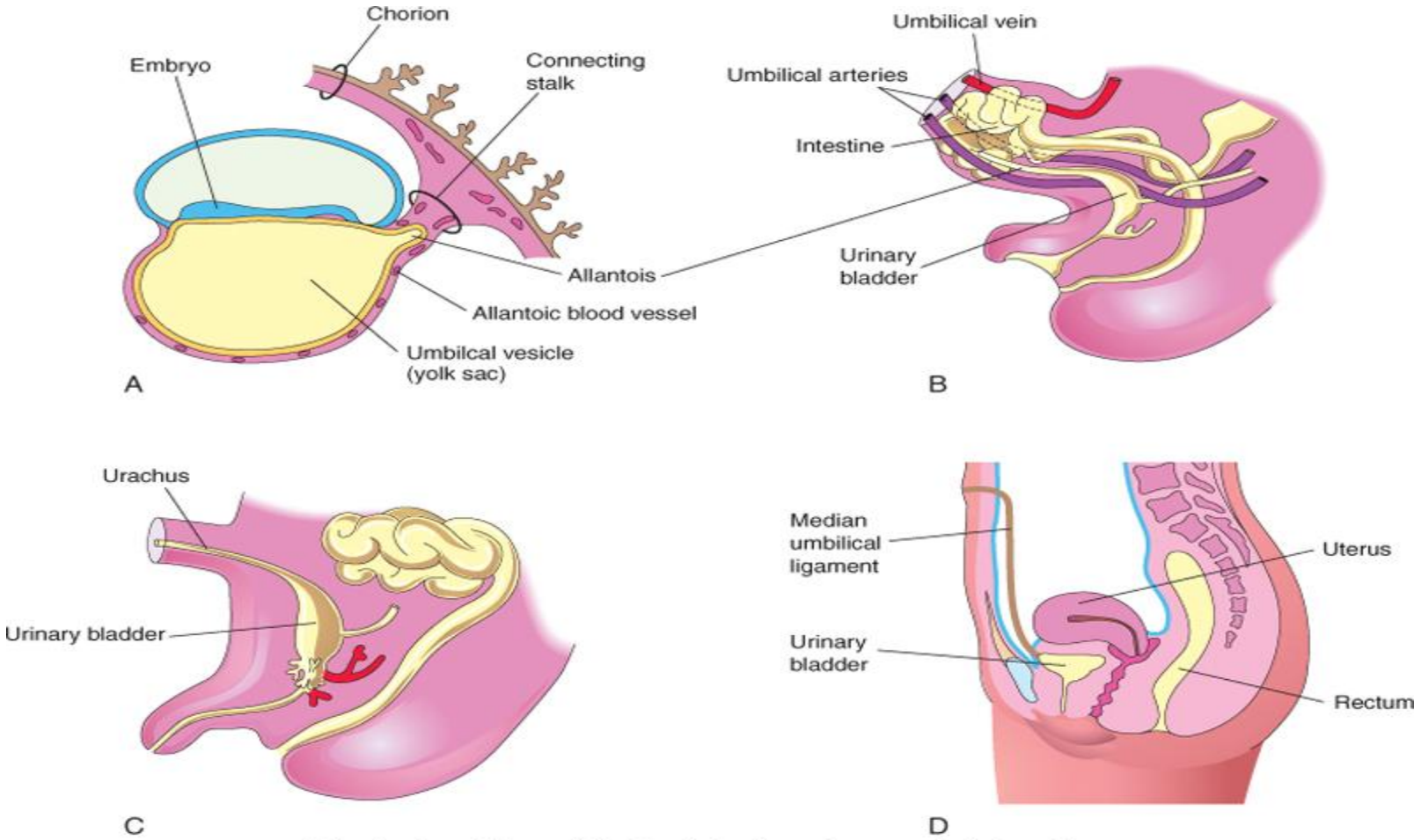
- In the **3rd week**, it appears as a sausage - like diverticulum from the caudal wall of the umbilical vesicle that extends into the connecting stalk.
- Although the allantois is not functional in human embryos, it is important for three reasons:
  - **Blood formation** occurs in its wall during the **3rd to 5th** weeks.
  - Formation of **umbilical vein** and **arteries**.
  - The intraembryonic part of the allantois runs from the umbilicus to the **urinary bladder**, with which it is continuous.

THE ALLANTOIS (2)

- During the **2nd** month, the extraembryonic part of the allantois degenerates.
- As the bladder enlarges, the allantois involutes to form a thick tube, the urachus.
- After birth, the urachus becomes a fibrous cord, the **median umbilical ligament**, that extends from the apex of the urinary bladder to the umbilicus.

Illustrations of developing notochordal process. The small sketch at the upper left is for orientation. **A,** Dorsal view of the embryonic disc (approximately 16 days) exposed by removal of the amnion. The notochordal process is shown as if it were visible through the embryonic ectoderm. **B, C,** and **E,** Median sections at the plane shown in **A,** illustrating successive stages in the development of the notochordal process and canal. The stages shown in **C** and **E** occur at approximately 18 days. **D** and **F,** Transverse sections through the embryonic disc at the levels shown in **C** and **E**.

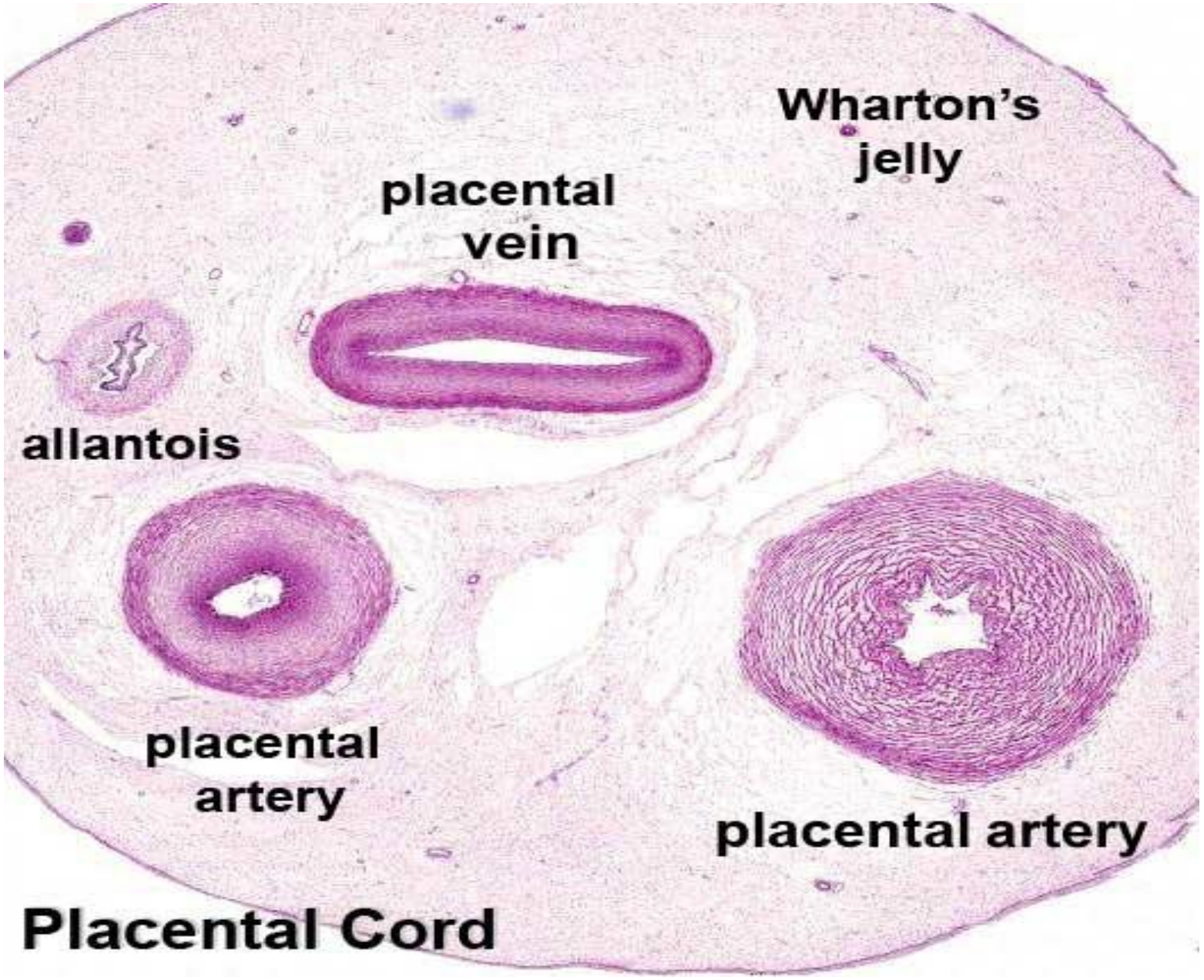




Illustrations of the development and usual fate of the allantois. **A,** A 3-week embryo. **B,** A 9-week fetus. **C,** A 3-month male fetus. **D,** Adult female. The nonfunctional allantois forms the urachus in the fetus and the median umbilical ligament in the adult.

ALLANTOIC CYSTS

- A cystic mass in the umbilical cord may represent the remains of the extraembryonic part of the allantois.
- These cysts usually resolve but may be associated with **omphalocele** - congenital herniation of viscera into the proximal part of the umbilical cord.
- The cysts are generally asymptomatic until childhood or adolescence, when they can become infected and inflamed.


Wharton's
jelly
placental
vein
allantois
placental
artery
placental artery
Placental Cord

AMNIOTIC FLUID(1)

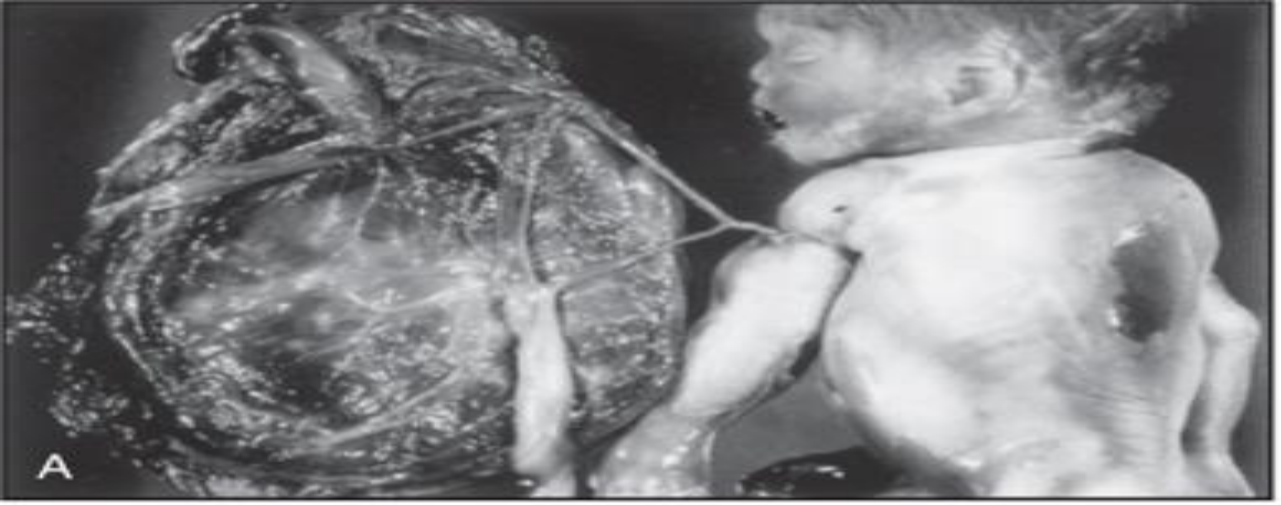
- Amnion is formed from embryoblast cells when lacunae appear among these cells which later coalesce to form amniotic cavity.
- Cells from embryoblast forms amnioblast which line the amniotic cavity forming the amniotic membrane.
- Sources of amniotic fluid
  - Secretion by amniotic cells;
  - Diffusion of maternal tissue and interstitial fluid across the amniochorionic membrane from the decidua parietalis.
  - Diffusion of fluid through the chorionic plate from blood in the intervillous space of the placenta.
  - Diffusion through fetal skin before keratinization of the skin; thus, amniotic fluid is similar to **fetal tissue fluid**.
  - Secretion by the fetal respiratory and gastrointestinal tracts.
  - Beginning in the 11th week, **urine** excreted by the fetus.
- The volume of amniotic fluid normally increases slowly, reaching approximately **30 mL at 10** weeks, **350 mL at 20** weeks, and **700 to 1000 mL by 37** weeks.

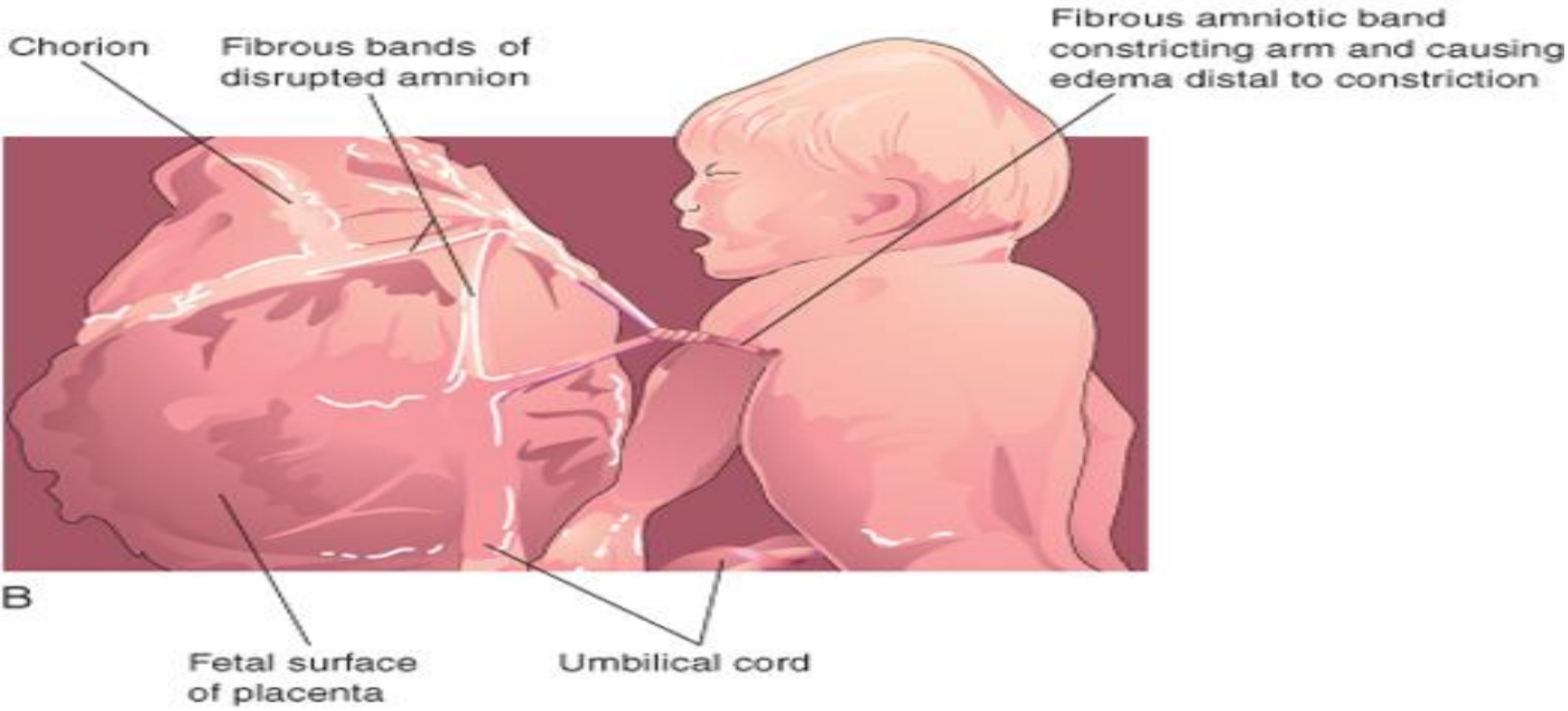
DISORDERS OF AMNIOTIC FLUID VOLUME (1)

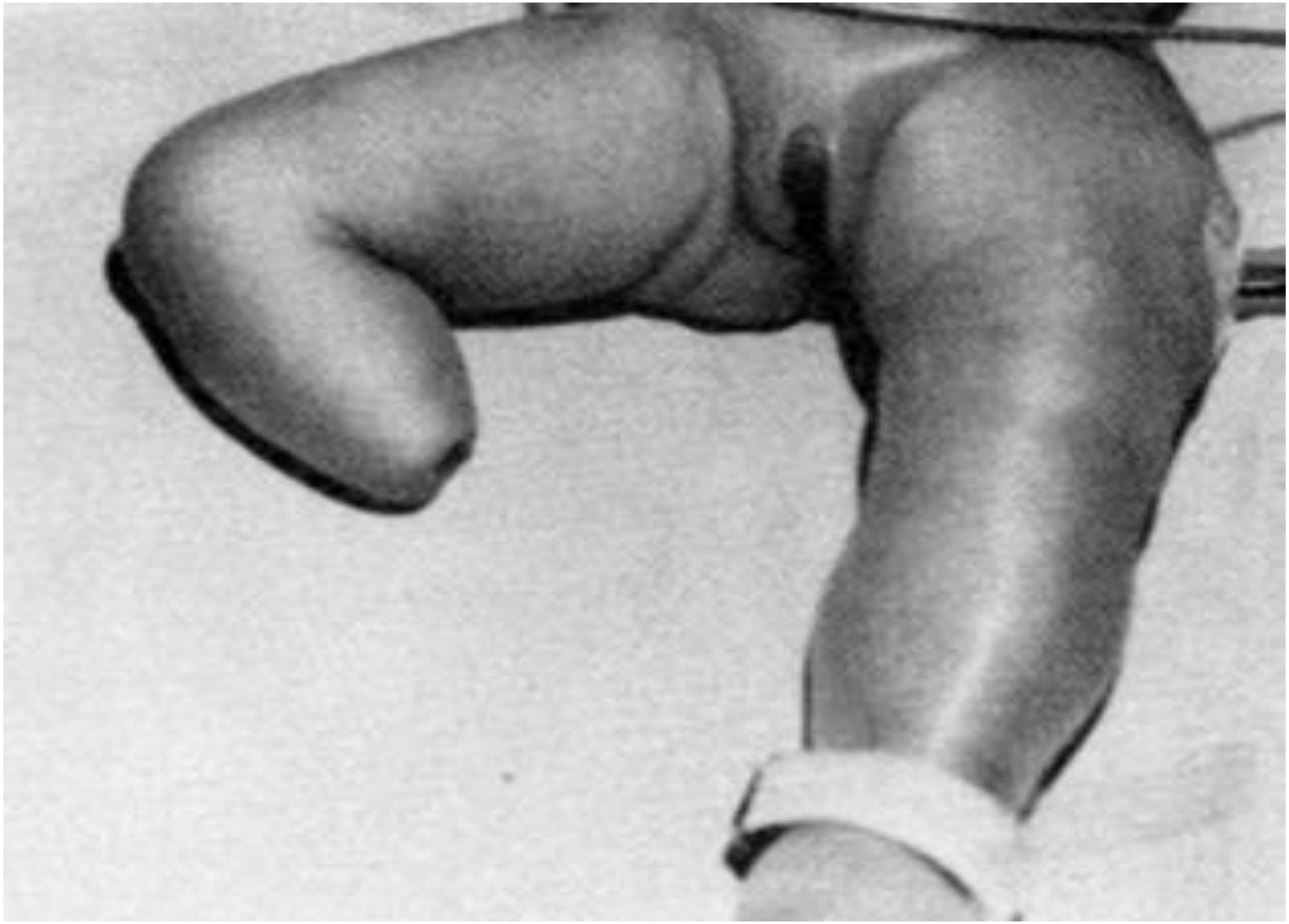
- Low volumes of amniotic fluid is called **oligohydramnios.**
- **Causes:**
  - Placental insufficiency.
  - Preterm rupture of the amniochorionic membrane.
  - Renal agenesis (failure of kidney formation).
  - Obstructive uropathy (urinary tract obstruction).

DISORDERS OF AMNIOTIC FLUID VOLUME (2)

- Complications of oligohydramnios include:
  - pulmonary hypoplasia,
  - facial defects,
  - limb defects that are caused by fetal compression by the uterine wall
  - compression of the umbilical cord is a potential complication if severe







DISORDERS OF AMNIOTIC FLUID VOLUME (3)

- High volumes of amniotic fluid is called **polyhydramnios.**
- **Causes**
- Causes of polyhydramnios:
  - 60% are idiopathic (unknown cause),
  - 20% are caused by maternal factors,
  - 20% are fetal in origin
- Failure of the fetus to swallow the usual amount of amniotic fluid e.g. in esophageal atresia (blockage).
- Severe anomalies of the central nervous system, such as meroencephaly (anencephaly).

COMPOSITION OF AMNIOTIC FLUID (1)

- Amniotic fluid is an aqueous solution in which undissolved material (desquamated fetal epithelial cells) is suspended.
- Amniotic fluid contains approximately equal portions of **organic and inorganic salts**.
- Organic constituents:
  - 50%-protein;
  - 50%-carbohydrates, fats, enzymes, hormones, and pigments.
- As pregnancy advances, the composition of the amniotic fluid changes as fetal excreta (meconium [fetal feces] and urine) are added.

SIGNIFICANCE OF AMNIOTIC FLUID (1)

- The embryo, suspended in amniotic fluid by the umbilical cord, floats freely.
- Amniotic fluid has critical functions in the normal development of the fetus.
- The buoyant amniotic fluid:
  - Permits symmetric external growth of the embryo and fetus
  - Acts as a barrier to infection
  - Permits normal fetal lung development
  - Prevents adherence of the amnion to the embryo and fetus

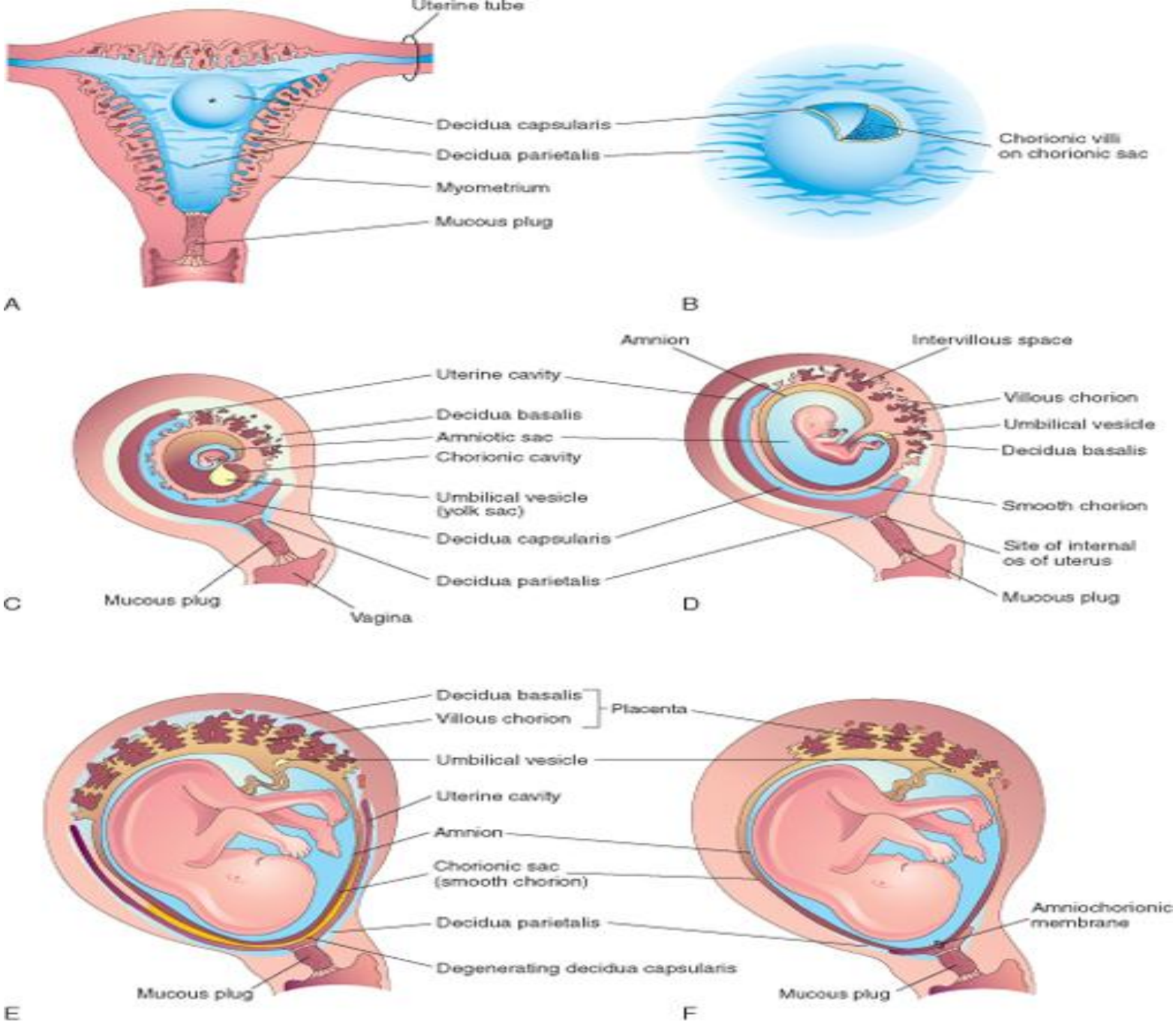
SIGNIFICANCE OF AMNIOTIC FLUID (2)

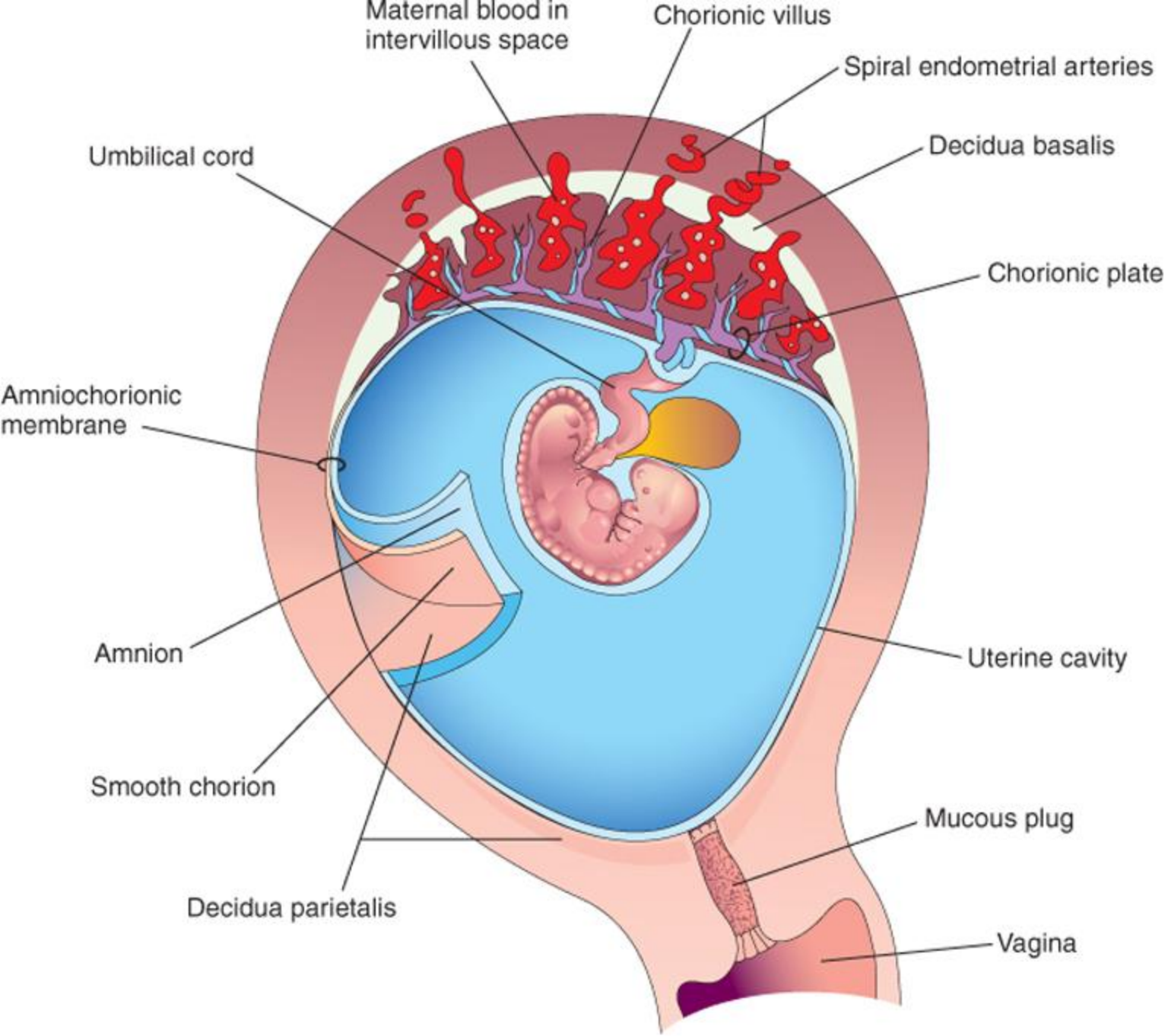
- Cushions the embryo and fetus against injuries by distributing impacts the mother receives
- Helps control the embryo's body temperature by maintaining a relatively constant temperature
- Enables the fetus to move freely, thereby aiding muscular development in the limbs
- Assists in maintaining homeostasis of fluid and electrolytes
- Amniotic fluid can be obtained for diagnostic purposes

THE PLACENTA

- The placenta is a fetomaternal organ that has two components:
  - A fetal part that develops from the chorionic sac
  - A maternal part that is derived from the endometrium
- The placenta and umbilical cord form a transport system for substances passing between the mother and fetus.

- Functions and activities of the placenta and fetal membranes:
  - protection,
  - nutrition,
  - respiration,
  - excretion,
  - hormone production.
- Shortly after birth, the placenta and fetal membranes are expelled from the uterus as the **afterbirth**.



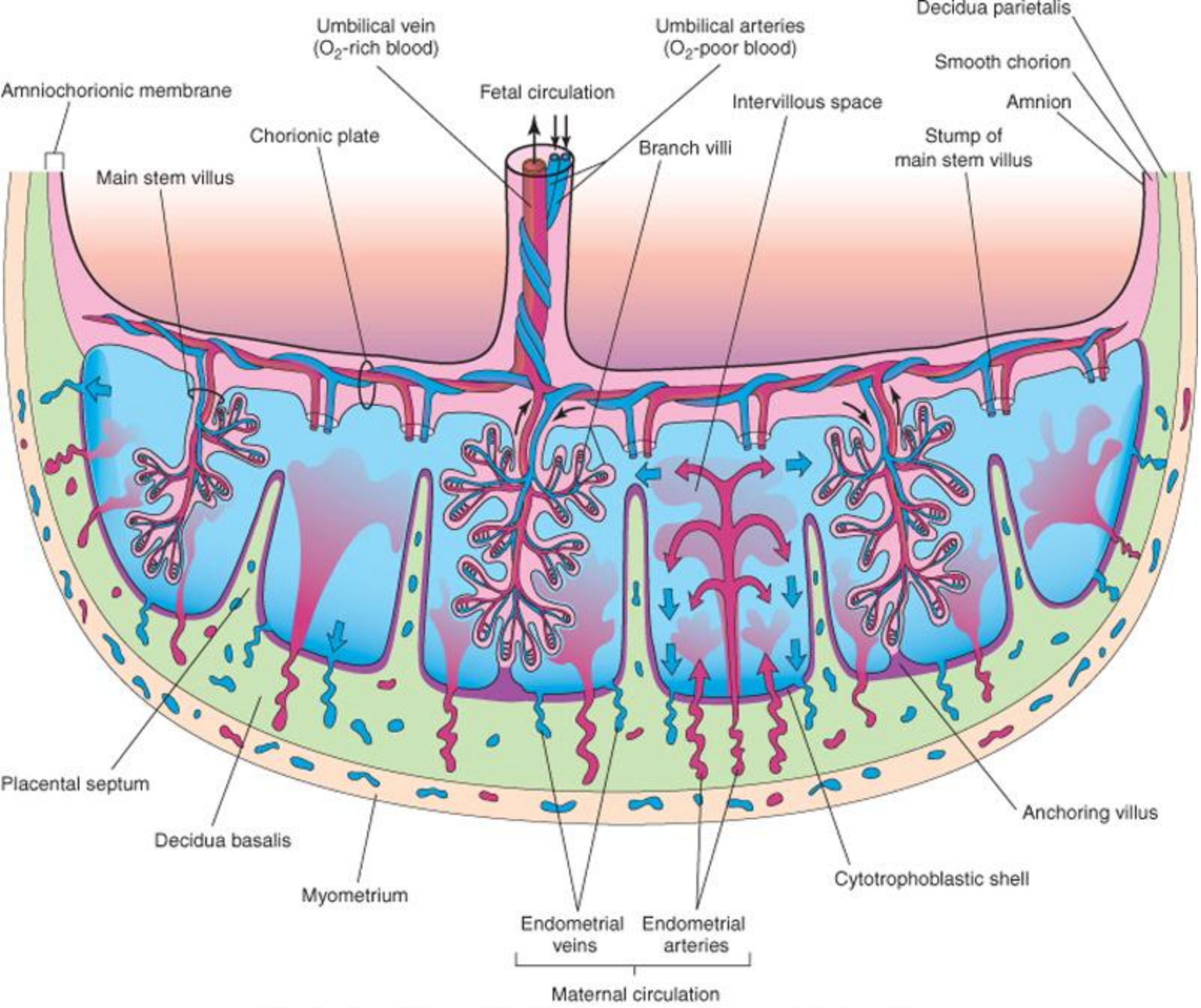


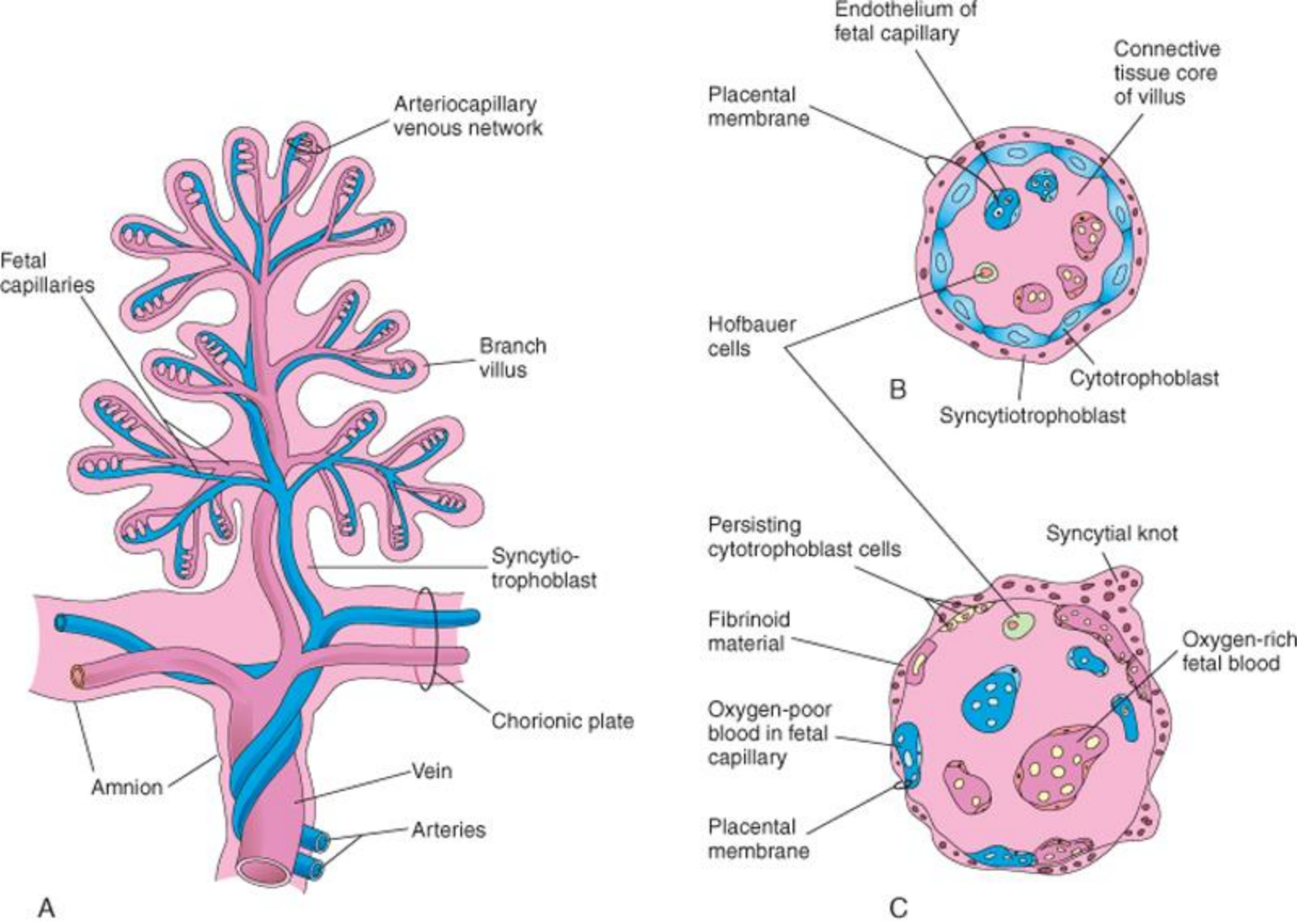
Development of the Placenta

- Early placental development is characterized by the rapid proliferation of the trophoblast and development of the chorionic sac and chorionic villi.
- By the end of the **third week**, the anatomic arrangements necessary for physiologic exchanges between the mother and her embryo are established.
- A complex vascular network is established in the placenta by the end of the **fourth week**, which facilitates maternal-embryonic exchanges of gases, nutrients, and metabolic waste products.

- Growth in the size and thickness of the placenta continues rapidly until the fetus is approximately 18 weeks old (20 weeks' gestation).
- The fully developed placenta covers **15% to 30%** of the decidua and weighs approximately **one sixth** that of the fetus.
- Decidual cells may protect the maternal tissue against **uncontrolled invasion** by the syncytiotrophoblast and that they may be involved in **hormone production**.

- The fetal part of the placenta (villous chorion) is attached to the maternal part of the placenta (decidua basalis) by the **cytotrophoblastic shell**, the external layer of trophoblastic cells on the maternal surface of the placenta.
- The chorionic villi attach firmly to the decidua basalis and anchor the chorionic sac to the decidua basalis.
- The shape of the placenta is determined by the persistent area of chorionic villi .
- Usually this is a circular area, giving the placenta a discoid shape.





- As the chorionic villi invade the decidua basalis, decidual tissue is eroded to enlarge the intervillous space.
- This erosion produces several wedge-shaped areas of decidua, **placental septa**, that project toward the chorionic plate.
- The placental septa divide the fetal part of the placenta into irregular convex areas - **cotyledons**.
- Each cotyledon consists of two or more stem villi and their many branch villi.
- By the end of the 4^{th} month, the decidua basalis is almost entirely replaced by the cotyledons.

- The **intervillous space** of the placenta, which contains maternal blood, is derived from the lacunae that developed in the syncytiotrophoblast during the 2nd week of development.
- The intervillous space of the placenta is divided into compartments by the **placental septa**; however, there is free communication between the compartments because the septa do not reach the chorionic plate.

- Maternal blood enters the intervillous space from the **spiral endometrial arteries** in the decidua basalis and discharge blood into the intervillous space.
- The intervillous space is drained by **endometrial veins** that also penetrate the cytotrophoblastic shell.
- The numerous branch chorionic villi arising from stem villi are continuously showered with maternal blood that circulates through the intervillous space.

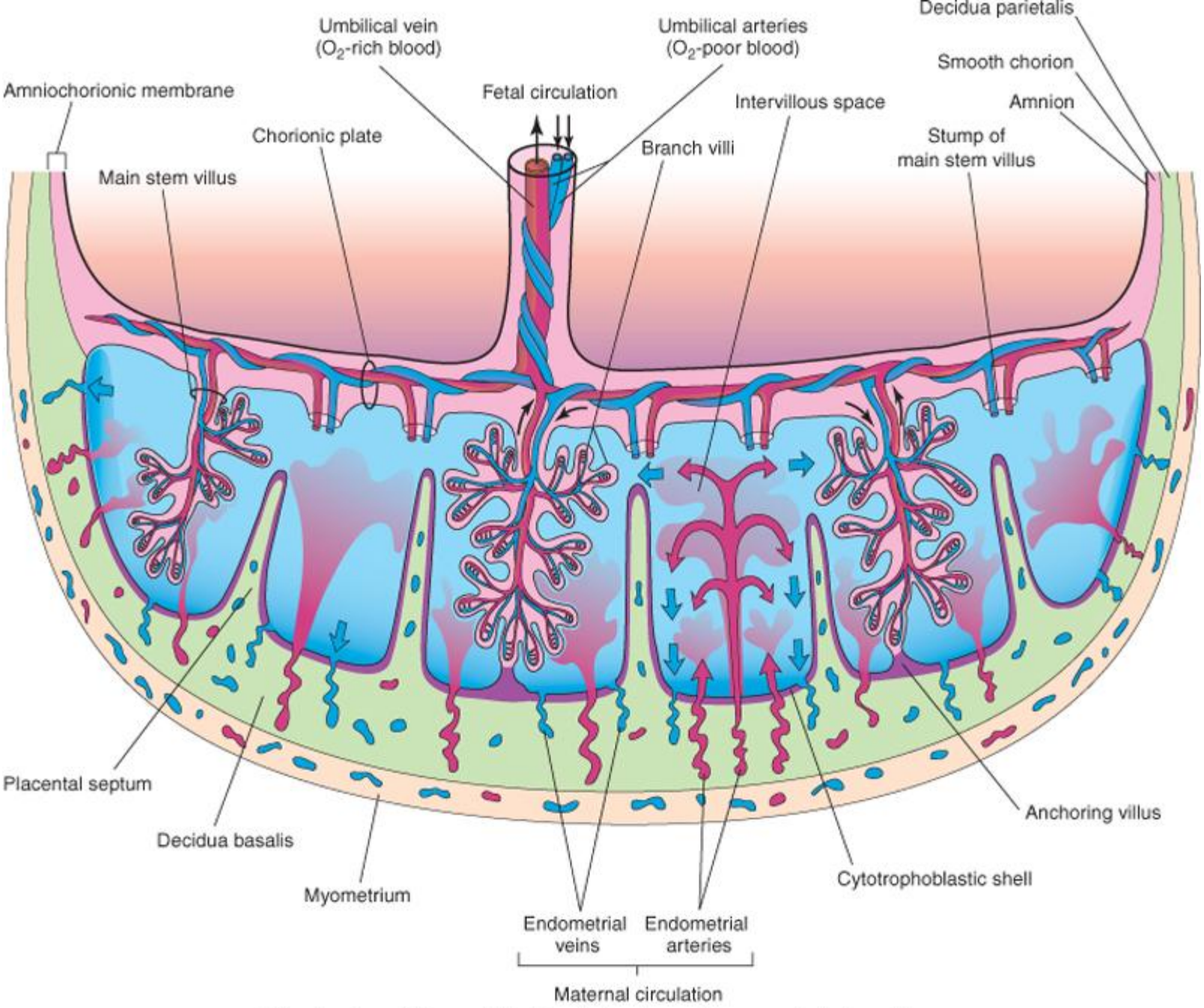
Placental Circulation

- The branch chorionic villi of the placenta provide a large surface area where materials may be exchanged across the very thin placental membrane ("barrier") interposed between the fetal and maternal circulations.
- It is through the numerous branch villi that the main exchange of material between the mother and fetus takes place.
- The circulations of the fetus and the mother are separated by the placental membrane consisting of extrafetal tissues.

Fetal Placental Circulation

- Poorly oxygenated blood leaves the fetus and passes through the umbilical arteries to the placenta.
- The blood vessels in the placenta form an **extensive arteriocapillary-venous system** within the chorionic villi, which brings the fetal blood extremely close to the maternal blood.
- This system provides a very large surface area for the exchange of metabolic and gaseous products between the maternal and fetal bloodstreams.

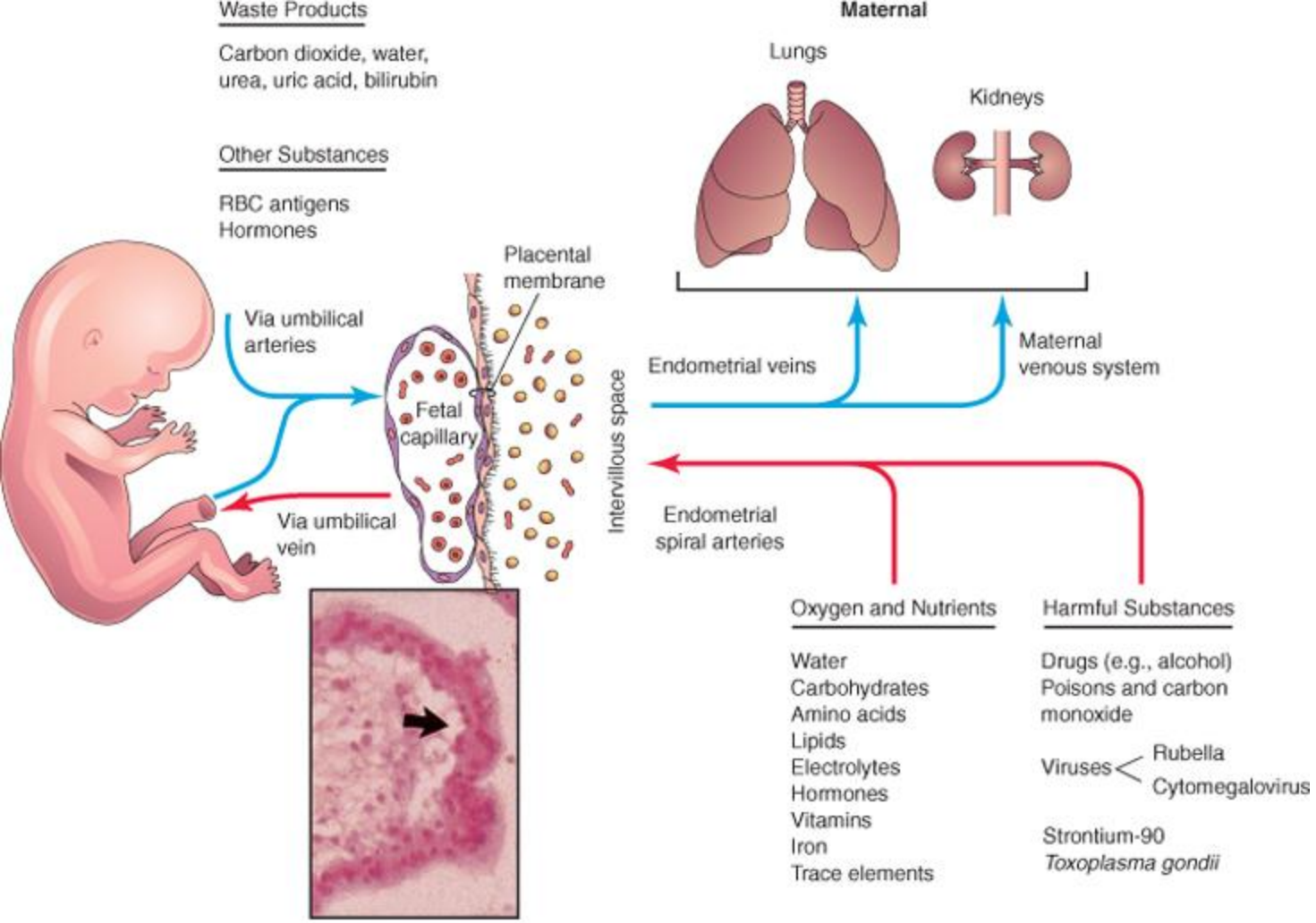
- There is normally no intermingling of fetal and maternal blood; **however, very small amounts of fetal blood may enter the maternal circulation when minute defects develop in the placental membrane.**
- The well-oxygenated fetal blood in the fetal capillaries passes into thin-walled veins that follow the chorionic arteries to the site of attachment of the umbilical cord.
- They converge here to form the umbilical vein.
- This large vessel carries oxygen rich blood to the fetus.



Maternal Placental Circulation

- The maternal blood in the intervillous space is **temporarily outside the maternal circulatory system**.
- It enters the intervillous space through 80 to 100 spiral endometrial arteries in the decidua basalis.
- These vessels discharge into the intervillous space through gaps in the cytotrophoblastic shell.
- The blood flow from the **spiral arteries** is pulsatile and is propelled in jetlike fountains by the maternal blood pressure .

- The entering blood is at a considerably higher pressure than that in the intervillous space and spurts toward the **chorionic plate** forming the "roof" of the intervillous space.
- As the pressure dissipates, the blood flows slowly over the branch villi, allowing an exchange of metabolic and gaseous products with the fetal blood.
- The blood eventually returns through the endometrial veins to the maternal circulation.
- The intervillous space of the mature placenta contains approximately **150 mL** of blood that is replenished **three or four times per minute**.



The Placental Membrane

- The placental membrane is a composite structure that consists of the extrafetal tissues separating the maternal and fetal blood.
- Until approximately 20 weeks, the **placental membrane** consists of four layers:
  - syncytiotrophoblast,
  - cytotrophoblast,
  - connective tissue of villus,
  - endothelium of fetal capillaries
- After the 20th week, histologic changes occur in the branch villi that result in the cytotrophoblast in many of the villi becoming attenuated.
- Eventually cytotrophoblastic cells disappear over large areas of the villi, leaving only thin patches of syncytiotrophoblast.

- As a result, the placental membrane consists of **three layers in most places**.
- In some areas, the placental membrane becomes markedly thinned and attenuated.
- At these sites, the syncytiotrophoblast comes in direct contact with the endothelium of the fetal capillaries to form a **vasculosyncytial placental membrane.**

- Electron micrographs of the syncytiotrophoblast show that its free surface has many **microvilli, more than 1 billion/cm^2 at term**, that increase the surface area for exchange between the maternal and fetal circulations.
- During the third trimester, numerous nuclei in the syncytiotrophoblast aggregate to form multinucleated protrusions called nuclear aggregations or **syncytial knots**.

- These aggregations continually break off and are carried from the intervillous space into the maternal circulation.
- Some knots lodge in capillaries of the maternal lung where they are rapidly destroyed by local enzyme action.
- Toward the end of pregnancy, fibrinoid material forms on the surfaces of villi.
- **Fibrinoid** material results mainly from aging and appears to reduce placental transfer.

Placental Transfer

- The transport of substances in both directions between the fetal and maternal blood is facilitated by the great surface area of the placental membrane.
- Almost all materials are transported across the placental membrane by one of the following four main transport mechanisms:
  - simple diffusion,
  - facilitated diffusion,
  - active transport,
  - pinocytosis

- Passive transport by **simple diffusion** is usually characteristic of substances moving from areas of higher to lower concentration until equilibrium is established.
- In **facilitated diffusion**, there is transport through electrical gradients.
- **Active transport** against a concentration gradient requires energy.
  - Such systems may involve carrier molecules that temporarily combine with the substances to be transported.

- **Pinocytosis** is a form of endocytosis in which the material being engulfed is a small amount of extracellular fluid.
  - This method of transport is usually reserved for large molecules.
  - Some proteins are transferred very slowly through the placenta by pinocytosis.

Other Placental Transport Mechanisms (1)

- There are three other methods of transfer across the placental membrane.
- **First**, fetal red blood cells pass into the maternal circulation, particularly during parturition, through microscopic breaks in the placental membrane.
  - Labeled maternal red blood cells have also been found in the fetal circulation.
  - Consequently, red blood cells may pass in either direction through very small defects in the placental membrane.

Other Placental Transport Mechanisms (2)

- **Second** method of transport, cells cross the placental membrane under their own power, e.g., maternal leukocytes and *Treponema pallidum*, the organism that causes syphilis.
- **Third** method of transport, some bacteria and protozoa such as *Toxoplasma gondii* infect the placenta by creating lesions and then cross the placental membrane through the defects that are created.

Transfer of Gases

- Oxygen, carbon dioxide, and carbon monoxide cross the placental membrane by simple diffusion.
- The placental membrane approaches the efficiency of the lungs for gas exchange.
- The quantity of oxygen reaching the fetus is primarily flow limited rather than diffusion limited; hence, fetal hypoxia (decreased levels of oxygen) results primarily from factors that diminish either the uterine blood flow or fetal blood flow.

Placental Endocrine Synthesis and Secretion

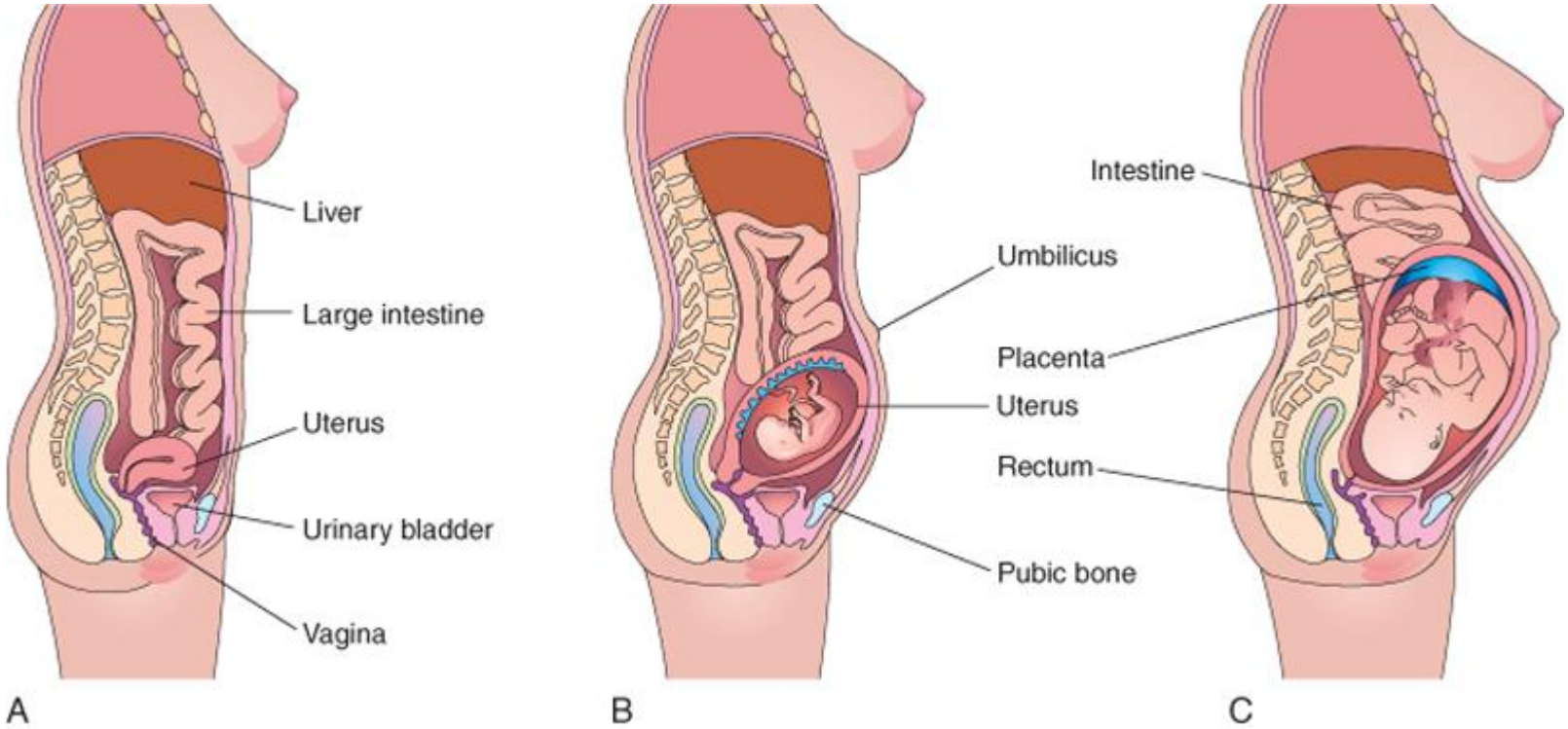
- Using precursors derived from the fetus and/or the mother, the syncytiotrophoblast of the placenta synthesizes protein and steroid hormones.
- The protein hormones synthesized by the placenta are:
  - hCG
  - Human chorionic somatomammotropin or human placental lactogen
  - Human chorionic thyrotropin
  - Human chorionic corticotropin

The Placenta as an Allograft

- The placenta can be regarded as an **allograft** with respect to the mother.
- The fetal part of the placenta is a derivative of the conceptus, which inherits both paternal and maternal genes.
- What protects the placenta from rejection by the mother's immune system?
- The syncytiotrophoblast of the chorionic villi, although exposed to maternal immune cells within the blood sinusoids, lacks major histocompatibility (MHC) antigens and thus does not evoke rejection responses.
- Thus, it appears that the decidua plays a dual role in uteroplacental homeostasis by immunoprotection of the placenta and protection of the uterus from placental overinvasion.

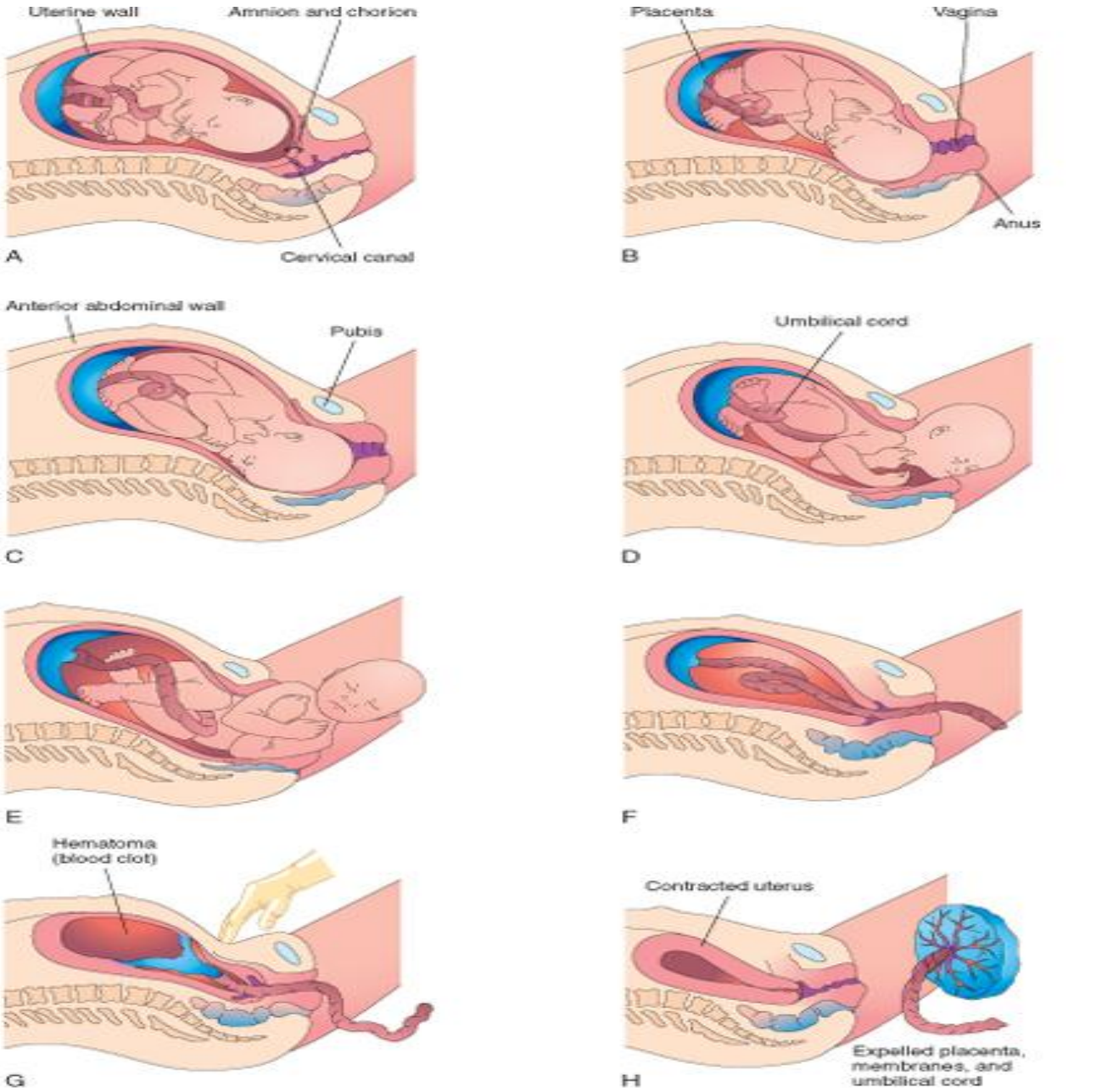
Uterine Growth during Pregnancy

- The uterus of a nonpregnant woman lies in the pelvis. To accommodate the growing conceptus, the uterus increases in size.
- It also increases in weight, and its walls become thinner.
- During the first trimester, the uterus moves out of the pelvis and by 20 weeks reaches the level of the umbilicus.
- By 28 to 30 weeks, the uterus reaches the epigastric region, the area between the xiphoid process of the sternum and the umbilicus.
- The increase in size of the uterus largely results from hypertrophy of preexisting smooth muscular fibers and partly from the development of new fibers.



PARTURITION

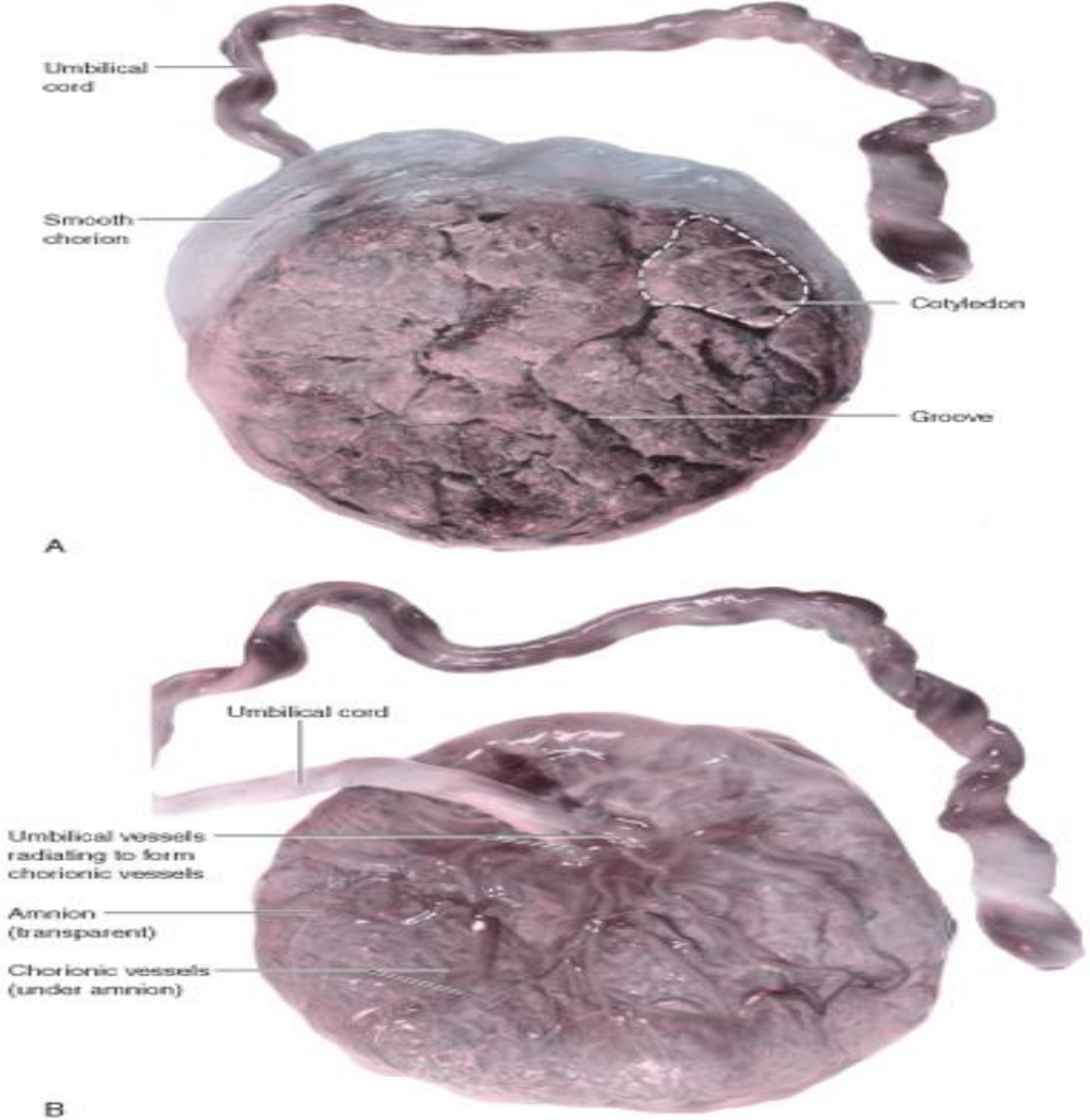
- Parturition (childbirth) is the process during which the fetus, placenta, and fetal membranes are expelled from the mother's reproductive tract.
- **Labor** is the sequence of involuntary uterine contractions that result in dilation of the uterine cervix and expulsion of the fetus and placenta from the uterus.
- Several factors control onset of labor including steroids, hormones etc
- 3 stages of labor:
- First stage – uterine dilatation
- Second stage – cervix fully dilated and delivery of baby
- Third stage – delivery of the placenta

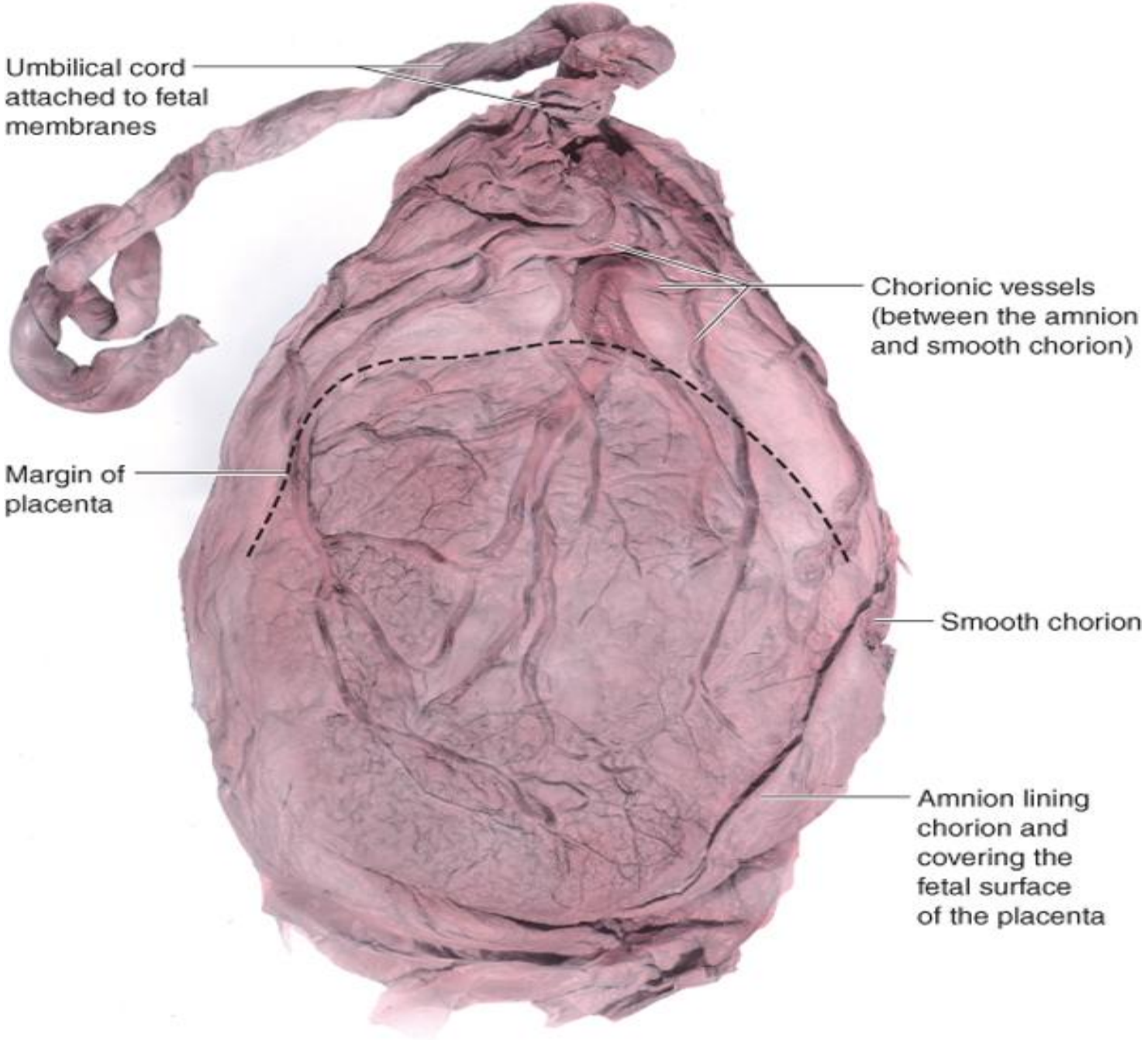


The Placenta and Fetal Membranes after Birth

- The **placenta** commonly has a discoid shape, with a diameter of 15 to 20 cm and a thickness of 2 to 3 cm.
- It weighs 500 to 600 g, which is approximately one sixth the weight of the average fetus.
- The margins of the placenta are continuous with the ruptured amniotic and chorionic sacs.
- When villi persist on the entire surface of the chorionic sac (an uncommon occurrence), a thin layer of placenta attaches to a large area of the uterus.

- This type of placenta is a membranous placenta-placenta membranacea.
- When villi persist elsewhere, several variations in placental shape occur:
  - accessory placenta,
  - bidiscoid placenta,
  - horseshoe placenta.
- Although there are variations in the size and shape of the placenta, most of them are of little physiologic or clinical significance.





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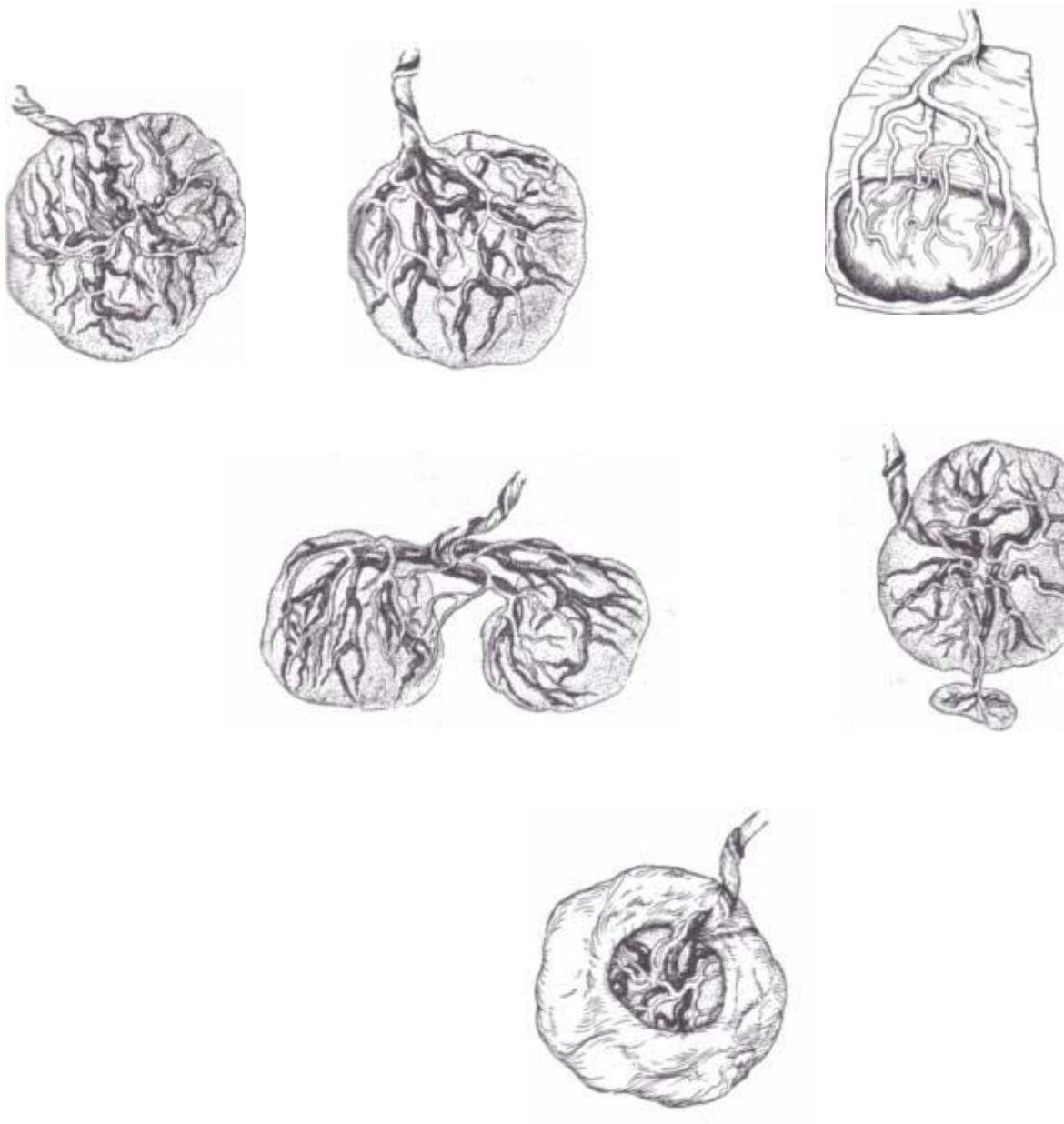
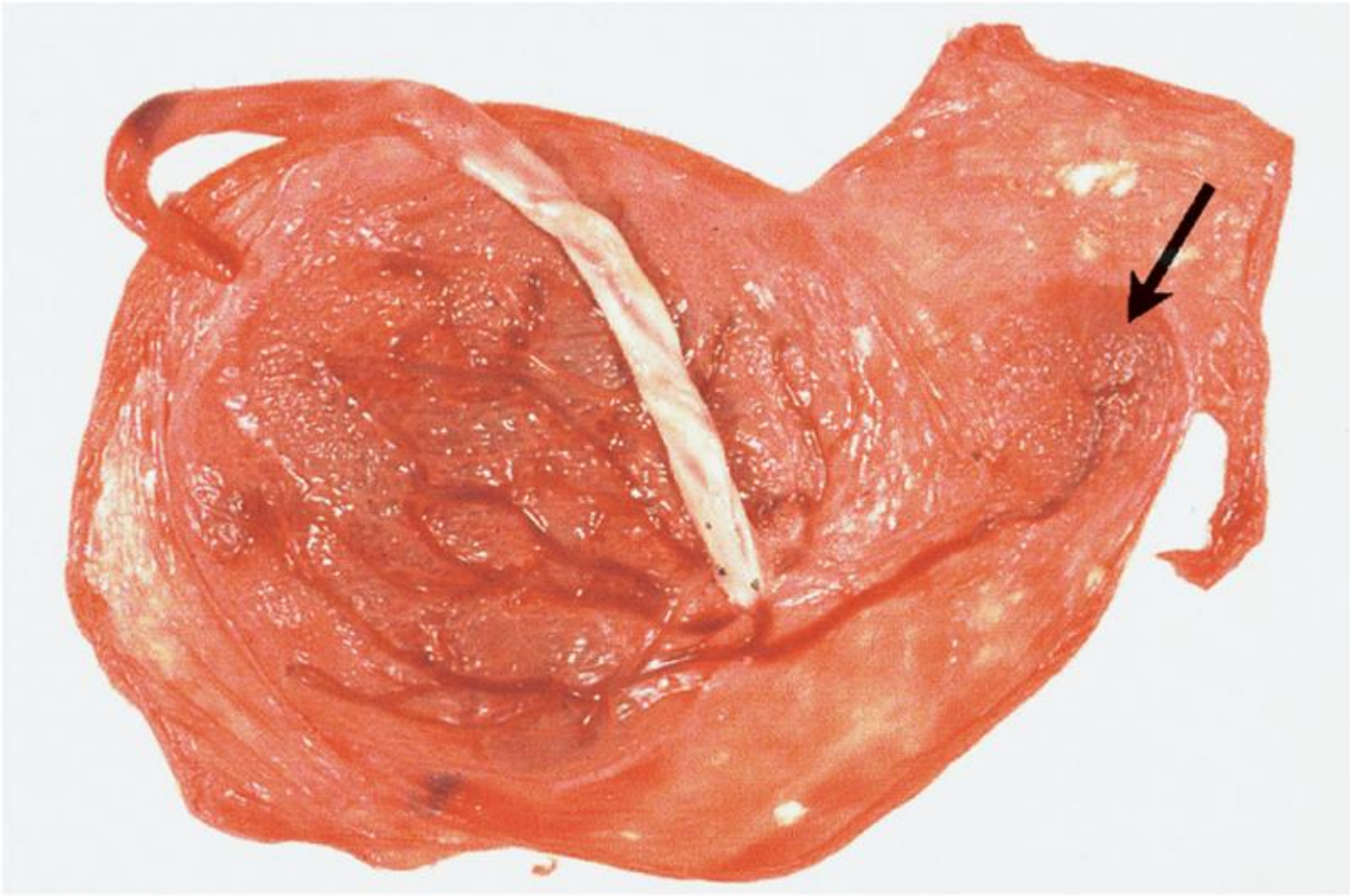


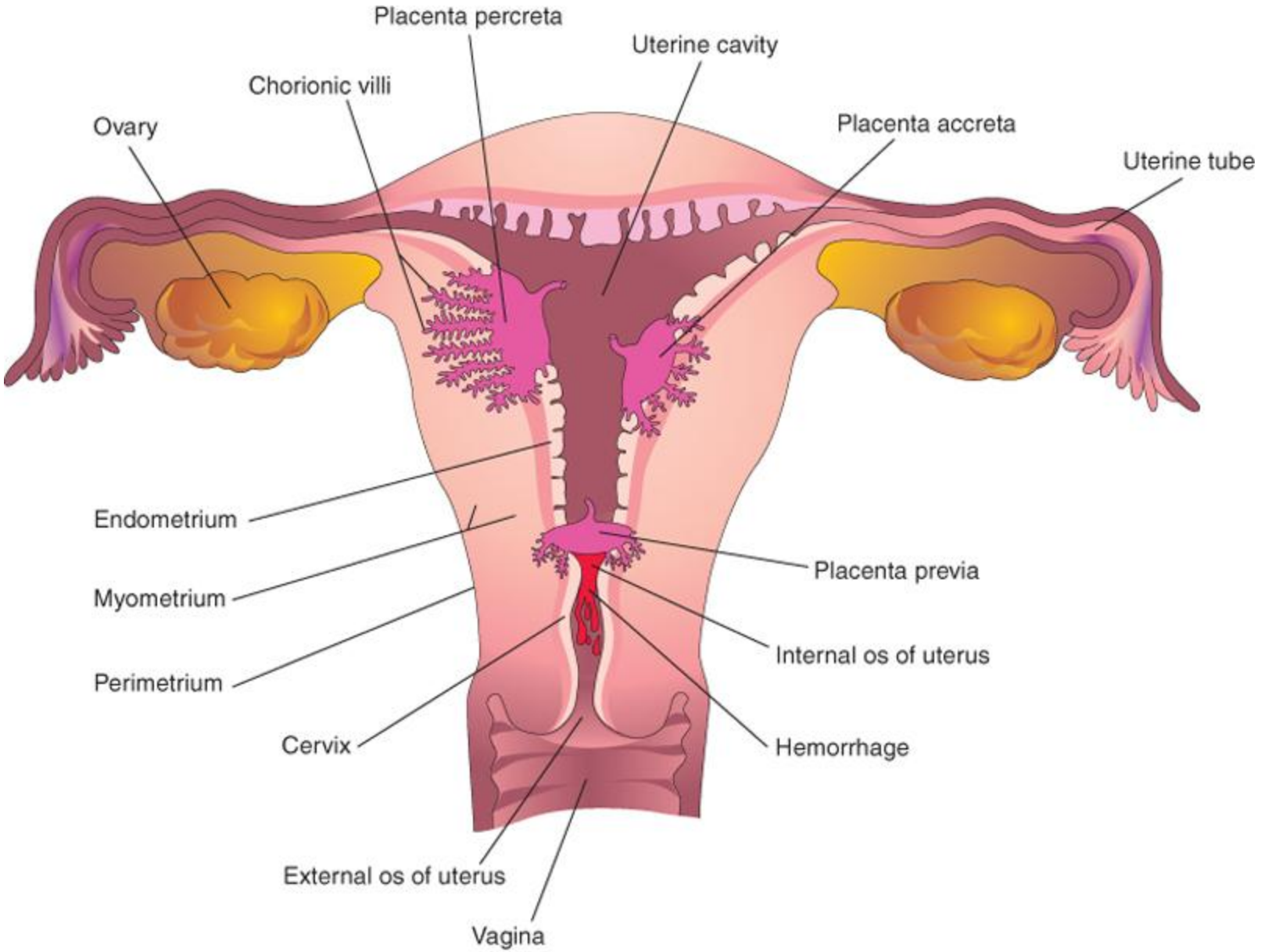
Maternal Surface of the Placenta

- The characteristic cobblestone appearance of the maternal surface is produced by slightly bulging villous areas-**cotyledons**-that are separated by grooves that were formerly occupied by placental septa.
- The surface of the cotyledons is covered by thin grayish shreds of decidua basalis that separated from the uterine wall when the placenta was extruded.
- These shreds of tissue are recognizable in sections of the placenta that are examined under a microscope.

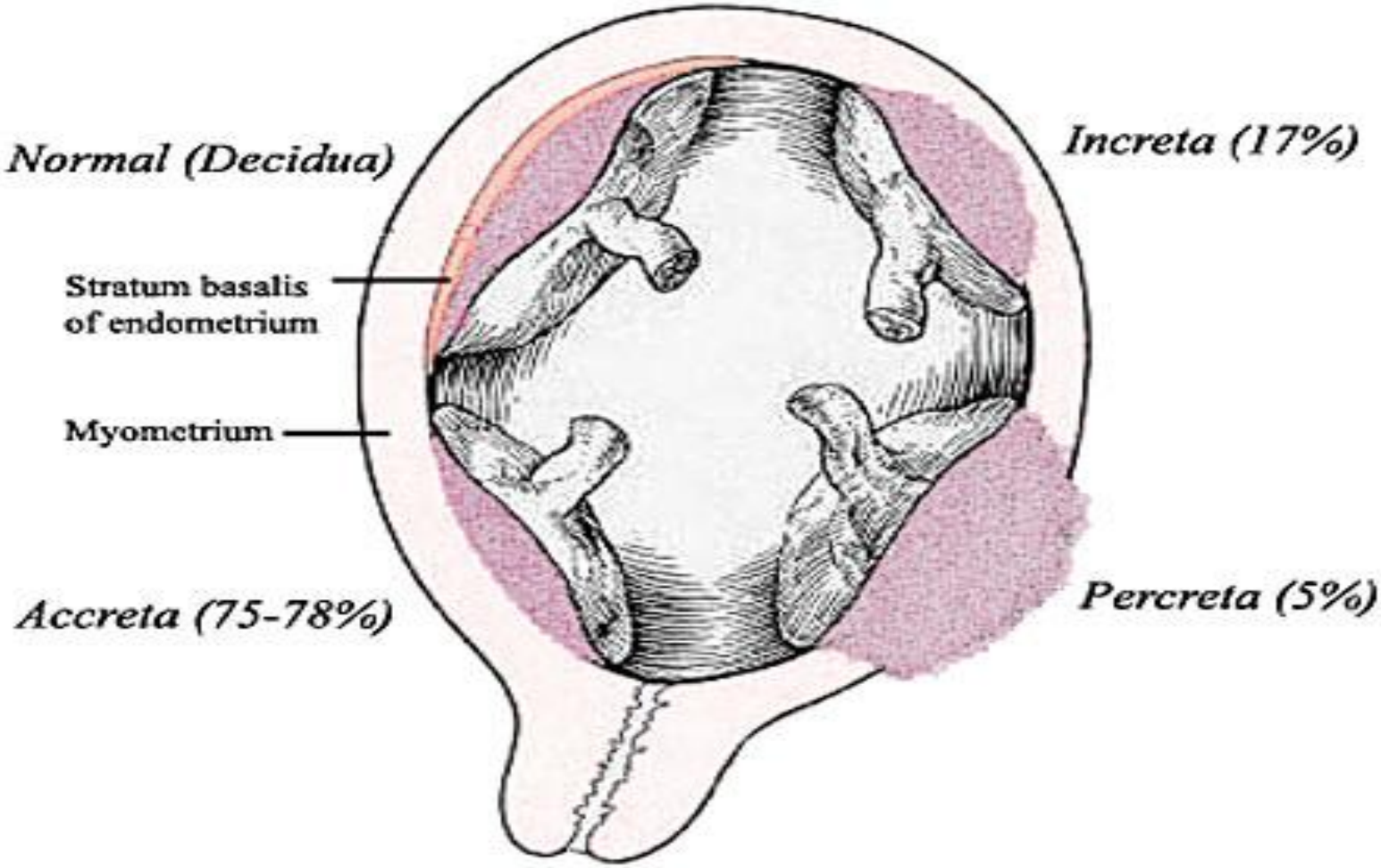


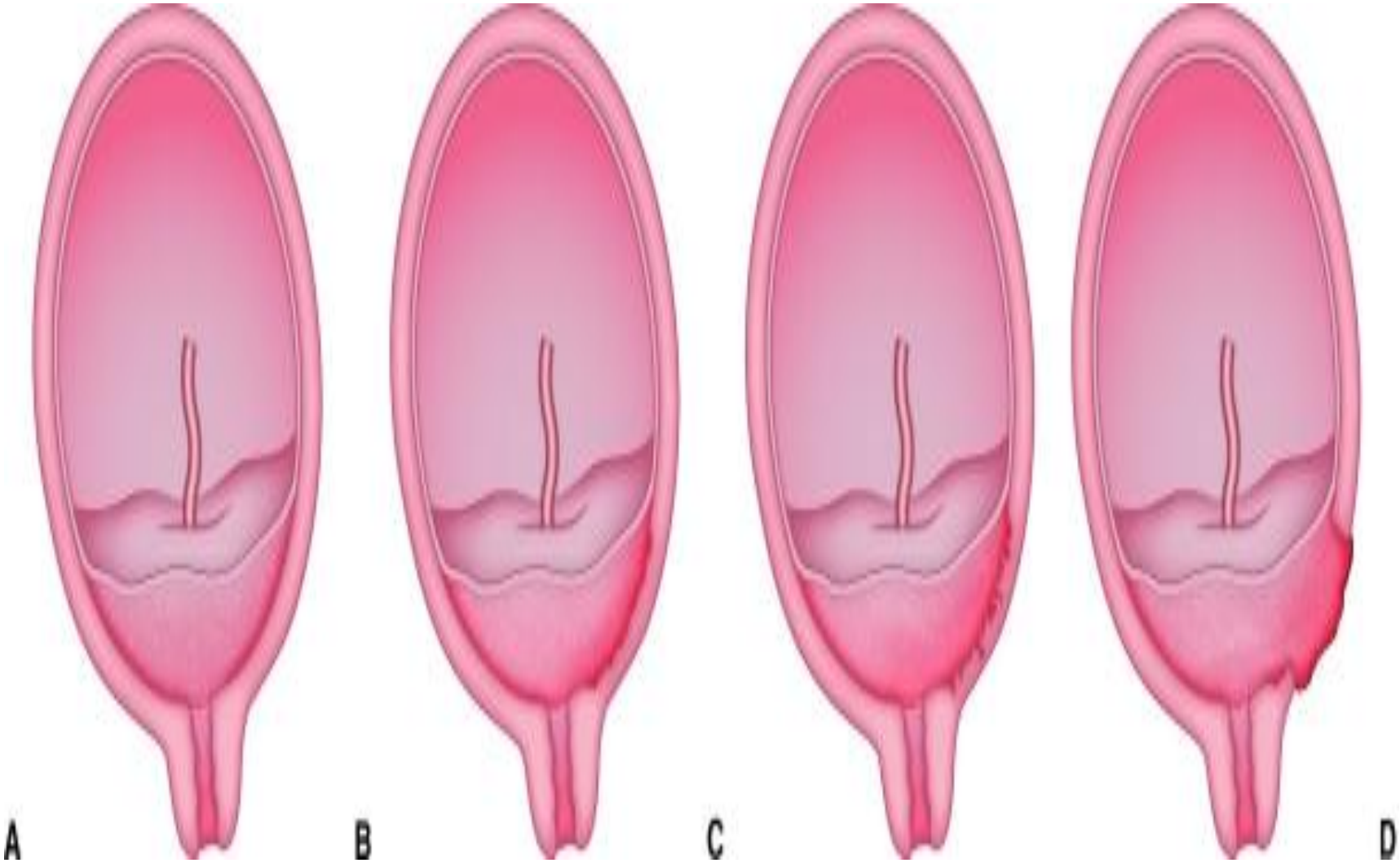
Placental implantation Abnormalities

- Abnormal adherence of chorionic villi to the myometrium is called **placenta accreta**.
- **Placenta increta** is when the placenta invades the myometrium but does not reach the serosa
- When chorionic villi penetrate the full thickness of the myometrium to or through the perimetrium (peritoneal covering), the abnormality is called **placenta percreta**.
- Third-trimester bleeding is the common presenting sign of these placental abnormalities.
- Most patients with placenta accreta have normal pregnancies and labors.
- **Placenta previa** is when the placenta is attached to the lower uterine segment



HISTOLOGICAL CLASSIFICATION




A
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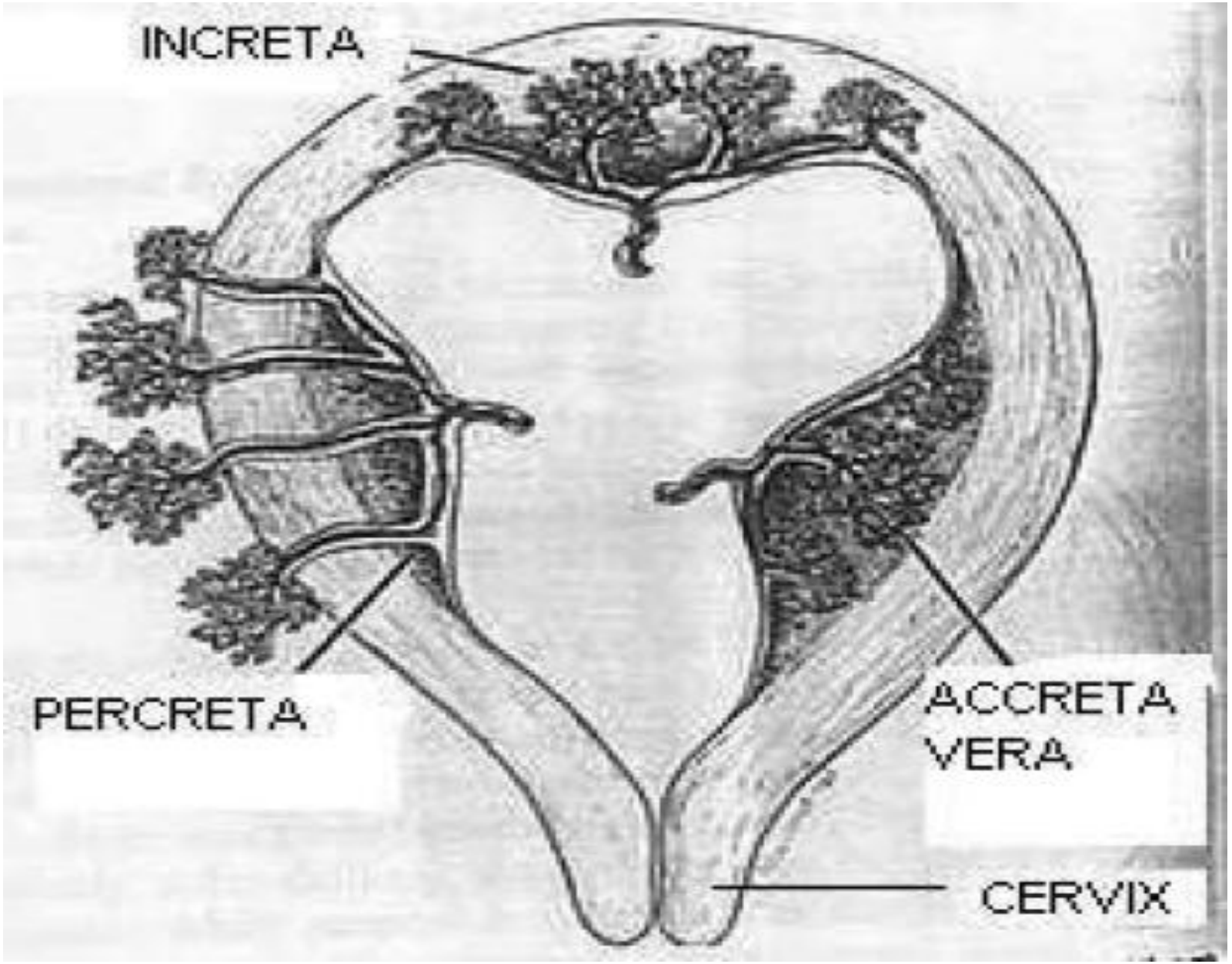
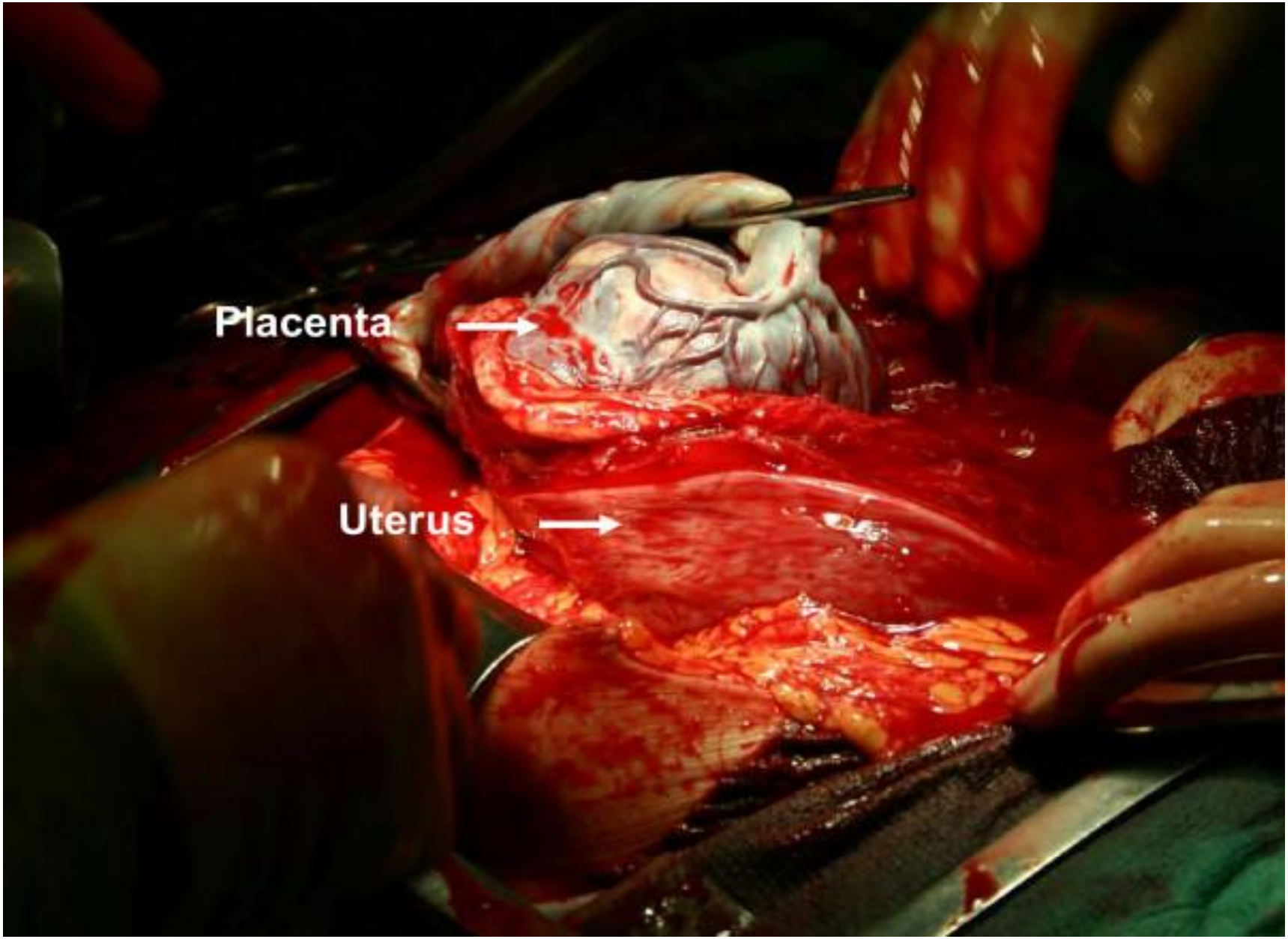
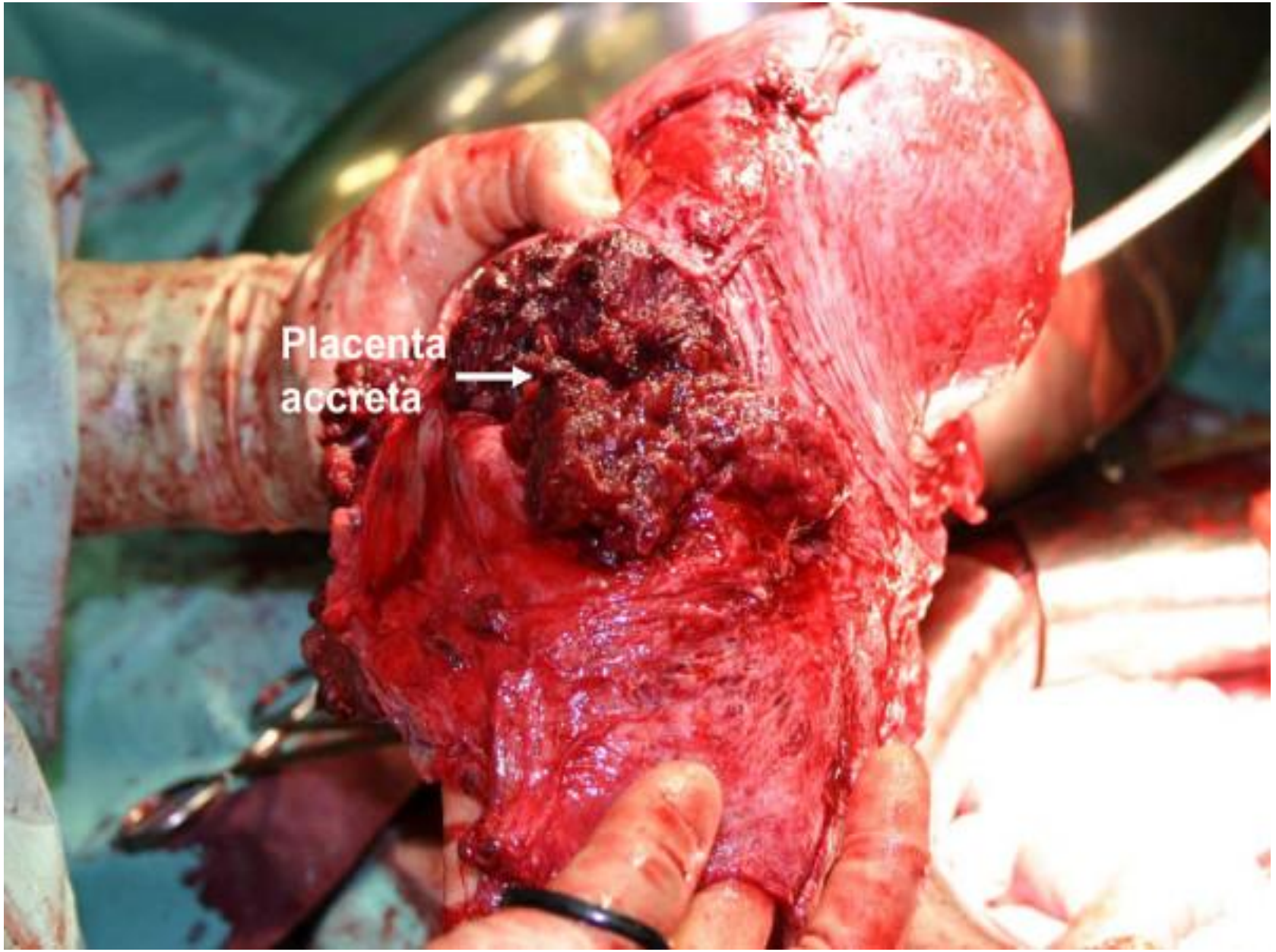

INCRETA
PERCRETA
ACCRETA
VERA
CERVIX


Placenta
Uterus


Placenta
accreta

The Umbilical Cord

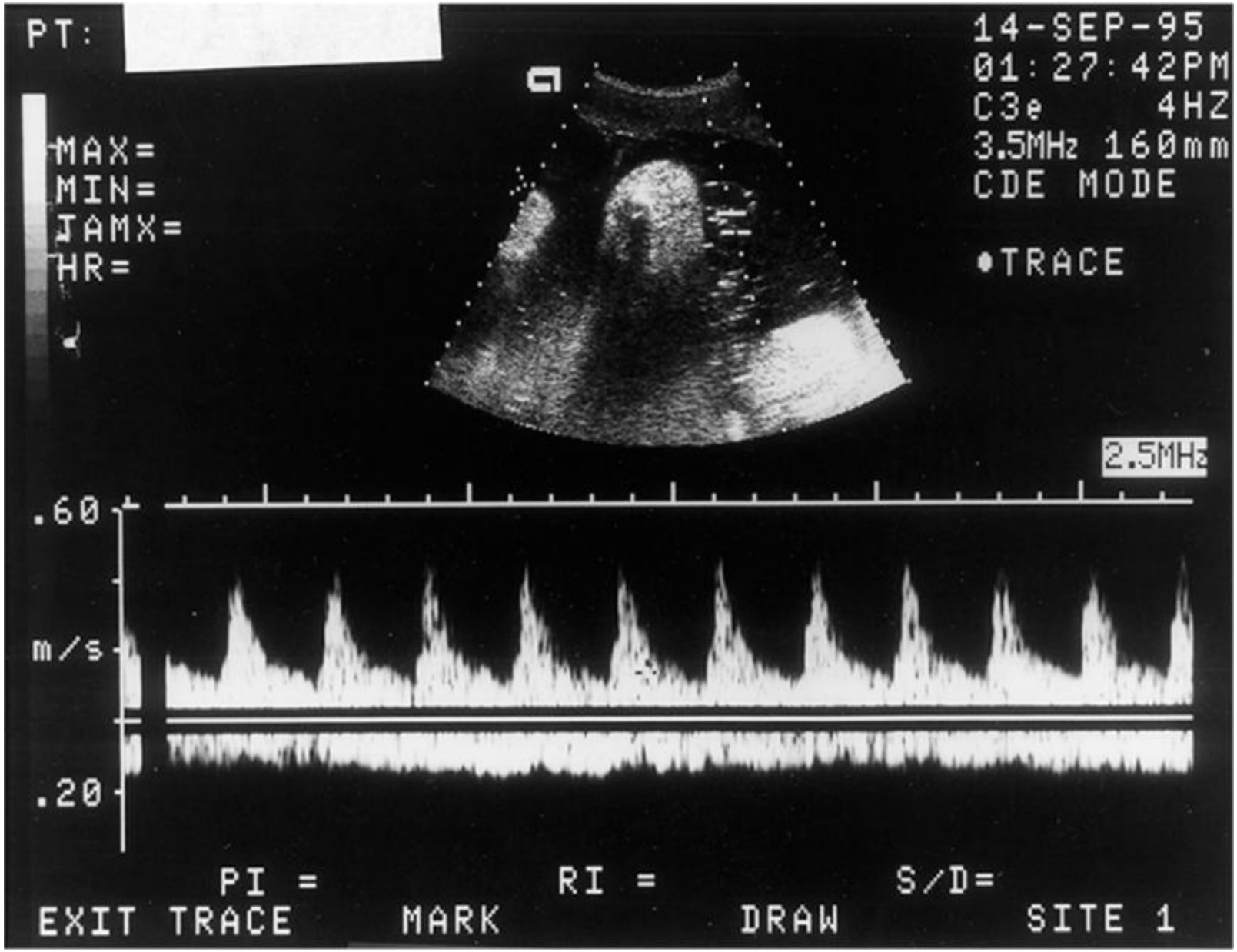
- The attachment of the umbilical cord to the placenta is usually near the center of the fetal surface of this organ, but it may attach at any point.
- Insertion of it at the placental margin produces a battledore placenta
- Attachment to the fetal membranes is a velamentous insertion of the cord
- The umbilical cord is usually 1 to 2 cm in diameter and 30 to 90 cm in length (average, 55 cm).

- Excessively long or short cords are uncommon.
- Long cords have a tendency to prolapse and/or to coil around the fetus.
- Prompt recognition of prolapse of the umbilical cord is important because the cord may be compressed between the presenting body part of the fetus and the mother's bony pelvis, causing fetal hypoxia or anoxia.
- A very short cord may cause premature separation of the placenta from the wall of the uterus during delivery.

- The umbilical cord usually has two arteries and one vein that are surrounded by mucoid connective tissue (Wharton jelly).
- Because the umbilical vessels are longer than the cord, twisting and bending of the vessels are common.
- In most cases, the knots form during labor as a result of the fetus passing through a loop of the cord. Simple looping of the cord around the fetus occasionally occurs.
- In approximately one fifth of deliveries, the cord is loosely looped around the neck without increased fetal risk.

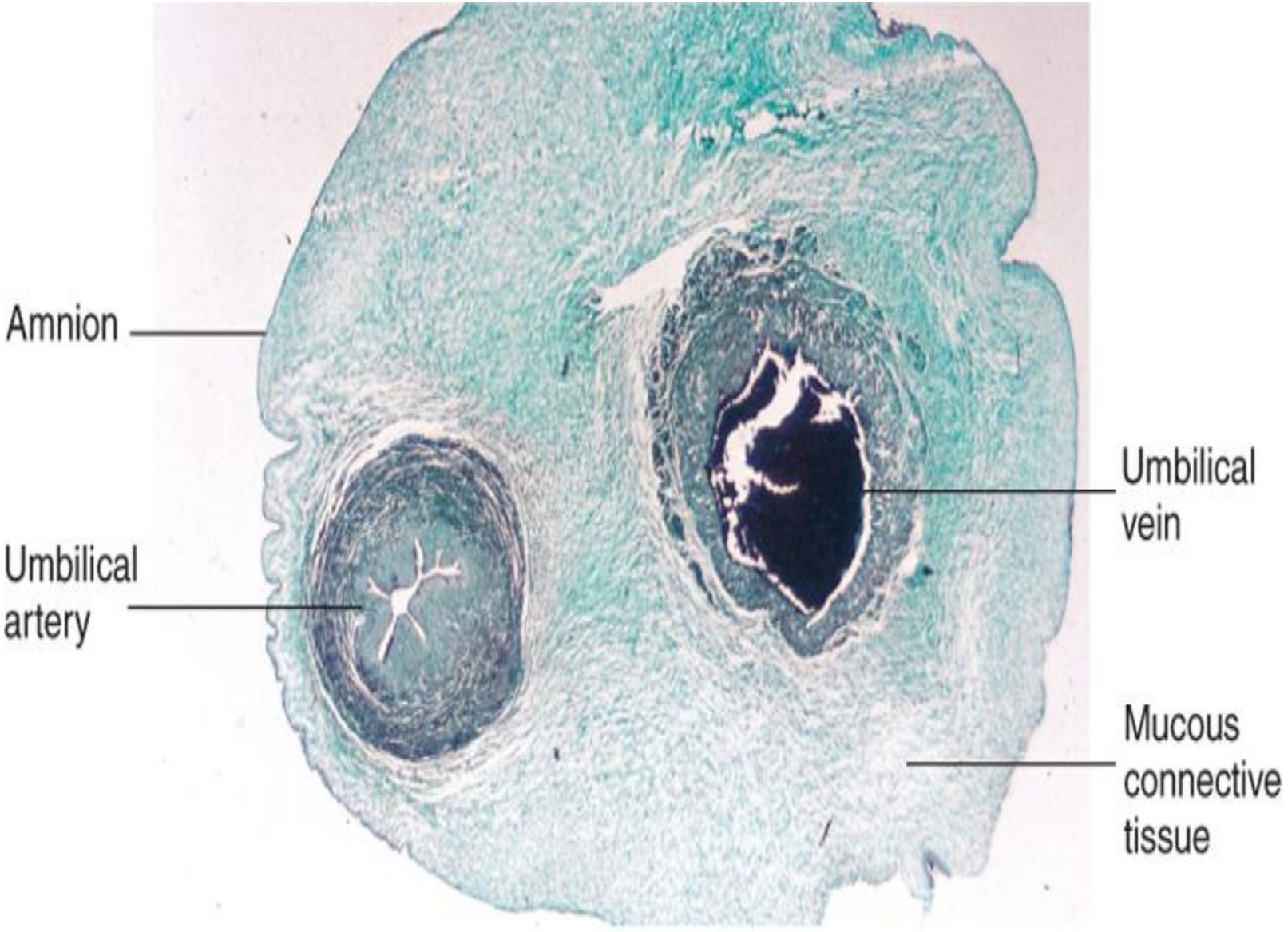
Umbilical Artery Doppler Velocimetry

- As gestation and trophoblastic invasion of the decidua basalis progress, there is a progressive increase in the diastolic flow velocity in the umbilical arteries.
- Doppler velocimetry of the uteroplacental and fetoplacental circulation is used to investigate complications of pregnancy such as IUGR and fetal distress resulting from fetal hypoxia and asphyxia.
- For example, there is a statistically significant association between IUGR and abnormally increased resistance in an umbilical artery.



Absence of an Umbilical Artery

- In approximately one in 100 newborns, only one umbilical artery is present, a condition that may be associated with chromosomal and fetal abnormalities.
- Absence of an umbilical artery is accompanied by a **15% to 20%** incidence of **cardiovascular anomalies** in the fetus.
- Absence of an artery results from either agenesis or degeneration of one of the two umbilical arteries.
- A single umbilical artery and the anatomic defects associated with it can be detected before birth by ultrasonography.

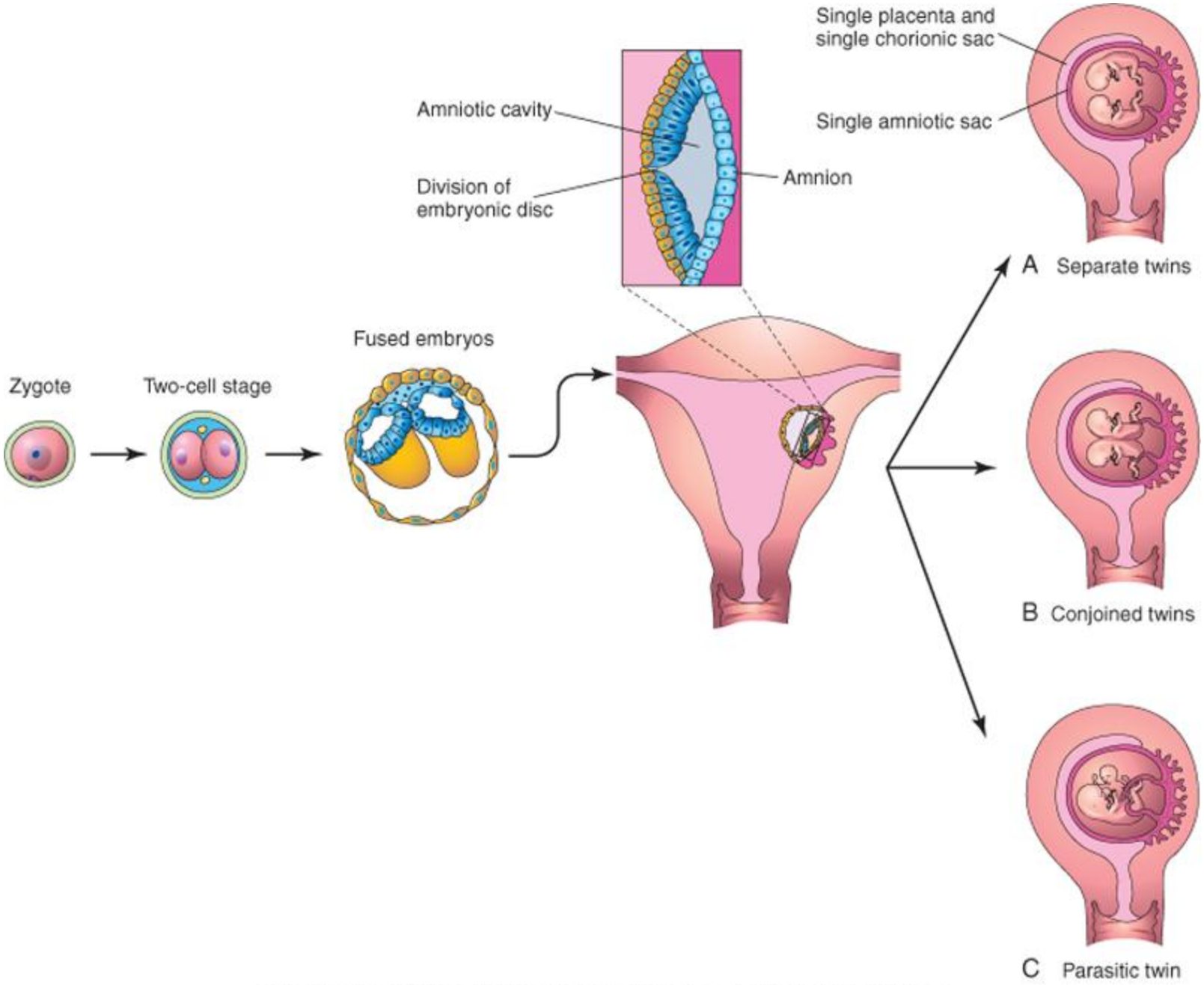


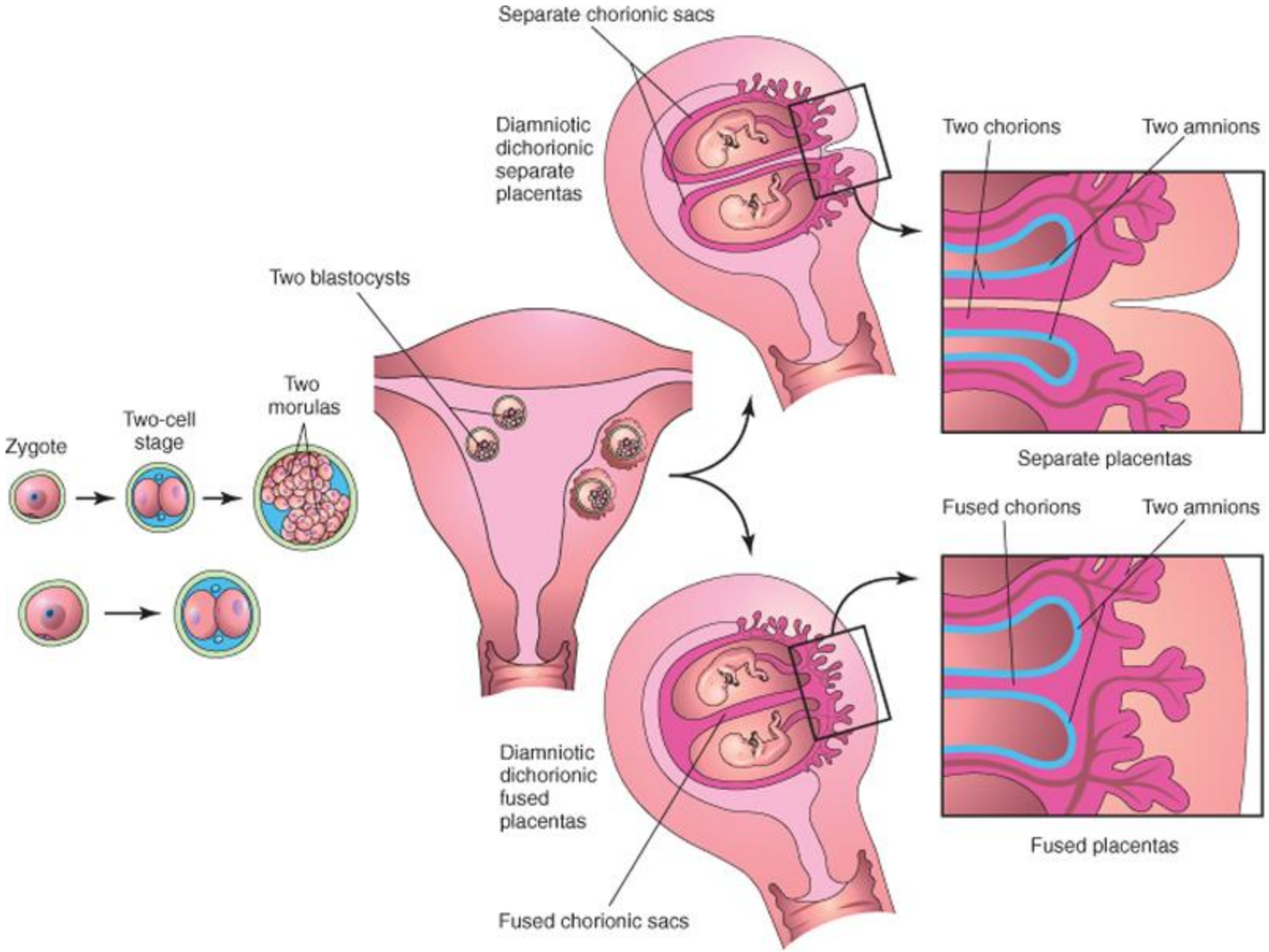
MULTIPLE PREGNANCIES

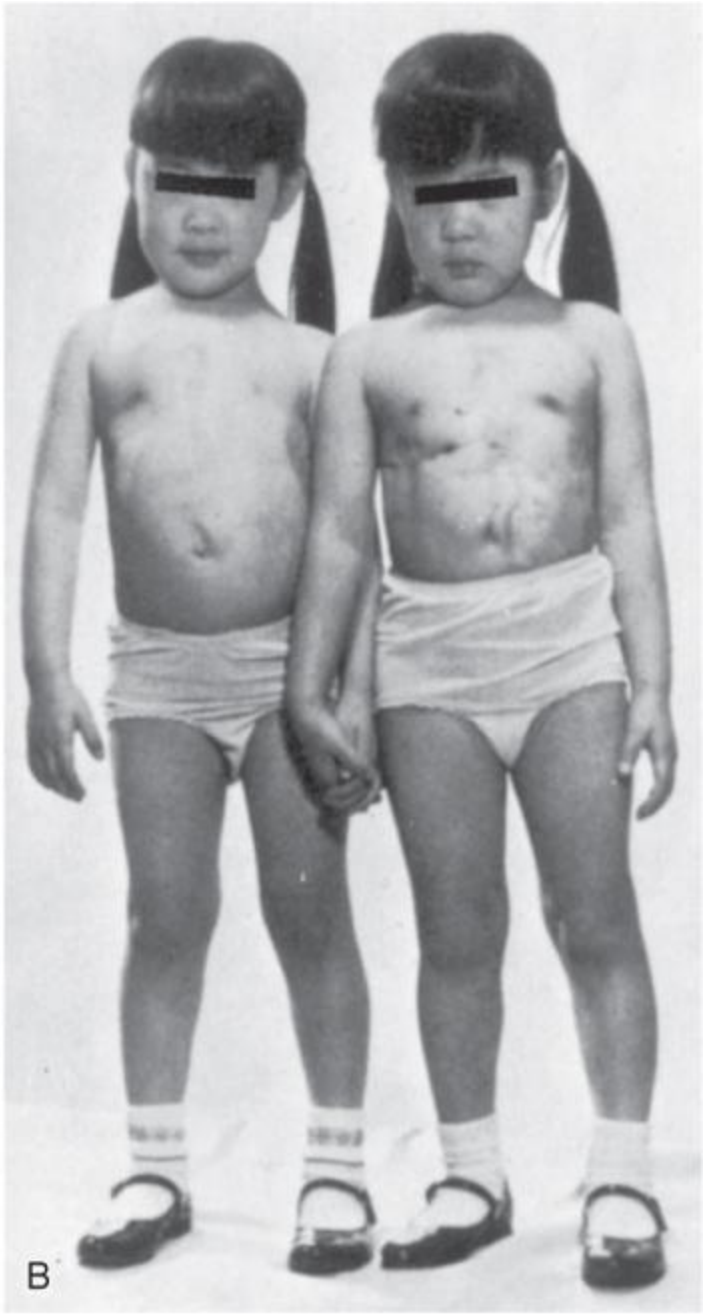
- Multiple pregnancy or gestation is a situation where more than one embryo/fetus is growing in a woman
- The risks of chromosomal anomalies and fetal morbidity and mortality are higher in multiple gestations than in single gestations.
- As the number of fetuses increases, the risks are progressively greater.
- Multiple births are more common now because of greater access to fertility therapies, including induction of ovulation for assisted reproductive technologies.

Twins and Fetal Membranes

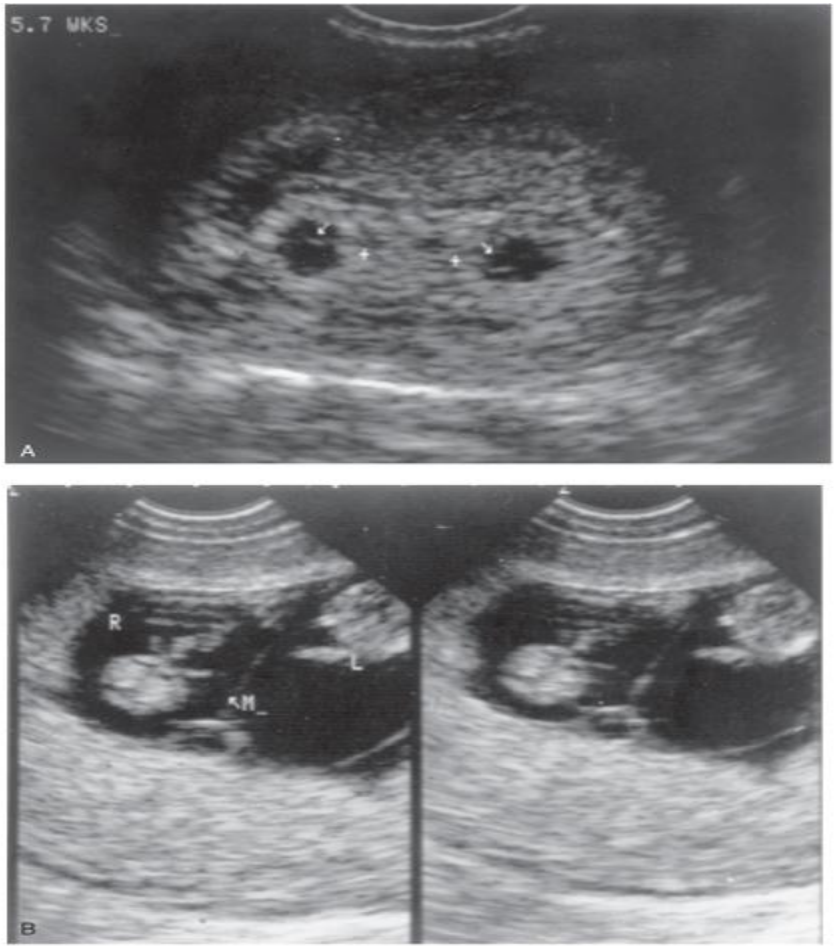
- Twins that originate from two zygotes are dizygotic (DZ) twins or fraternal twins, whereas twins that originate from one zygote are monozygotic (MZ) twins or identical twins.
- The fetal membranes and placentas vary according to the origin of the twins.
- In the case of MZ twins, the type of placenta and membranes formed depends on when the twinning process occurs.



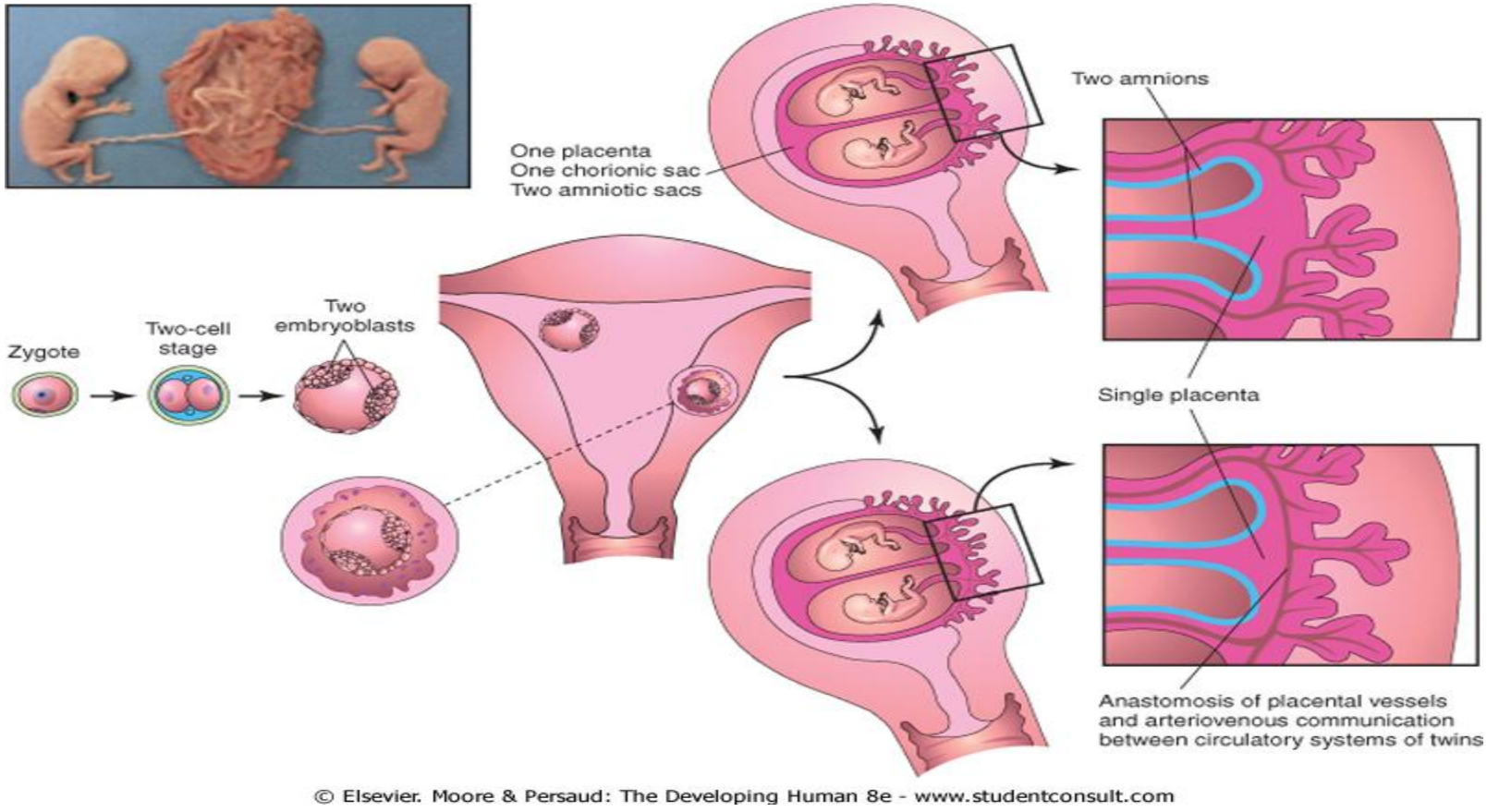




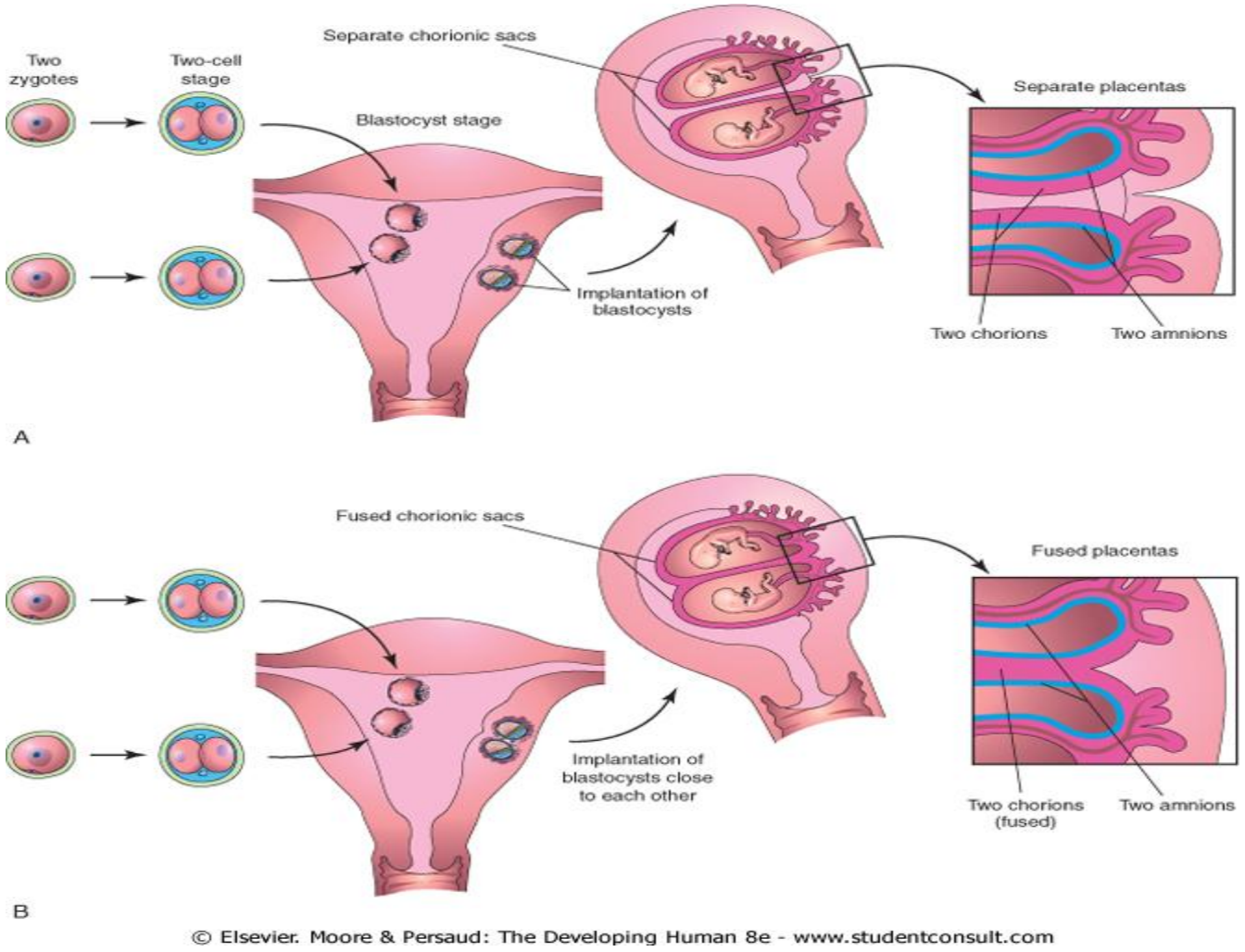
Dicephalic (two heads) conjoined twins, alizarin stained, showing bone (red) and cartilage (blue). Note the two clavicles supporting the midline upper limb, fused thoracic cage, and parallel vertebral columns. (Courtesy of Dr. Joseph R. Siebert, Children's Hospital and Regional Center, Seattle, WA.)



Ultrasound scans of pregnant women. **A,** Diamniotic/dichorionic twin gestation at 5.7 weeks, 3.7 weeks after fertilization. The *arrows* indicate the umbilical vesicles of the dizygotic twins in their chorionic sacs. **B,** Diamniotic/monochorionic twin gestation at 11 weeks, 9 weeks after fertilization. The fused amnions (M) separate the monozygotic fetuses (R and L). (Courtesy of Dr. Lyndon M. Hill, Department of Obstetrics and Gynecology, Division of Maternal-Fetal Medicine, University of Pittsburgh, Pittsburgh, PA.)



Diagrams illustrating how approximately 65% of monozygotic twins develop from one zygote by division of the embryoblast (inner cell mass) of the blastocyst. These twins always have separate amnions, a single chorionic sac, and a common placenta. *Inset*, Monozygotic twins, 17 weeks' gestation. (Courtesy of Dr. Robert Jordan, St. Georges University Medical School, Grenada.)



Diagrams illustrating how dizygotic twins develop from two zygotes. The relationships of the fetal membranes and placentas are shown for instances in which the blastocysts implant separately (**A**) and the blastocysts implant close together (**B**). In both cases, there are two amnions and two chorions. The placentas are usually fused when they implant close together.

- Approximately two thirds of twins are DZ.
- The frequency of DZ twinning shows marked racial differences, but the incidence of MZ twinning is approximately the same in all populations.
- In addition, the rate of MZ twinning shows little variation with the mother's age, whereas the rate of DZ twinning increases with maternal age.

- Studies in a Mormon population showed that the genotype of the mother affects the frequency of DZ twins, but the genotype of the father has no effect.
- It has also been observed that if the firstborn are twins, a repetition of twinning or some other form of multiple birth is approximately five times more likely to occur with the next pregnancy than in the general population.

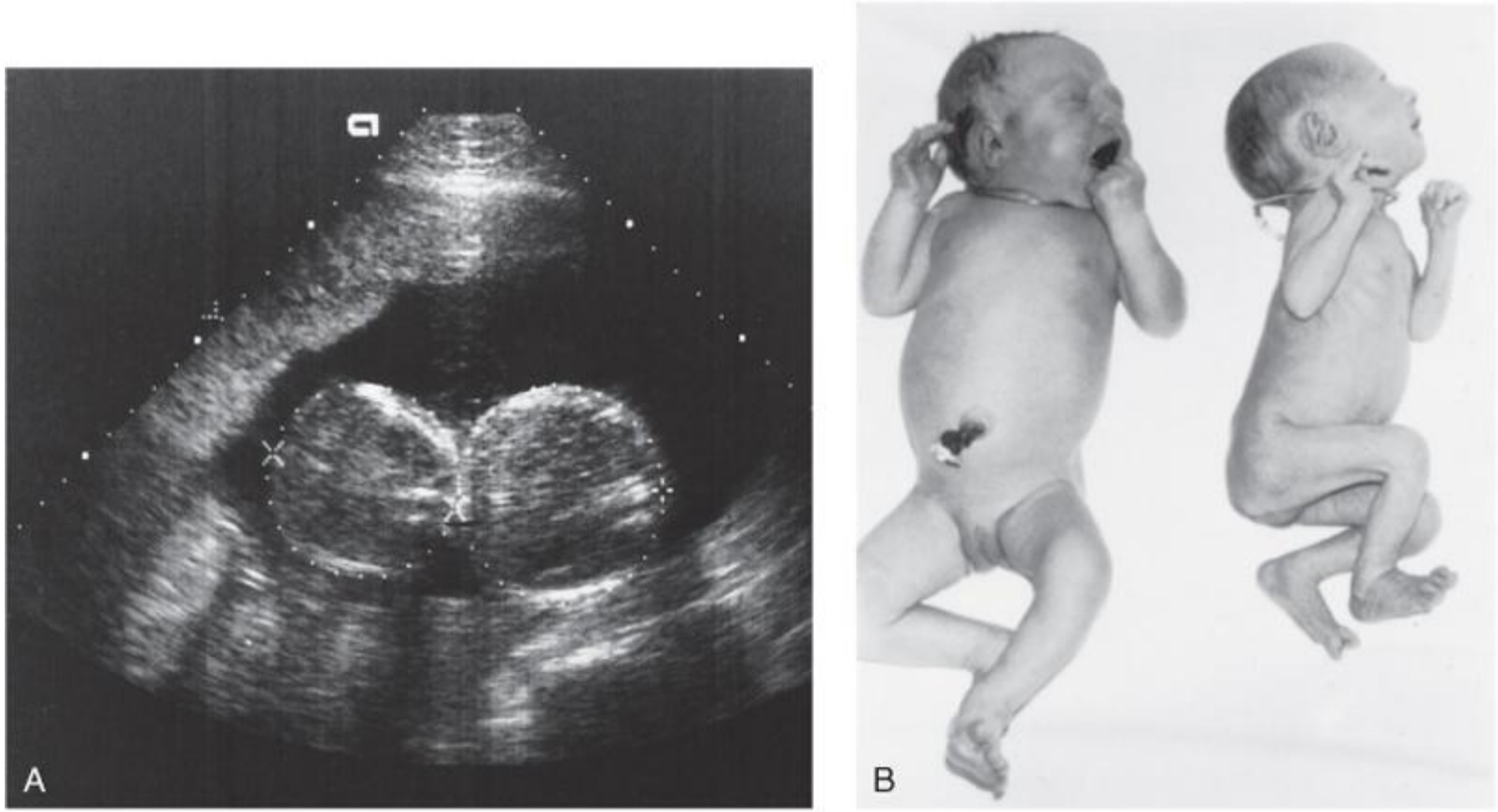
Anastomosis of Placental Blood Vessels

- Anastomoses between blood vessels of fused placentas of DZ twins may result in **erythrocyte mosaicism**.
- The members of these DZ twins have red blood cells of two different types because red cells were exchanged between the circulations of the twins.
- In cases in which one fetus is a male and the other is female, masculinization of the female fetus does not occur.

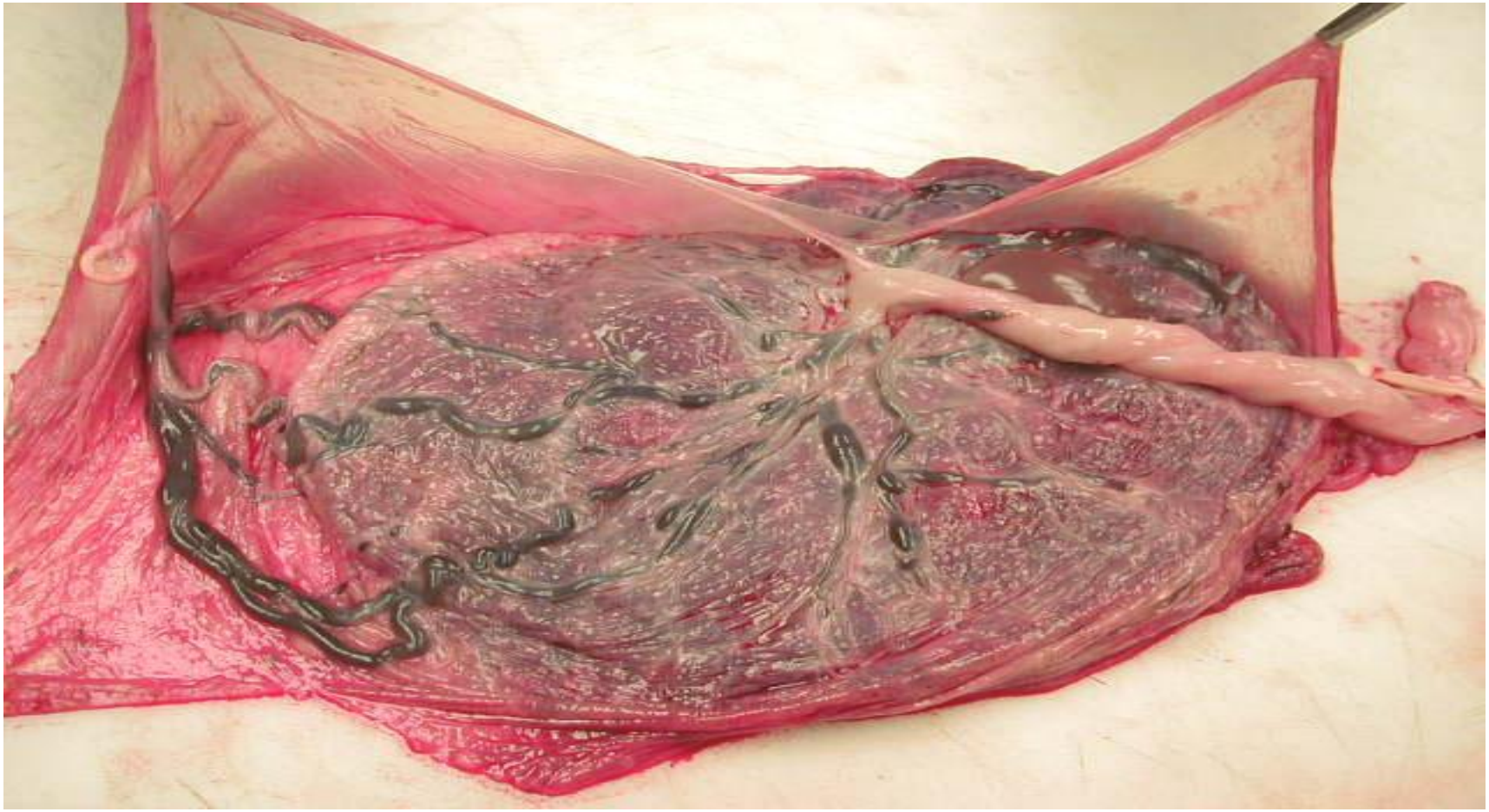
Twin Transfusion Syndrome

- This syndrome occurs in as many as 30% of monochorionic-diamniotic MZ twins.
- There is shunting of arterial blood from one twin through arteriovenous anastomoses into the venous circulation of the other twin.
- The donor twin is small, pale, and anemic, whereas the recipient twin is large and polycythemic - an increase above the normal in the number of red blood cells.

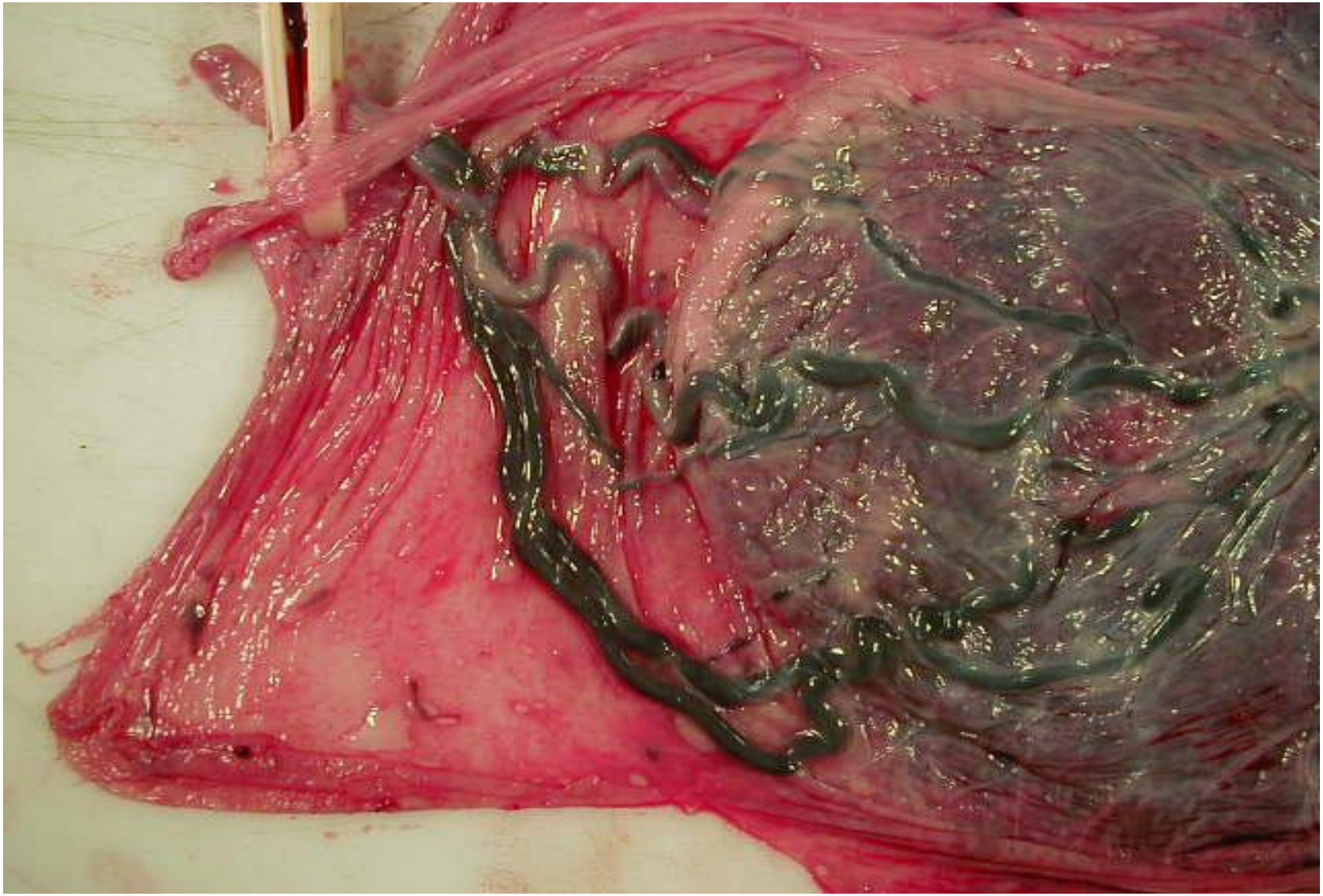
- The placenta shows similar abnormalities; the part of the placenta supplying the anemic twin is pale, whereas the part supplying the polycythemic twin is dark red.
- In lethal cases, death results from anemia in the donor twin and congestive heart failure in the recipient twin.



A, Ultrasound image of discordant (MZ) twins (24 weeks' gestation), twin transfusion syndrome. **B,** Monozygotic, monochorionic, diamniotic twins showing a wide discrepancy in size resulting from an uncompensated arteriovenous anastomosis of placental vessels. Blood was shunted from the smaller twin to the larger one, producing the twin transfusion syndrome. (**A,** Courtesy of Dr. G.J. Reid, Department of Obstetrics, Gynecology, and Reproductive Sciences, University of Manitoba, Women's Hospital, Winnipeg, Manitoba, Canada.)



This is a picture of a monochoionic diamnionic placenta with twin to twin transfusion syndrome. There is velamentous insertion of the cord on the left side. This was the smaller donor twin (B). When one looks carefully at the blood vessels that came from the insertion of the cord and go to the placenta, one will see some white streaks in the veins – they are thrombi. Birth weights were recipient baby (A) 1400g and donor baby (B) 925g at 29 weeks. Both did well.



This shows a higher magnification of the velamentous insertion and the thrombi.

Dizygotic Twins

- Because they result from fertilization of two oocytes, DZ twins develop from two zygotes and may be of the same sex or different sexes.
- For the same reason, they are no more alike genetically than brothers or sisters born at different times.
- The only thing they have in common is that they were in their mother's uterus at the same time (i.e., "womb mates").

- DZ twins always have two amnions and two chorions, but the chorions and placentas may be fused.
- DZ twinning shows a hereditary tendency.
- Recurrence in families is approximately three times that of the general population.
- The incidence of DZ twinning shows considerable variation, being approximately 1 in 500 in Asians, 1 in 125 in whites, and as high as 1 in 20 in some African populations.

Monocygotic twins

- Because they result from the fertilization of one oocyte and develop from one zygote, MZ twins are of the same sex, genetically identical, and very similar in physical appearance.
- Physical differences between MZ twins are environmentally induced, e.g., because of anastomosis of placental vessels.
- MZ twinning usually begins in the blastocyst stage, approximately at the end of the first week, and results from division of the embryoblast into two embryonic primordia.

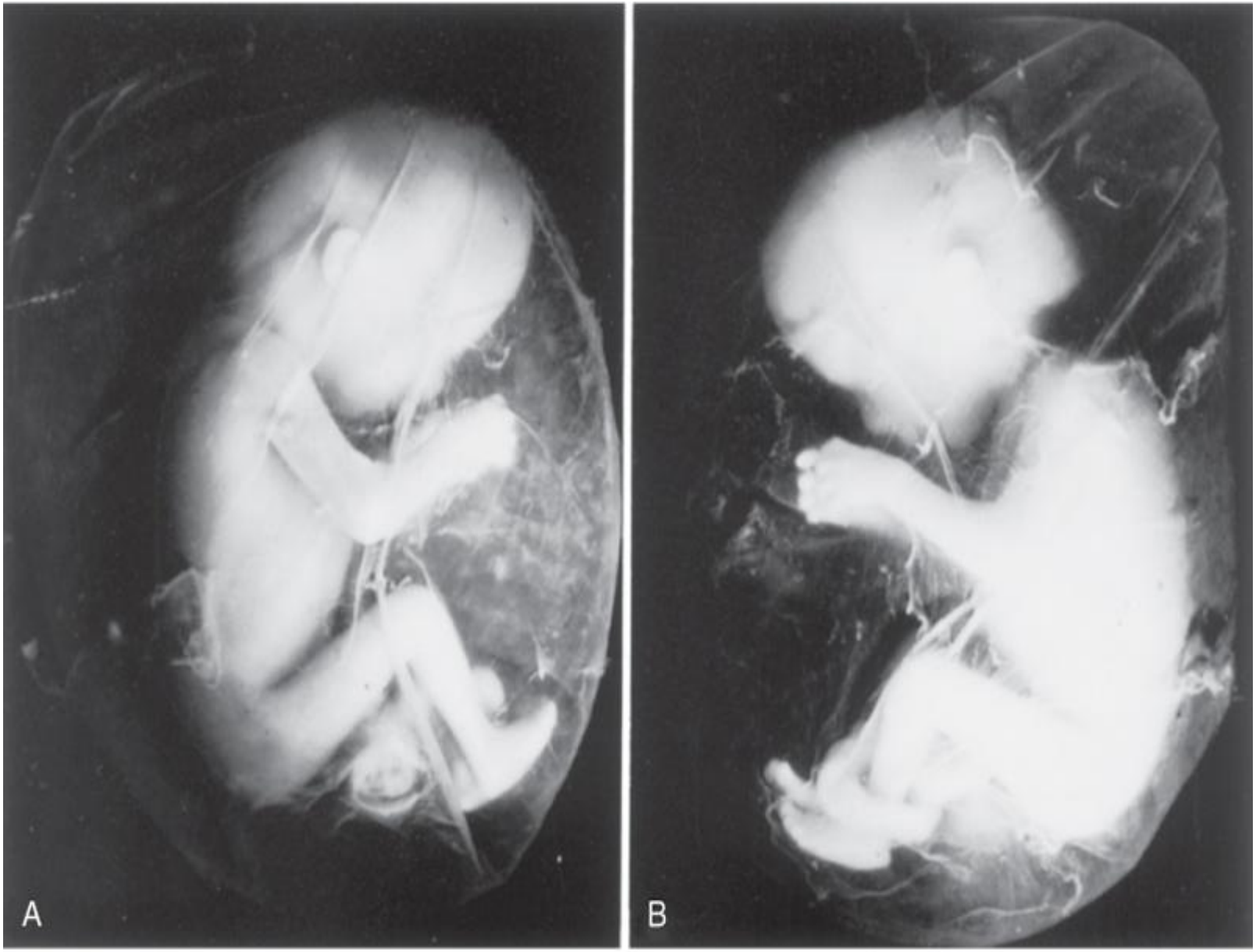
- Subsequently, two embryos, each in its own amniotic sac, develop within the same chorionic sac and share a common placenta-a monochorionic-diamniotic twin placenta.
- Uncommonly, early separation of embryonic blastomeres (e.g., during the two- to eight-cell stages) results in MZ twins with two amnions, two chorions, and two placentas that may or may not be fused.
- In such cases, it is impossible to determine from the membranes alone whether the twins are MZ or DZ.

Establishing the Zygosity of Twins

- Establishing the zygosity of twins is important in tissue and organ transplantation (e.g., bone marrow transplantations).
- The determination of twin zygosity is now done by molecular diagnosis because any two people who are not MZ twins are virtually certain to show differences in some of the large number of DNA markers that can be studied.
- Approximately 35% of MZ twins result from early separation of the embryonic blastomeres, i.e., during the **first 3 days of development**.
- The other 65% of MZ twins originate at the end of the **first week** of development .
- Late division of early embryonic cells, such as division of the embryonic disc during the **second week, results in MZ twins that are in one amniotic sac and one chorionic sac**.

- A monochorionic-monoamniotic twin placenta is associated with a fetal mortality rate approaching 50%.
- These MZ twins are rarely delivered alive because the umbilical cords are frequently so entangled that circulation of blood through their vessels ceases and one or both fetuses die.
- Sonography plays an important role in the diagnosis and management of twin pregnancies .
- Ultrasound evaluation is necessary to identify various conditions that may complicate MZ twinning such as IUGR, fetal distress, and premature labor.

- MZ twins may be discordant for a variety of birth defects and genetic disorders, despite their origin from the same zygote.
- In addition to environmental differences and chance variation, the following have been implicated:
  - Mechanisms of embryologic development, such as vascular abnormalities, that can lead to discordance for anomalies
  - Postzygotic changes, such as somatic mutation leading to discordance for cancer, or somatic rearrangement of immunoglobulin or T cell-receptor genes
  - Chromosome aberrations originating in one blastocyst after the twinning event
  - Uneven X chromosome inactivation between female MZ twins, with the result that one twin preferentially expresses the paternal X and the other the maternal X.



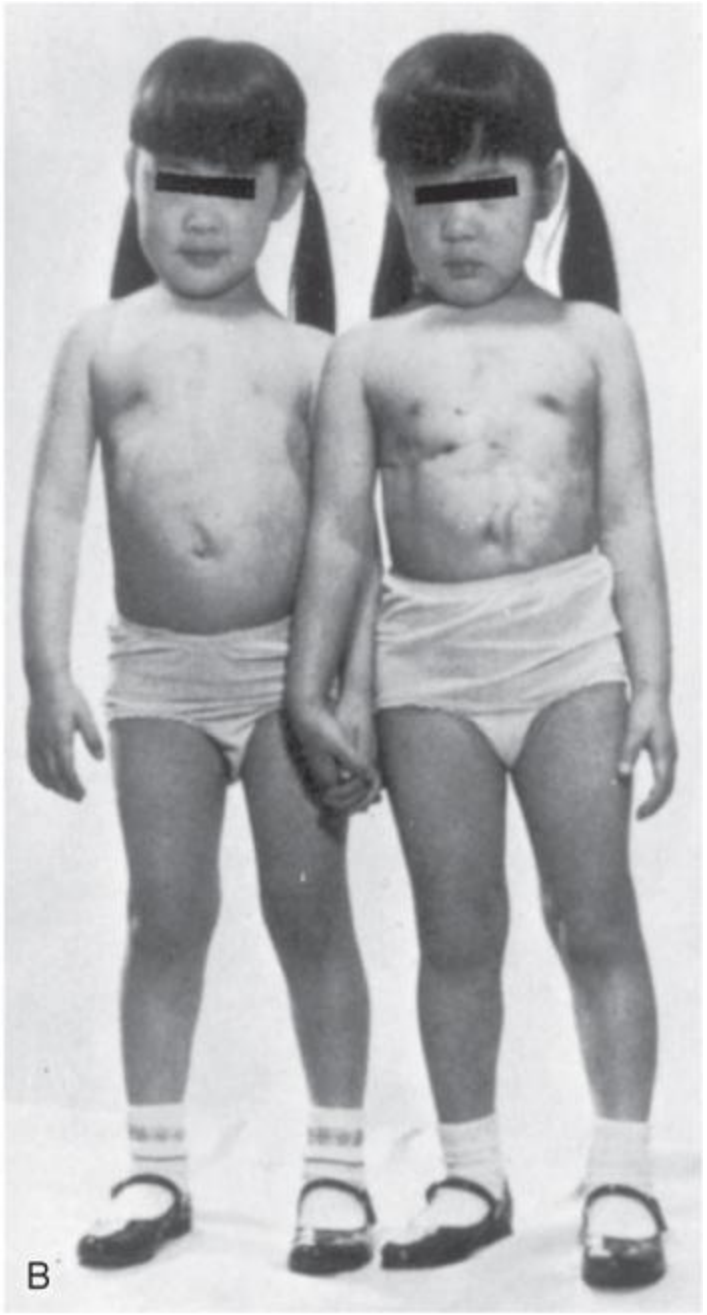
Early Death of a Twin

- Because ultrasonographic studies are a common part of prenatal care, it is known that early death and resorption of one member of a twin pair is fairly common.
- Awareness of this possibility must be considered when discrepancies occur between prenatal cytogenetic findings and the karyotype of an infant.
- Errors in prenatal cytogenetic diagnosis may arise if extraembryonic tissues (e.g., part of a chorionic villus) from the resorbed twin are examined.

Conjoined Monozygotic Twins

- If the embryonic disc does not divide completely, or adjacent embryonic discs fuse, various types of conjoined MZ twins may form .
- The attached twins are named according to the regions that are attached, e.g., thoracopagus indicates that there is anterior union of the thoracic regions.
- It has been estimated that the incidence of conjoined twins is 1 in 50,000 to 100,000 births.

- In some cases, the twins are connected to each other by skin only or by cutaneous and other tissues, e.g., fused livers .
- Some conjoined twins can be successfully separated by surgical procedures ; however, the anatomic relations in most conjoined twins do not permit surgical separation with sustained viability .



Dicephalic (two heads) conjoined twins, alizarin stained, showing bone (red) and cartilage (blue). Note the two clavicles supporting the midline upper limb, fused thoracic cage, and parallel vertebral columns. (Courtesy of Dr. Joseph R. Siebert, Children's Hospital and Regional Center, Seattle, WA.)

Superfecundation

- Superfecundation is the fertilization of two or more oocytes at different times.
- In humans, the presence of two fetuses in the uterus caused by fertilization at different times (superfetation) is rare.
- DZ human twins with different fathers have been confirmed by genetic markers.

Other Types of Multiple Births

- Triplets may be derived from:
  - One zygote and be identical
  - Two zygotes and consist of identical twins and a singleton
  - Three zygotes and be of the same sex or of different sexes
  - In the last case, the infants are no more similar than infants from three separate pregnancies. Similar combinations occur in quadruplets, quintuplets, sextuplets, and septuplets.

THANK YOU