Human Embryology-4

- ✓ Development of Mesoderm
- ✓ Development of Endoderm
- ✓ Teratology
- ✓ Most Common Birth Defects

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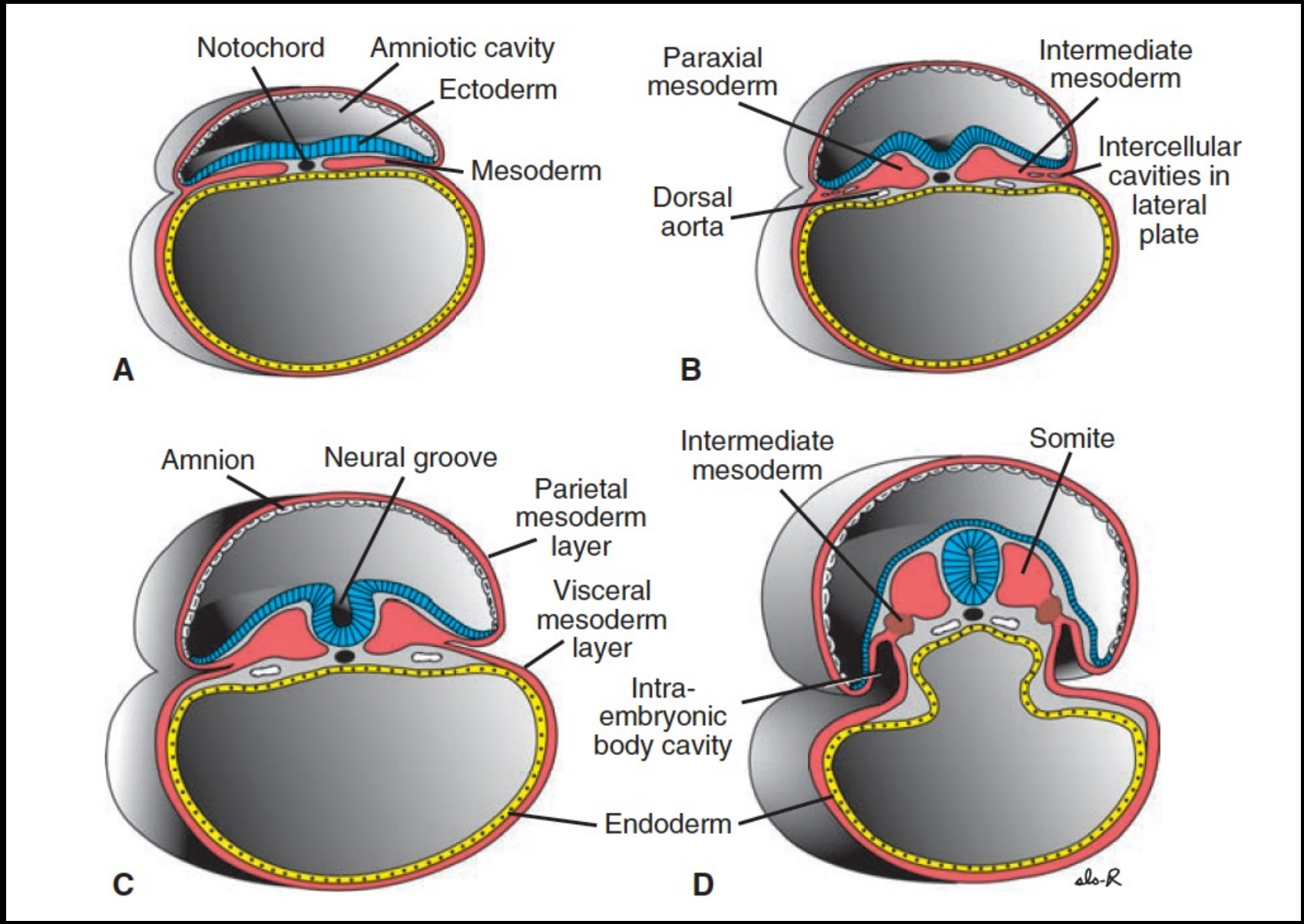
Further Development of Mesoderm



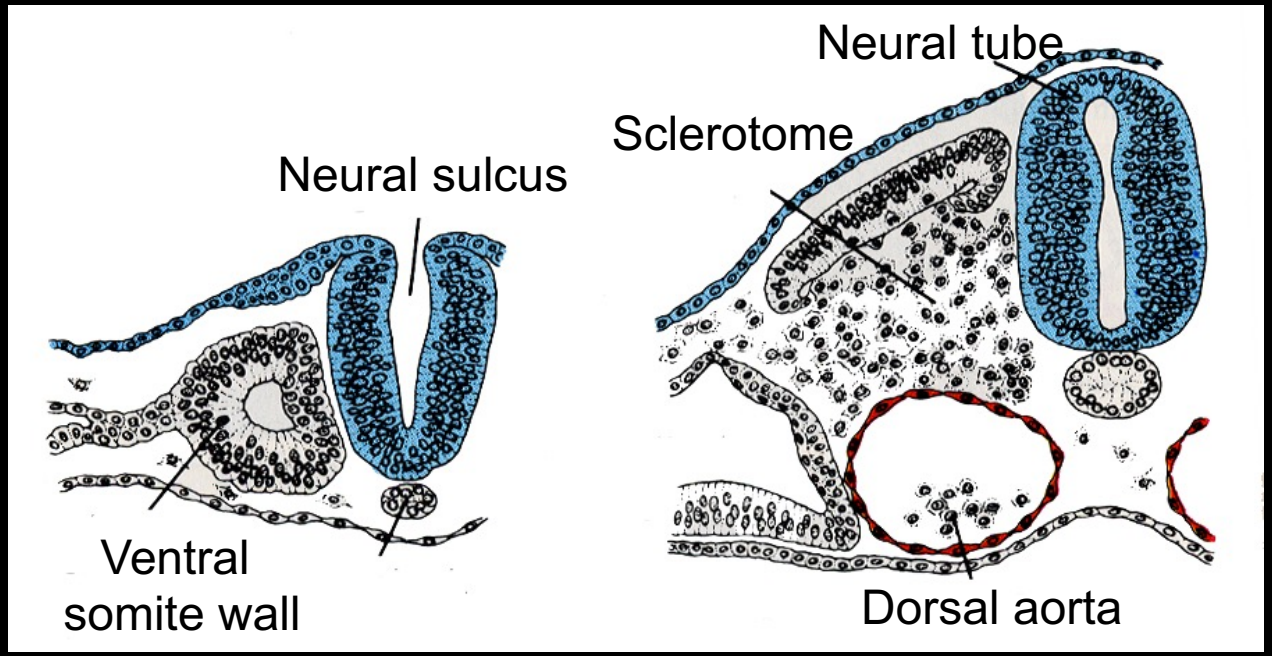
Development of Somites

- Beginning of 3rd Week: Somitomeres begin to differentiated from paraxial mesoderm and gradually transform into somites.
  - First pair: Cervical region (day 20)
  - 42-44 pairs by the end of 5th week (3 pairs/day)
  - 4 occipital
  - 8 cervical
  - 12 thoracic
  - 5 lumbar
  - 5 sacral
  - 8-10 coccygeal → 5-7 disappear later

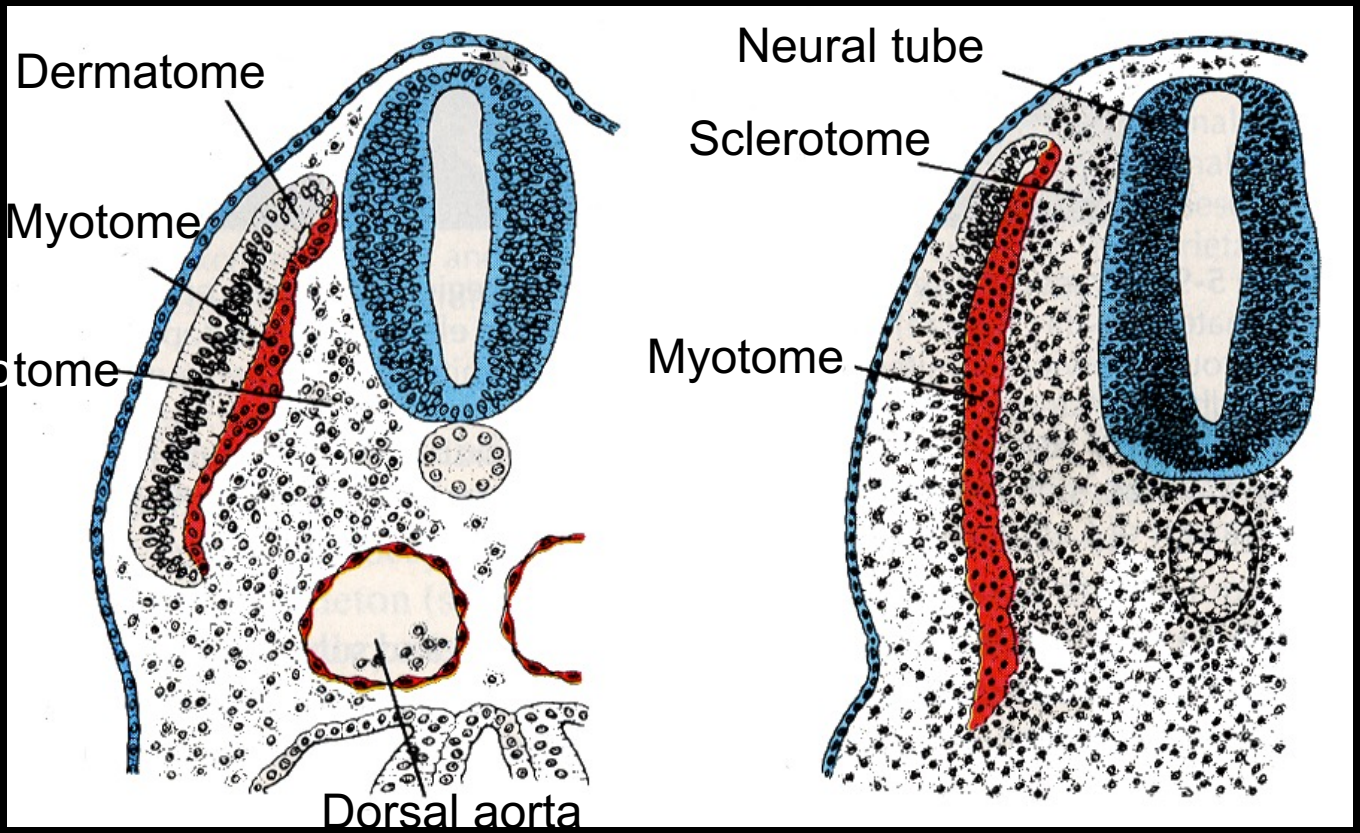
Age (day)	Somite formed
20	1-4
21	4-7
22	7-10
23	10-13
24	13-17
25	17-20
26	20-23
27	23-26
28	26-29
30	34-35

Somite Differentiation

- Beginning of 4th Week
  - Somites begin to grow and move towards notochord.
  - These structures are called sclerotomes, which are mesenchymal tissue.
  - Sclerotomes give rise to bone, cartilage and connective tissues.



- By the end of 4th week
  - Outer part of the somites transforms into dermatome; inner part turns into myotome.
  - Each dermatome give rise to dermis and hypodermis
  - Each myotome give rise to regional muscles.



Terminology Note:

Mesoderm refers to cells derived from the epiblast and extraembryonic tissues.

Mesenchyme refers to loosely organized embryonic connective tissue regardless of origin.

Cell Populations Derived from Somites

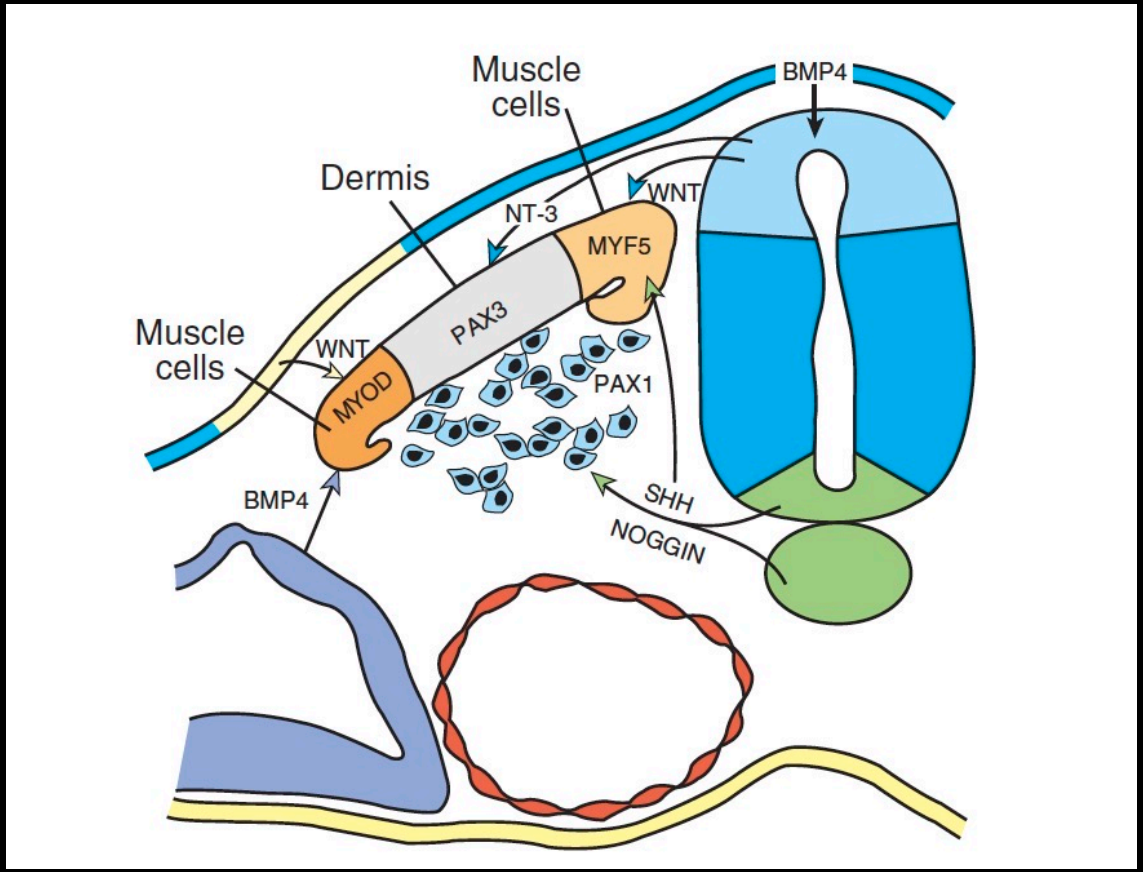
Some cells in the head are derived from ectoderm and neural crest

Adipocytes
Chondrocytes
Osteocytes
Endothelial cells (arteries, veins, capillaries, lymphatics)
Pericytes
Fibroblasts (connective tissue, dermis, tendon and ligaments)
Muscle cells (skeletal and smooth)
Neural tissues (arachnoid cells, epineural cells, perineural cells, dura mater fibroblasts)

Regulation of Somite Differentiation

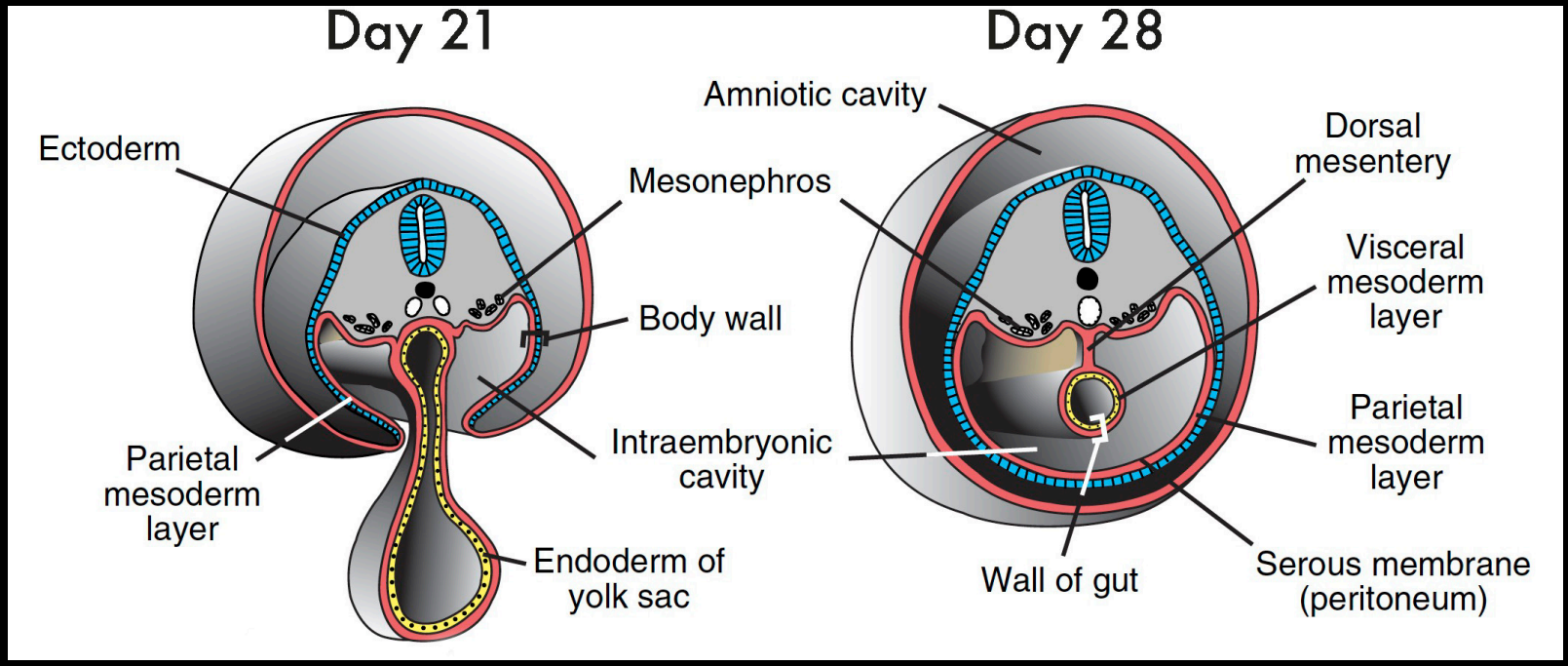
- Notochord
- Neural tube
- Epidermis
- Lateral mesoderm

Responsible inducers



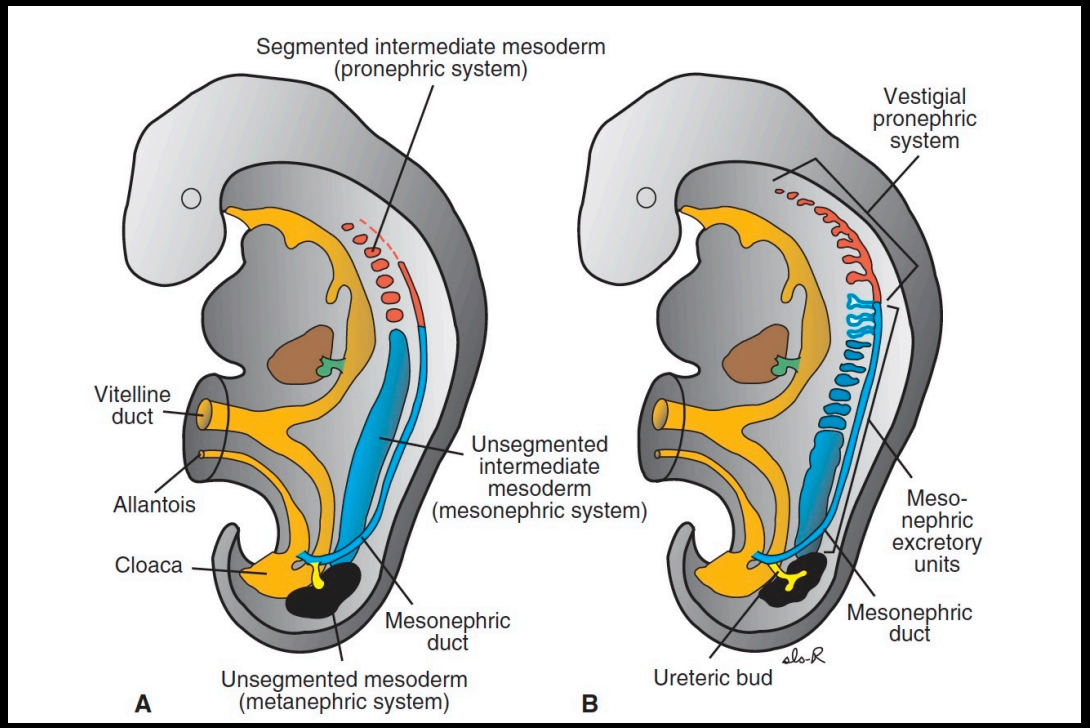
Parietal and Visceral Mesoderm

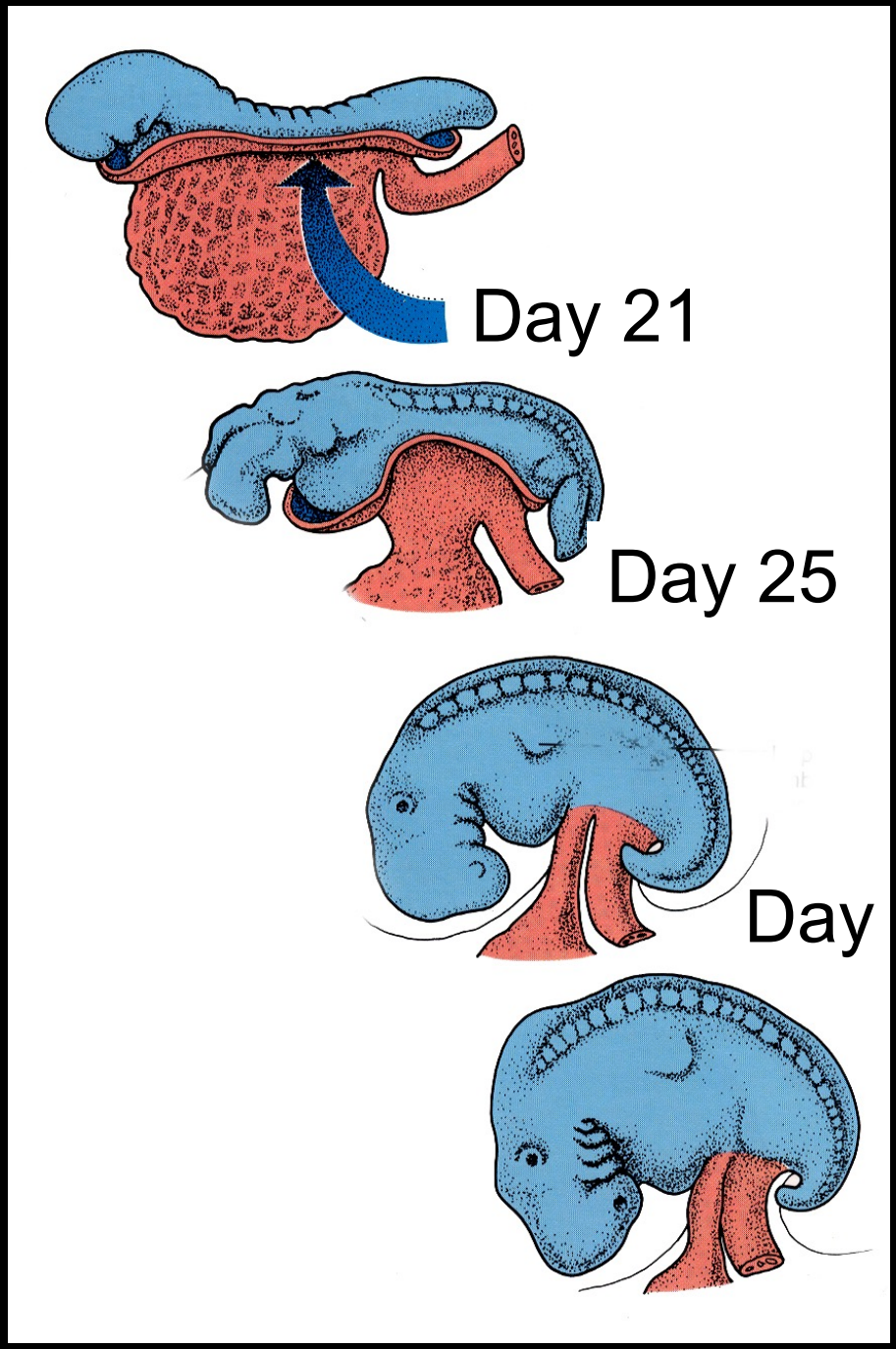
Both give rise to the inner and outer linings of intraembryonic coelom (cavity). In later life, these linings form the inner and outer body walls.



Intermediate Mesoderm

- Cervical region give rise to pronephros (regresses)
- Upper thoracic and upper lumbar regions give rise to mesonephros (regresses)
- Metanephros (metanephric system) forms the permanent kidney and collectory ducts

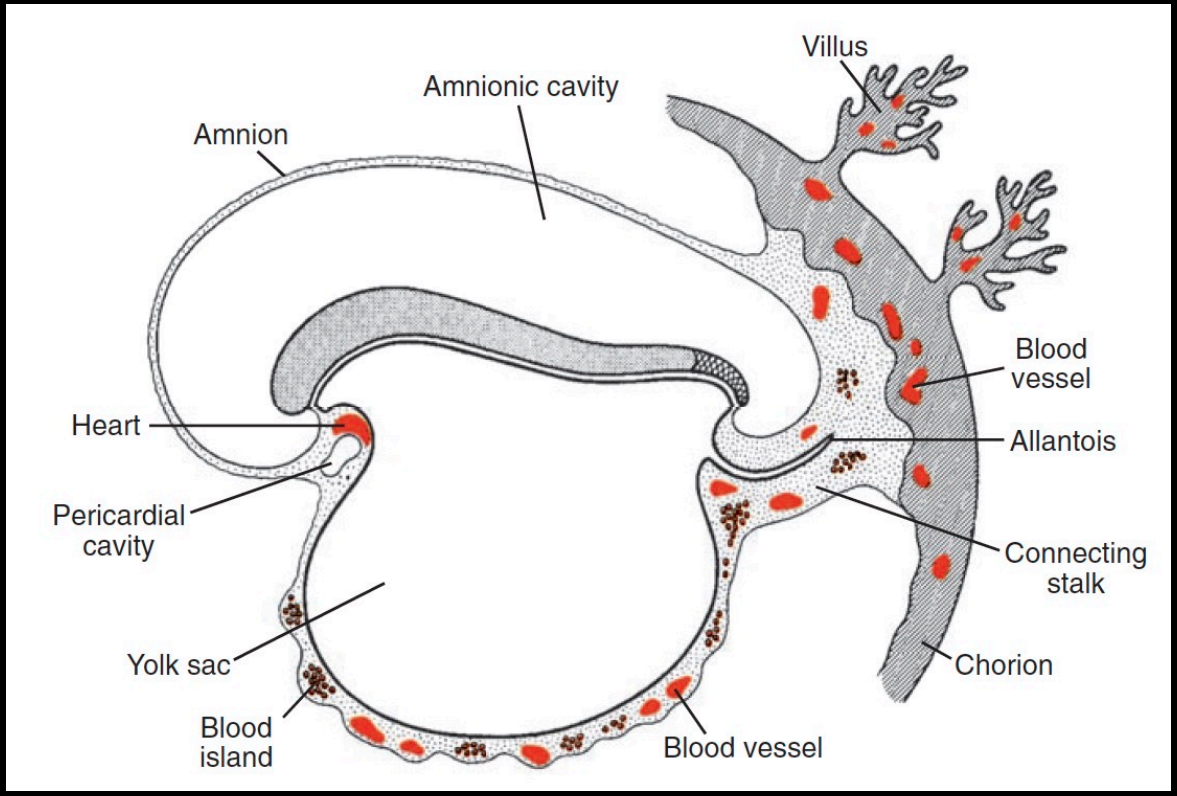




Cephalocaudal folding

Blood and Blood Vessels

- Mesangioblasts which originate from visceral mesoderm and then migrate to the wall of yolk sac
- Differentiate into blood cells and blood vessels.

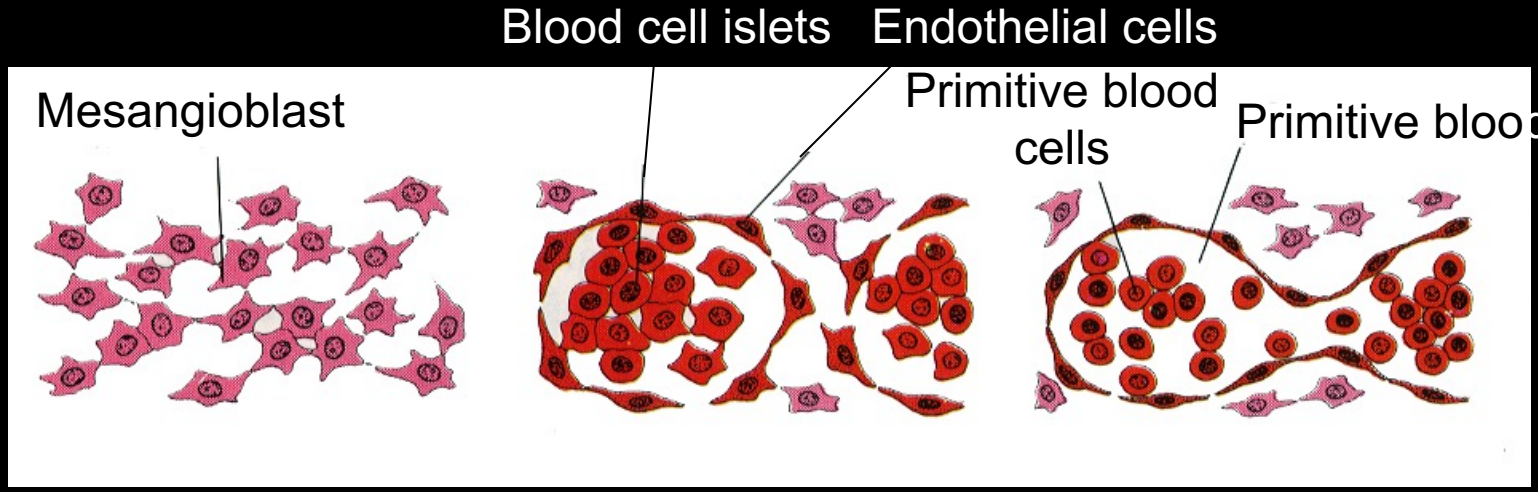


Mesangioblasts

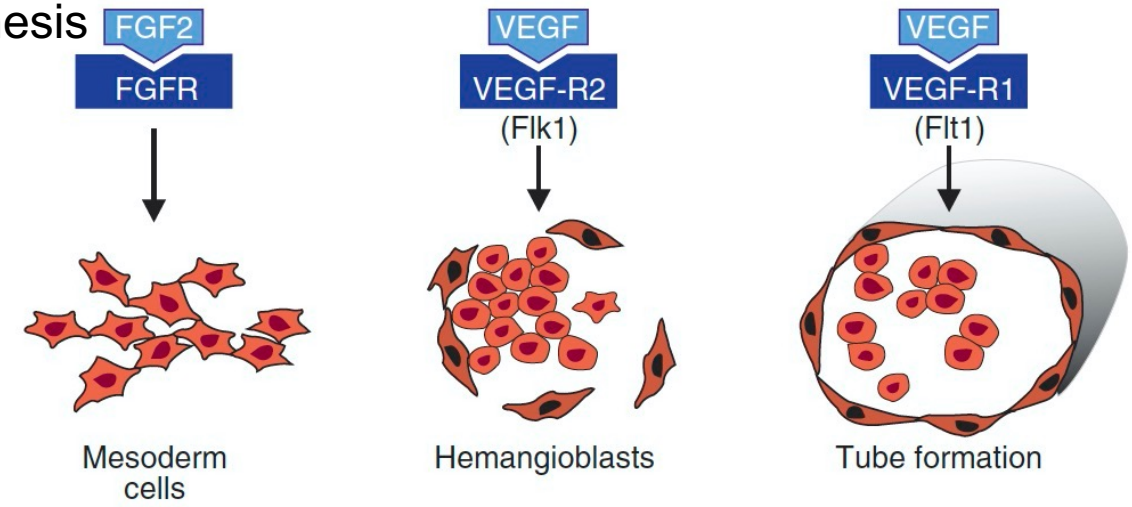
Hemangioblasts

Endothelial cells

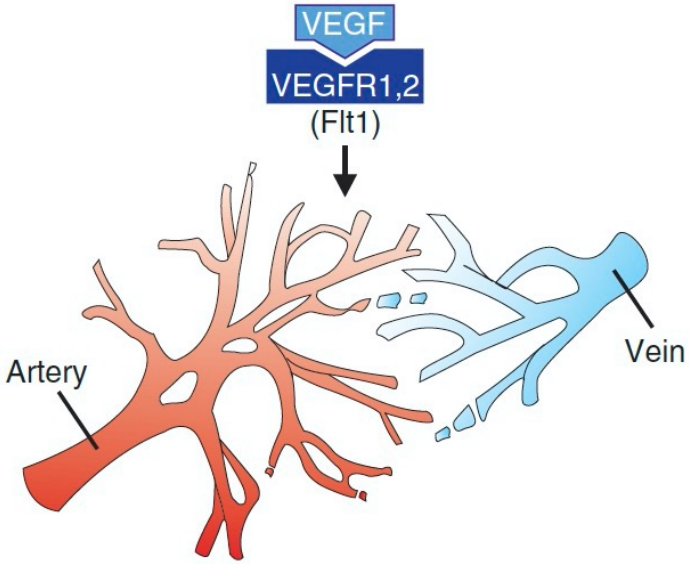
Blood cells



Vasculogenesis



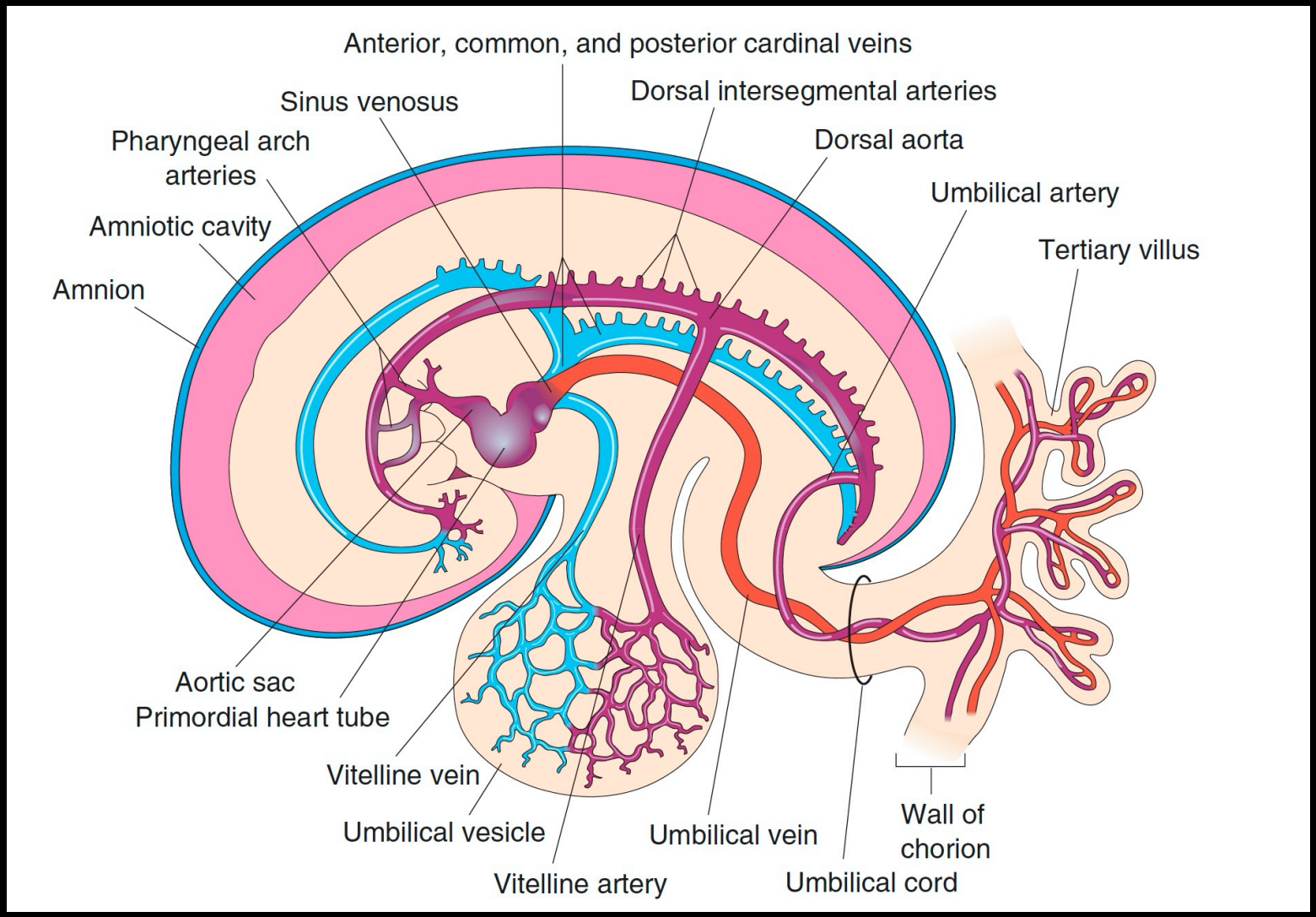
Angiogenesis



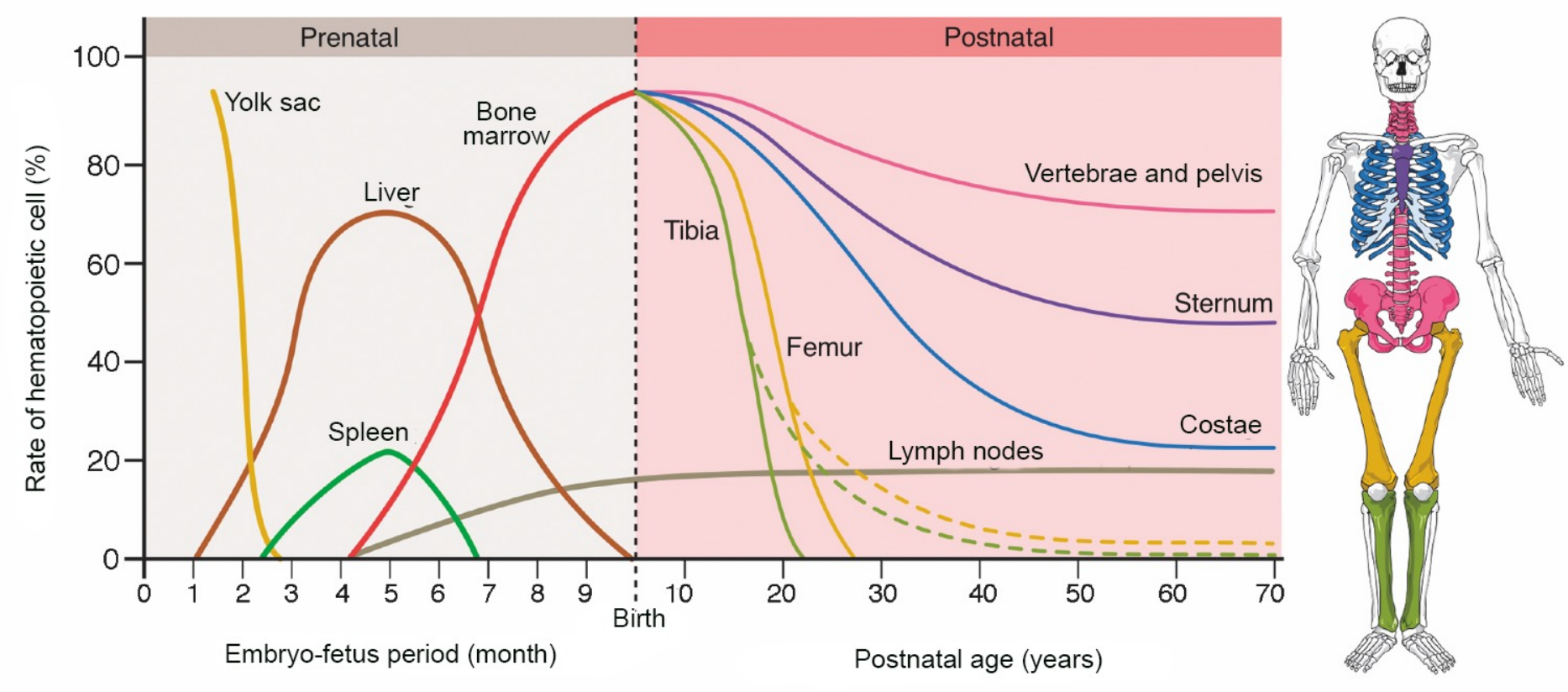
PDGF & TGFβ

Final modeling and stabilization

Blood circulation by the end of 3rd week in human embryo



Hematopoiesis (Production of blood cells)

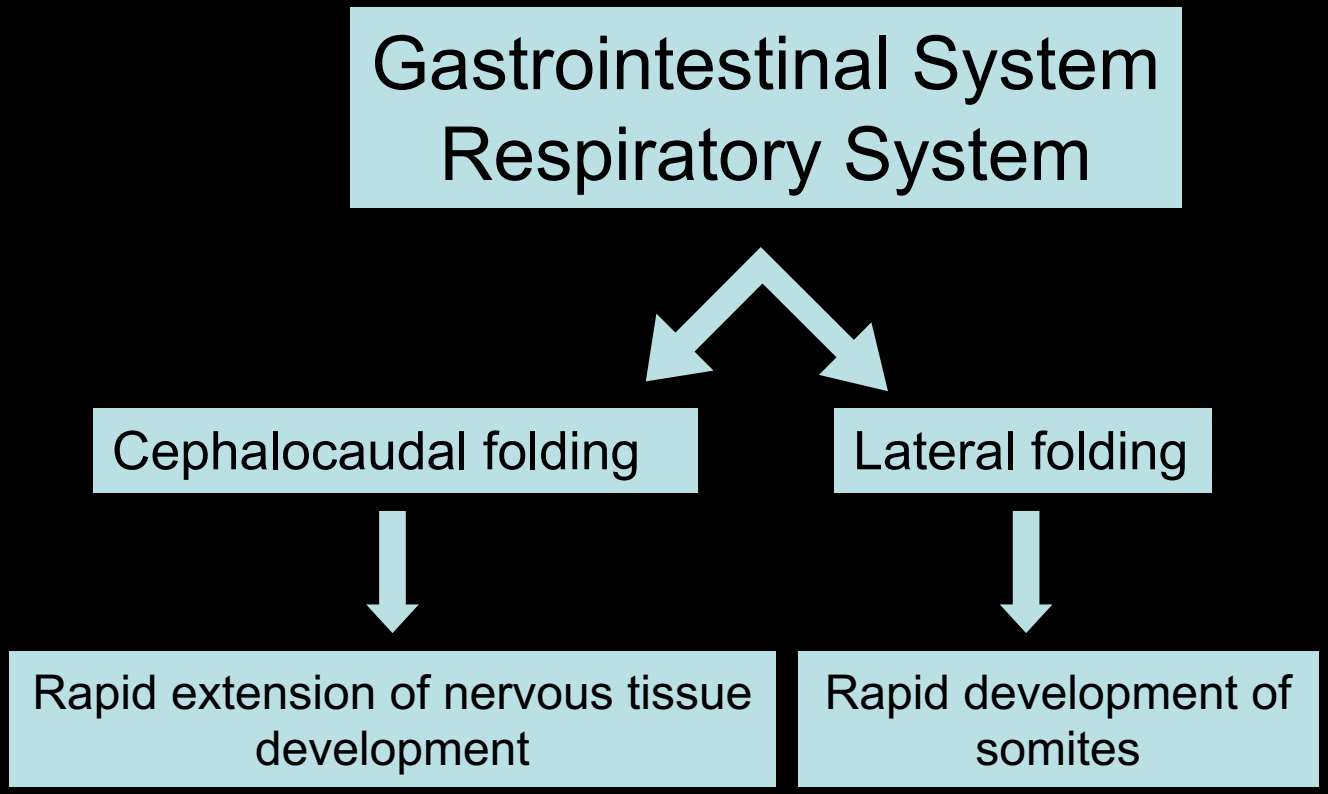


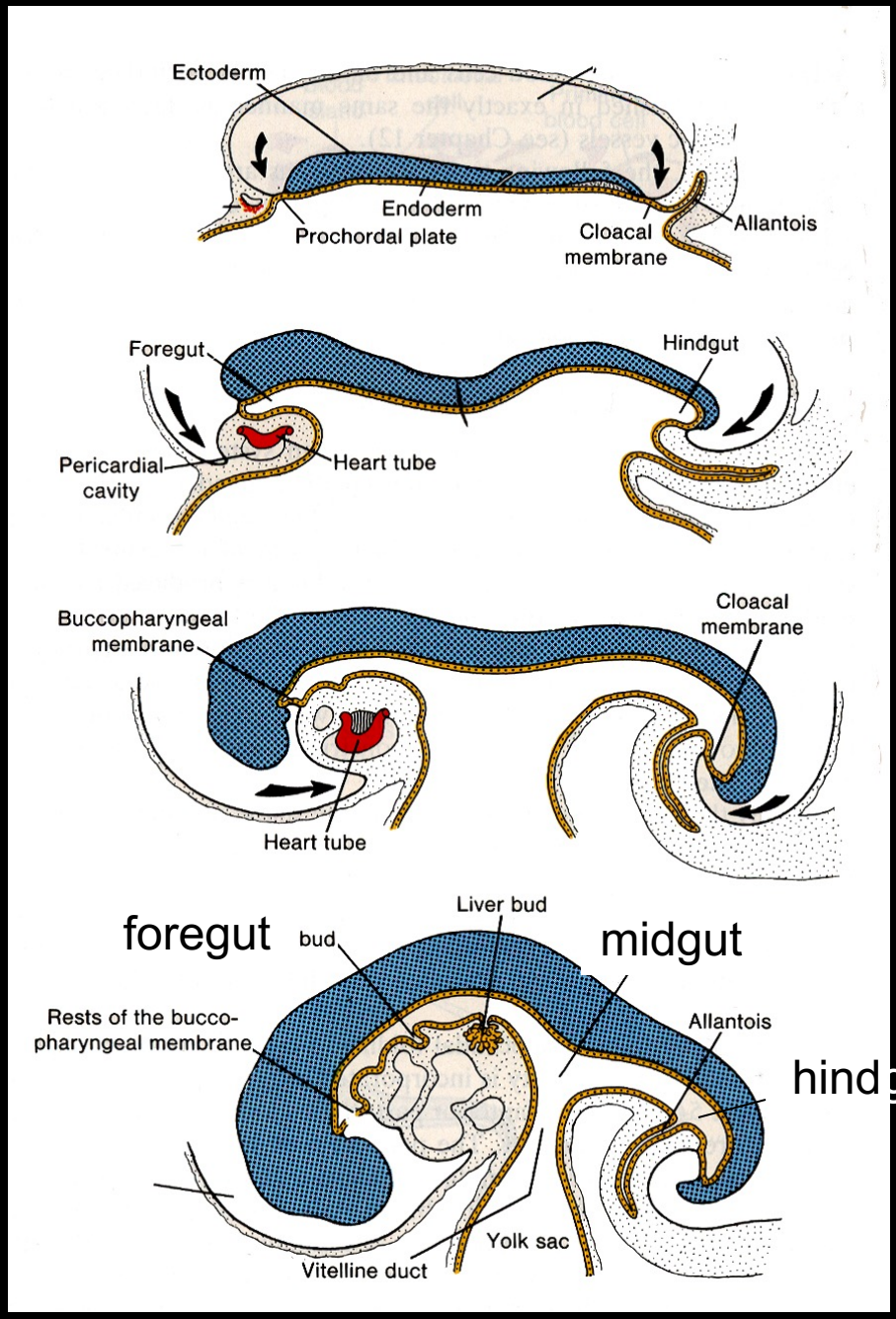
A. Can, Kök Hücre, 2014

Summary of Mesoderm

- Supporting tissues (connective, bone and cartilage)
- Dermis
- Striated and smooth muscle
- Heart muscle, blood and lymphatic vessels
- Kidneys, gonads and related tubules
- Adrenal cortex
- Spleen

Development of Endoderm



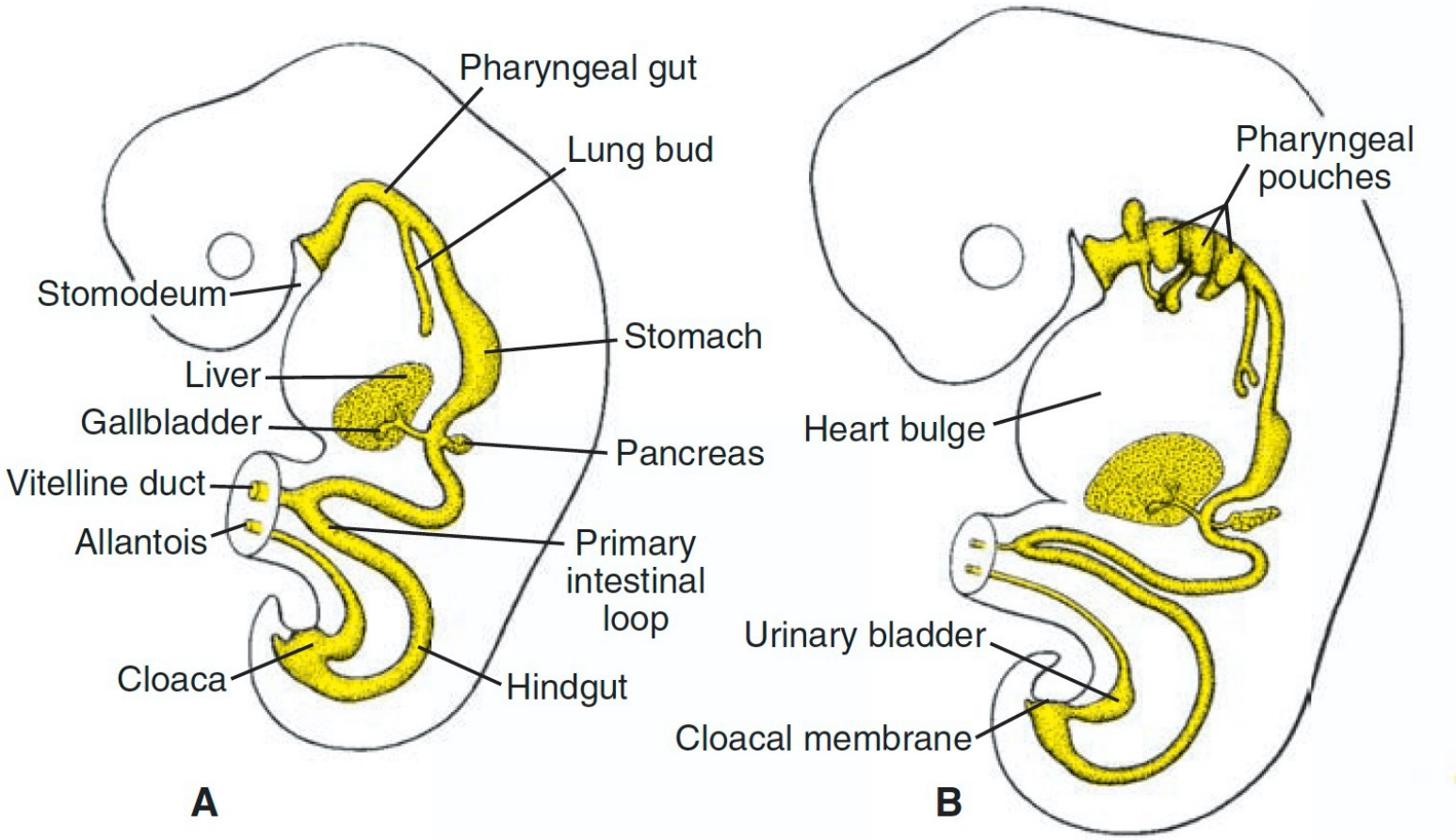


Cranial folding

Caudal folding

Cephalocaudal folding

Endoderm Layer

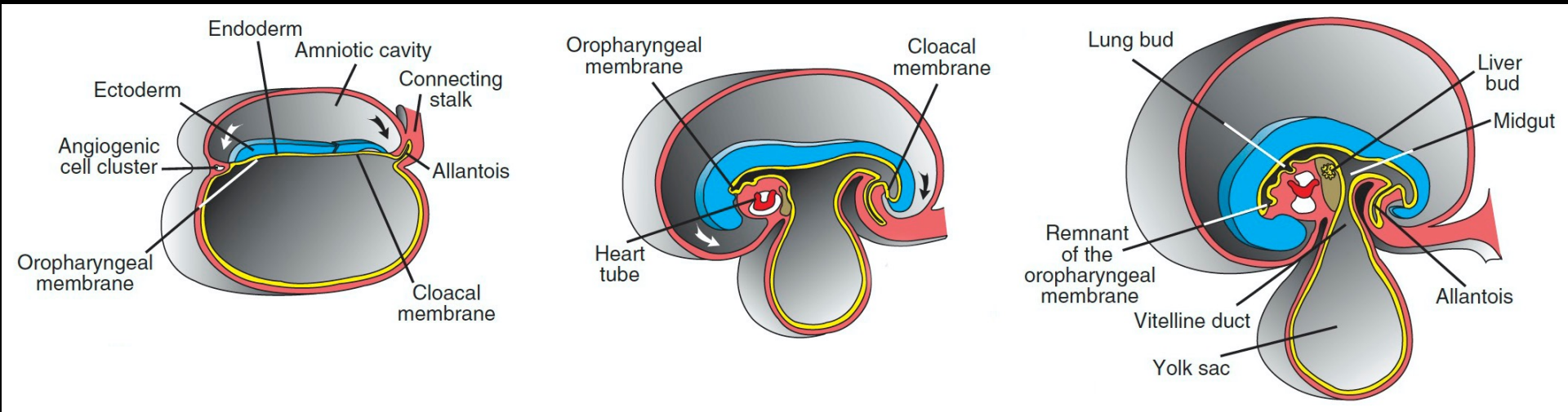


4th week

5th week

Allantois

- A temporary sac occurs during early development of mammals, birds and reptiles
- In human, it appears as an endodermal process at hindgut lies proximity to connecting stalk
- Since it is connected to fetus bladder, it facilitates to excrete nitrogen waste products
- It helps the development of umbilical vessels



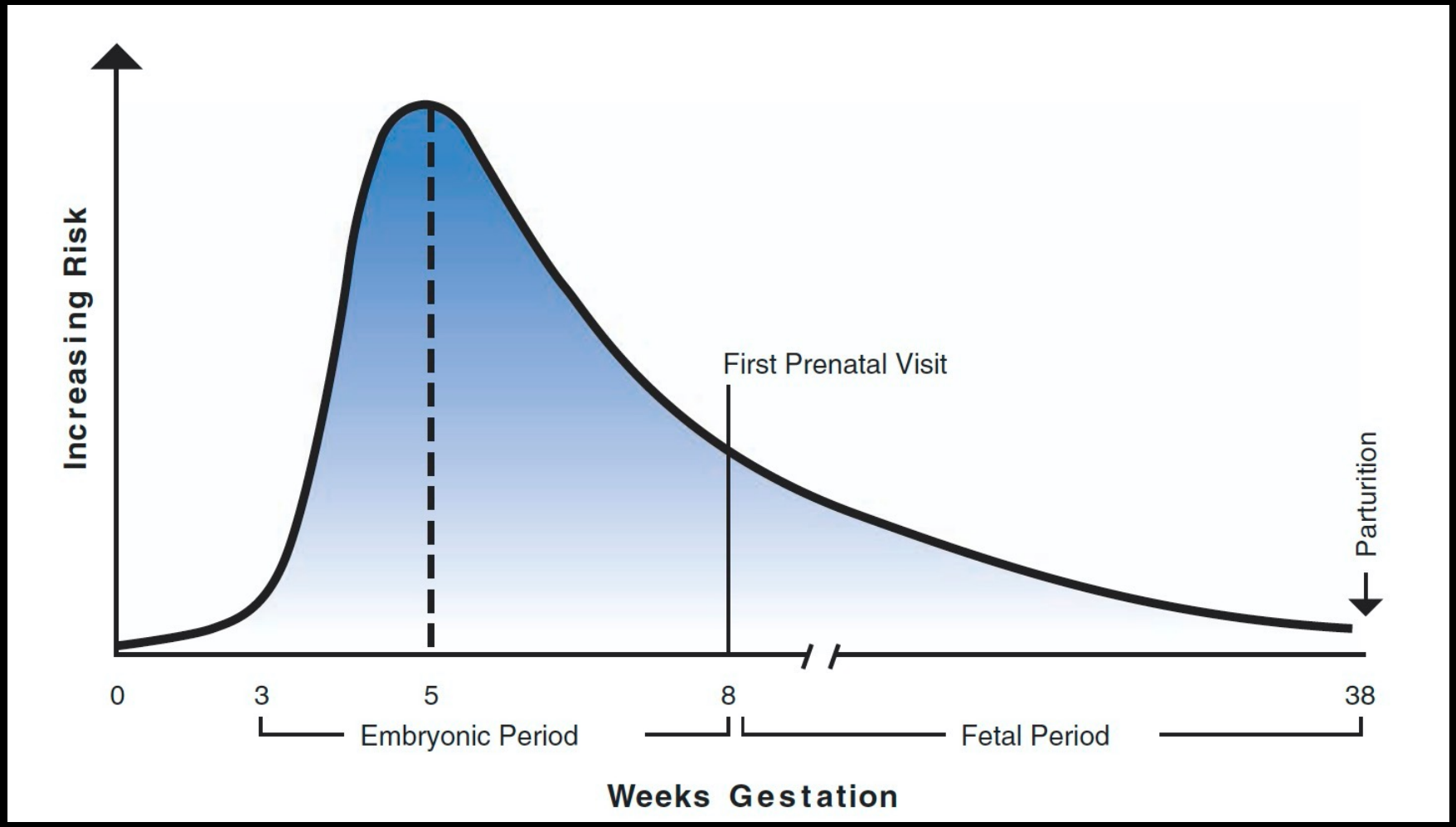
Endodermal Derivatives

- Epithelia of all gastrointestinal system.
- Epithelia of all respiratory system.
- Parenchyma of thyroid, parathyroid, liver and pancreas.
- Stroma of tonsils and thymus.
- Epithelia of bladder and urethra.
- Tympanic cavity and Eustachian tube.

Teratology

- Study of abnormalities of arise from developmental stages.
- Related term is developmental toxicity that includes all manifestations of abnormal development caused by environmental insult including growth retardation, delayed mental development or other congenital disorders without any structural malformations.

Clinical Importance of 3rd-8th Weeks



Major structural malformations

Minor structural malformations
Functional anomalies

Congenital Anomalies (Birth Defects)

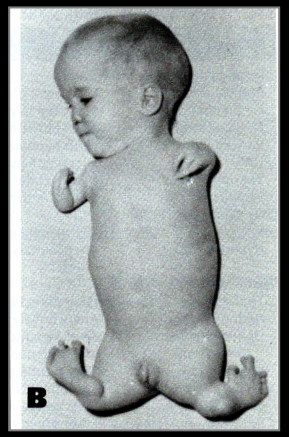
(Structural-functional malformations caused by various reasons in embryonic and fetal period)

- Major structural anomalies 3% of live born infants
- 2-3% is detected in the first 5 years

} 4-6%

- 20% of all in utero ex (before reaching term)
- 80% anomalies born live
- Frequencies of birth defects are the same for Asians, African, Americans, Latin Americans, Whites, and Native Americans
- In 40-45% the cause is unknown
- 28% chromosome anomalies, mutations etc.
- 3-4% environmental factors
- 20-25% genetic + environmental (multifactorial inheritance)
- % 0.5-1 twinning (multiple births)

Phocomelia



Thalidomide Effect

(originally used as a sedative and hypnotic Drug in pregnant women; now it is used in Multiple Myeloma to treat acute episodes of erythema nodosum leprosum)

Anencephaly

(Lack of brain & skull development)

Throughout the world, about 10,000 cases were reported of infants with phocomelia due to thalidomide; only 50% of the10,000 survived.

Cleft lip and palate

(cigarette smoking)

Most Common Birth Defects

1. Heart Defects
   - 1:100 in live births
   - Tetralogy of Fallot, coarctation of aorta, hypoplastic left heart syndrome, Marfan syndrome etc..)
2. Cleft Lip/Palate
   - 1:700 (bilateral)
   - More common in boys
3. Down Syndrome
   - 1:700
   - Increases with mother age (1:60 in women>42)
4. Spina bifida
   - 0.01-0.5%

Abdominal Wall Defects

- Omphalocele
  - Intestines, liver and remain outside of the abdomen in a sac because of failure of the normal return of intestines and other contents back to the abdominal cavity during around the 9th week of intrauterine development
  - Covered by amniotic membrane
  - 1:4000 births
  - 30% of infants with an omphalocele have other congenital abnormalities.
- Gastroschisis
  - Intestines extend outside of the body through a hole next to the belly button
  - 2-5:10.000 births

Omphalocele

Gastroschisis