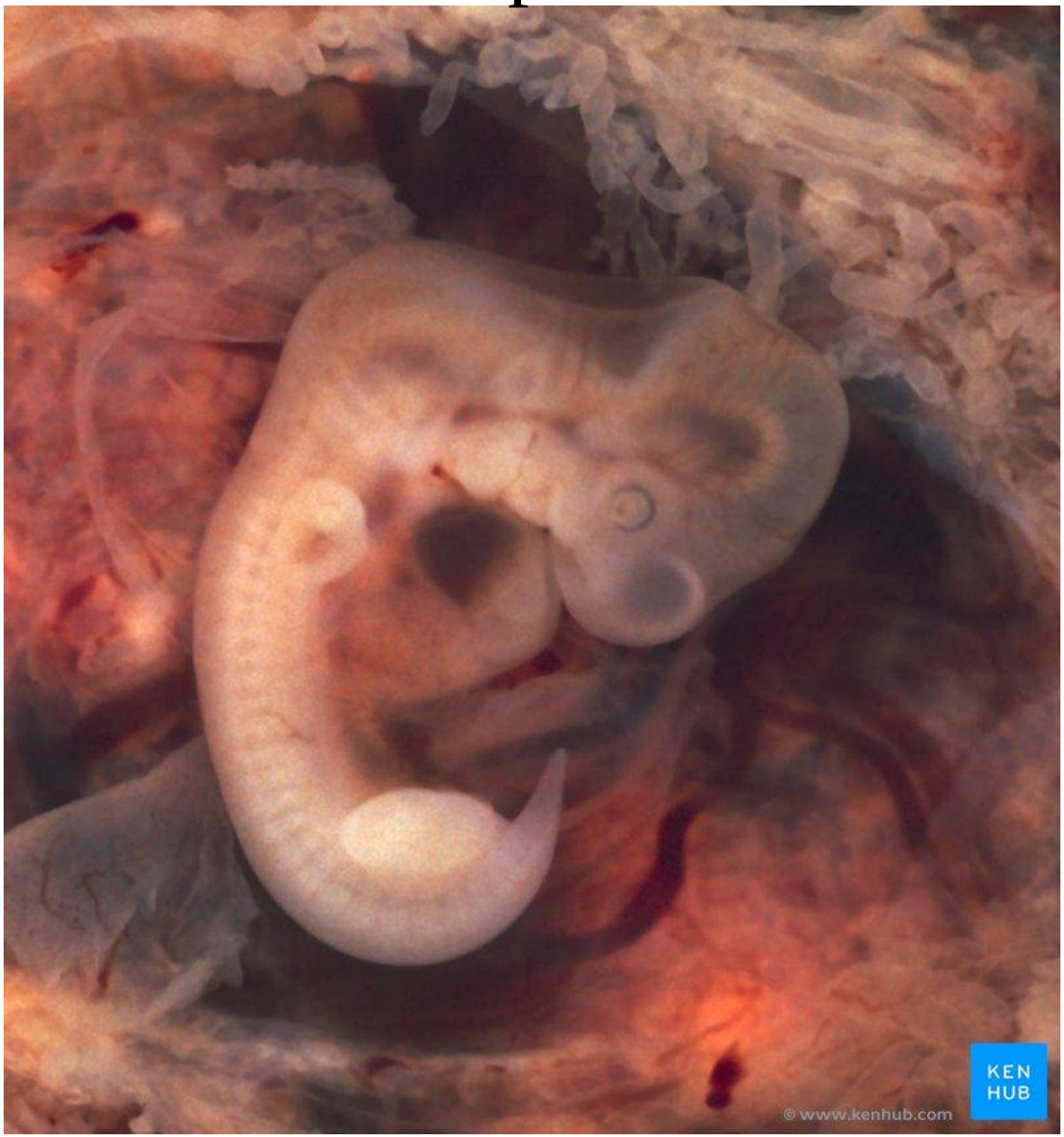
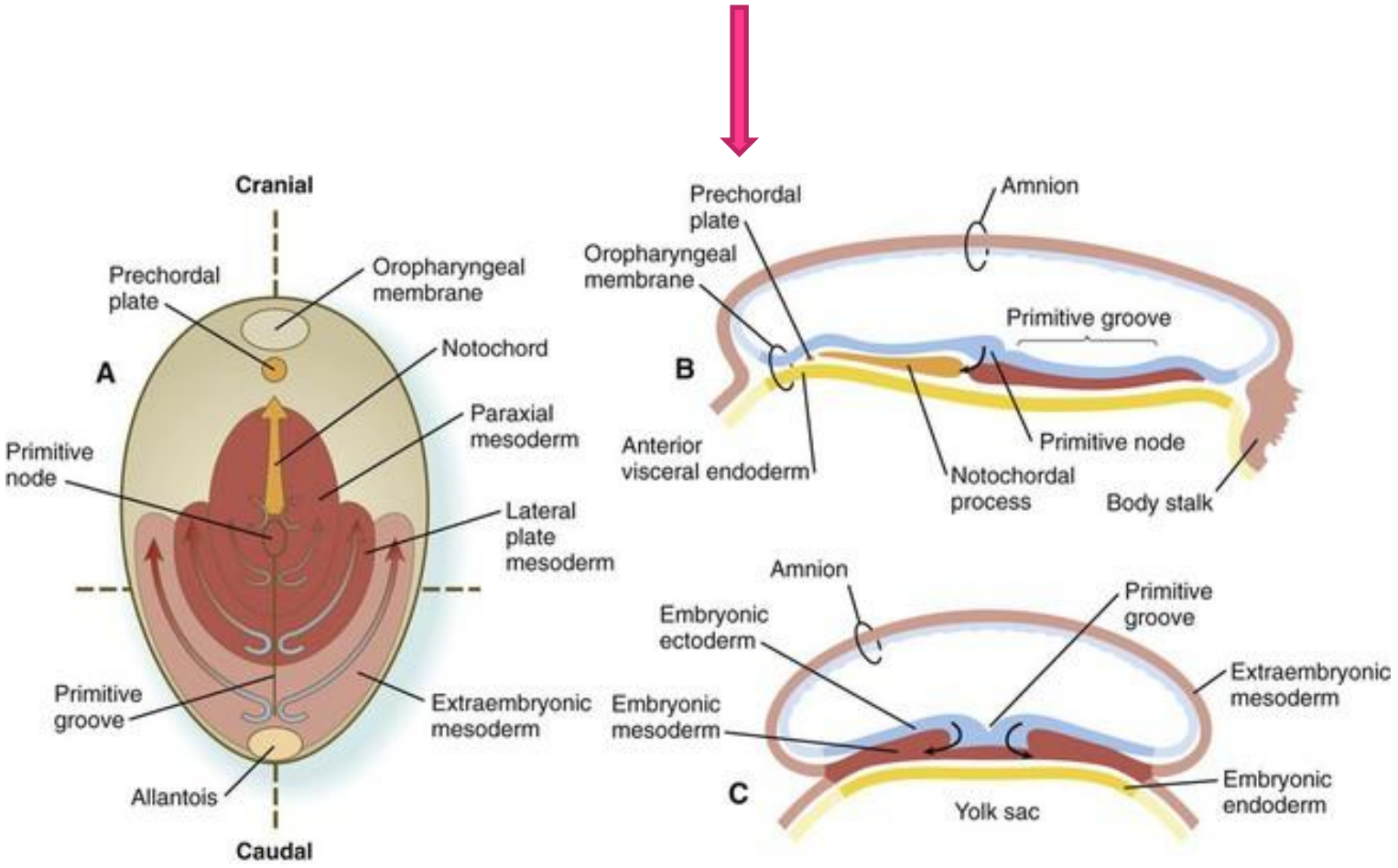
third week of development - continued

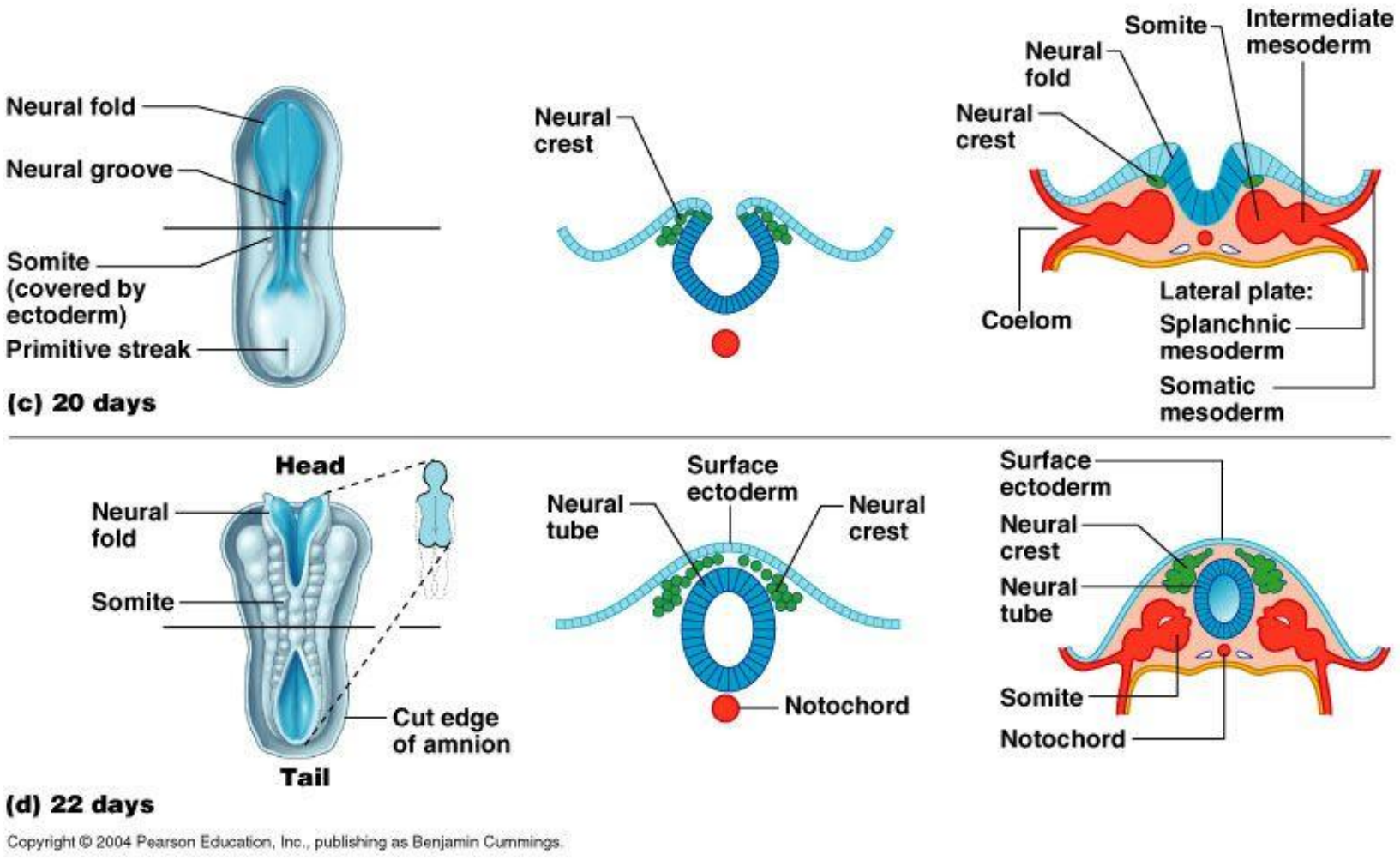


Prechordal plate



The prechordal plate is the anterior-most axial mesoderm, and a critical ventral patterning center that underlies the developing forebrain

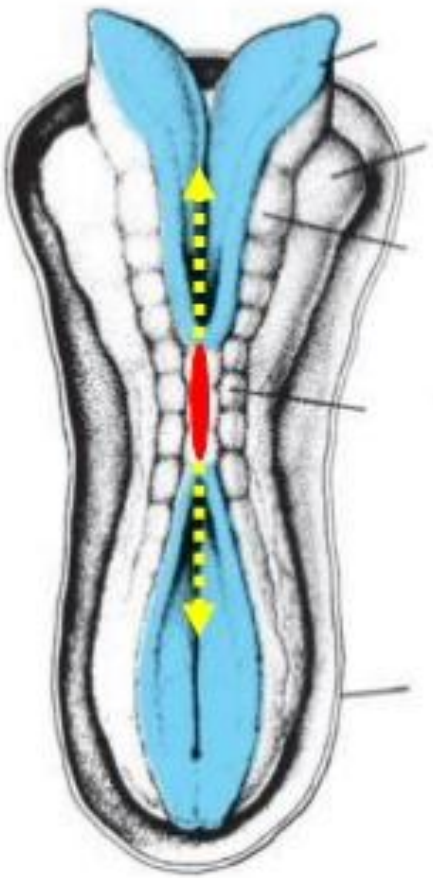
WEEK 3

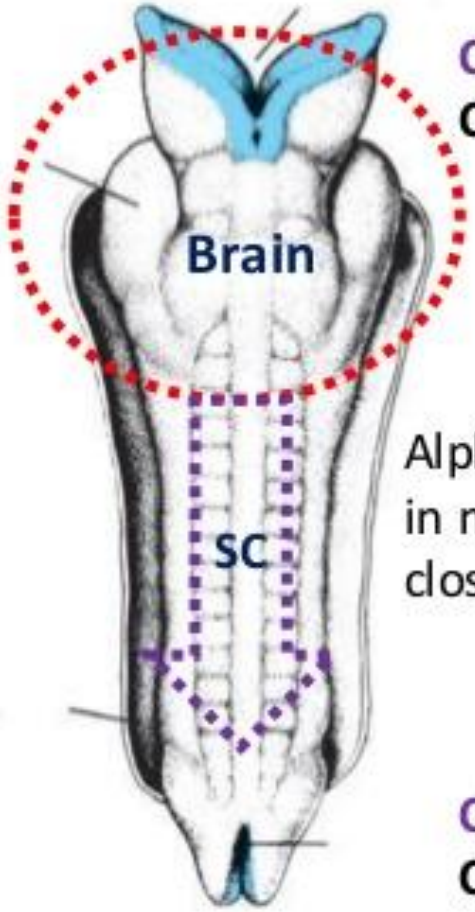


Fusion begins in the cervical region and proceeds cranially and caudally

WEEK 4

ectoderm

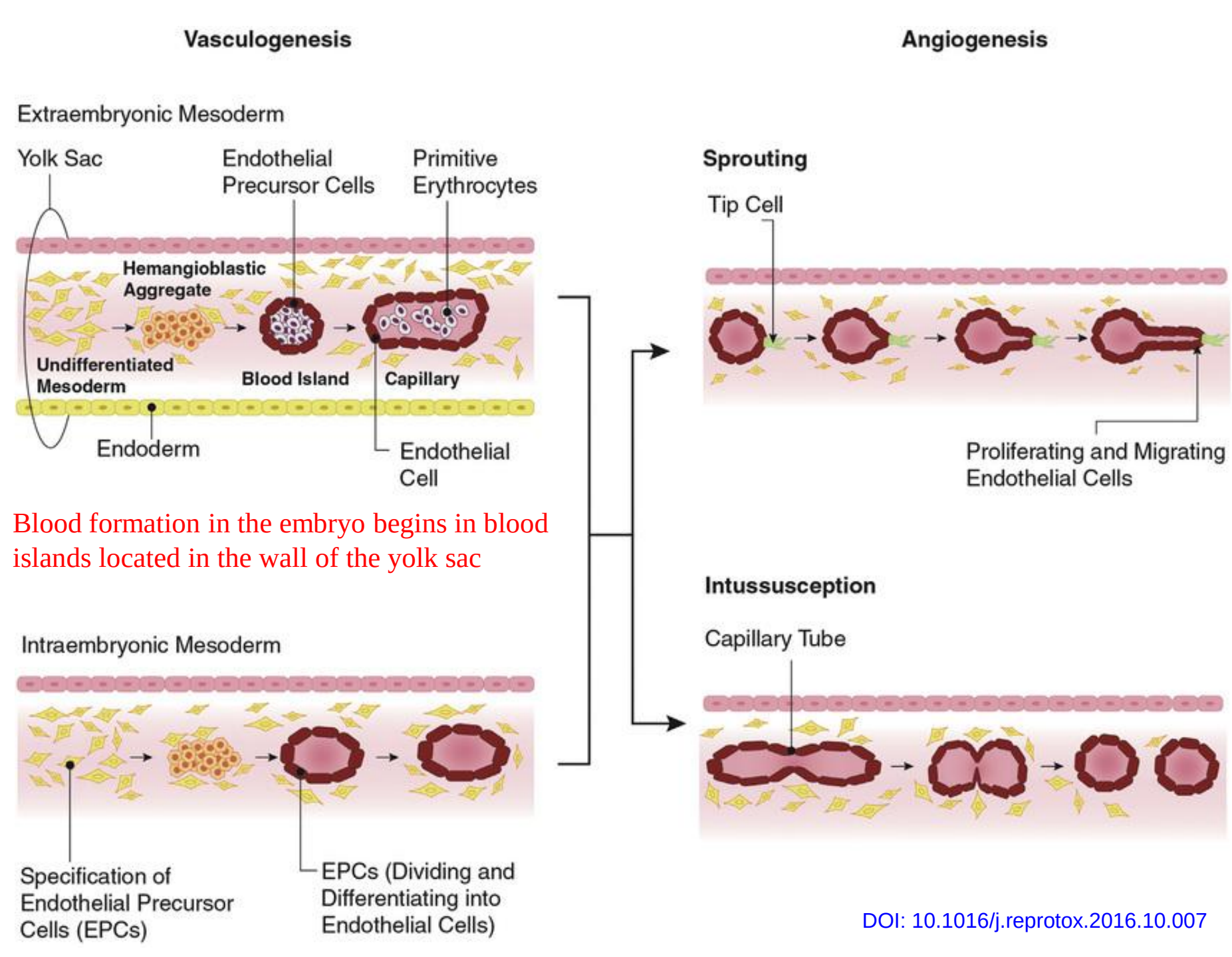




Cranial neuropore
Closure at 25th day

Alpha feto protein (AFP) increases in maternal AF if neuropores fail to close (neural tube defects).

Caudal neuropore
Closure at 27th day



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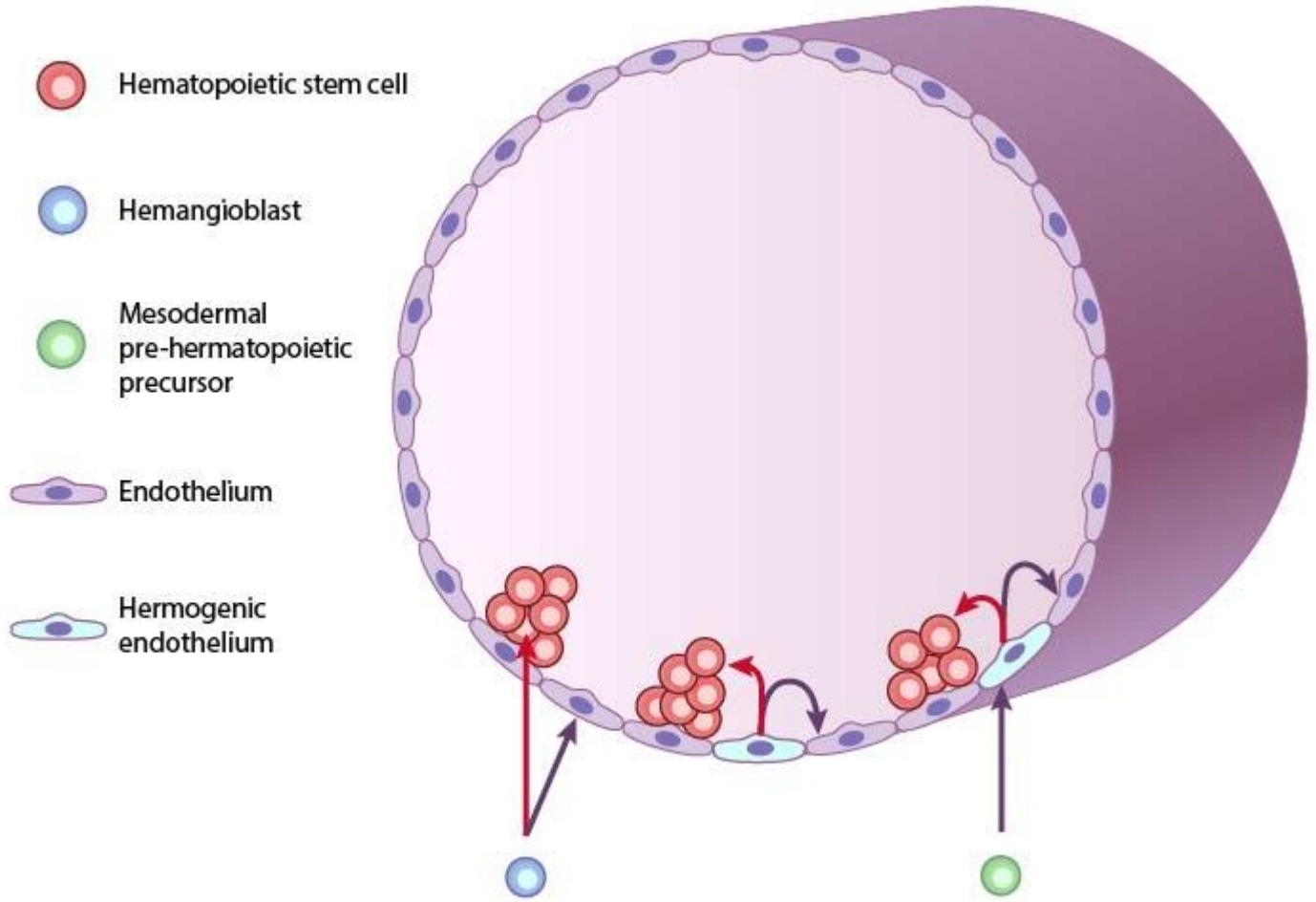
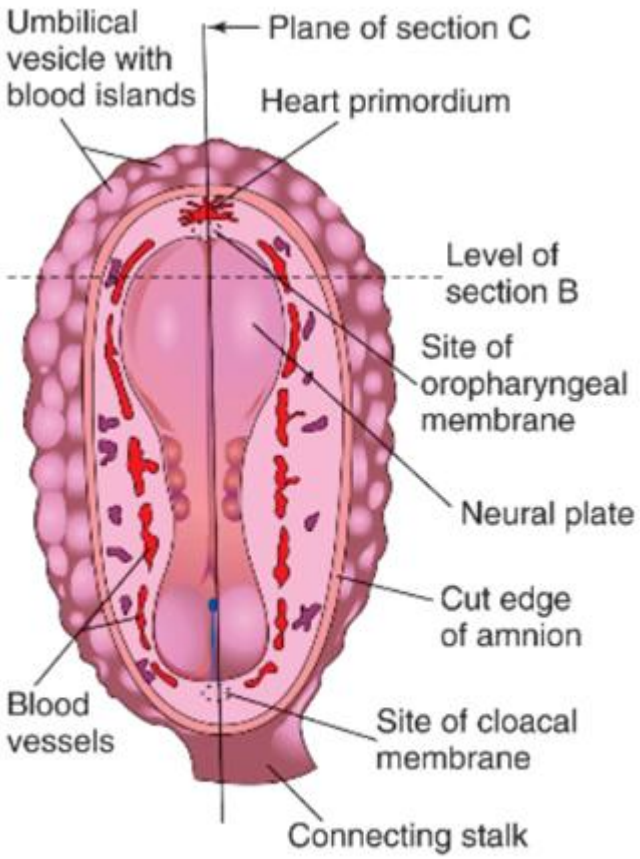
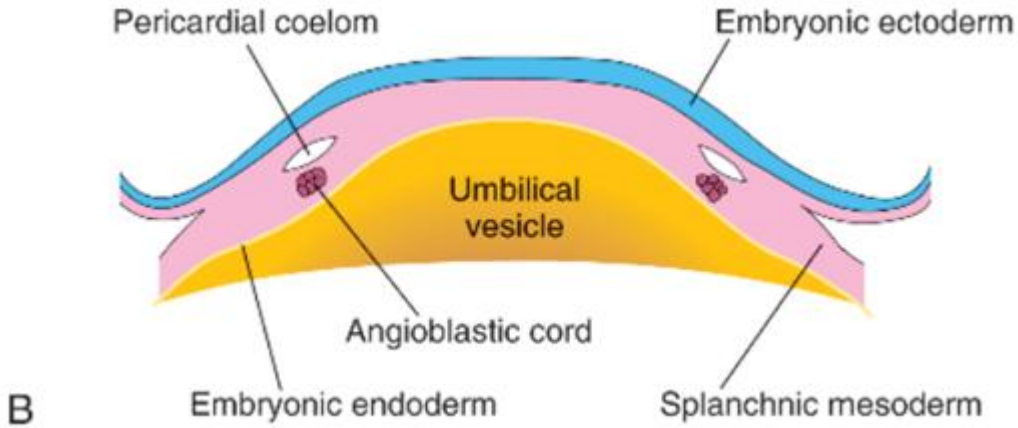
The definitive hematopoietic **stem cells** (HSCs) develop intra-embryonically in the **aorta-gonad-mesonephros** (AGM) region



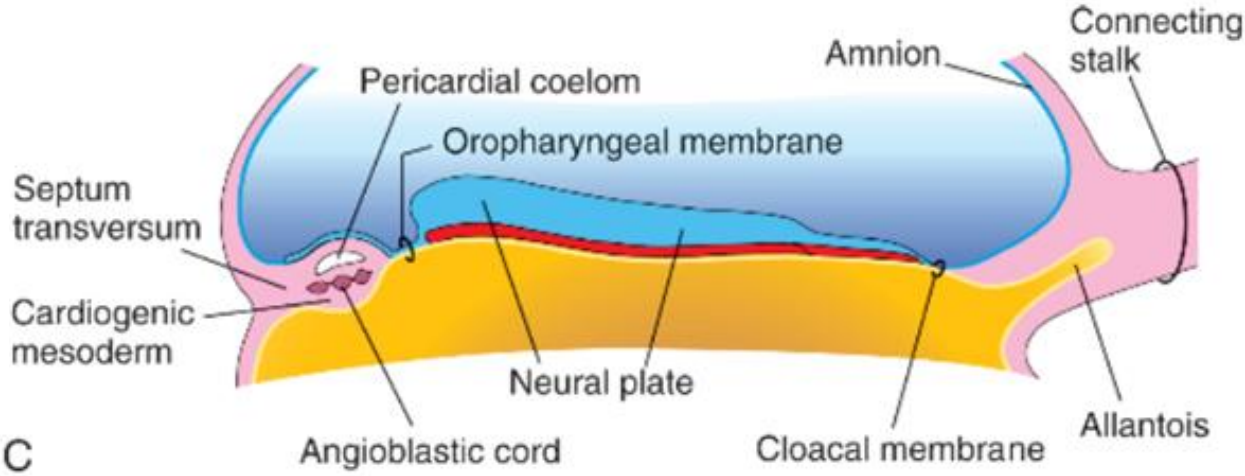

Umbilical vesicle with blood islands
Plane of section C
Heart primordium
Level of section B
Site of oropharyngeal membrane
Neural plate
Cut edge of amnion
Blood vessels
Site of cloacal membrane
Connecting stalk

A

Day 18

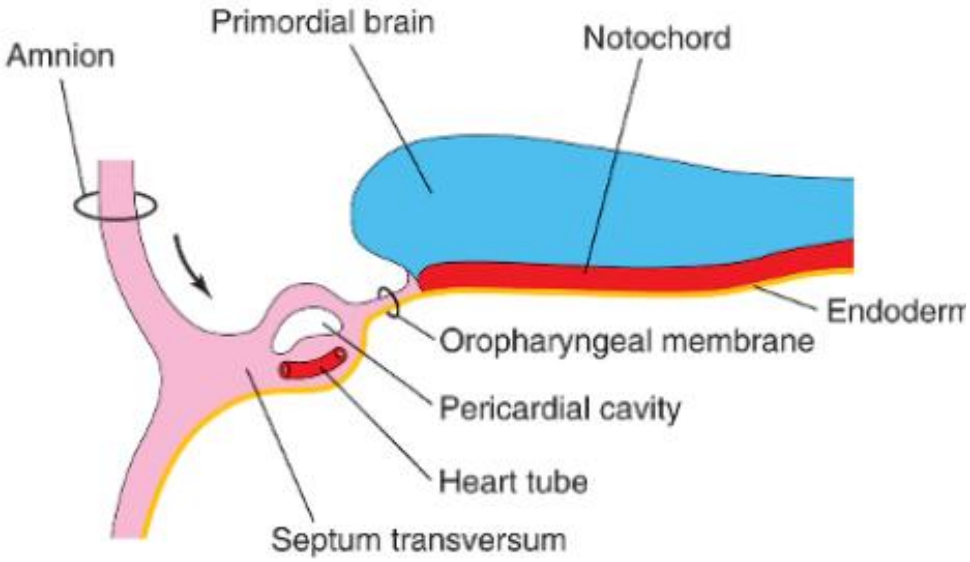

Pericardial coelom
Embryonic ectoderm
Umbilical vesicle
Angioblastic cord
Embryonic endoderm
Splanchnic mesoderm

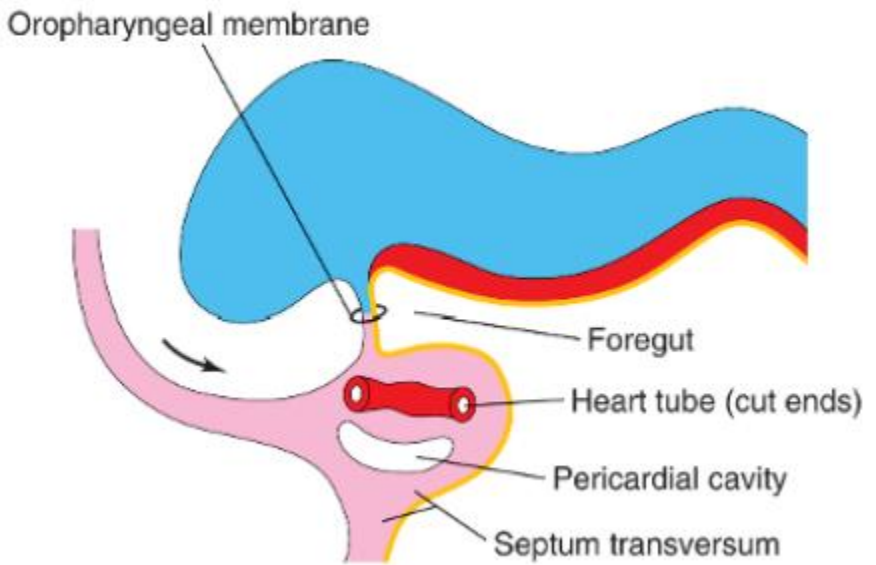
B


Amnion
Connecting stalk
Pericardial coelom
Oropharyngeal membrane
Septum transversum
Cardiogenic mesoderm
Neural plate
Angioblastic cord
Cloacal membrane
Allantois

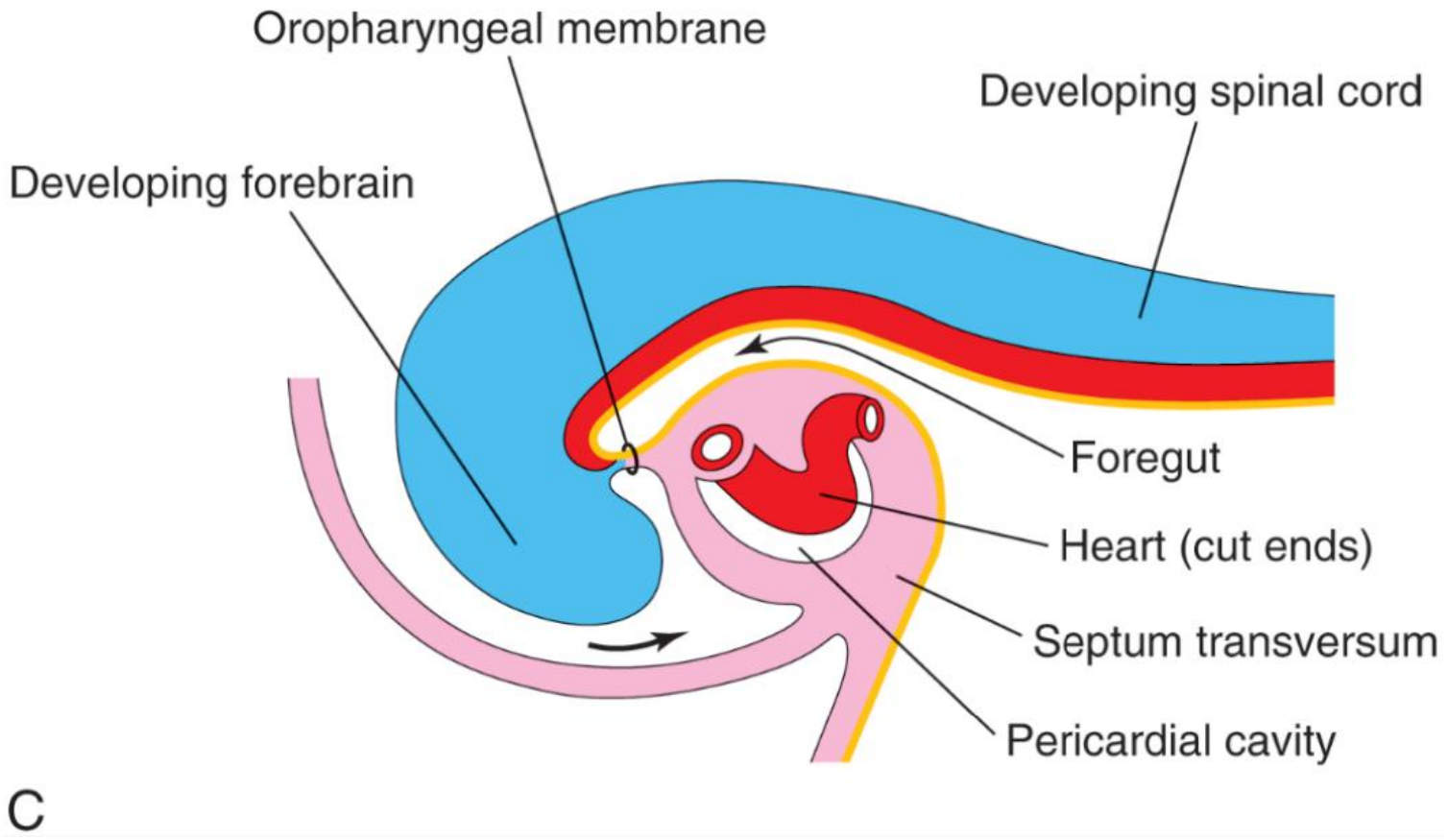
C

Longitudinal sections through the cranial half of human embryos during the **fourth week** of development.

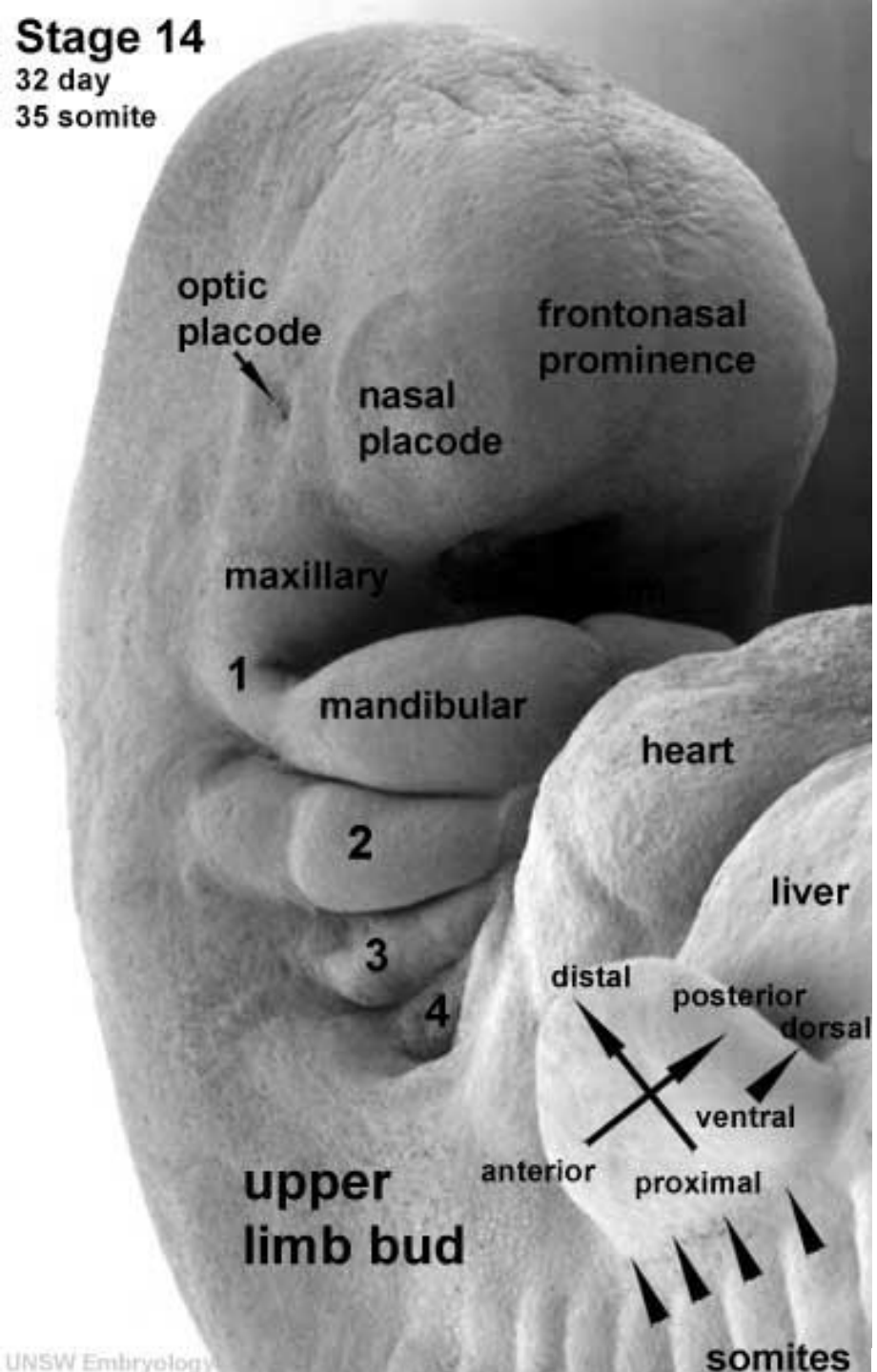




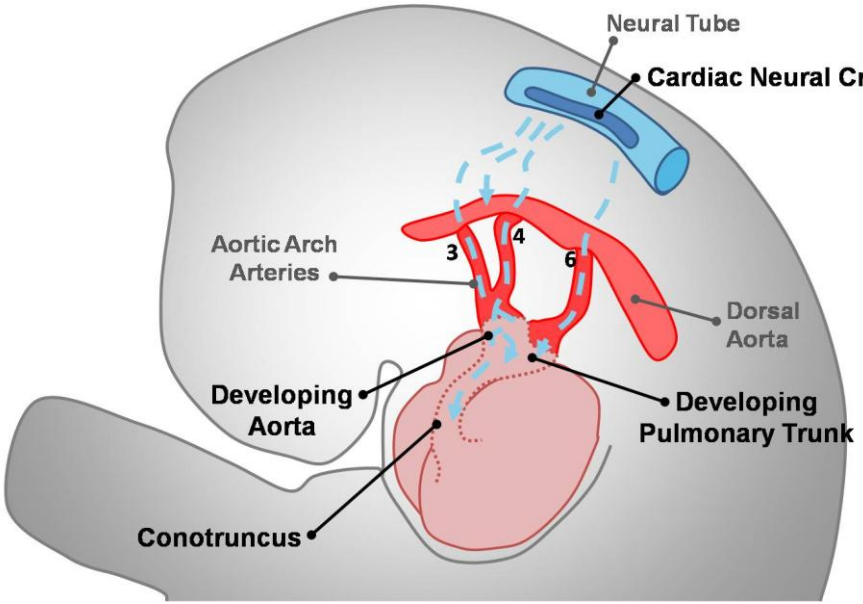
The effect of the head fold (*arrows*) on the position of the heart and other structures is shown. **A** and **B,** As the head fold develops, the heart tube and the pericardial cavity come to lie ventral to the foregut and caudal to the oropharyngeal membrane.

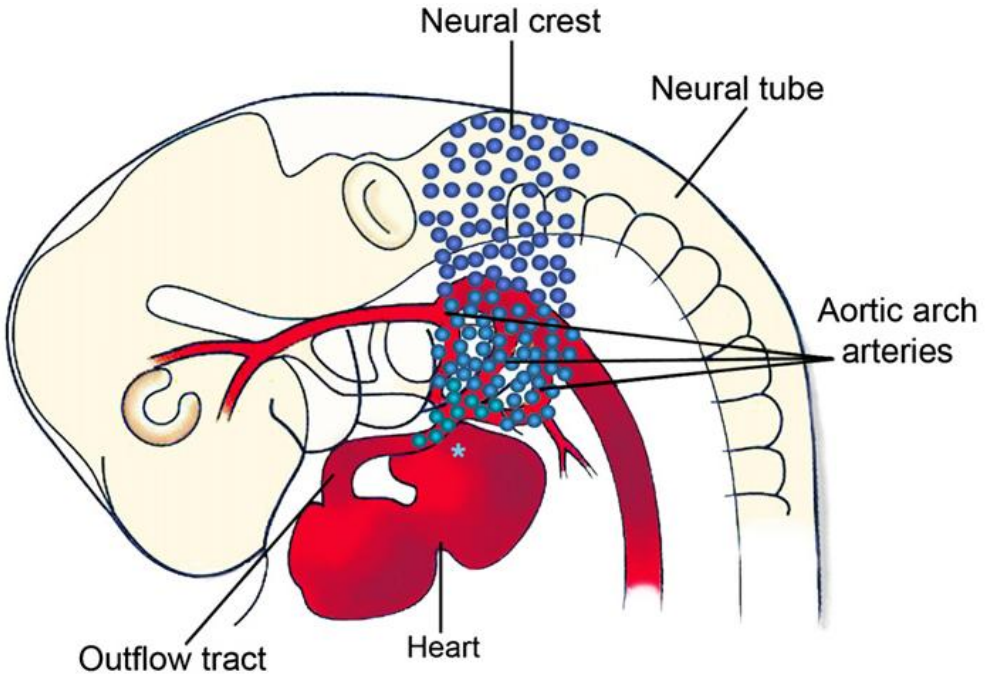


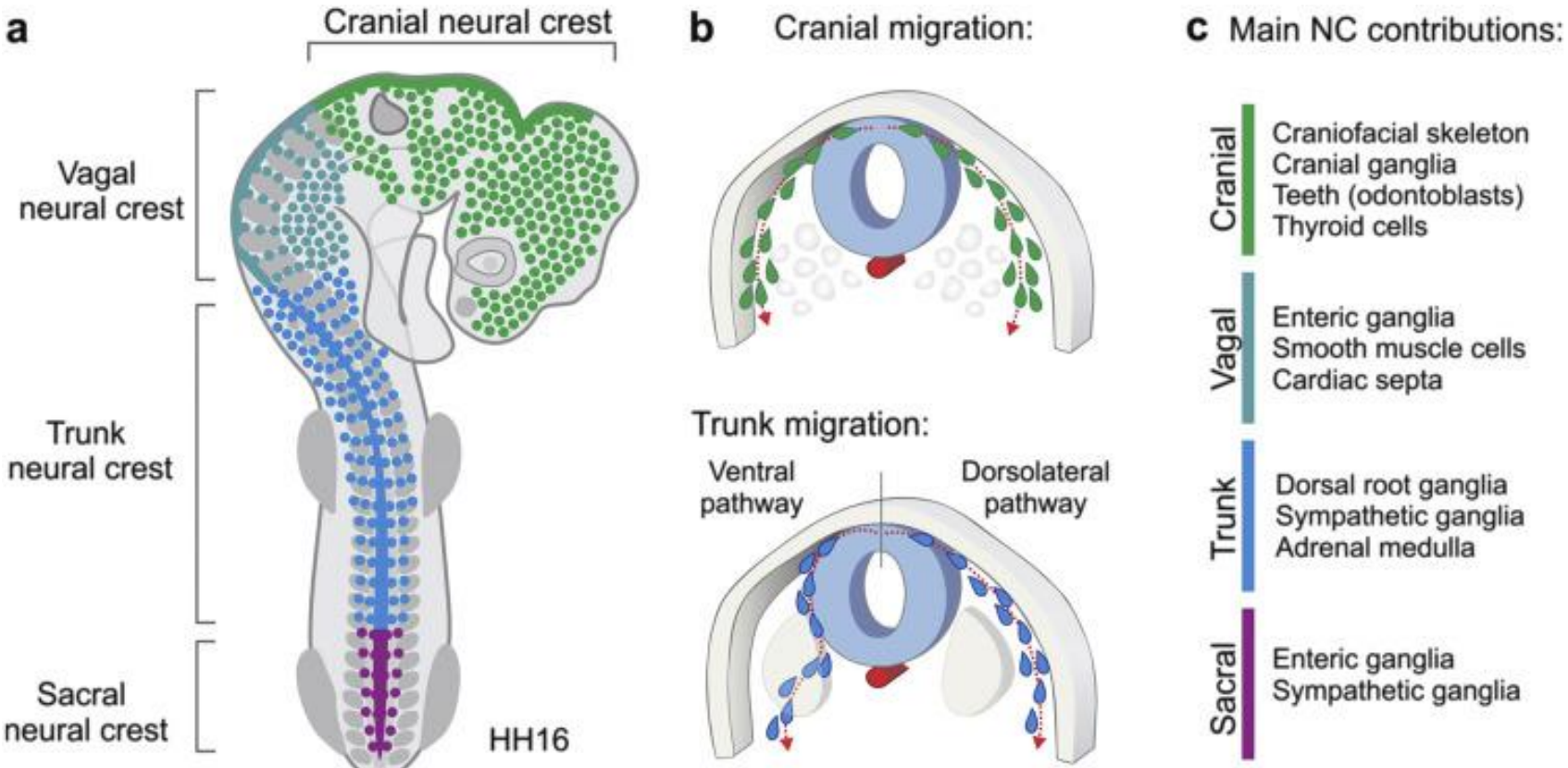
The positions of the pericardial cavity and the septum transversum have reversed with respect to each other. The **septum transversum** now lies posterior to the pericardial cavity, where it will form the central tendon of the diaphragm.

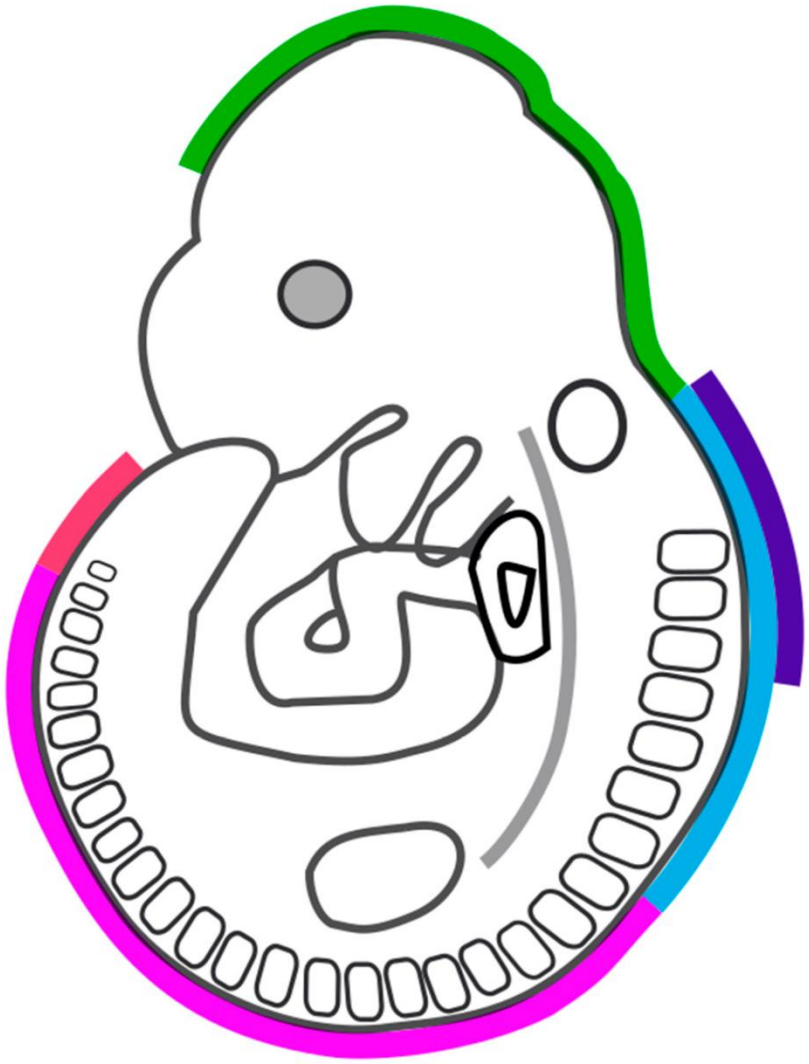


Embryo – Week 5: Migration of the Cardiac Neural Crest

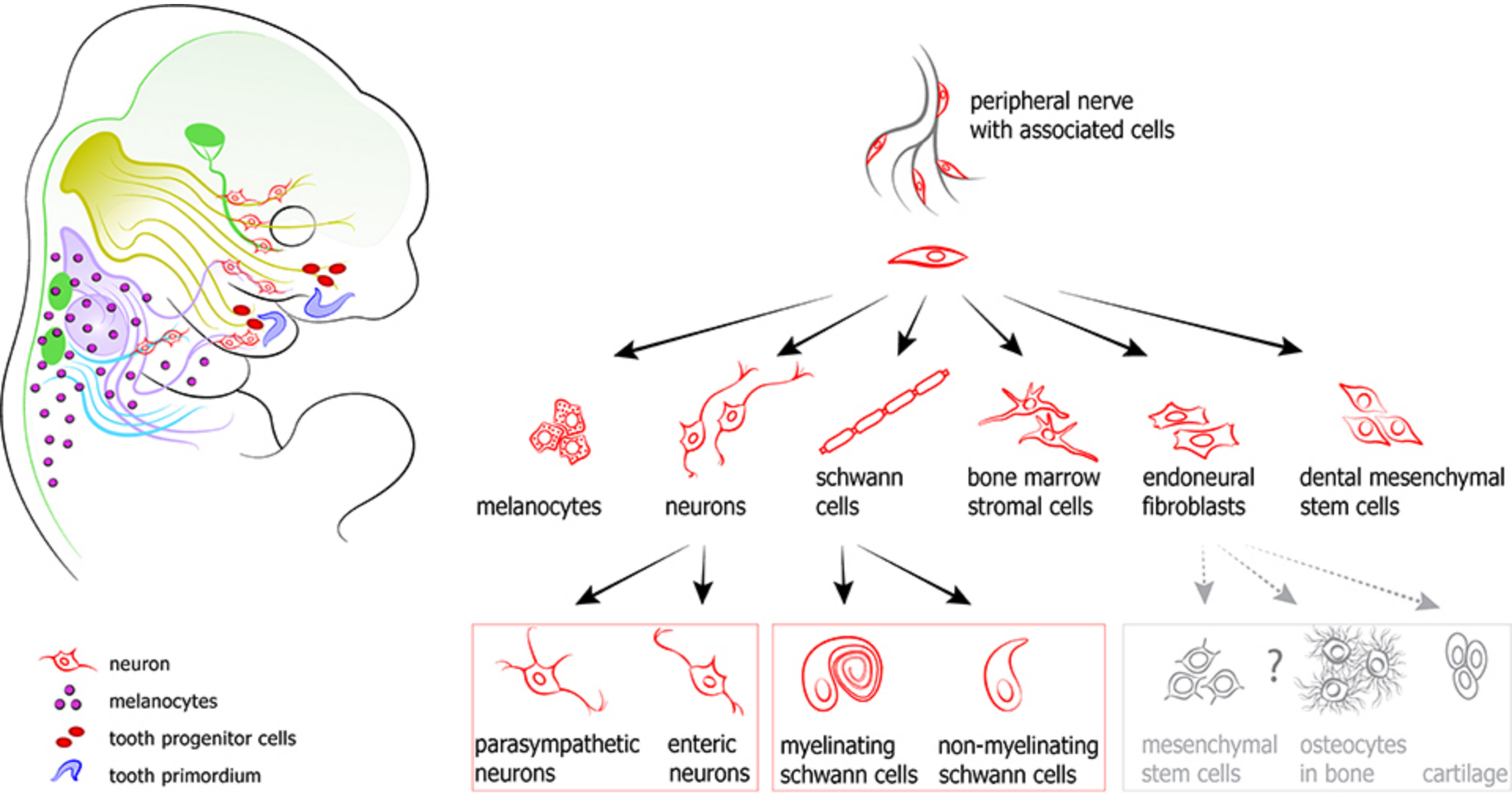





a
Cranial neural crest
Vagal neural crest
Trunk neural crest
Sacral neural crest
HH16
b
Cranial migration:
Trunk migration:
Ventral pathway
Dorsolateral pathway
c
Main NC contributions:
Cranial
Craniofacial skeleton
Cranial ganglia
Teeth (odontoblasts)
Thyroid cells
Vagal
Enteric ganglia
Smooth muscle cells
Cardiac septa
Trunk
Dorsal root ganglia
Sympathetic ganglia
Adrenal medulla
Sacral
Enteric ganglia
Sympathetic ganglia

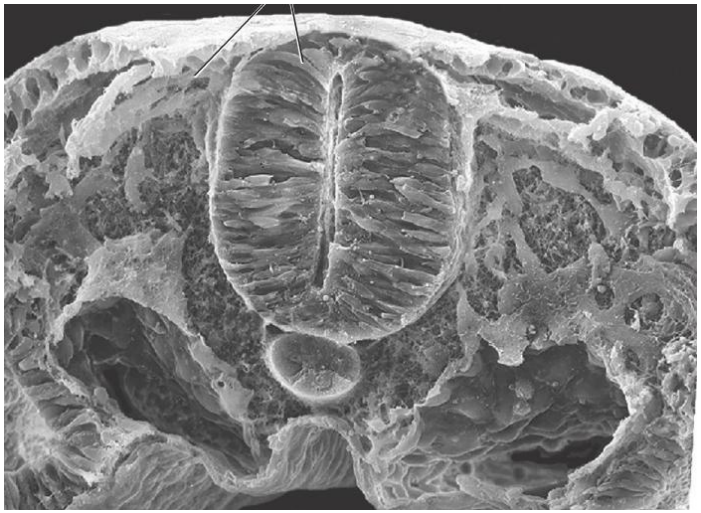


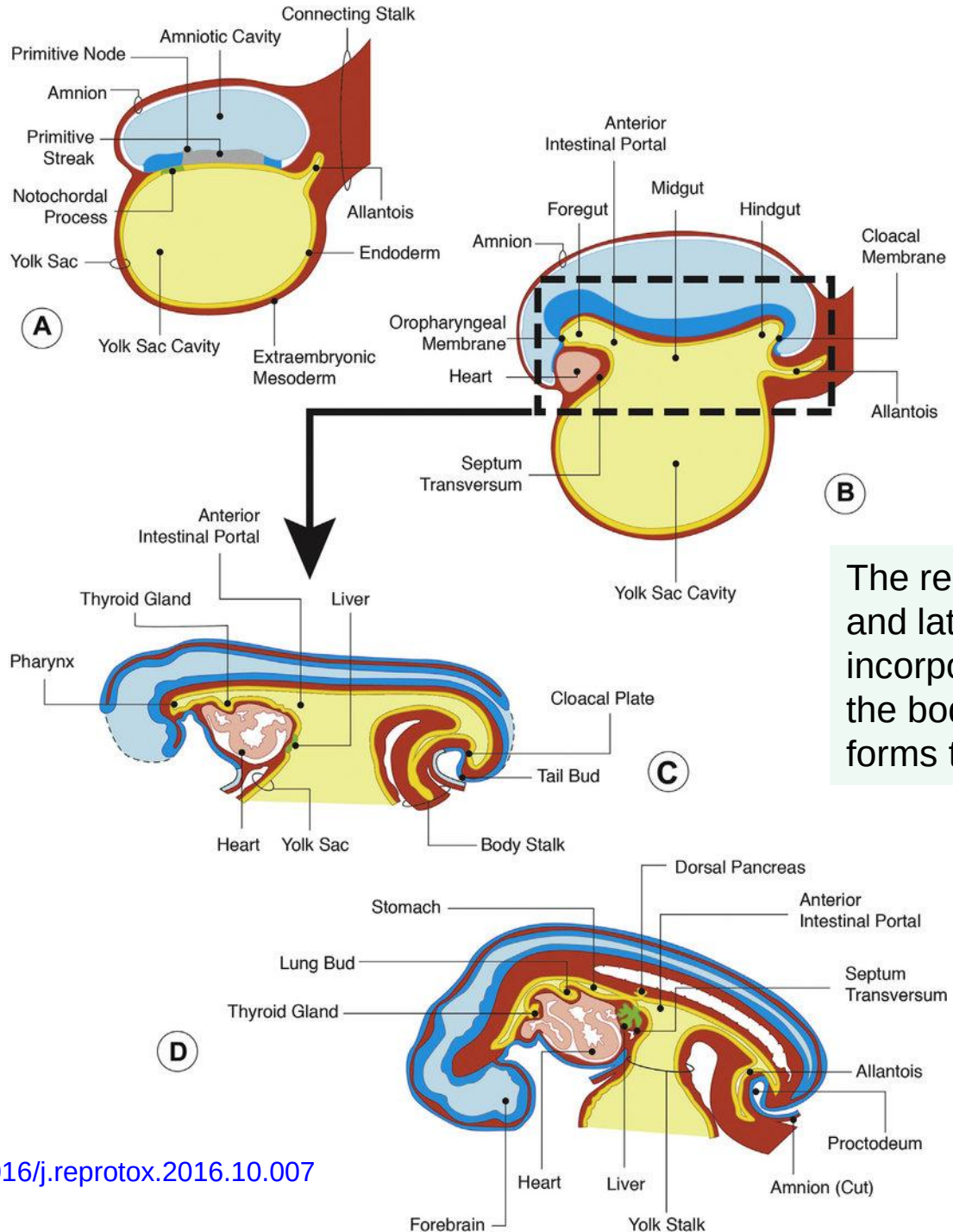
Cranial		Chondrocytes Osteocytes Cranial sensory ganglia Ciliary ganglia Odontoblasts Thyroid cells
Vagal	Cardic	Smooth muscle cells Cardiac septa Pericytes
Vagal		Ganglia Mesenchyme Pericytes
Trunk		Dorsal root ganglia Sympathetic ganglia Adrenal medulla Schwann cells Melanocytes
Sacral		Enteric ganglia Sympathetic ganglia


peripheral nerve
with associated cells
melanocytes
neurons
schwann
cells
bone marrow
stromal cells
endoneural
fibroblasts
dental mesenchymal
stem cells
parasympathetic
neurons
enteric
neurons
myelinating
schwann cells
non-myelinating
schwann cells
?
mesenchymal
stem cells
osteocytes
in bone
cartilage
neuron
melanocytes
tooth progenitor cells
tooth primordium

Neural crest cells

- Sometimes referred as a fourth germ layer
- Neural crest cells of the cranial neural folds leave the neural tube before closure
- Neural crest cells in the trunk region leave the neural tube after closure
- In the head region they form:
  - Craniofacial skeleton
  - Dermis of face and neck
  - Melanocytes
  - Cranial ganglia
  - C cells of thyroid gland
  - Odontoblasts and cementoblasts
  - Glial cells
  - Mesenchyme of thymus
  - Mesenchyme of parathyroid gland
  - Smooth muscle cells of blood vesseles





The result of cephalocaudal growth and lateral folding is partial incorporation of the allantois into the body of the embryo where it forms the cloaca.

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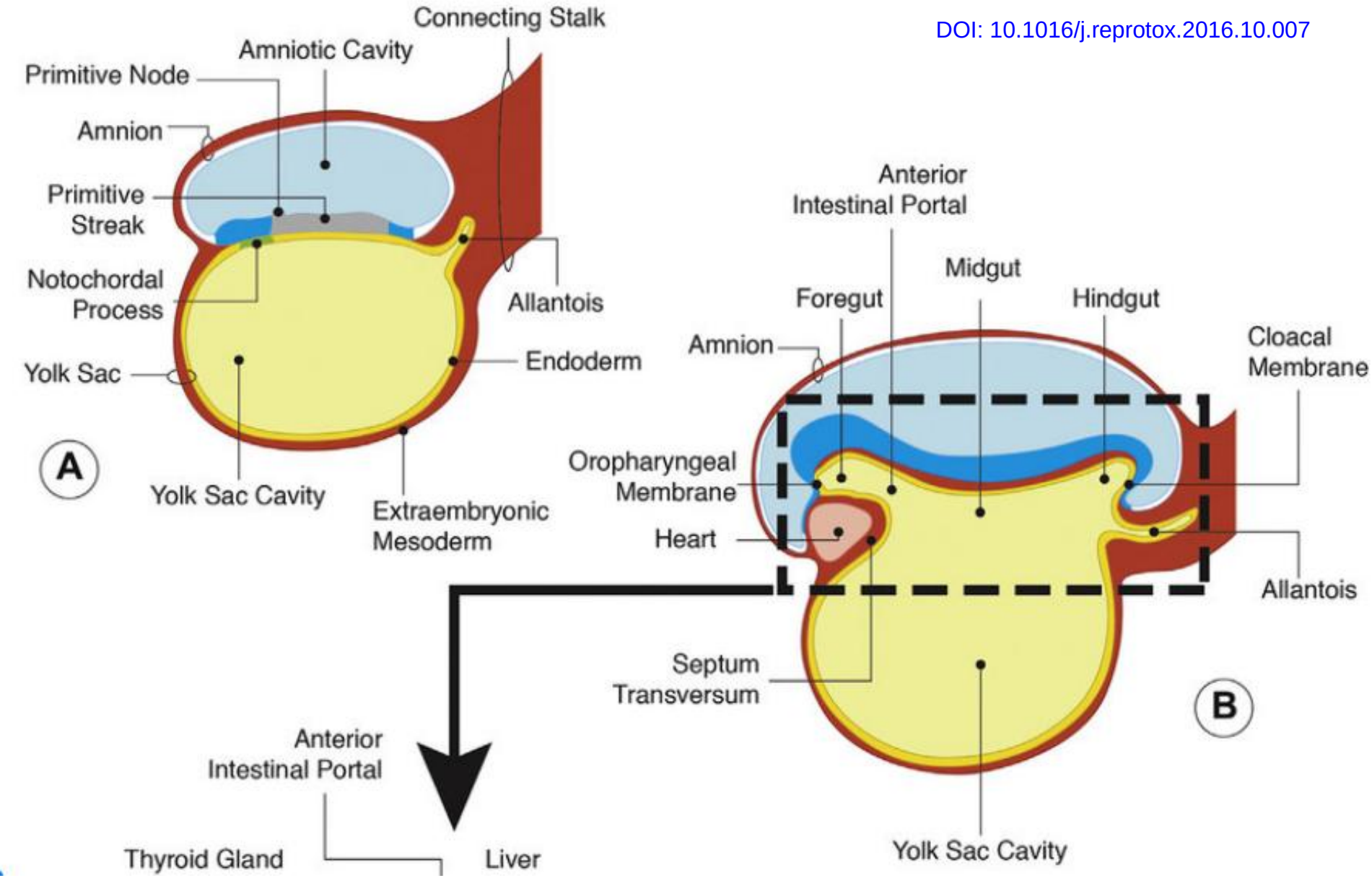
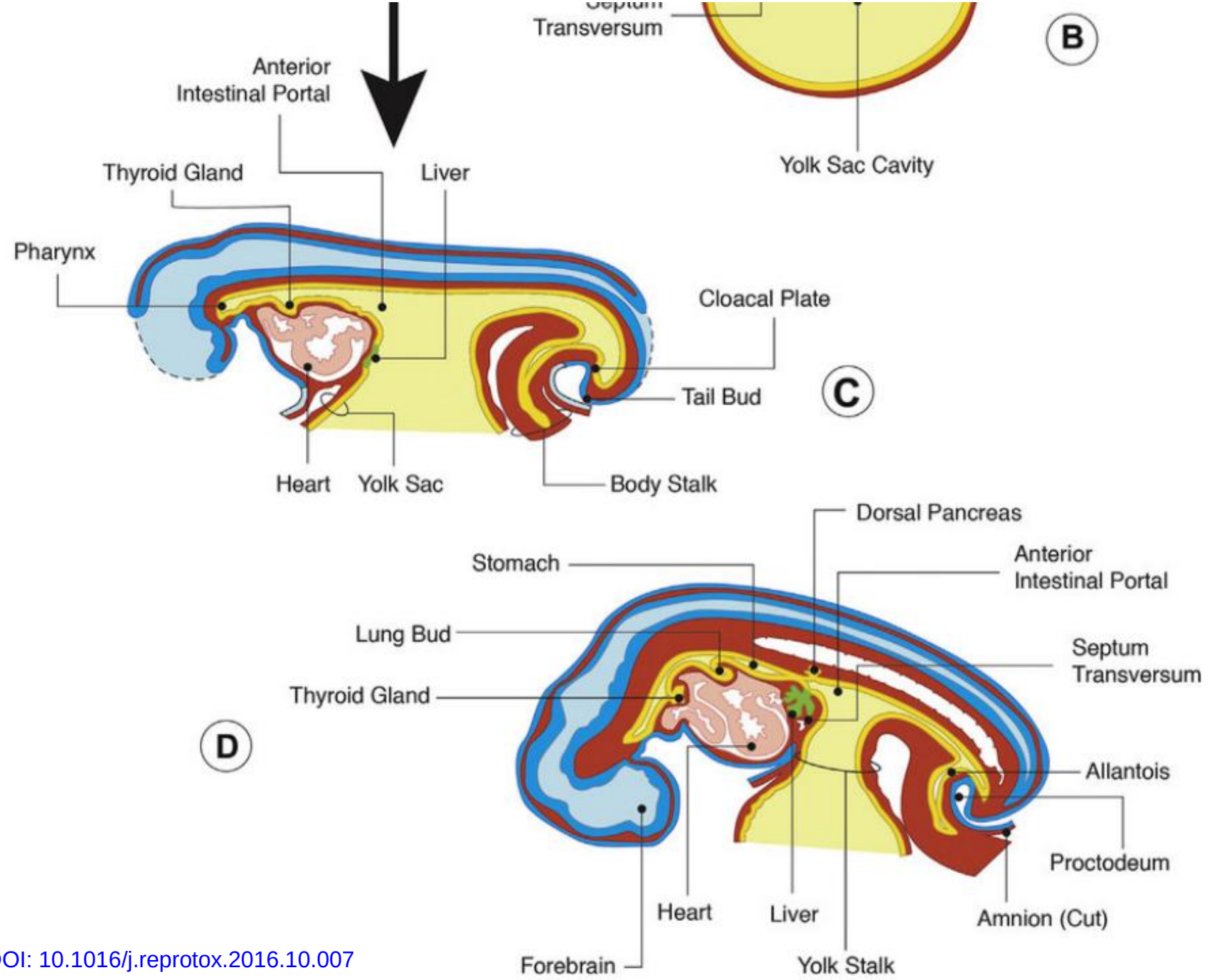


When the cloacal membrane appears, the posterior wall of the yolk sac forms a small diverticulum that extends into the connecting stalk. This diverticulum, **the allantoenteric diverticulum**, or **allantois**, appears around the **16th** day of development.



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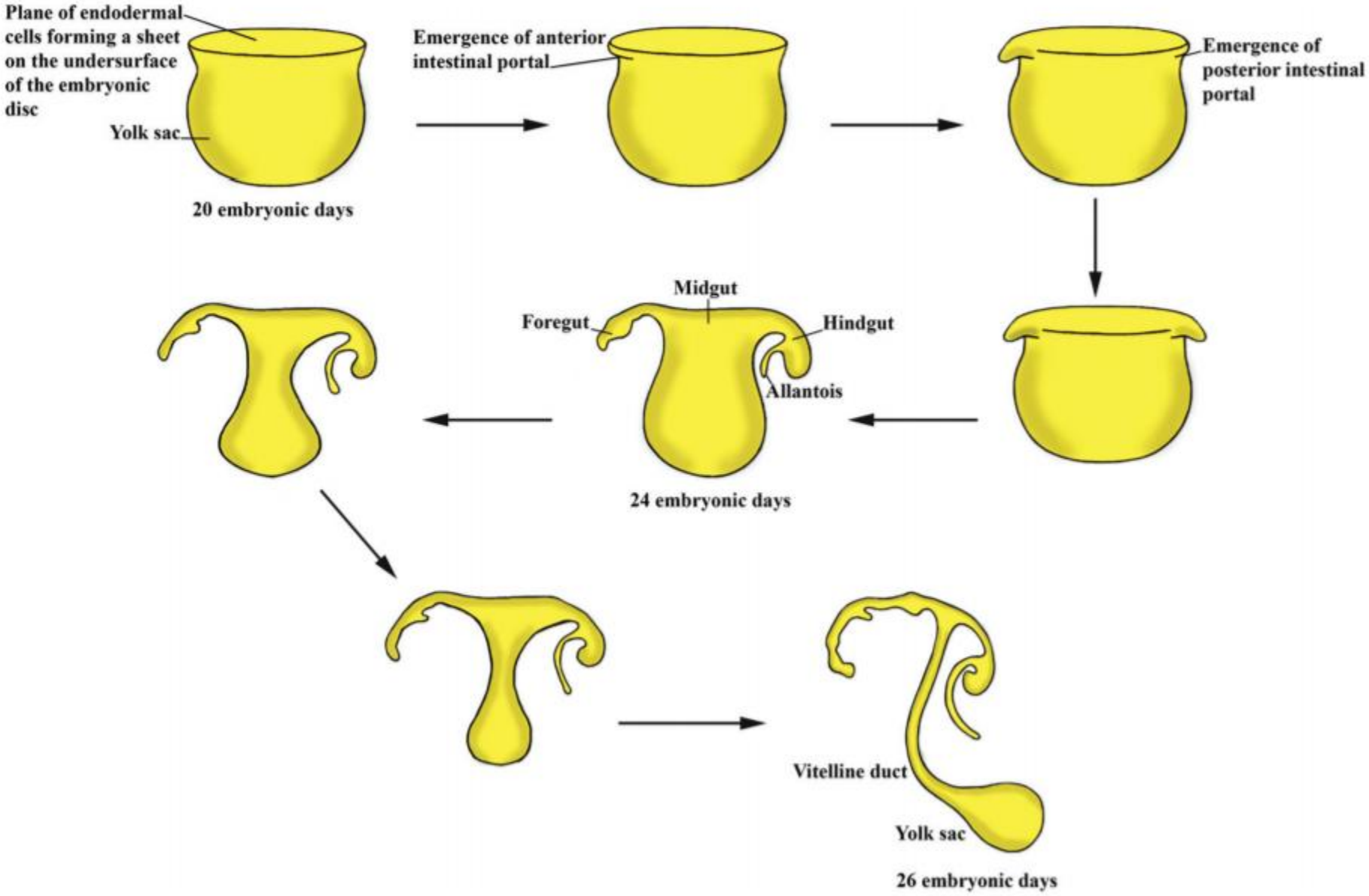
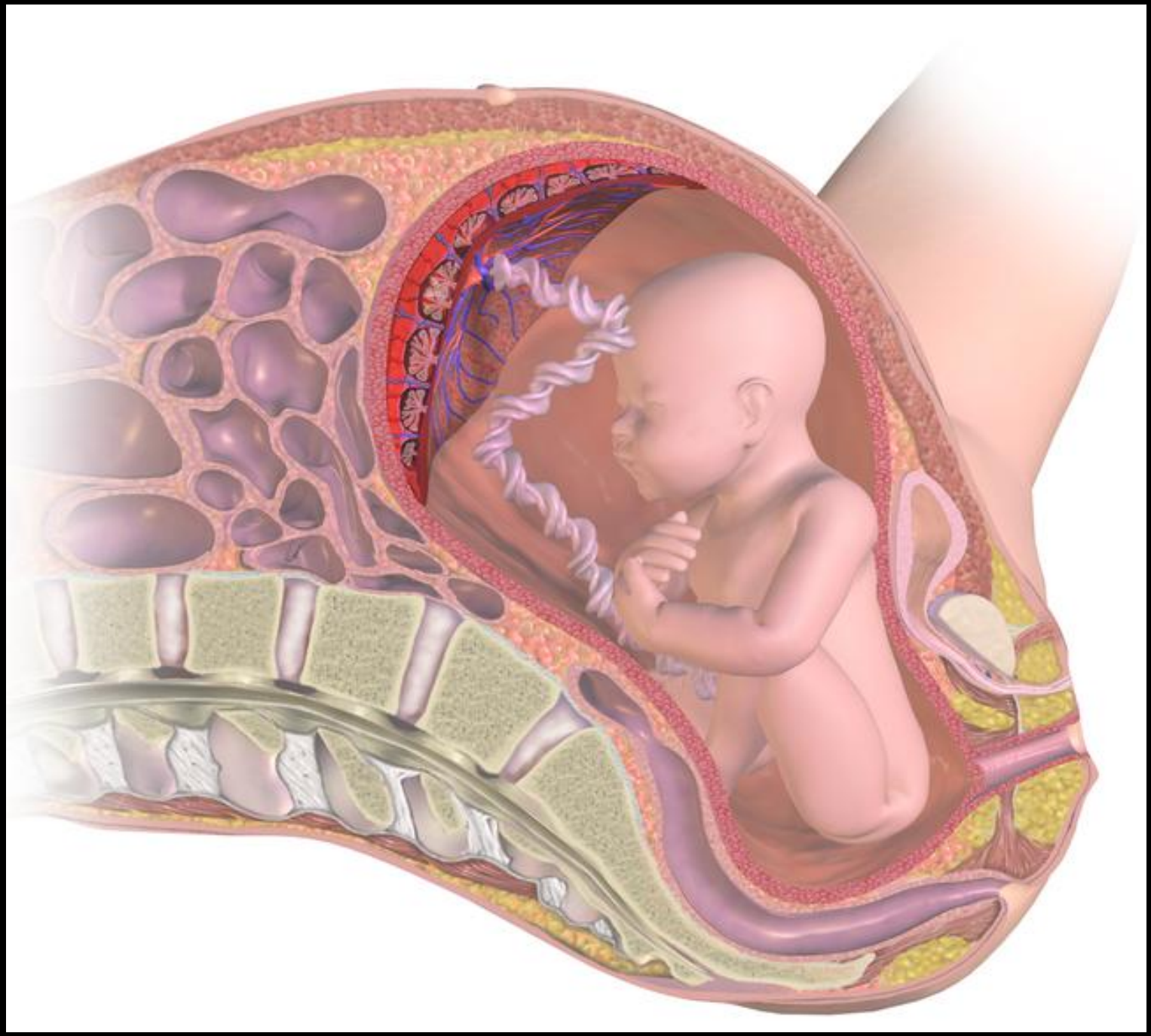
Drawings of just the endoderm (yellow) as it changes from a flat sheet at the upper edge of the yolk sac into the gut



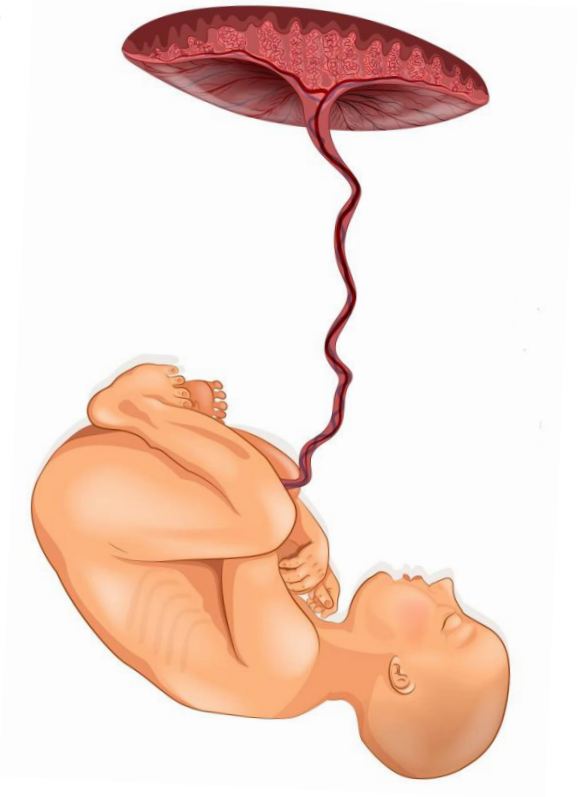
Neurographics 2016 January/February; 6(1):43– 63; www.neurographics.org

EMBRYOLOGY



PLACENTA

This is a fetomaternal organ



It has two components

- **Fetal part – develops from the chorionic sac (chorion frondosum)**
- **Maternal part - derived from the endometrium (functional layer – decidua basalis)**

The placenta and the umbilical cord are a transport system for substances between the mother and the fetus (vessels in umbilical cord)

PLACENTA FUNCTION

Exchange of metabolic and gaseous products between maternal and fetal bloodstreams:

Nutrition – exchange of nutrients and electrolytes; amino acids, free fatty acids, carbohydrates vitamins

Respiration – exchange of gases; oxygen and carbon dioxide

Excretion - filtering waste products (urea and creatinine) from the fetus

Protection – maternal immunoglobulin G (IgG) begins to be transported from mother to fetus at 14 weeks

Hormone production:

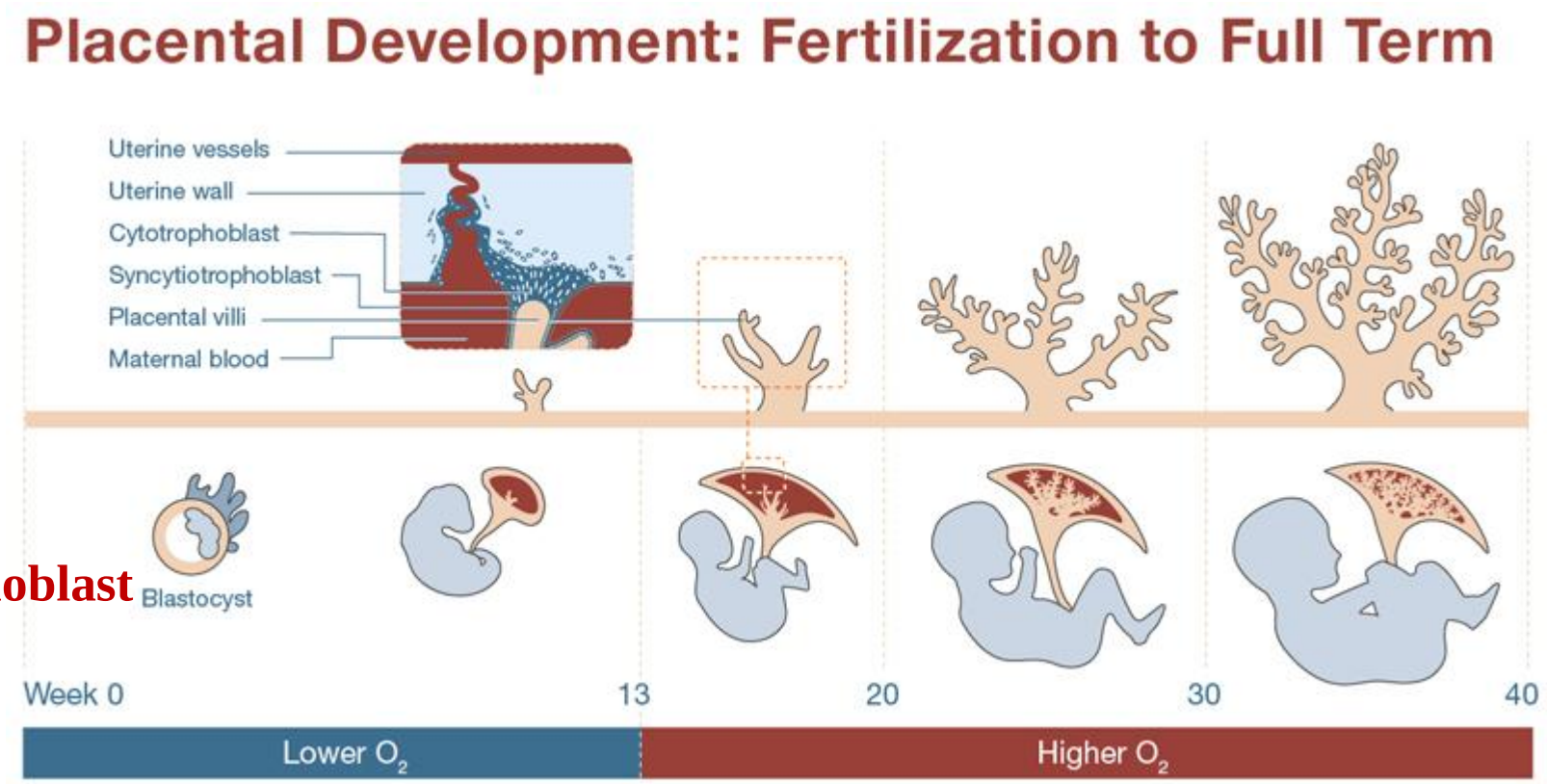
• during the first 2 months of pregnancy - **human chorionic gonadotrophin hCG**, which maintains the **corpus luteum** and can be used as an indicator of pregnancy

• **progesteron** in sufficient amounts to maintain pregnancy if the corpus luteum is removed

• **estrogenic hormones** (**estriol**) – stimulate uterine growth and development of mammary glands

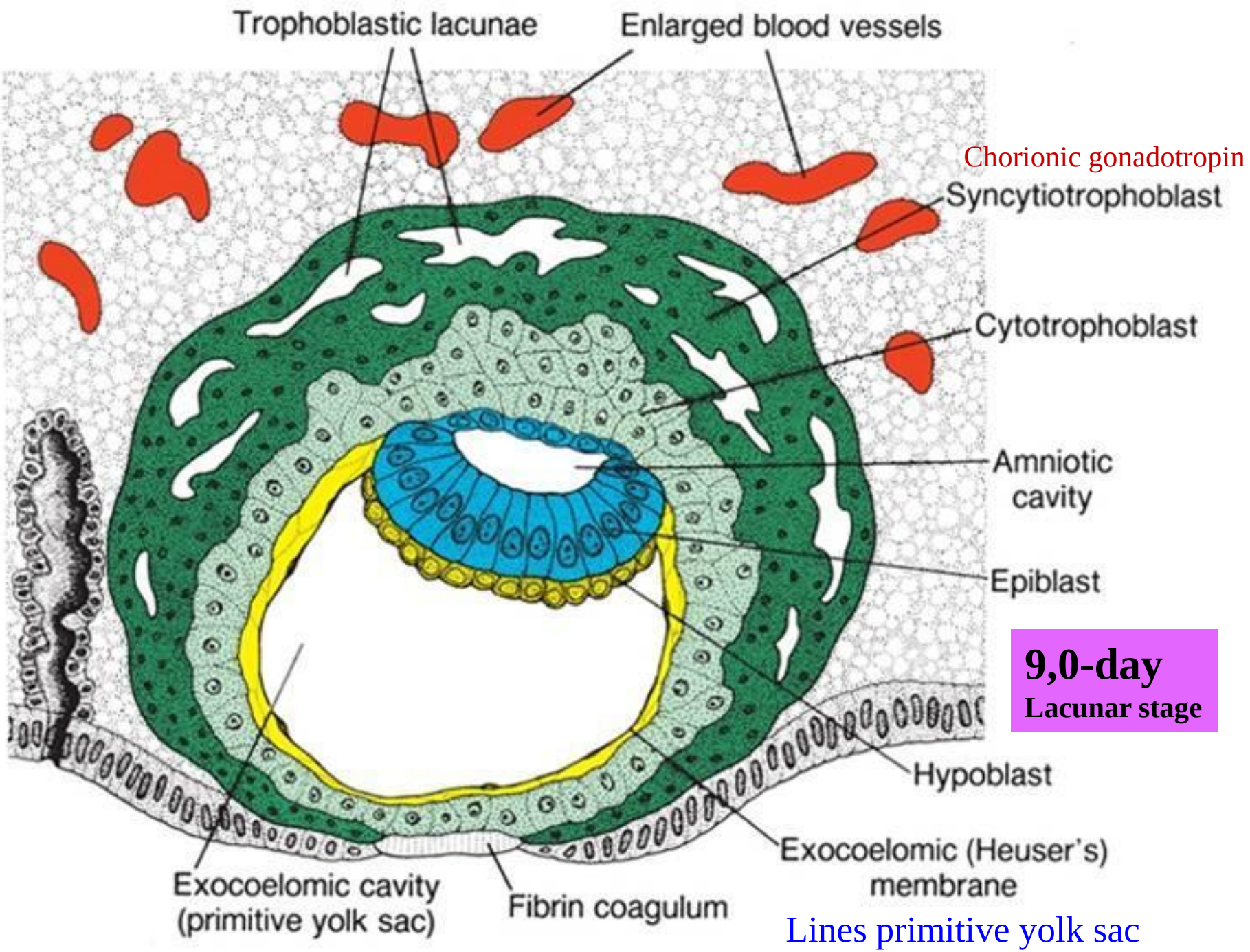
• **somatomammotropin** (**placental lactogen**) – give the fetus priority on maternal blood glucose and promotes breast development for milk production

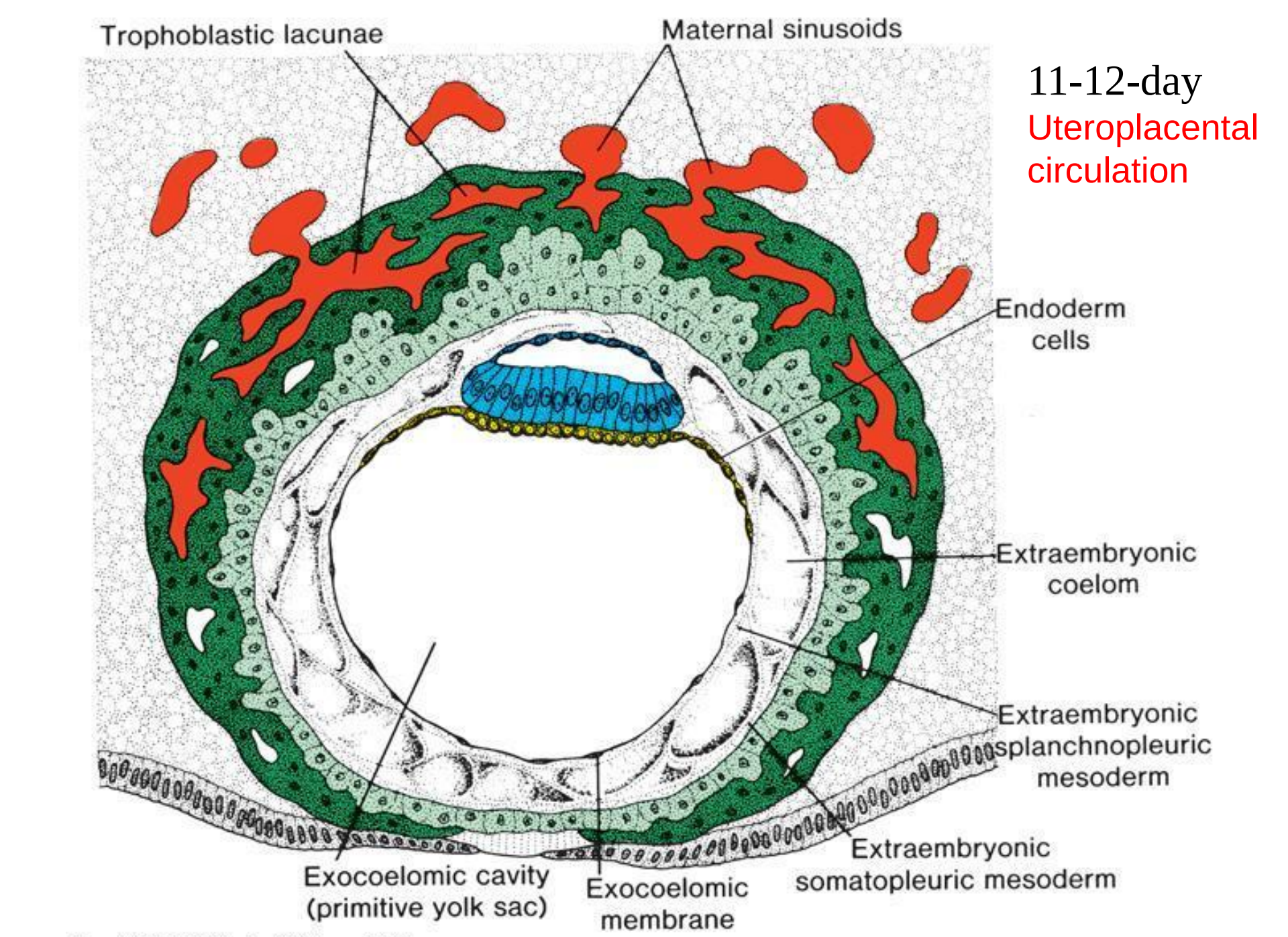
The placenta is the organ that facilitates nutrient an gas exchange between the maternal and fetal compartments



trophoblast

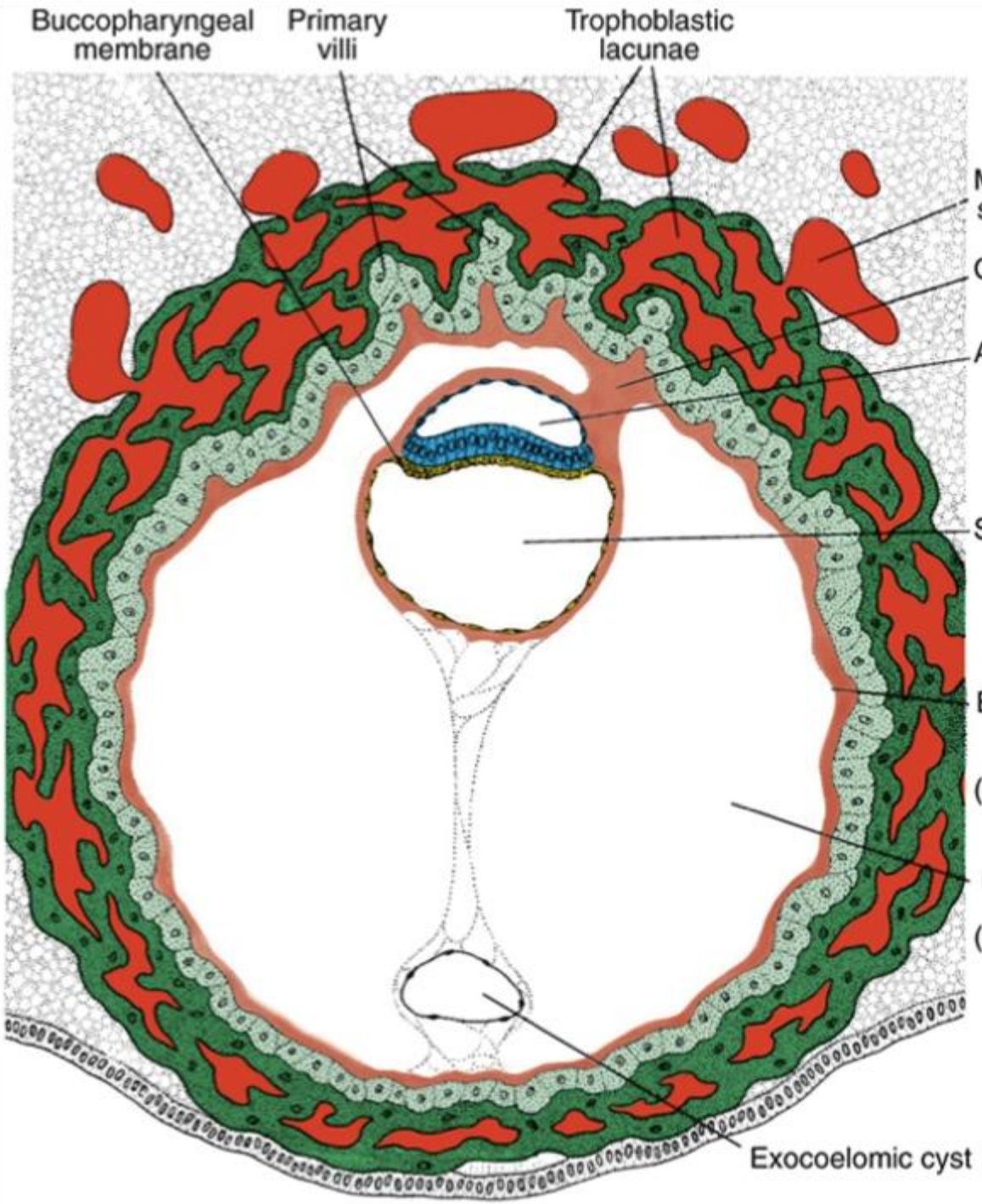
Extensive remodeling occurs toward the end of the first trimester when the definitive **placenta** is formed.





11-12-day
Uteroplacental circulation

13-day



→ Umbilical cord

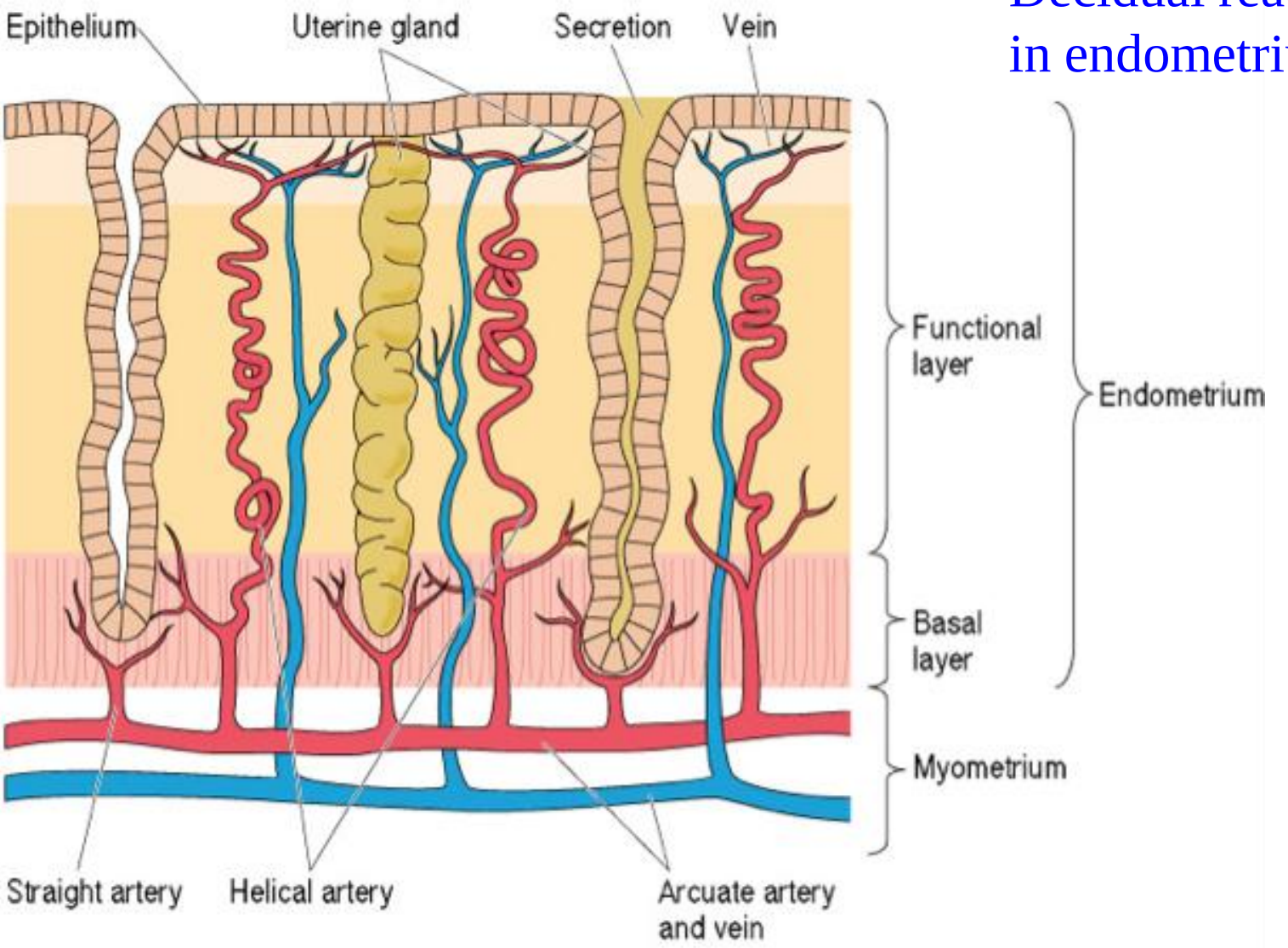
Chorion frondosum

!

Chorion laeve

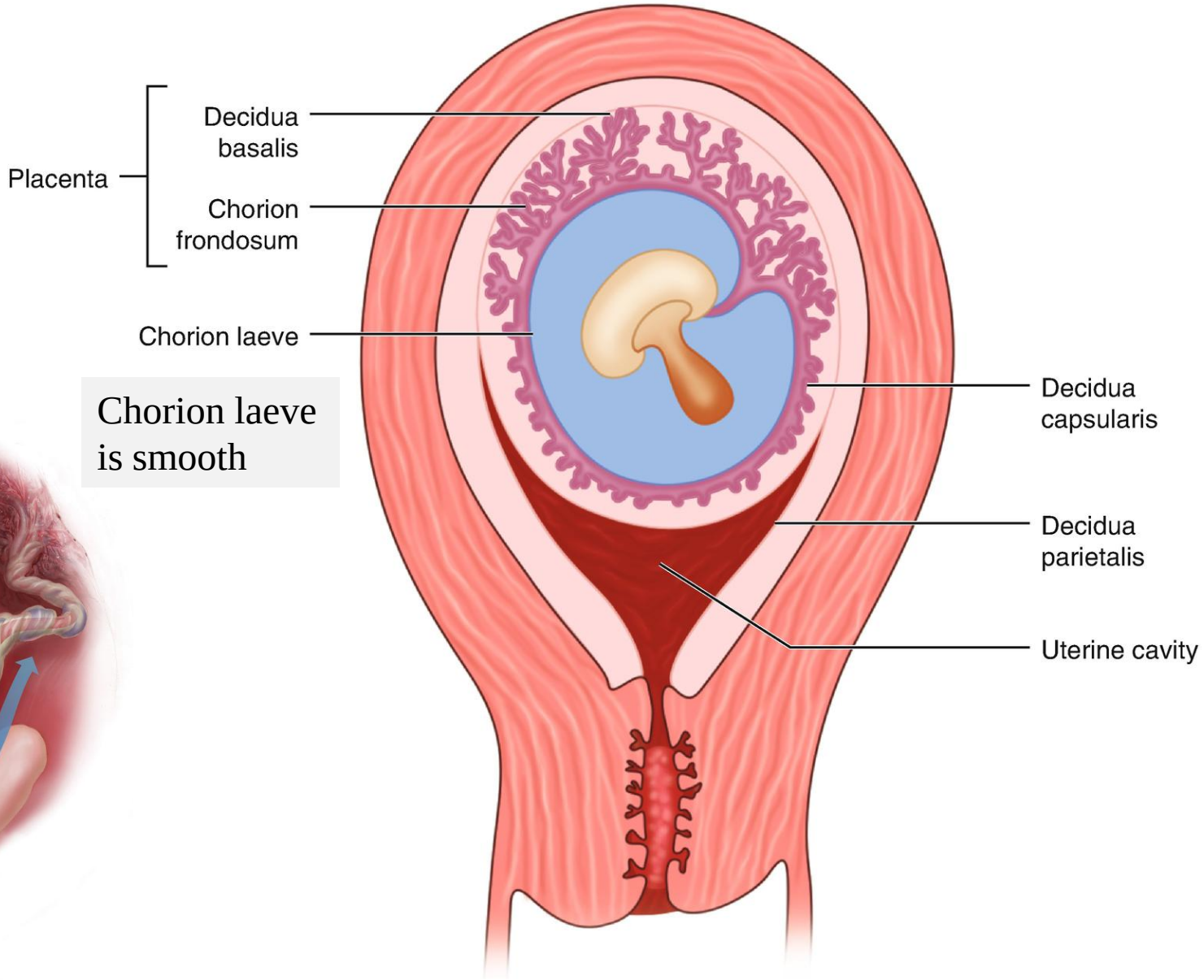
Bleeding near 28th day

Decidual reaction in endometrium

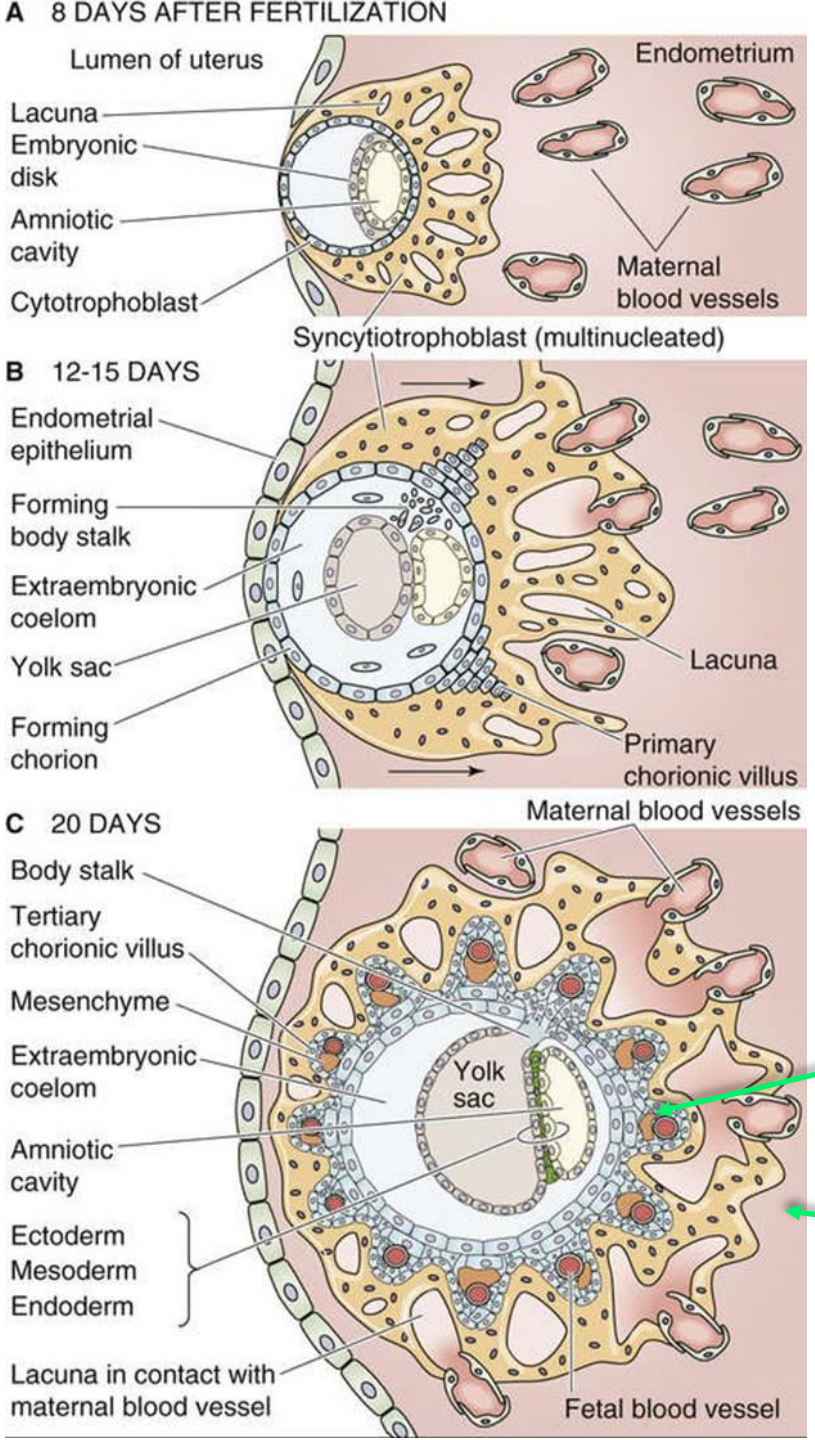


Decidual reaction refers to the physiological process of transformation of stromal cells in the endometrium, the lining of the uterus, into decidual cells during pregnancy.

Within days after implantation of the embryo, the stromal cells of the endometrium undergo a striking transformation called the decidual reaction



Chorion laeve is smooth

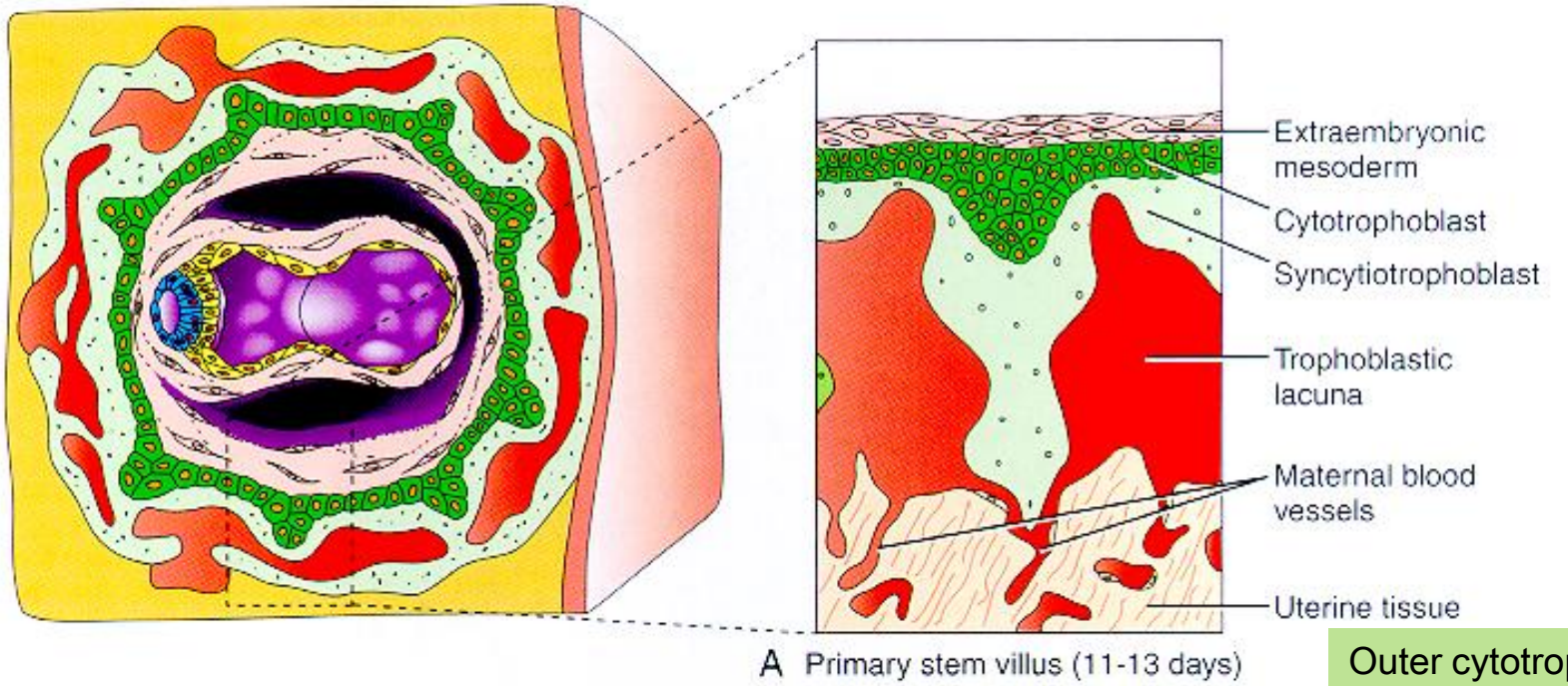


Fetal placenta

Cytotrophoblast

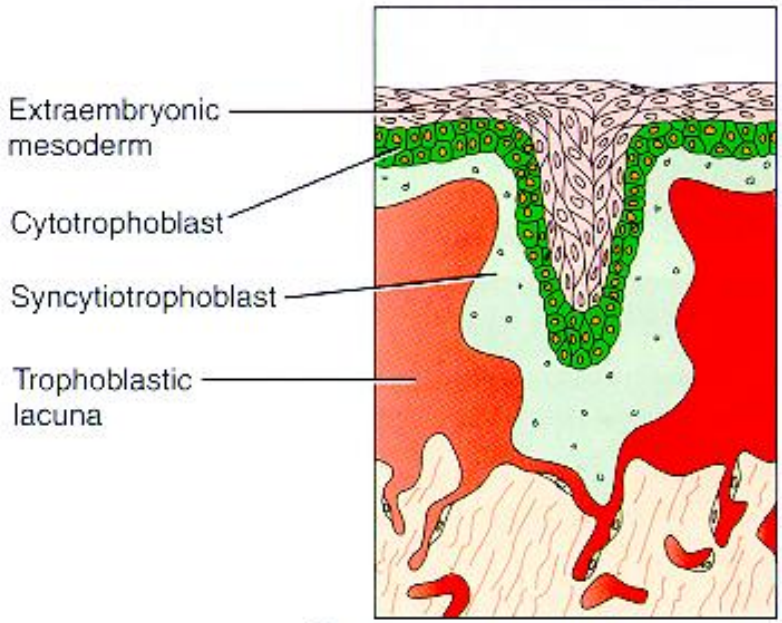
Extraembryonic mesoderm (the chorionic plate)

Uterine endometrium

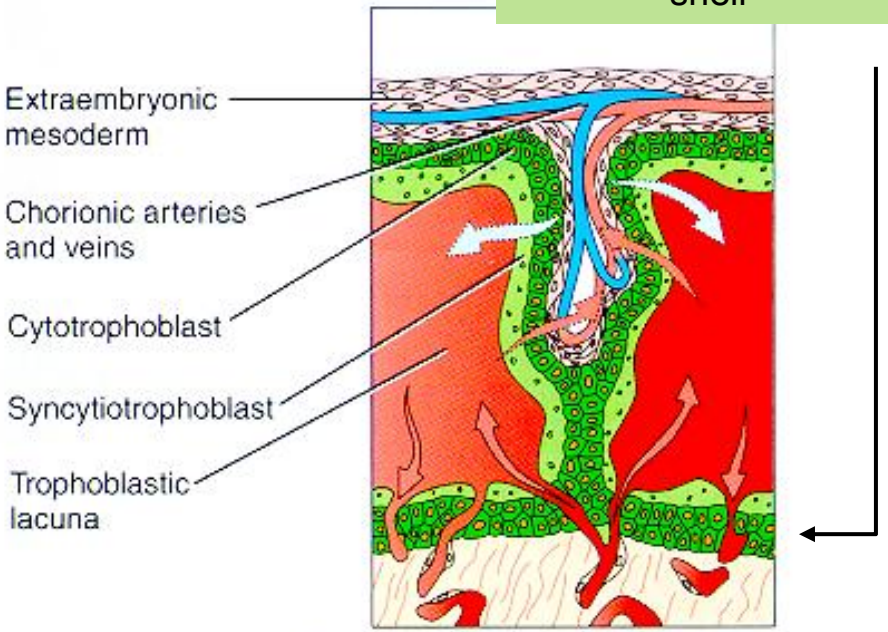


A Primary stem villus (11-13 days)

Outer cytotrophoblastic shell

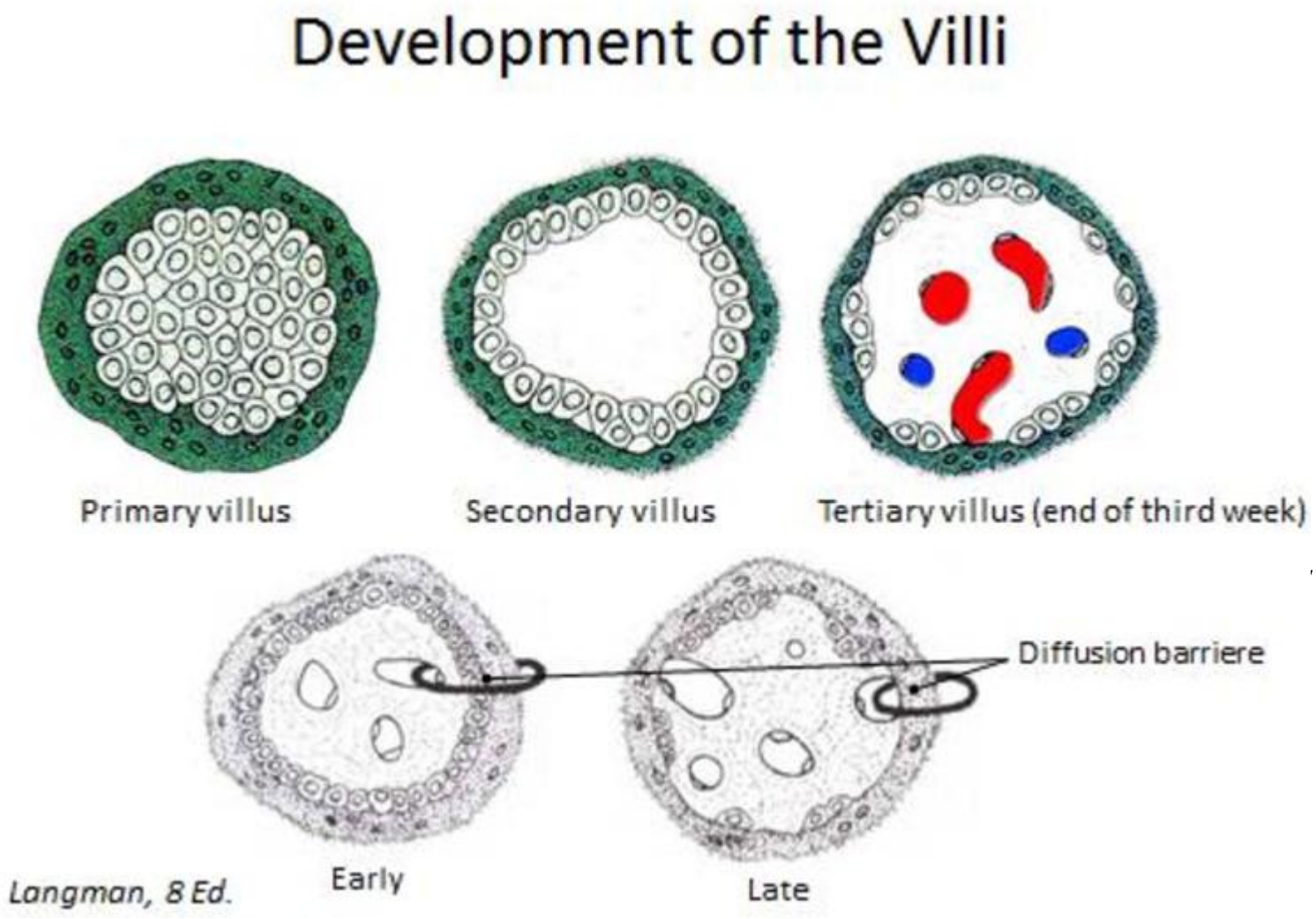


B Secondary stem villus (16 days)



C Tertiary stem villus (21 days)

Formation of primary, secondary and tertiary villi

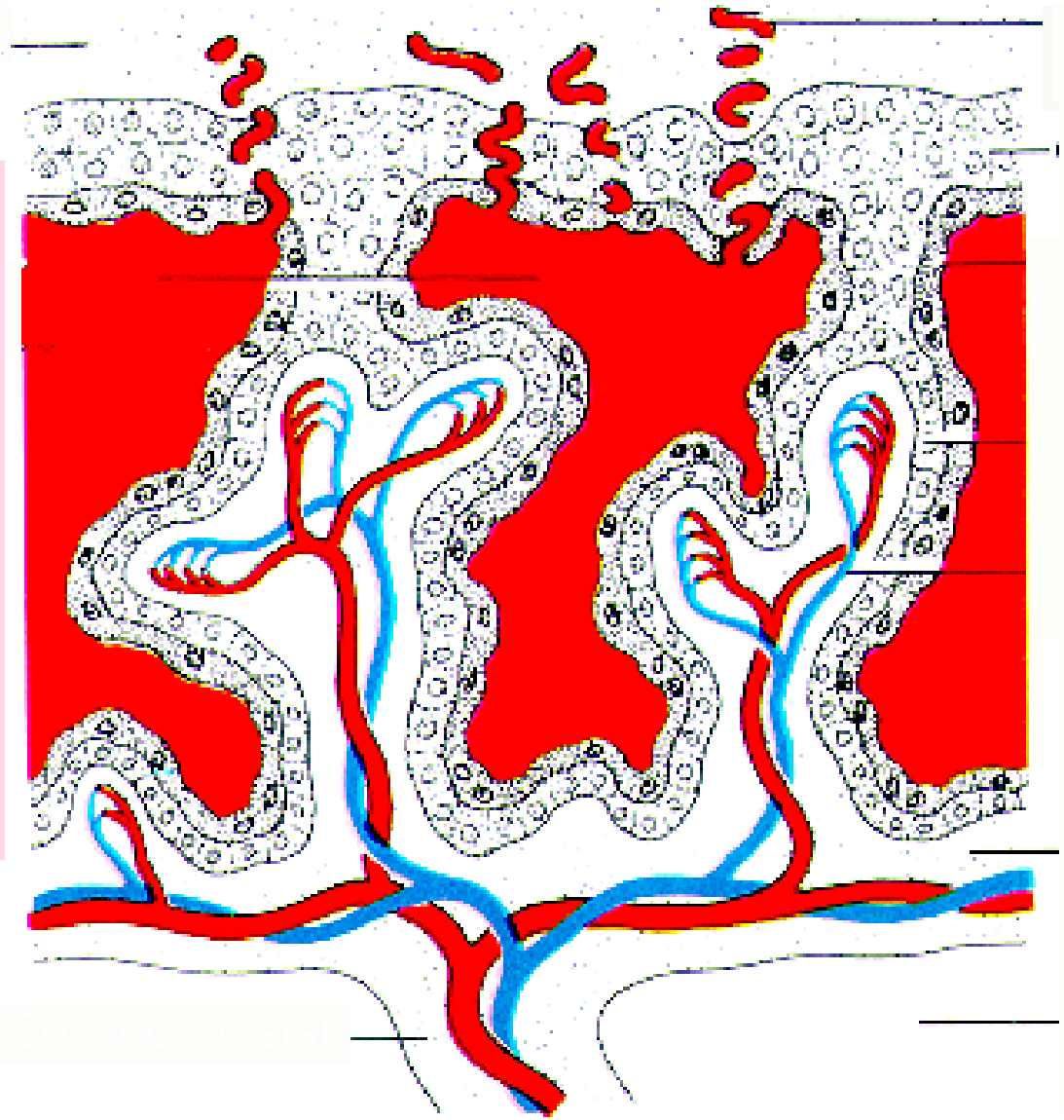


Villus at the end of the 3rd week of development

Decidua basalis

Endometrium

In the **junctional zone**, trophoblast (syncytial giant cells) and decidual cells intermingle. This zone i rich in amorphous extracellular material.



Spiral artery

Maternal vessels

Outer cytotrophoblastic shell

Syncytiotrophoblast

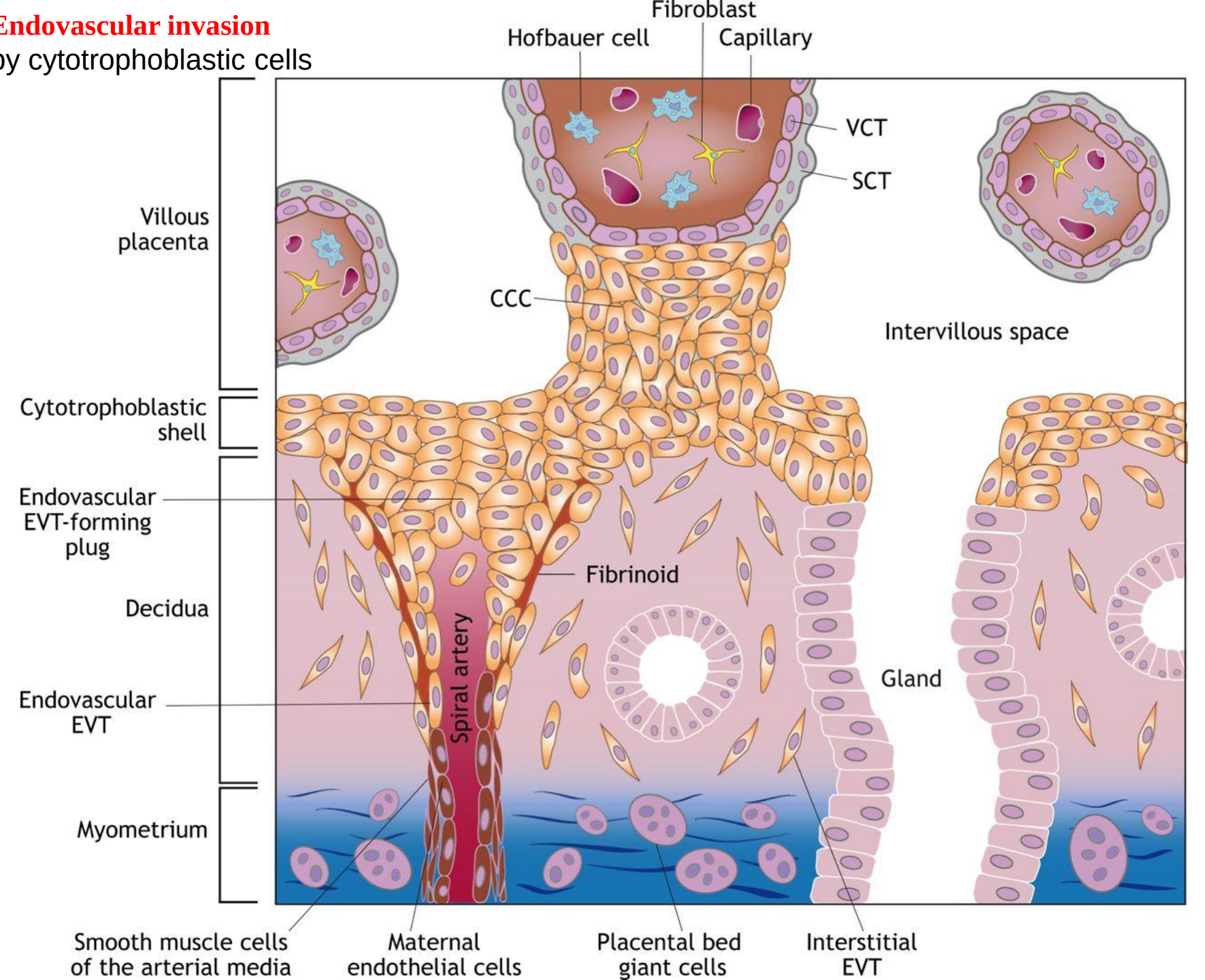
Cytotrophoblast

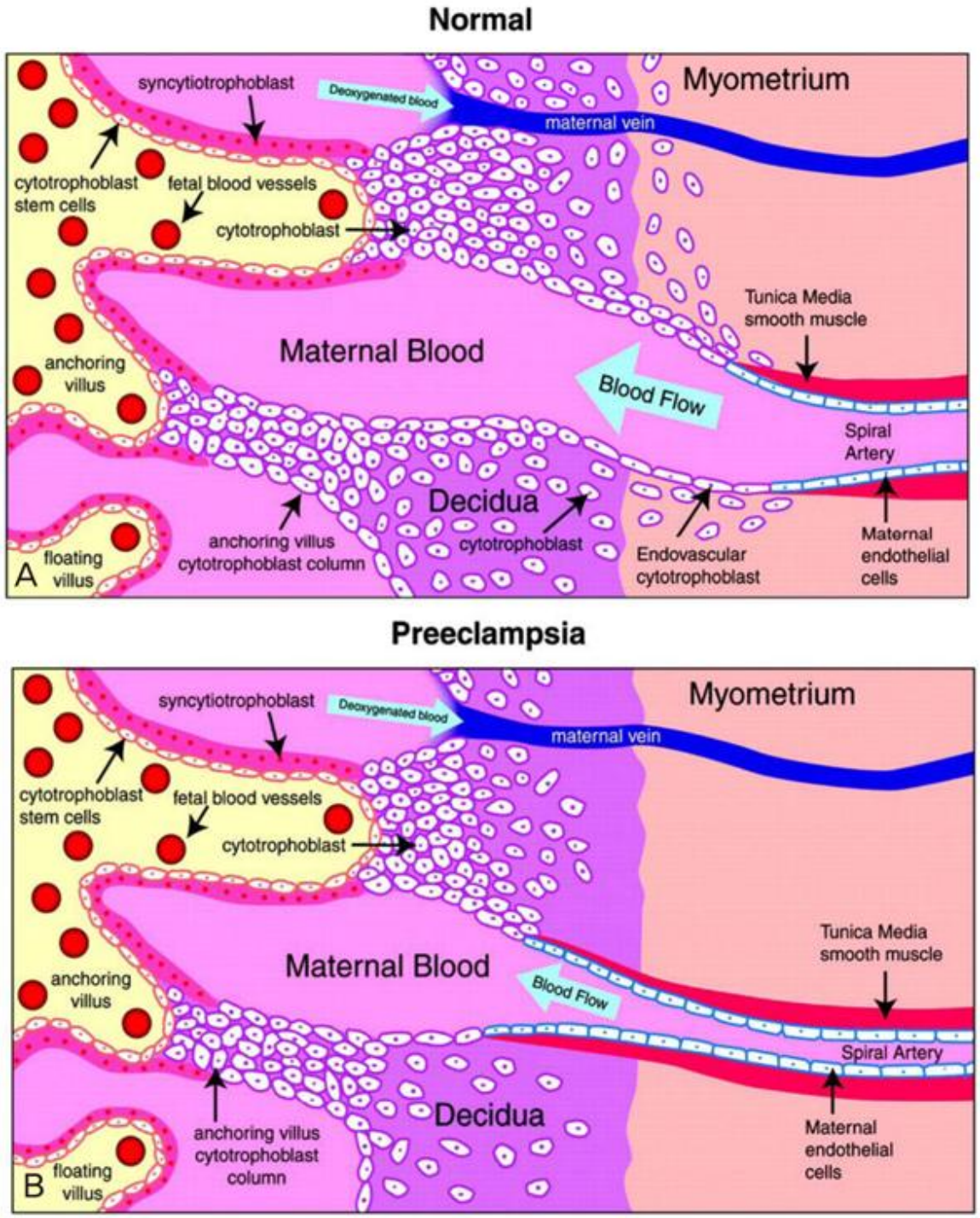
Mesoderm core with capillaries

Chorionic plate

Chorionic cavity

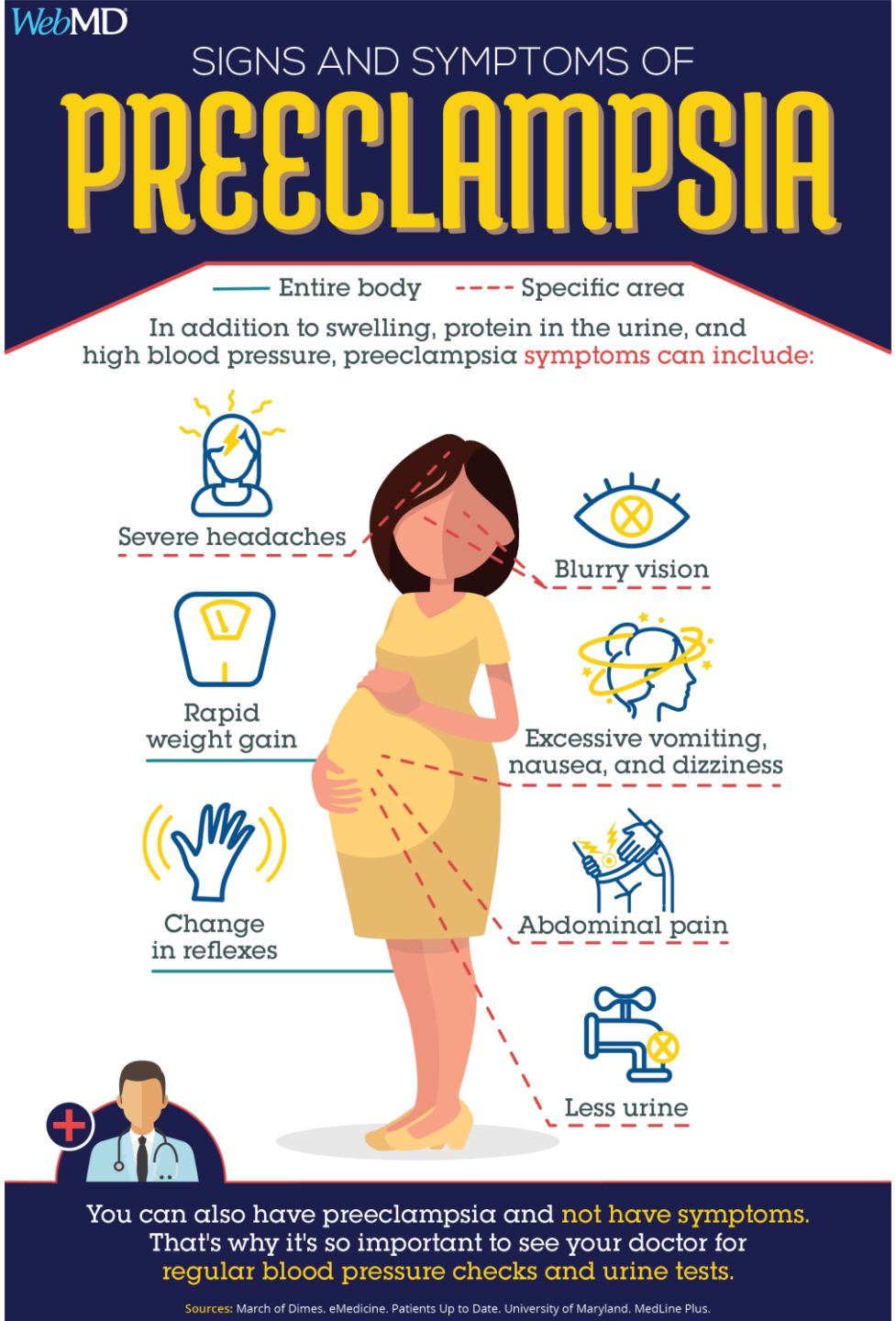
Endovascular invasion
by cytotrophoblastic cells





The developing placenta undergoes a process of vascular mimicry (referred to as pseudovasculogenesis) as cytotrophoblasts convert from an epithelial to an endothelial phenotype.

Pre-eclampsia (PE) is a disorder of pregnancy characterized by the maternal hypertension and proteinuria due to reduced organ perfusion



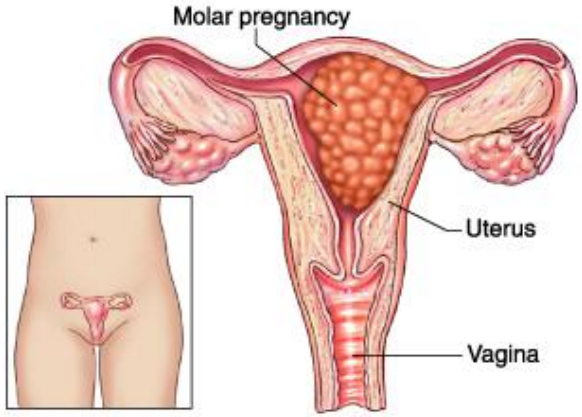
Preeclampsia begins suddenly anytime from approximatel 20 weeks gestation to term.

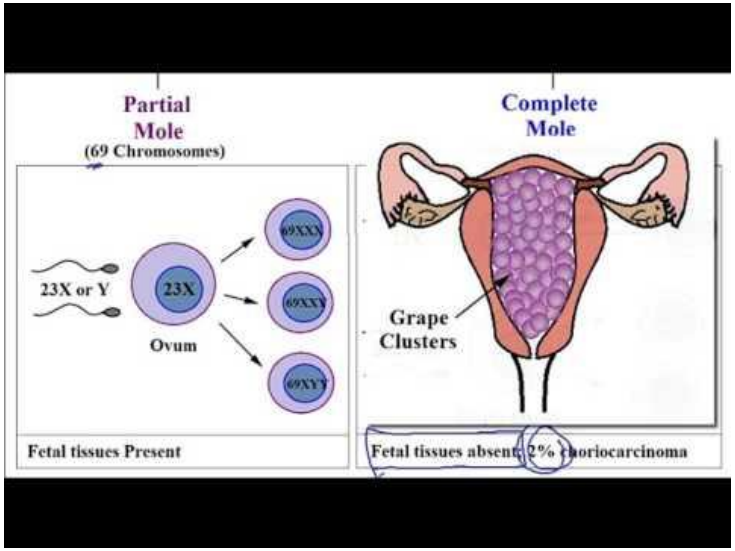
Preeclampsia commonly occurs in women with hydatidiform moles

Hydatidiform mole

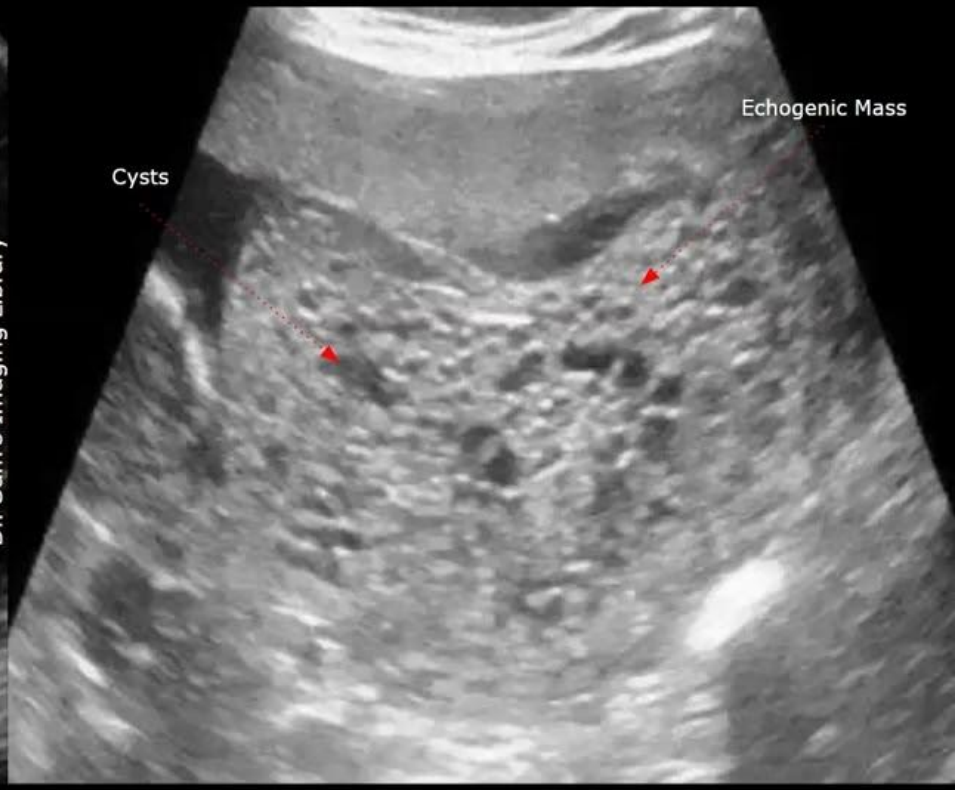
also known as molar pregnancy, is a subcategory of diseases under gestational trophoblastic disease, which originates from the placenta and can metastasize. It is unique because the tumor originates from gestational tissue rather than from maternal tissue.

In a molar pregnancy there is unusual and rapid growth of part or all of the placenta. The placenta becomes larger than normal and contains a number of cysts (sacs of fluid). The first part of the name 'hydatidiform' comes from the Greek word 'hydatid' meaning droplet. These droplets appear to burrow into the wall of the uterus, hence the name mole.





Longitudinal View

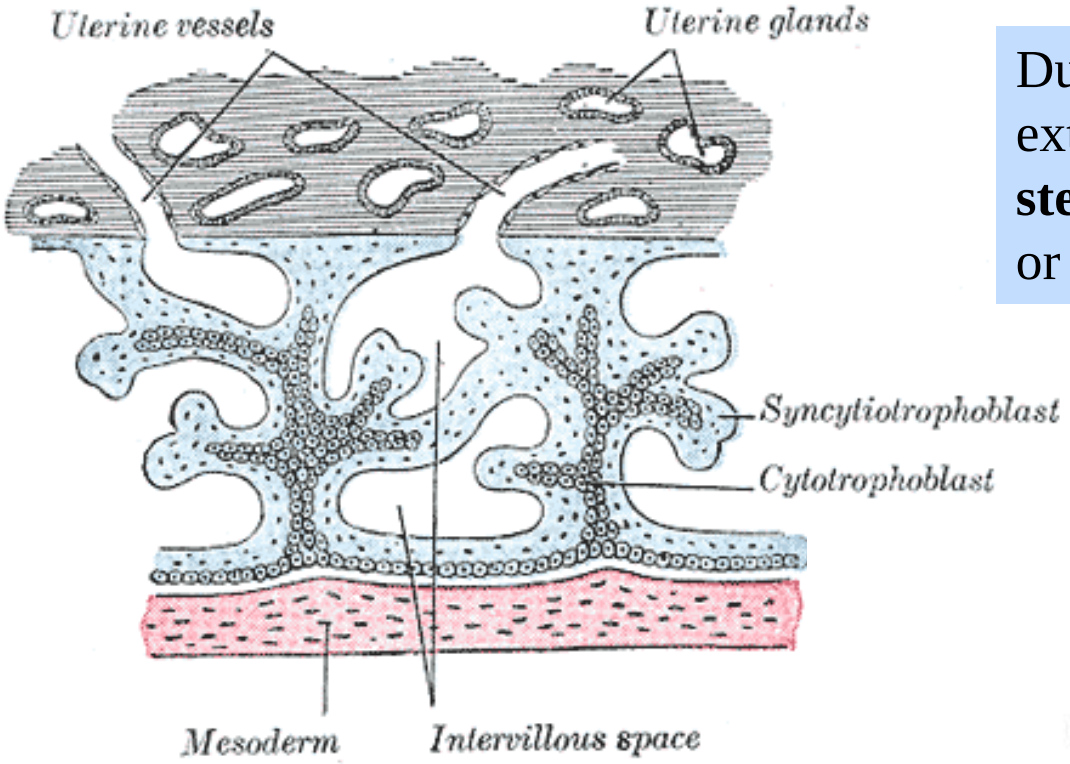


Normal Pregnancy

- Normal fetus and placenta

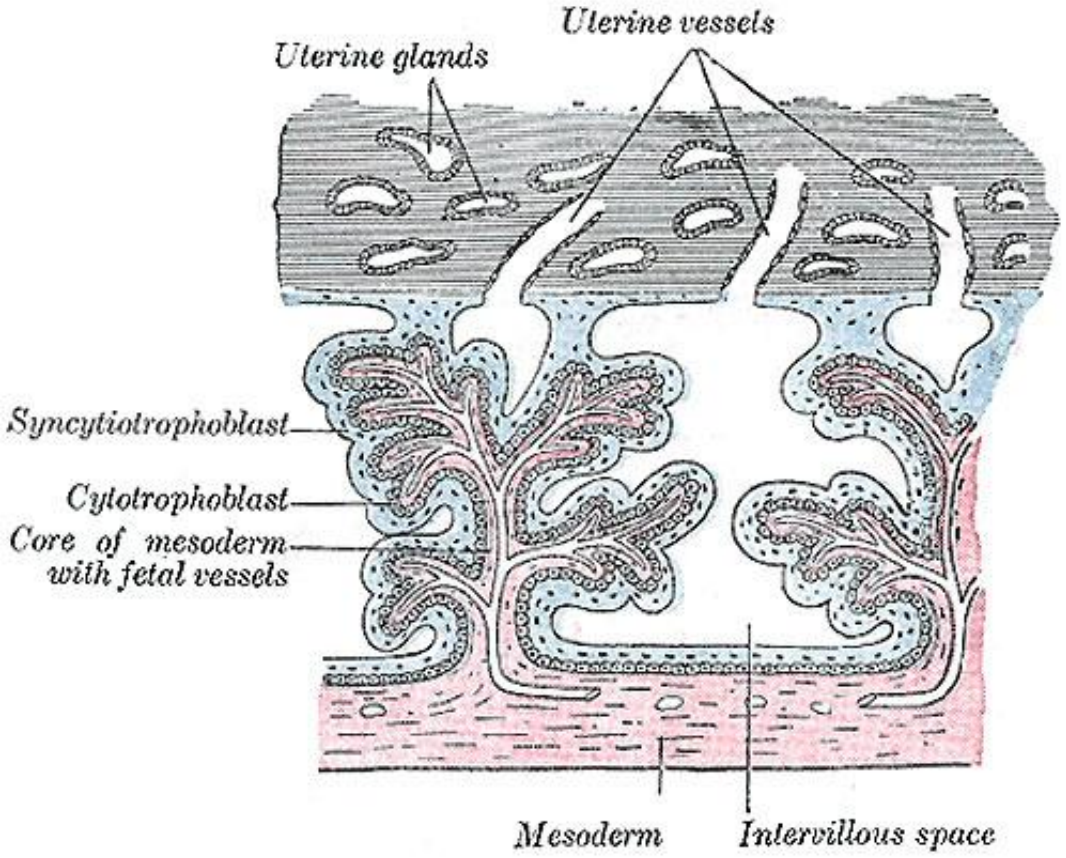
Complete Hydatidiform Mole

- No fetal parts visible
- **Snowstorm Appearance:** The "snowstorm" pattern is caused by a myriad of tiny cystic spaces (hydropic villi) interspersed within the echogenic mass.



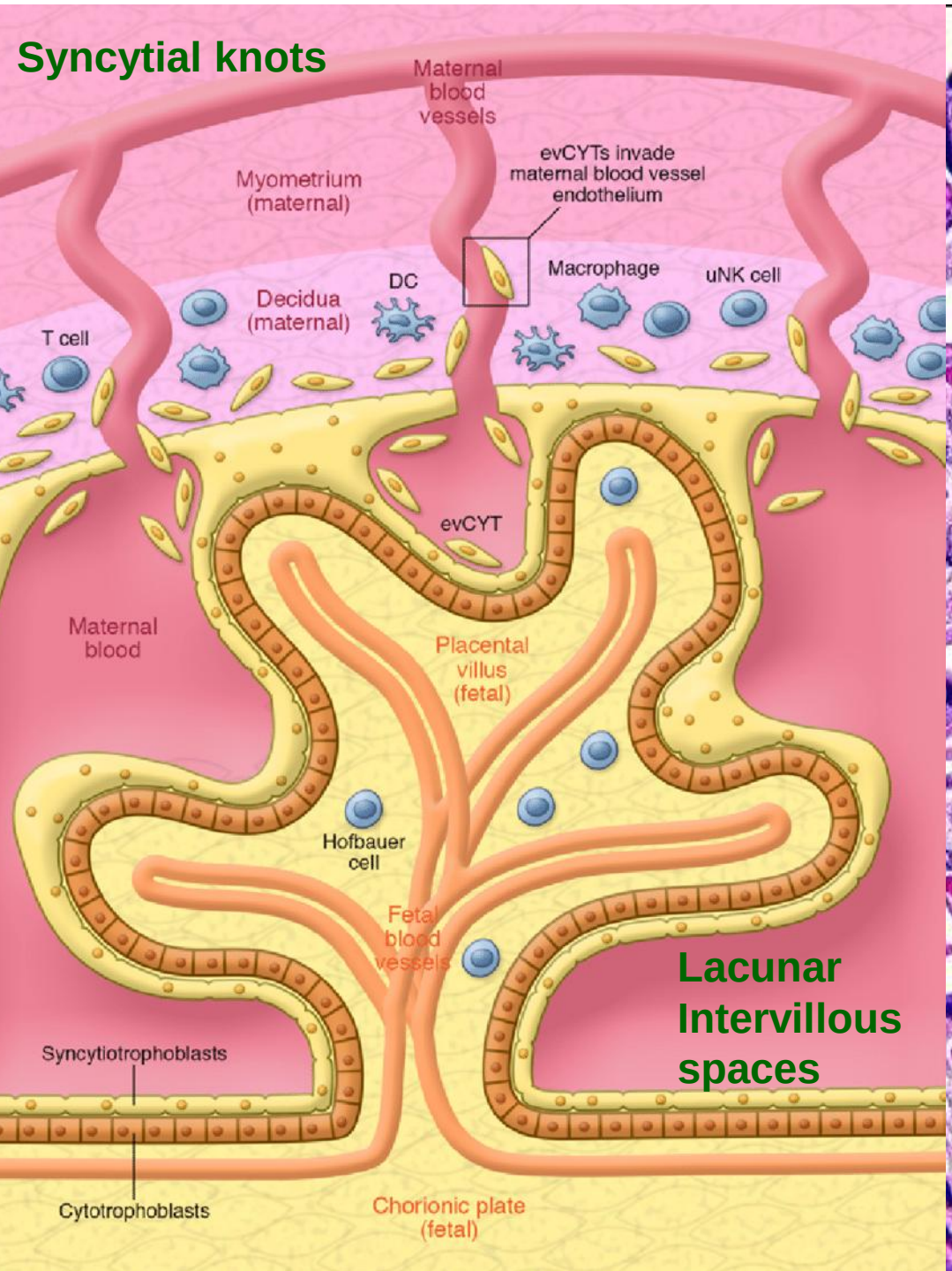
During the following months, small extensions grow out from existing **stem villi** into the surrounding lacunar or intervillous spaces

Free villi

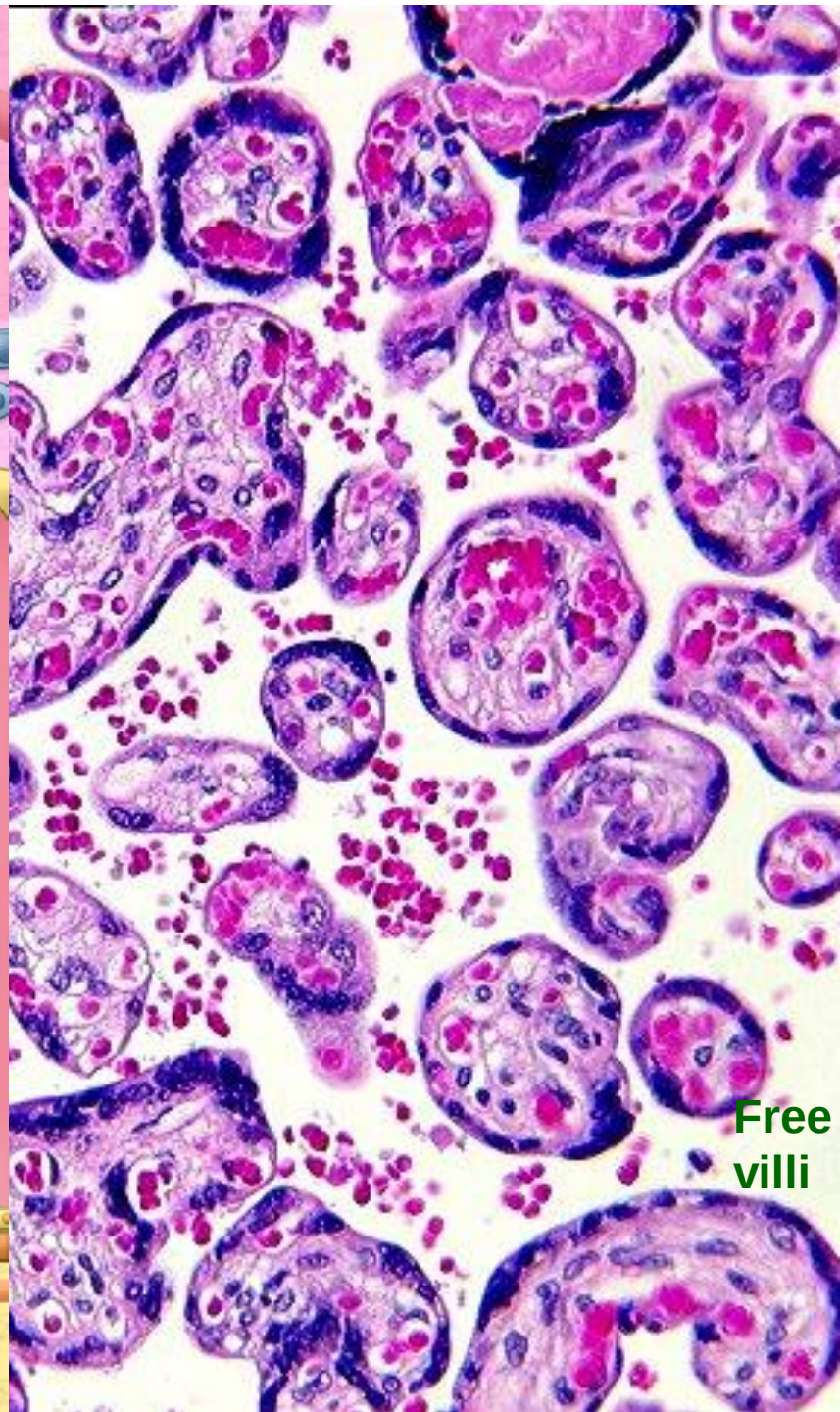


Lacunar Intervillous spaces

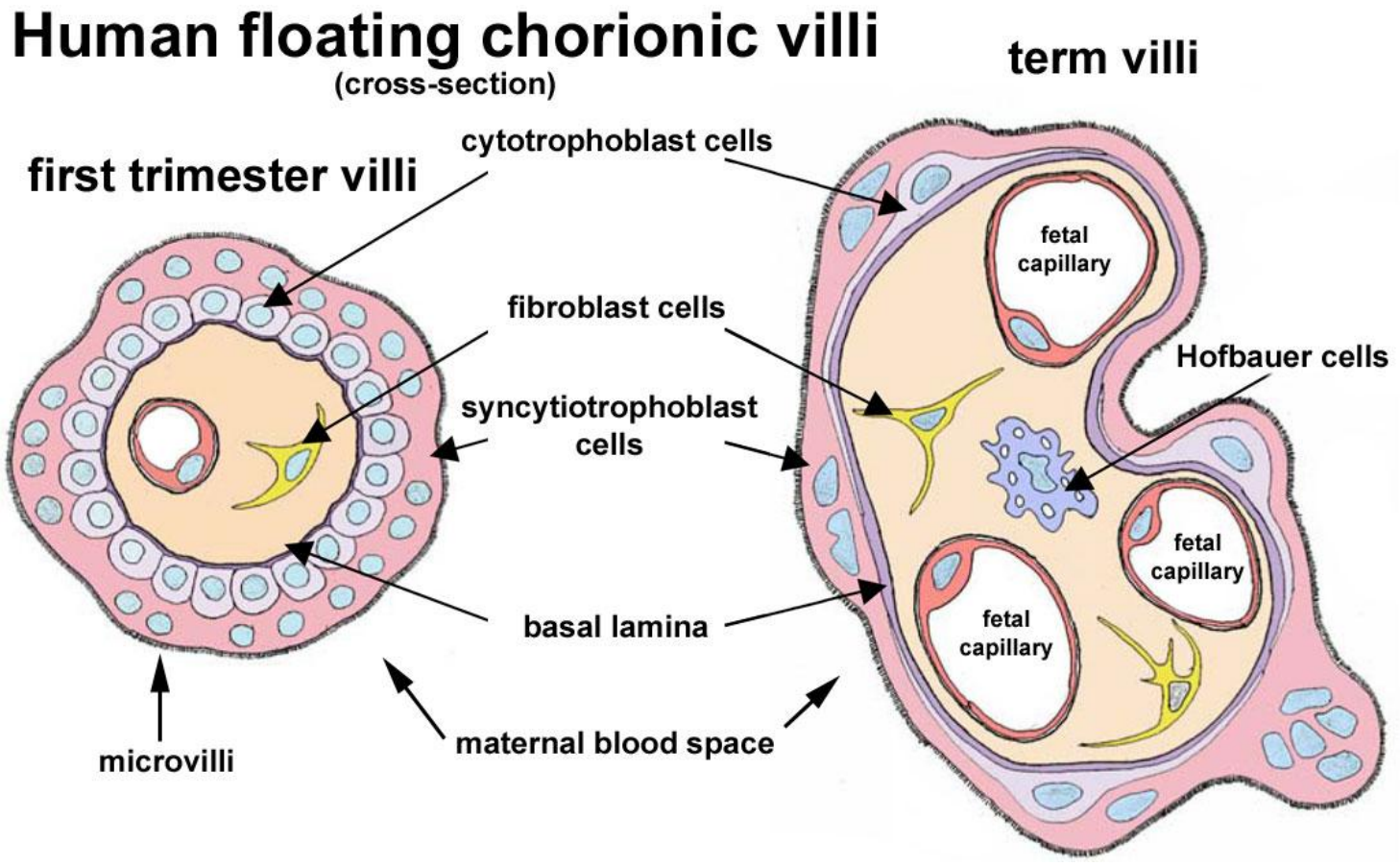
Syncytial knots



Lacunar Intervillous spaces



Free villi



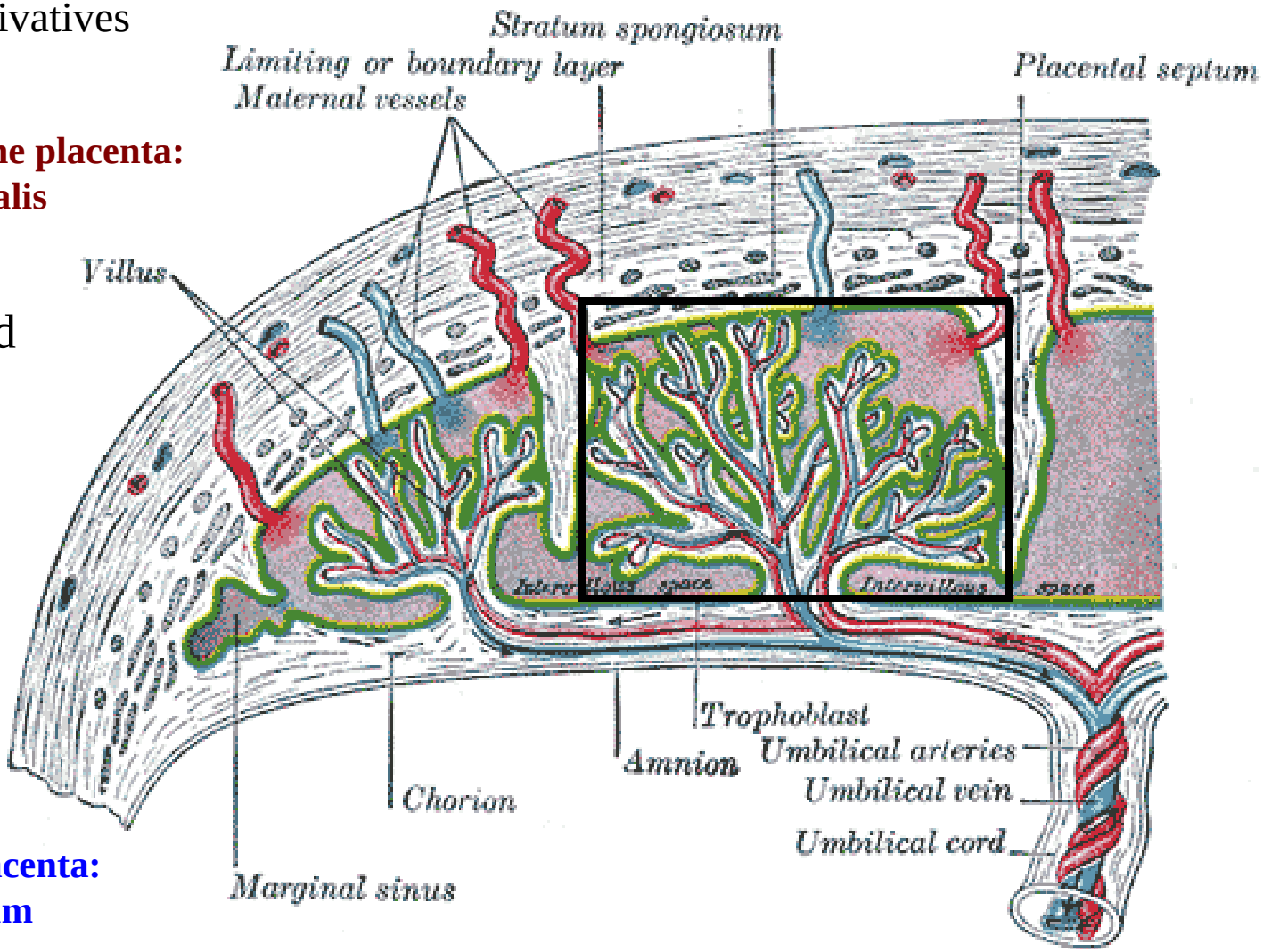
The syncytium and endothelial wall of the blood vessels are the **only layers** that separate maternal and fetal circulation
Placental barrier

The syncytium becomes very thin, and large pieces containing several nuclei (known as **syncytial knots**) may break off and drop into the intervillous spaces and enter the maternal circulation and usually degenerate without causing any symptoms

The human placenta is considered to be of the **hemochorial** type, because the maternal blood in the intervillous spaces is separated from the fetal blood by a chorionic derivatives

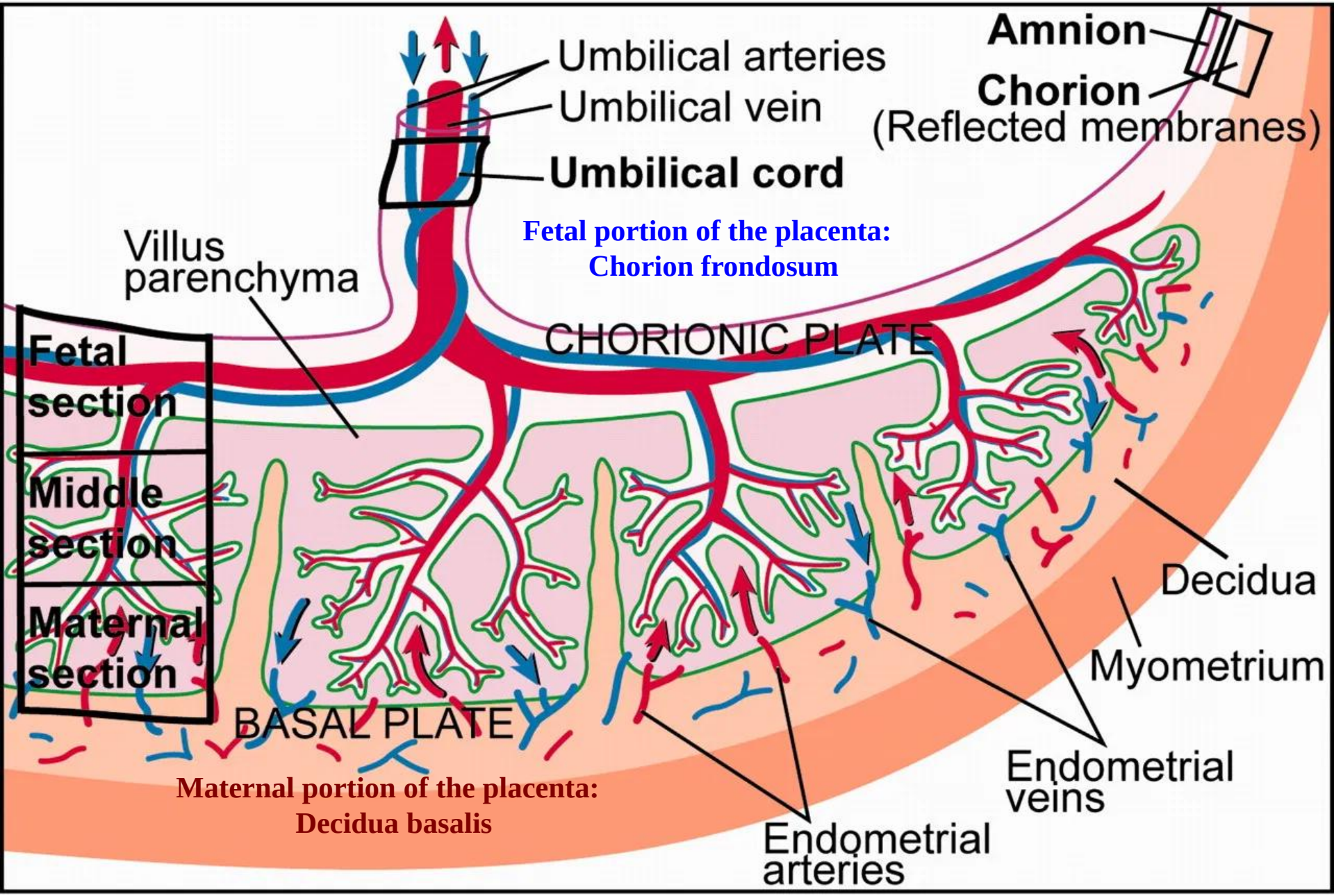
Maternal portion of the placenta:
Decidua basalis

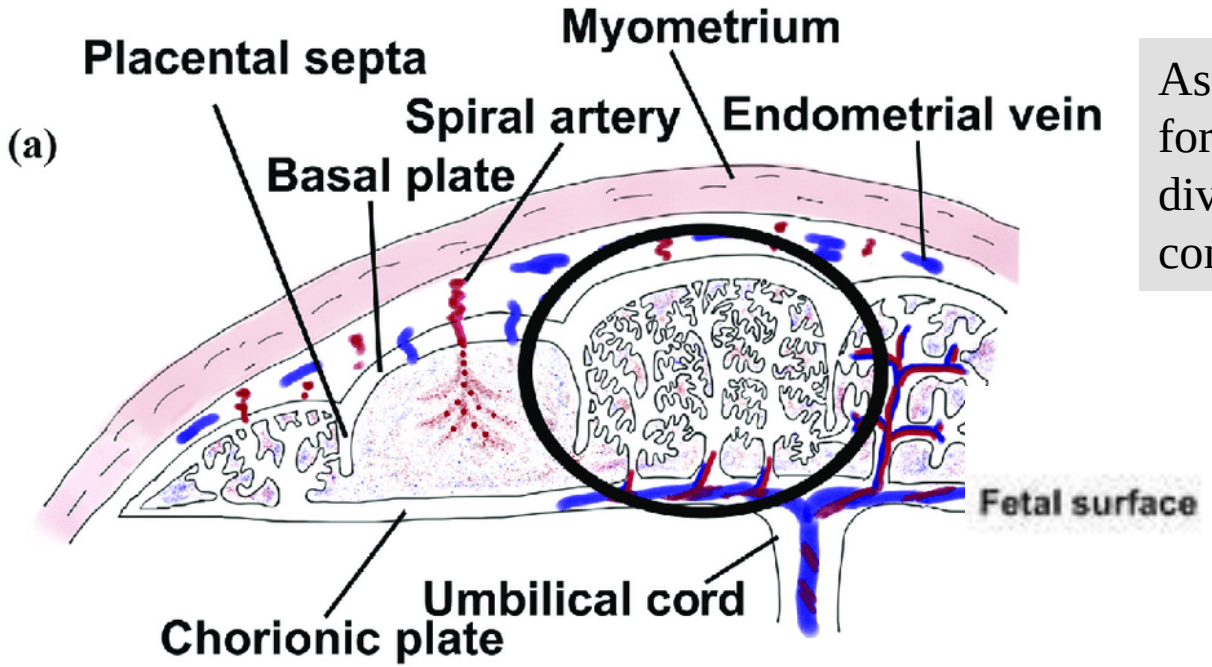
During the fourth and fifth months, the decidua forms a number of **decidual septa**



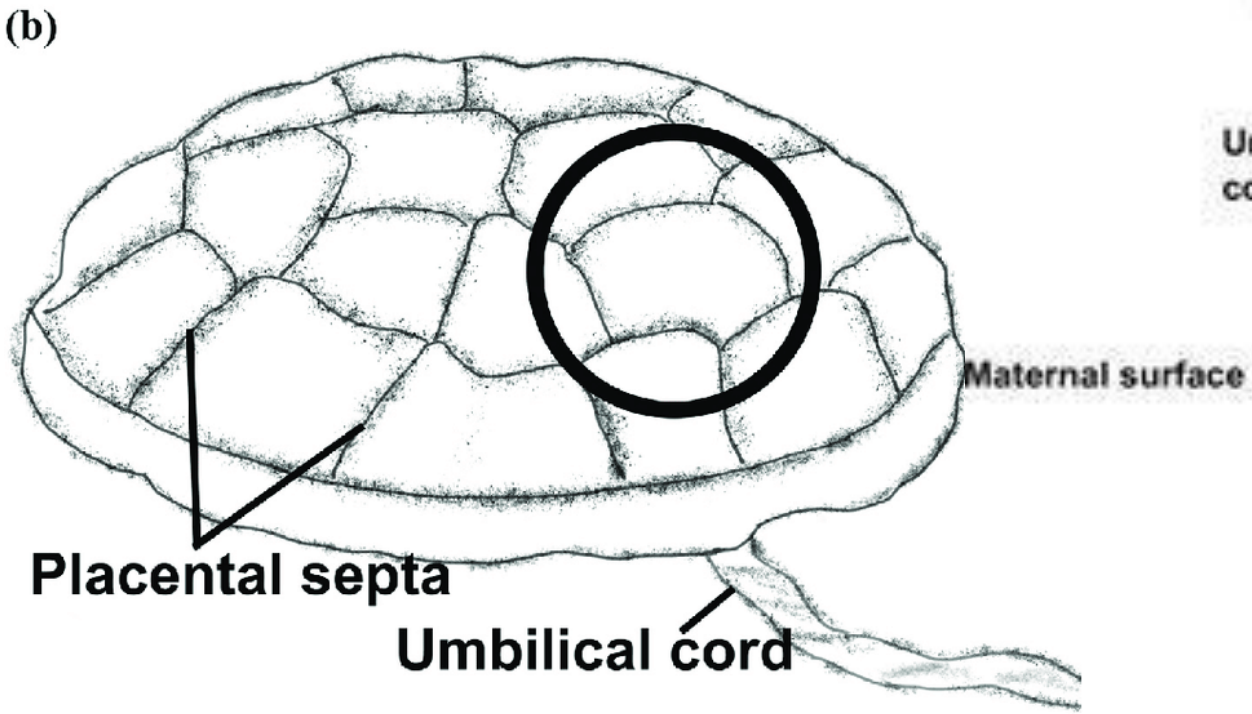
Fetal portion of the placenta:
Chorion frondosum

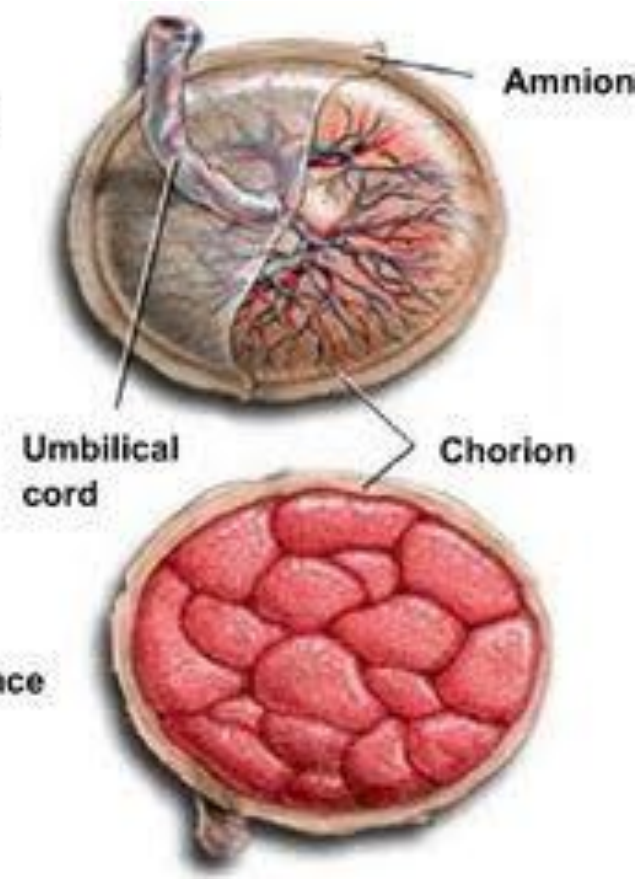
Because the decidual septa do not reach the chorionic plate, contact between intervillous spaces in the various cotyledons is maintained.

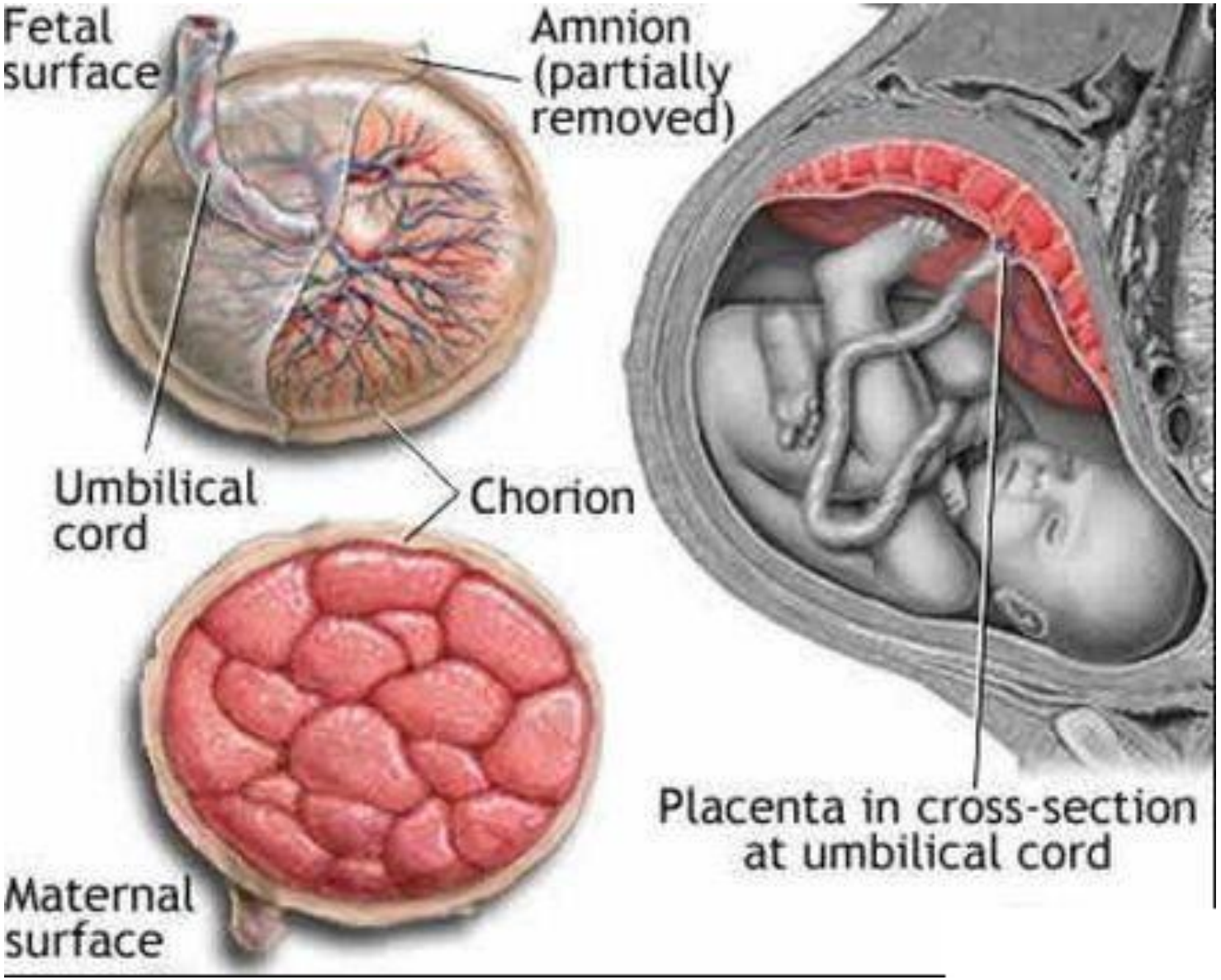

Amnion
Chorion
(Reflected membranes)
Umbilical arteries
Umbilical vein
Umbilical cord
Fetal portion of the placenta:
Chorion frondosum
Villus
parenchyma
CHORIONIC PLATE
Fetal
section
Middle
section
Maternal
section
Decidua
Myometrium
BASAL PLATE
Endometrial
veins
Maternal portion of the placenta:
Decidua basalis
Endometrial
arteries



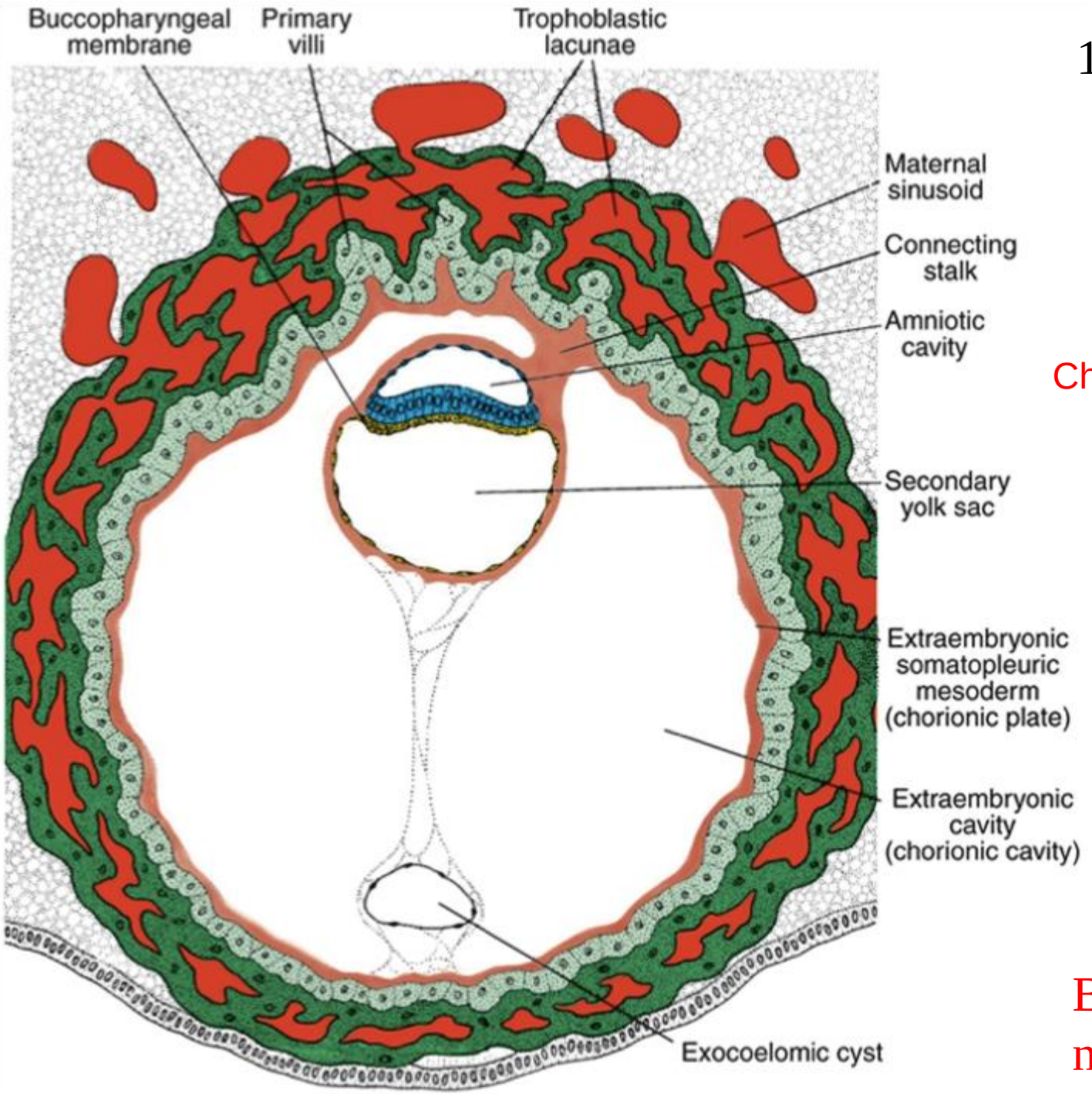
As a results of septum formation, the placenta is divided into a number of compartments, or **cotyledons**






Fetal surface
Amnion (partially removed)
Umbilical cord
Chorion
Maternal surface
Placenta in cross-section at umbilical cord

13-day

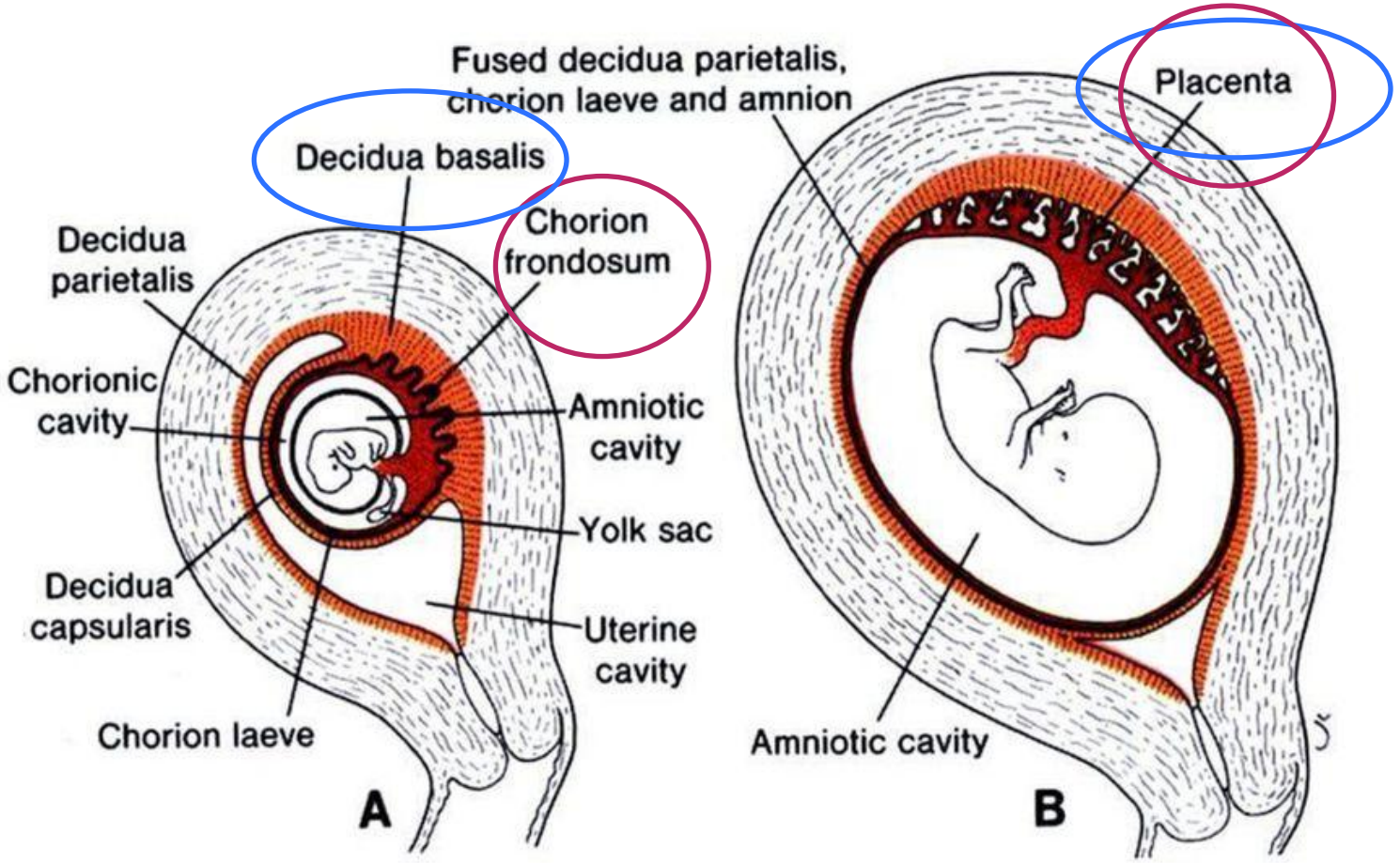


Chorion frondosum

Chorion laeve

Bleeding
near 28th day

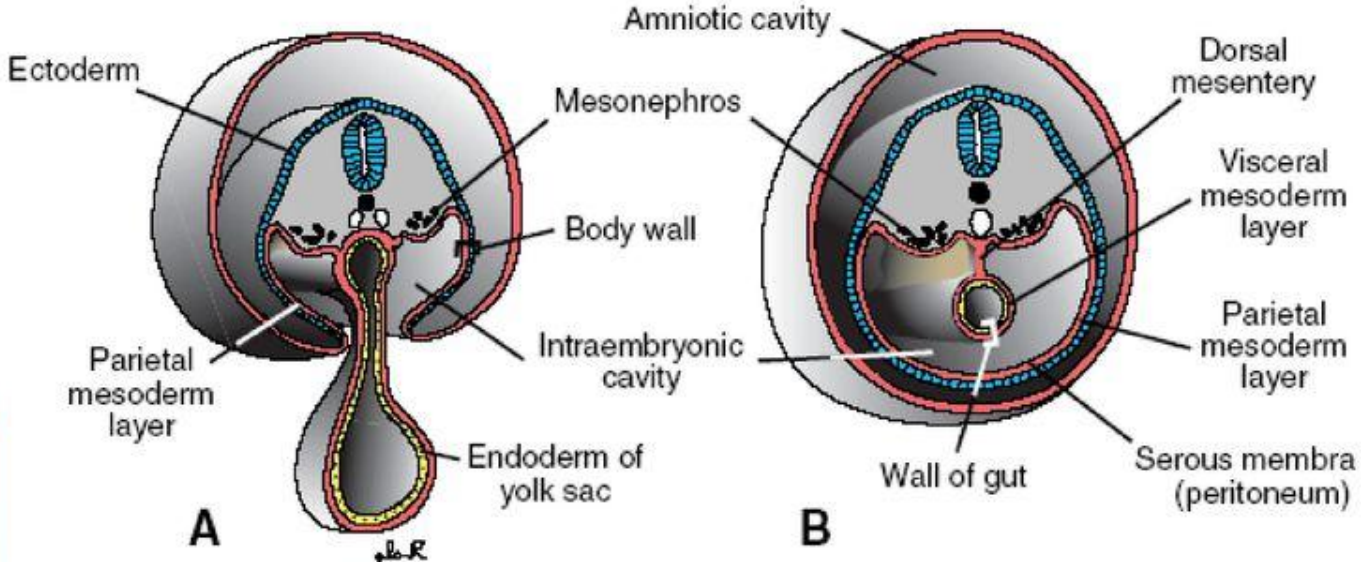
When the enlarging embryo finally completely fills the endometrial cavity during the third or fourth month of pregnancy, the **decidua capsularis fuses with the decidua parietalis** opposite it and obliterates the endometrial cavity.



Fusion of the amnion and chorion forms the **amniochorionic membrane,** Chorionic cavity obliterates, **amniochorionic membrane** rupture during labor

The umbilical cord and amnion:

- The cephalocaudal and lateral folding of the embryonic disk during the *2nd month* of development lead to the formation of a ring at the junction of the amnion and the ectoderm. This ring is called *the primitive umbilical ring* that contains the following:



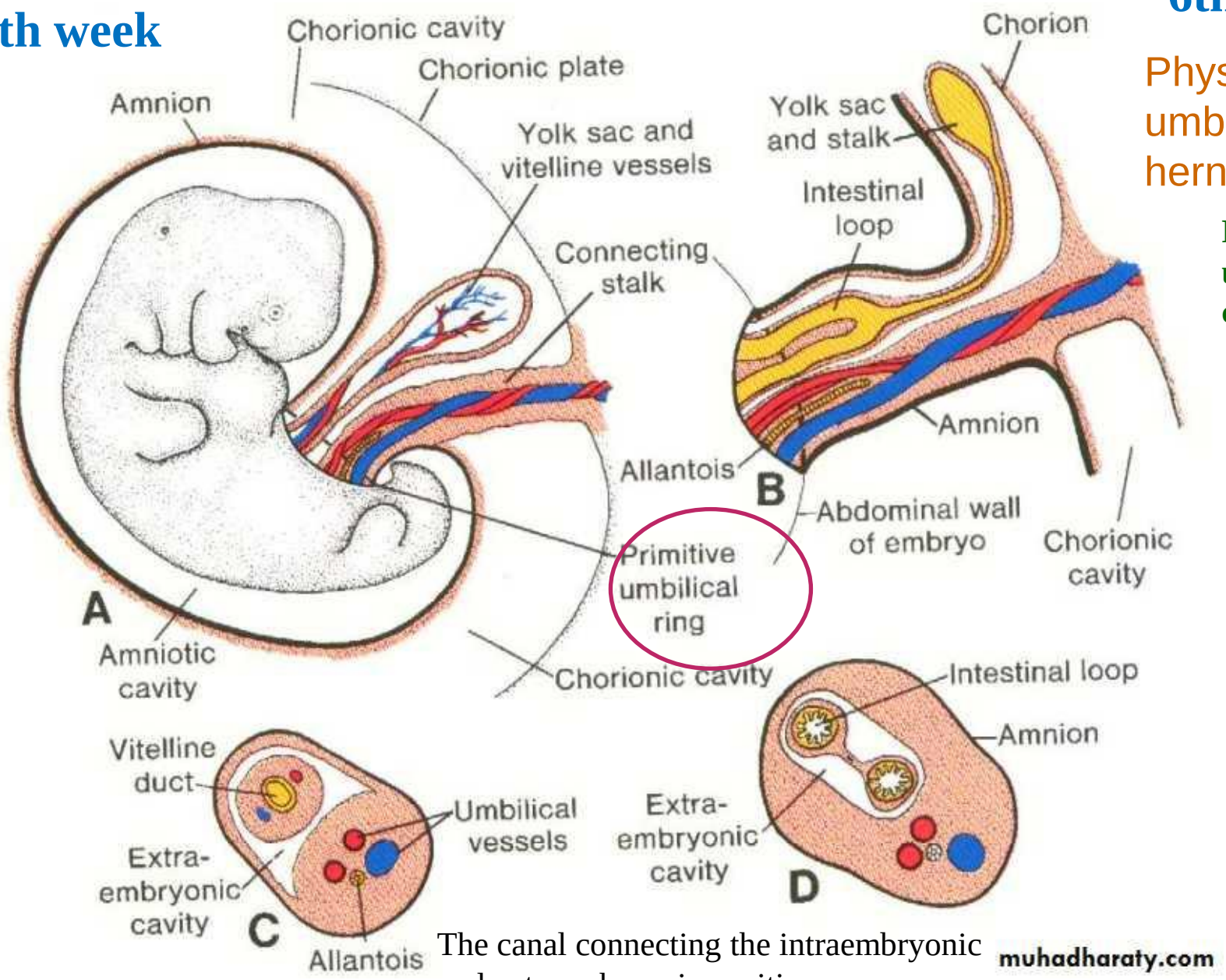
The ventral body wall closes completely exept for the umbilical region where the connecting stalk and yolk sac duct remain attached

Fifth week

6th week

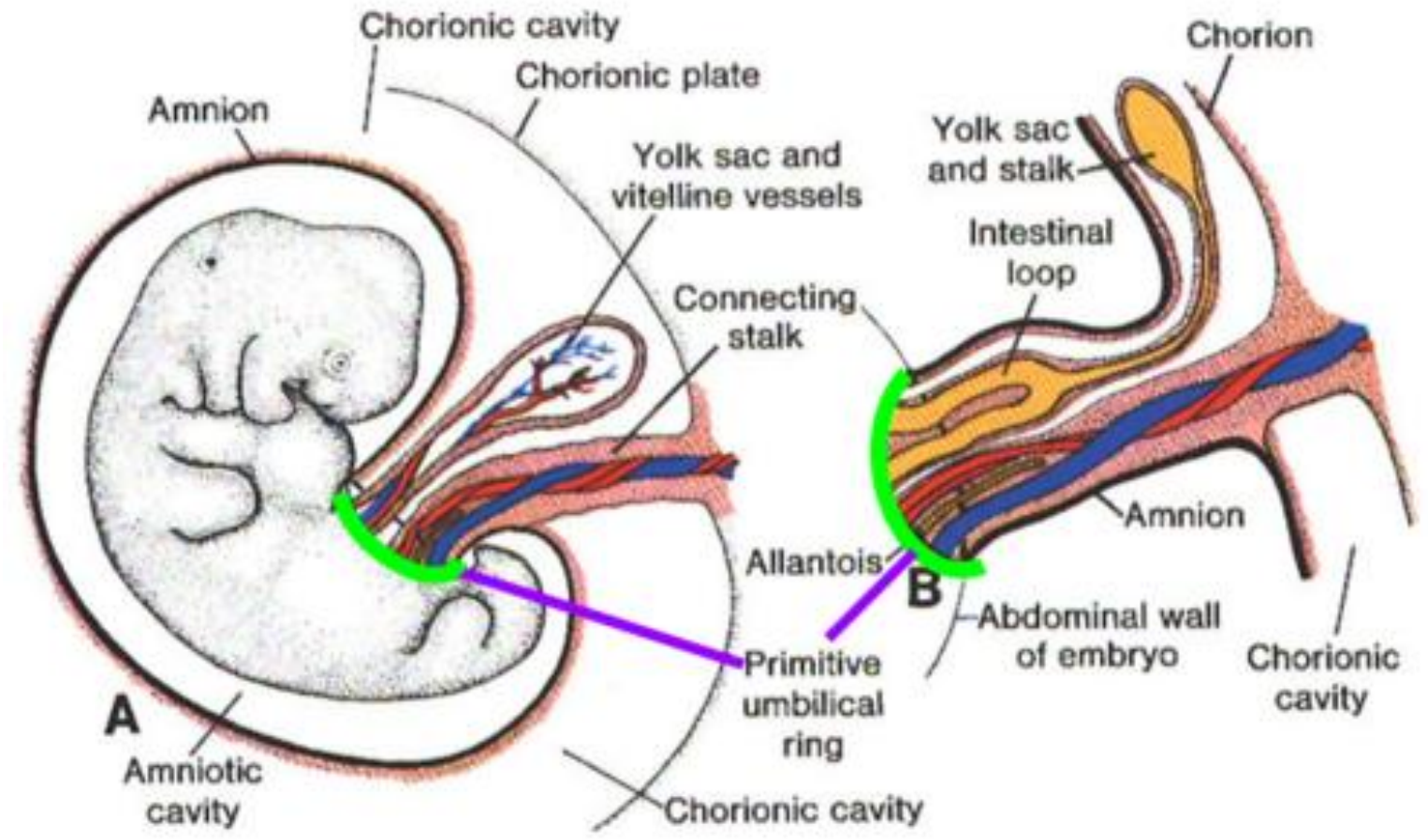
Physiological umbilical hernia

Primitive umbilical cord



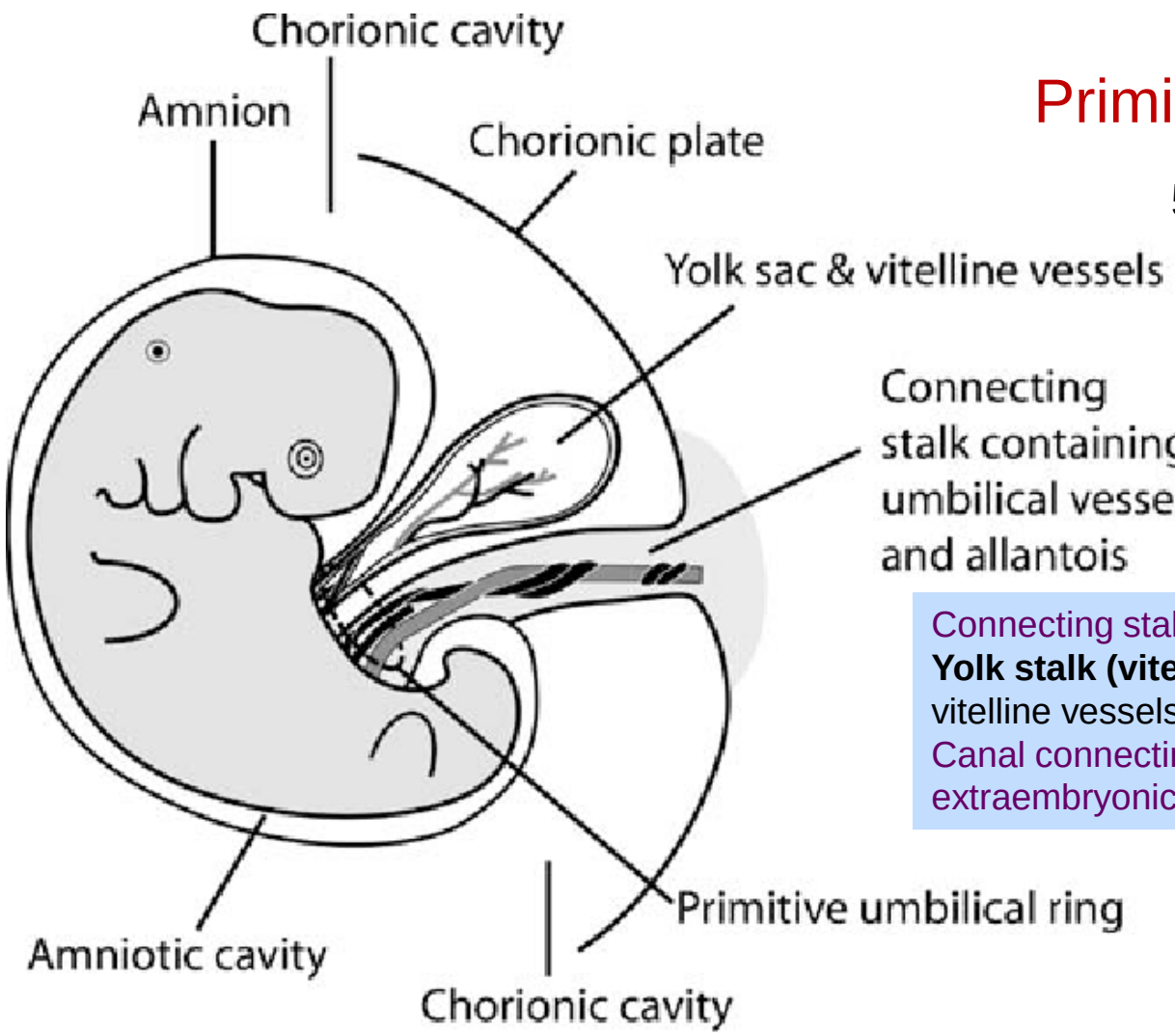
The canal connecting the intraembryonic and extraembryonic cavities

The oval line of reflections between the **amnion** and **embryonic ectoderm** is a **amnio-ectodermal junction = primitive umbilical ring**



Primitive umbilical **ring**

5th week of development

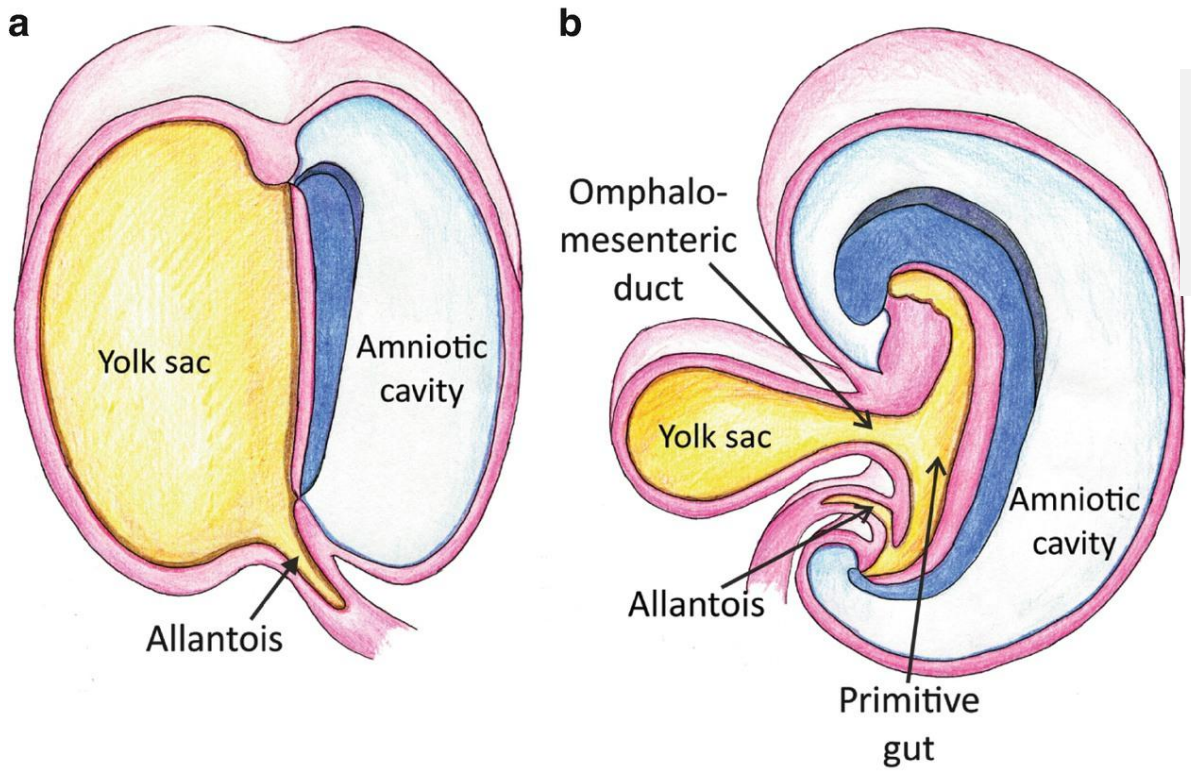


Connecting stalk: allantois and umbilical vessels
Yolk stalk (vitelline duct) accompanied by the vitelline vessels
Canal connecting the intraembryonic and extraembryonic cavities

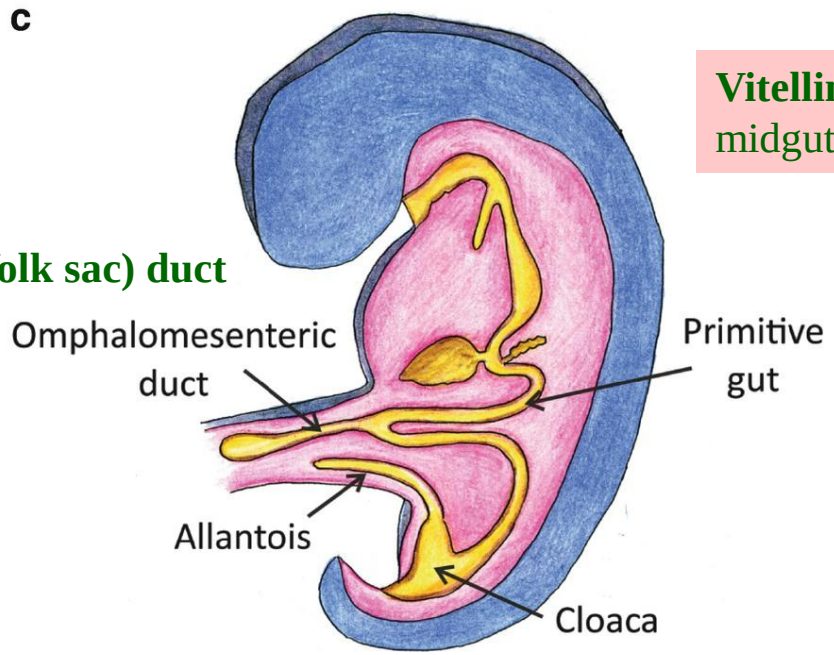
When the amniotic cavity enlardes, the amnion begins to envelop the connecting and yolk sac stalks, crowding them together and giving rise to the **primitive umbilical cord**

Definitive Umbilical Cord

- Return of intestinal loop to abdominal cavity at 3rd month.
- Obliteration of extra-embryonic part of vitelline vessels and one umbilical vein with persistence of other vein and 2 umbilical arteries.
- Degeneration of vitelline duct and allantois
- Transformation of mesoderm of connecting stalk into wharton's jelly.



Stomodeum is separates from the foregut by **oropharyngeal membrane** (only ectoderm and endoderm)

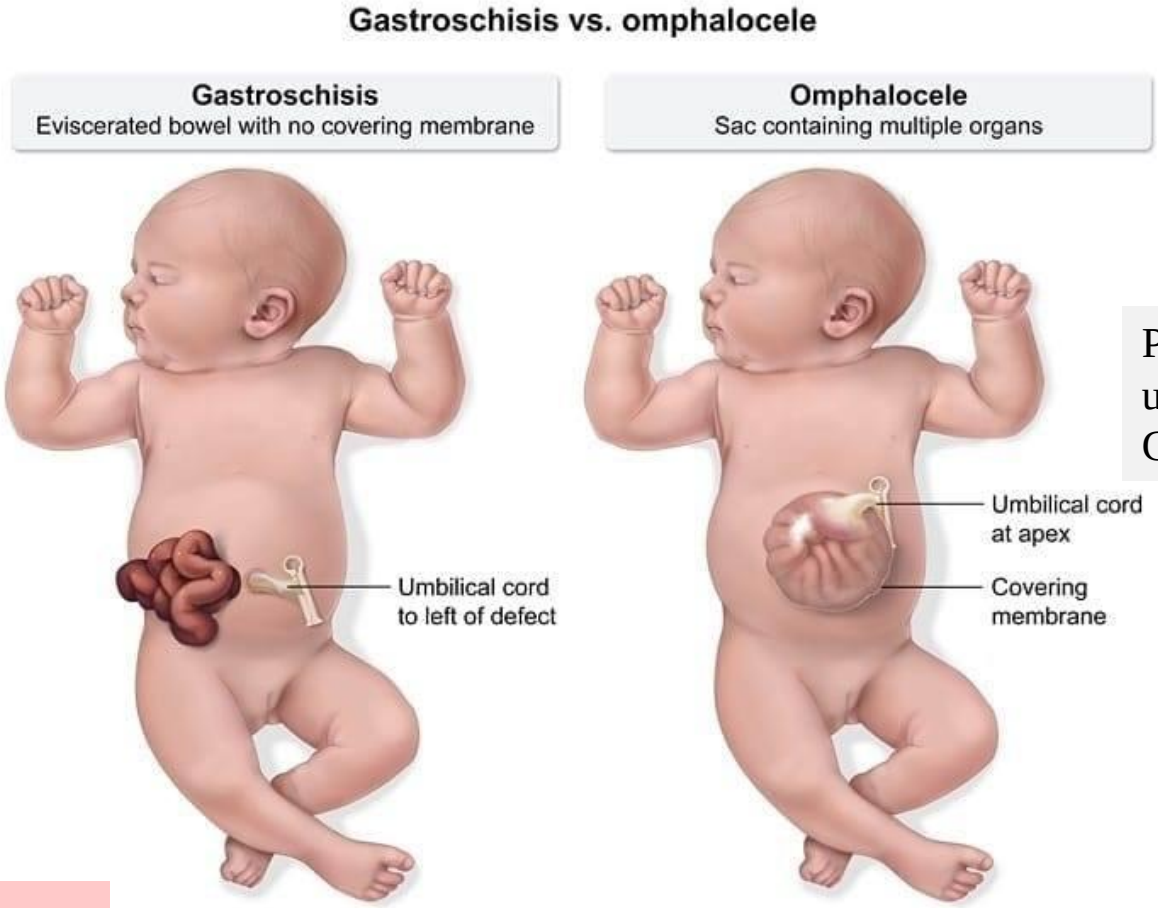


Vitelline (Yolk sac) duct connects midgut with the yolk sac

Vitelline (Yolk sac) duct

Upper part of the anal canal is separates from **proctodeum** (lower part of the anal canal) by **cloacal membrane** (only ectoderm and endoderm)

Ventral body wall defects



Protrudes into umbilical cord
Covered by amnion

After delivery
exposed to air
No peritoneal layer

Body wall closure fails in the abdominal region

It originate when portion of the gut tube that normally herniates into the umbilical cord during the 6th to the 10th weeks fails to return to the abdominal cavity

DEVELOPMENT OF THE FETUS

Monthly changes

12 week of development:

- Primary ossification centers are present in the long bones and skull

- External genitalia develop to such a degree that the sex of the fetus can be determined by external examination (ultrasound)

- The intestinal loops have withdrawn into the abdominal cavity

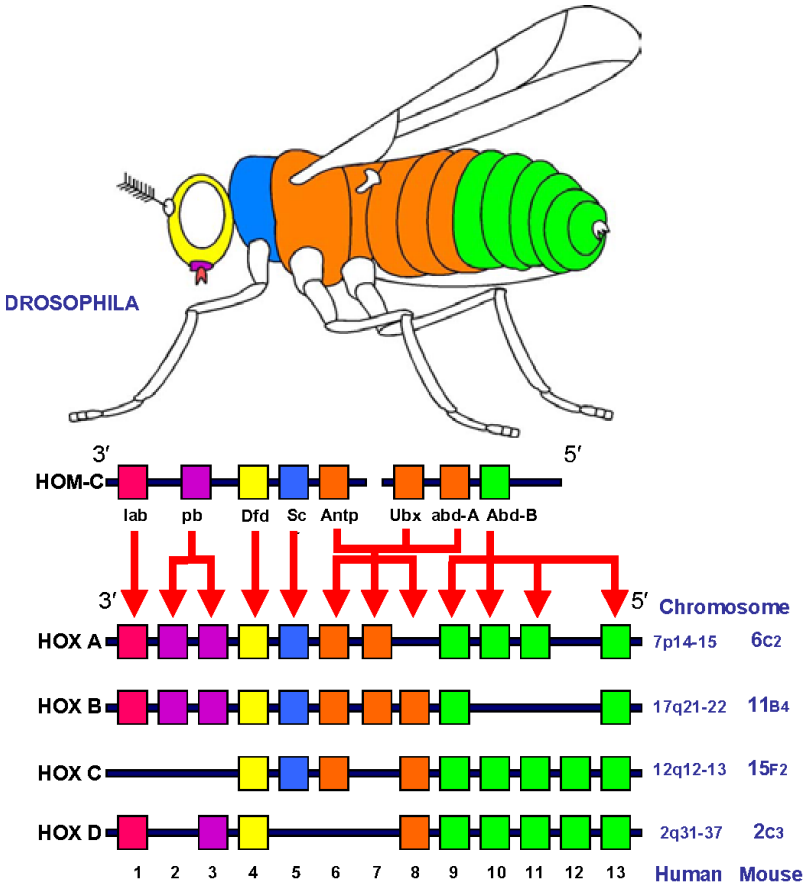
Alagille syndrome

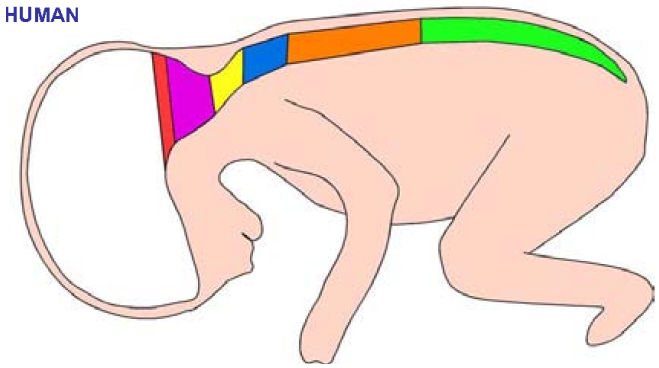
Rare genetic disorder that can affect multiple organ systems of the body including the liver, heart, skeleton, eyes and kidneys

Common symptoms, which often develop during the first three months of life, include blockage of the flow of bile from the liver (cholestasis), yellowing of the skin and mucous membranes (jaundice), poor weight gain and growth.

Caused by the mutation within NOTCH pathway

Patterning of the anteroposterior axis: Regulation by homeobox genes





HOX genes are evolutionarily highly conserved. The HOX proteins which they encode are master regulators of embryonic development and continue to be expressed throughout postnatal life. The 39 human HOX genes are located in four clusters (A-D) on different chromosomes at 7p15, 17q21.2, 12q13, and 2q31 respectively

PRENATAL DIAGNOSIS

• **Ultrasound** (fetal age and growth aassessed by crown-rump lenght during the 5th to the 10th weeks of gestations, neural tube, abdominal and facial defects, **nuchal translucency - Down syndrome**)

• **Maternal serum scrining** (alfa-fetoprotein: decreased – Down syndrome, trisomy 18….; increased: neural tube defects, bladder extrophy…..)

• **Amniocentesis** (for karyotyping and other genetic analysis, and AFP and acetylcholinesterase analysis)

• **Chorionic villus sampling** (genetic characterisation of the fetus)