Human Embryology-3

- ✓ Implantation
- ✓ Second – Fourth Week of Life

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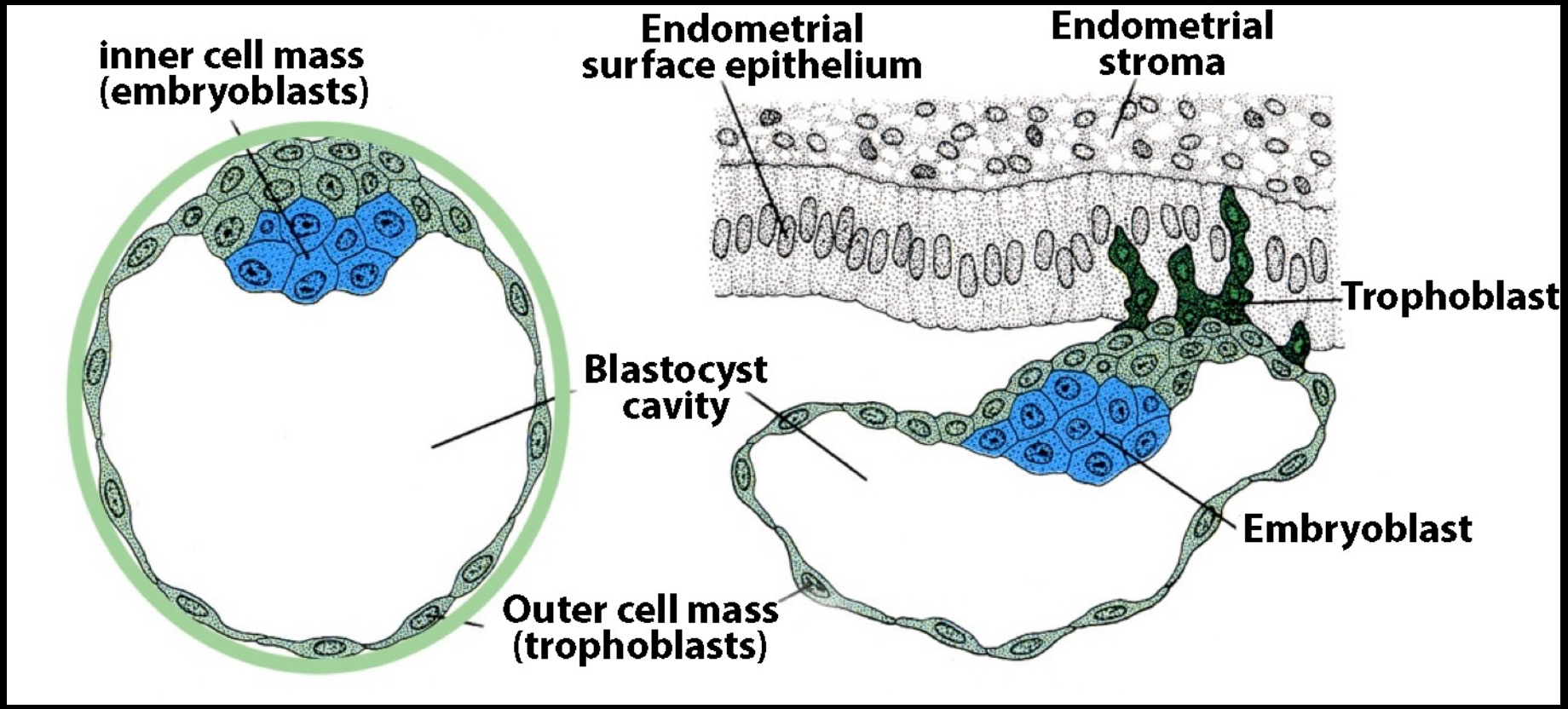
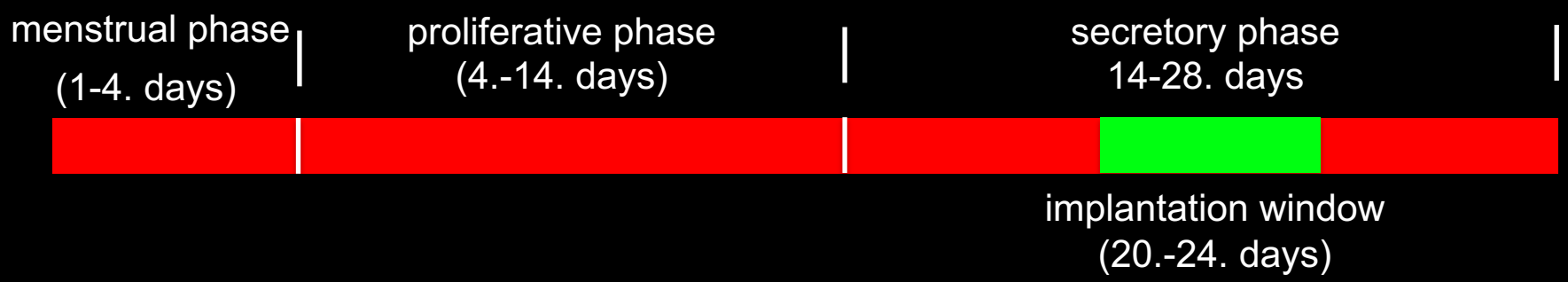
Implantation
(Postfertilization 6-7th day)



Hatching (removal of ZP)

Failure of Hatching = Implantation Failure

Implantation Window



Receptive Endometrium

- Endometrium is most suitable, thus acceptable for embryo at postovulatory 6-8 days.
- Receptivity lasts around 4 days (20-24th days of menstrual cycle)

Epithelial Mucins (MUCs)

- A group of high MW epithelial cell surface glycoproteins, which inhibits adhesion
- MUC-1 keeps the embryo away from the endometrium surface until it finds a proper place and time to attach
- Only MUC-1 and MUC-6 are found in human endometrium

Three Phases of Implantation

Apposition (finding a proper place to attach)

- Interleukin-8 (IL-8)
- Monocyte chemotactic protein-1 (MCP-1)
- RANTES

} Secretory products of endometrium surface and glandular epithelium

Adhesion (attachment)

- α5-β1 integrin
- HB-EGF and EGF-Receptor relation
- This interaction phosphorylates heparan sulphate proteoglycan (parlecan) on trophoblasts
- Colony stimulating factor-1 (CSF-1)
- Leukemia inhibiting factor (LIF)
- Interleukin-1 (IL-1)

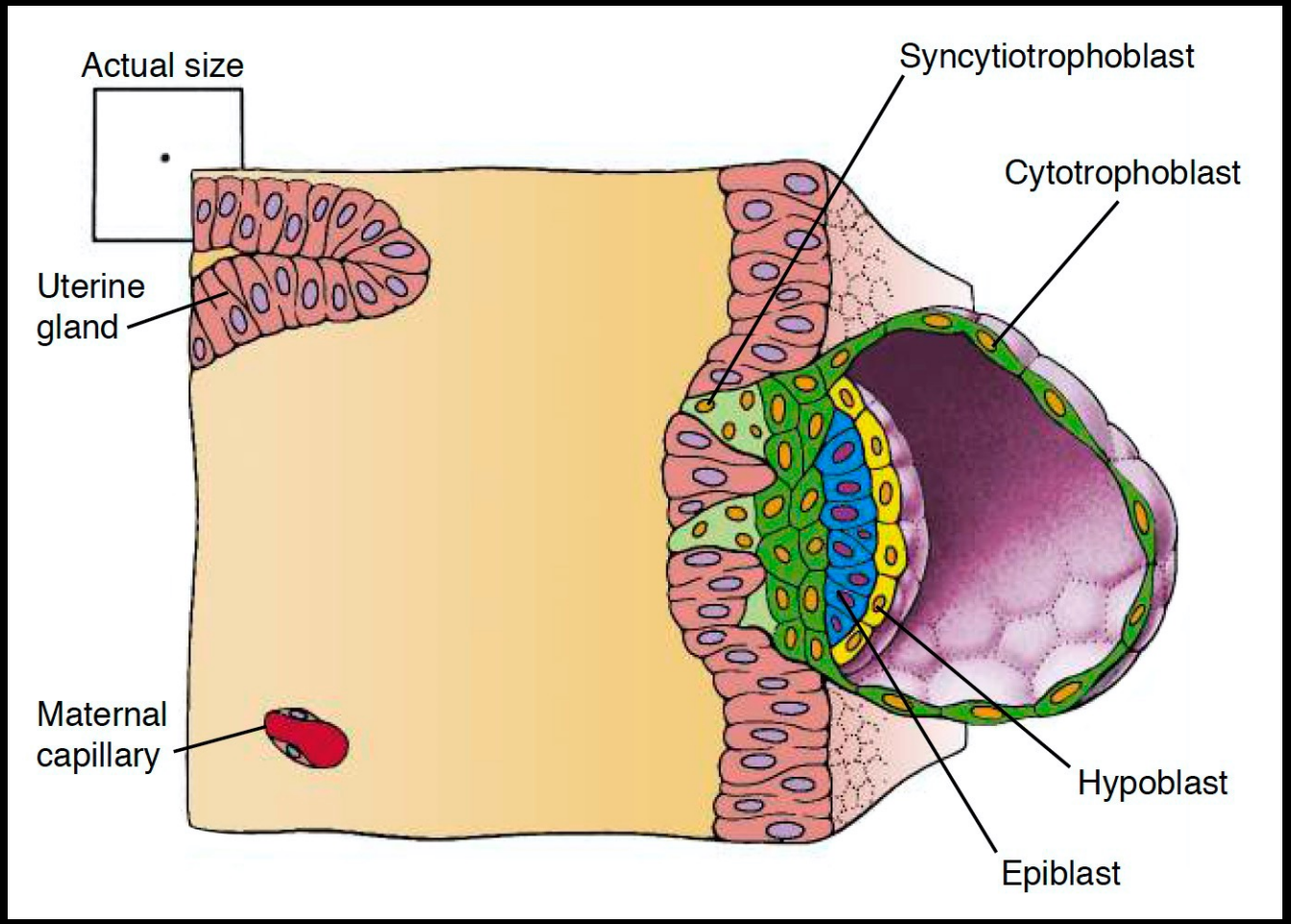
} Secretory products of endometrium surface and + Blastocyst

Invasion (homing)

- Collagenases (degrade collagen types 1,2,3,4,10)
- Gelatinases (degrade collagen type 4)
- Matrix metalloproteinases (MMP-2, MMP-9)
- MMP-3 (degrade fibronectin, laminin, proteoglycans, collagenase types 4,5,7)

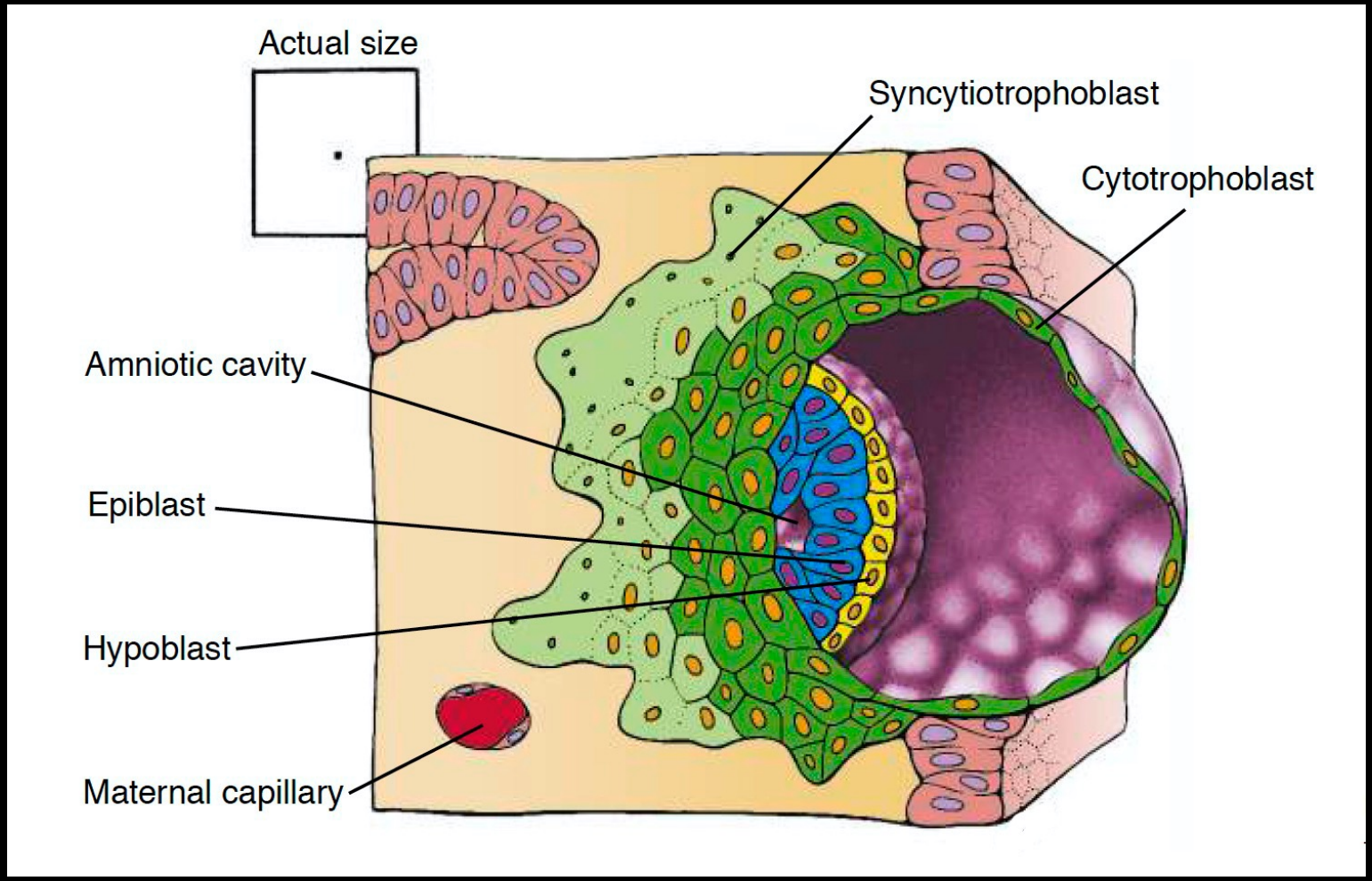
} Secretory products of trophoblasts

Day 7



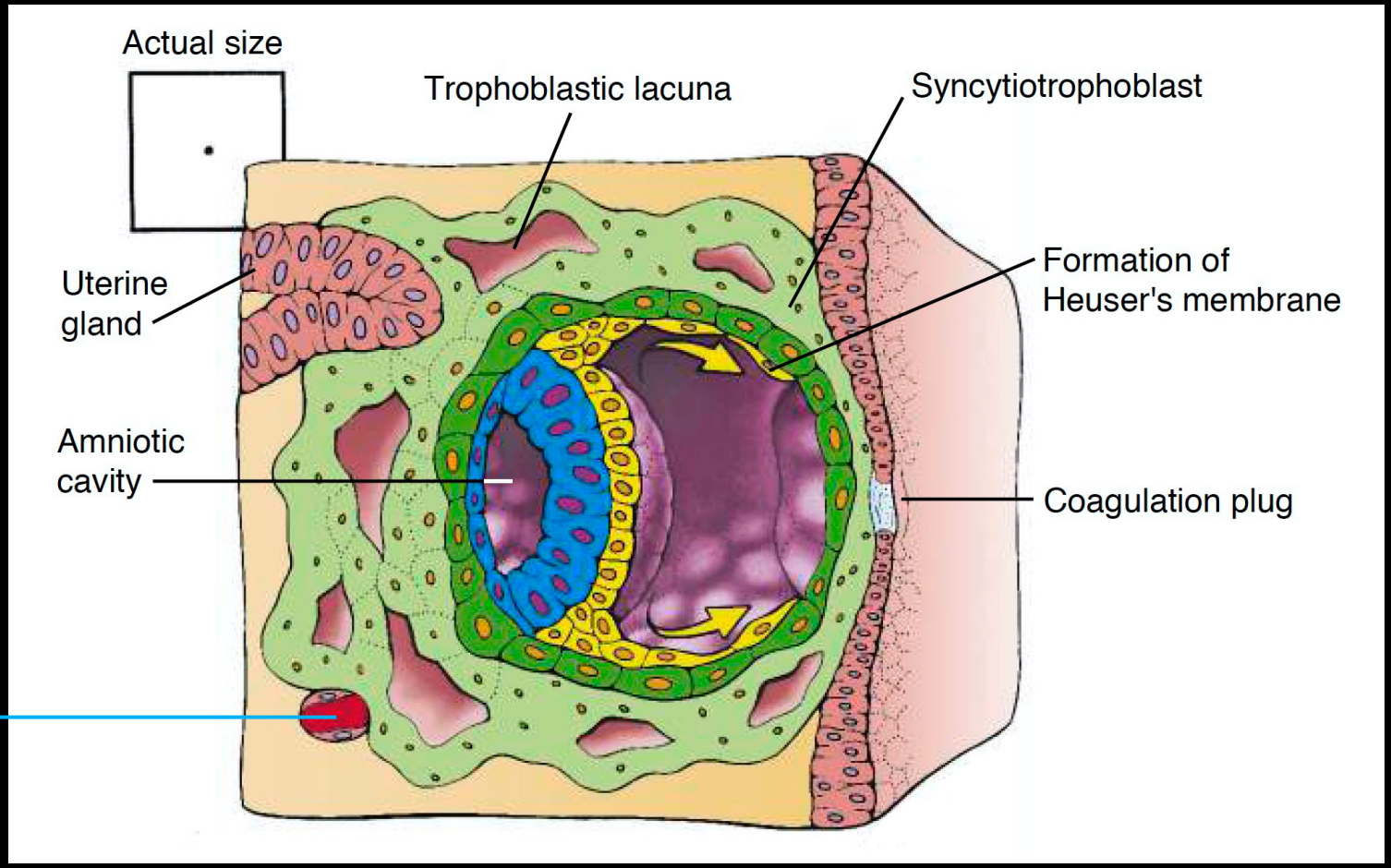
- Syncytiotrophoblasts secrete MMPs
- Embryoblasts differentiate into 2 cell layers (epiblast & hipoblast = 2-layer embryo disc)

Day 8



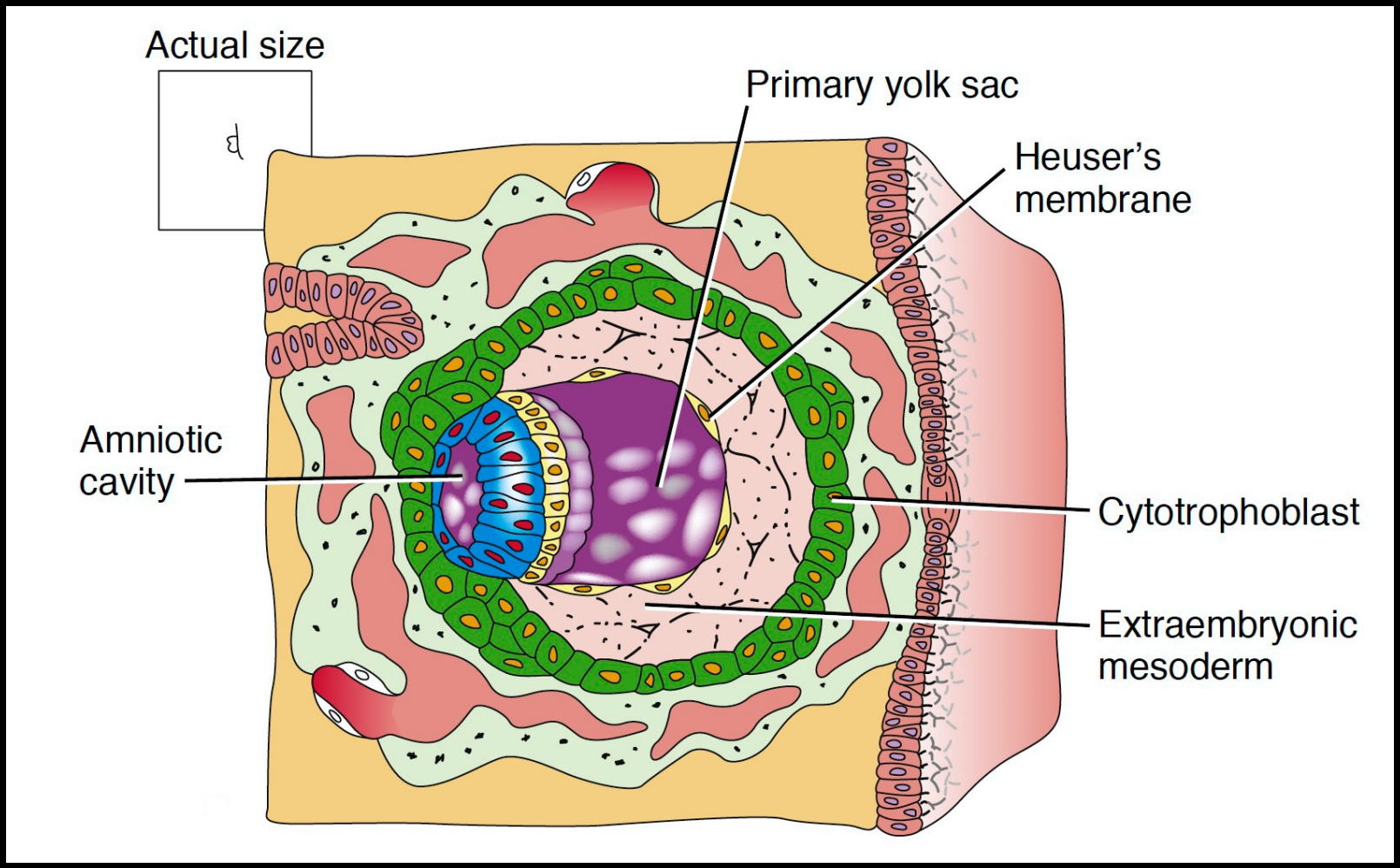
- Syncytiotrophoblasts secrete Collagenases & Gelatinases
- Differentiation of Amnioblasts from epiblasts
- Formation of Amniotic Sac and synthesis of Amniotic Fluid by amnioblasts

Day 9



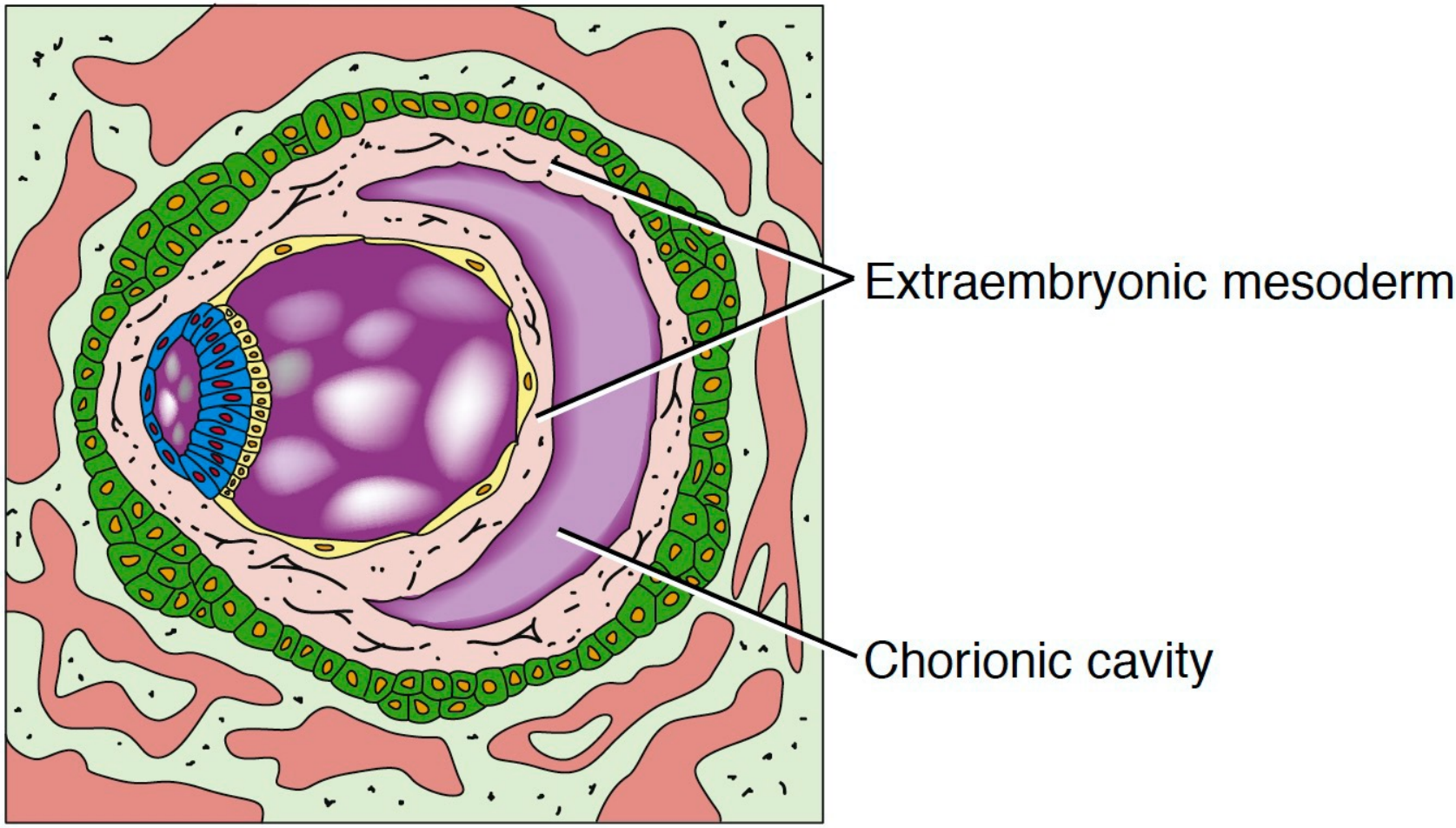
- Fully embedded conceptus (embryo and membranes), fibrin coagulum
- Conceptus is completely surrounded by a synctiotrophoblast shell
- Formation of exocoelomic membrane (Heuser's membrane)
- Formation of trophoblastic lacunae
- Synctiotrophoblast contact with maternal blood and begin secreting hCG

Days 10-11



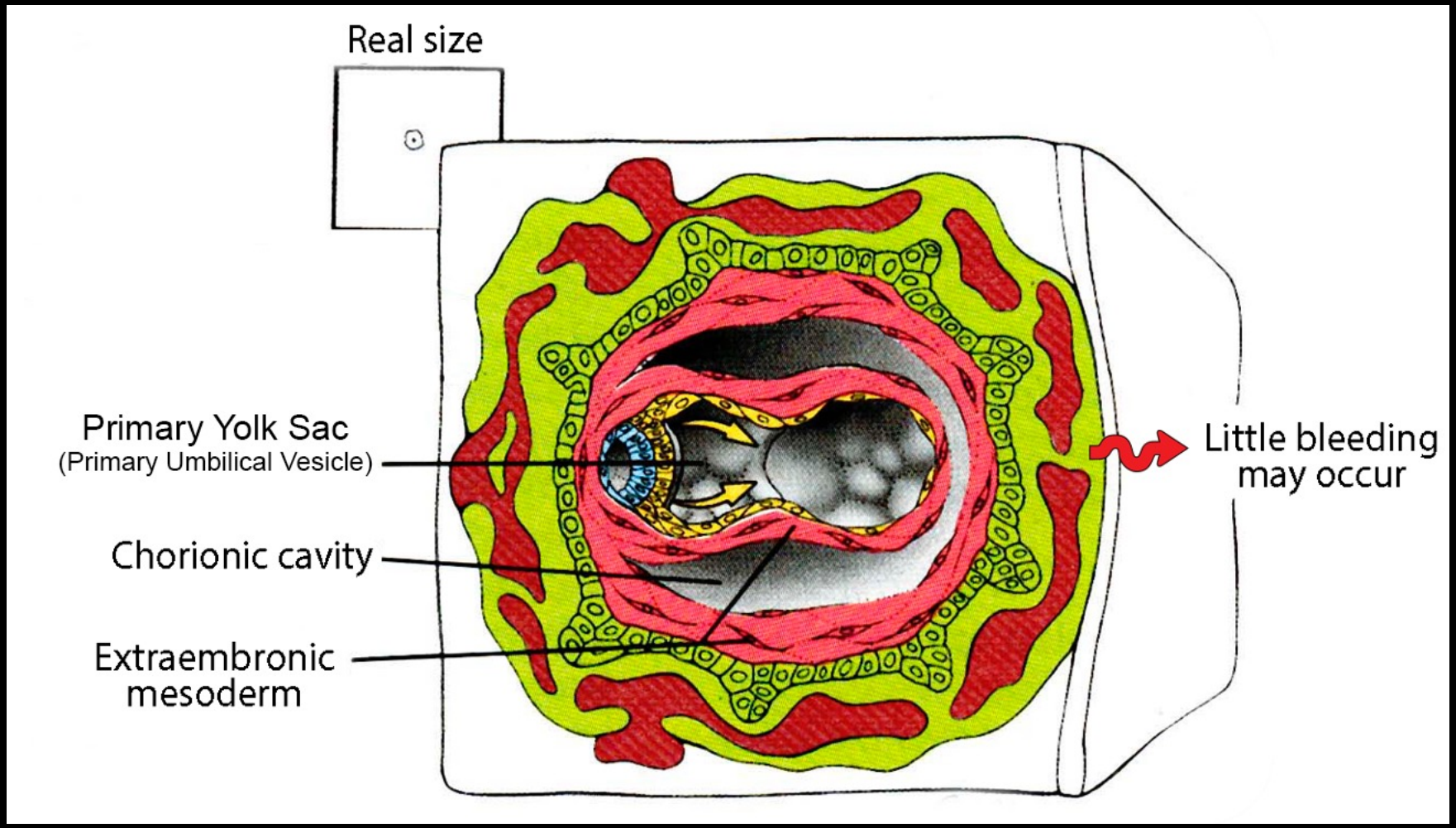
- Extended invasion of syncytiotrophoblasts
- Uteroplacental circulation begin as the lacunae are filled with blood
- Hypoblast + Heuser's membrane forms primitive yolk sac (exocoelomic cavity)
- Formation of extraembryonic mesoderm

Days 12-13



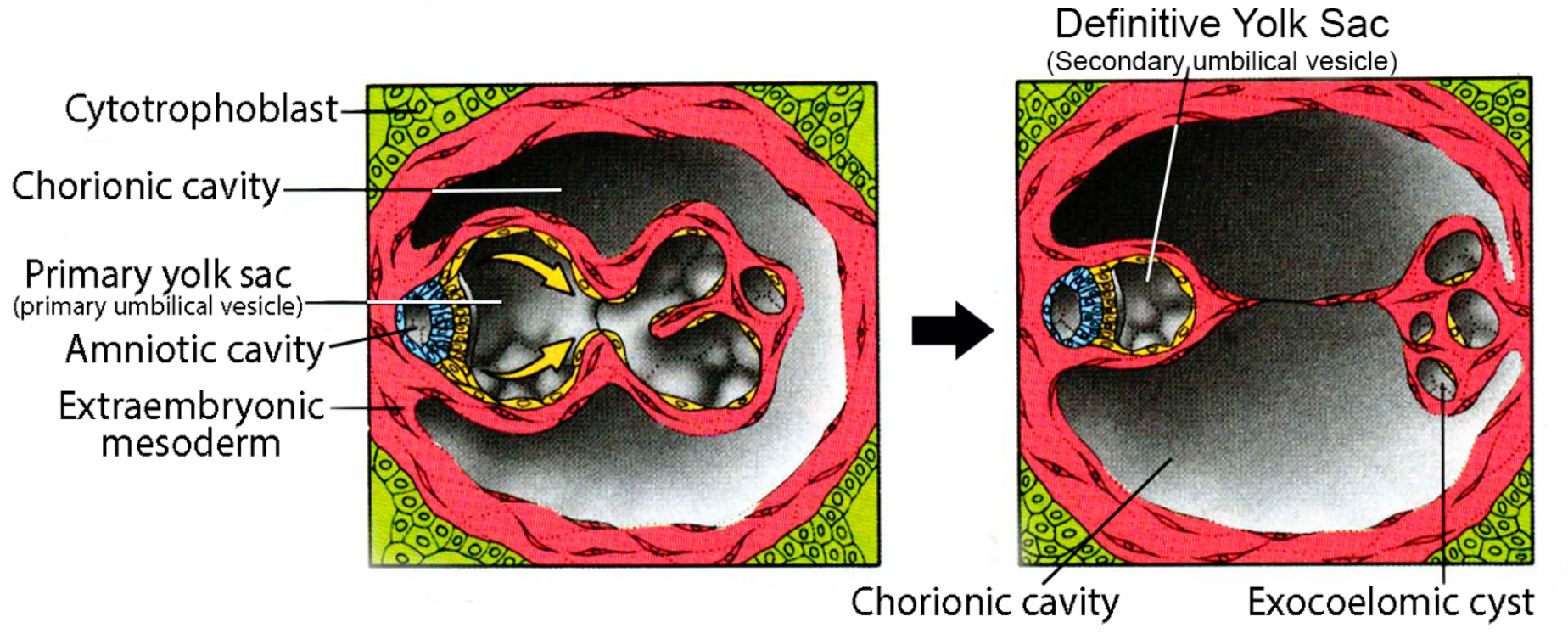
- Formation of Extraembryonic Mesoderm and then splits into 2 layers

Days 12-13



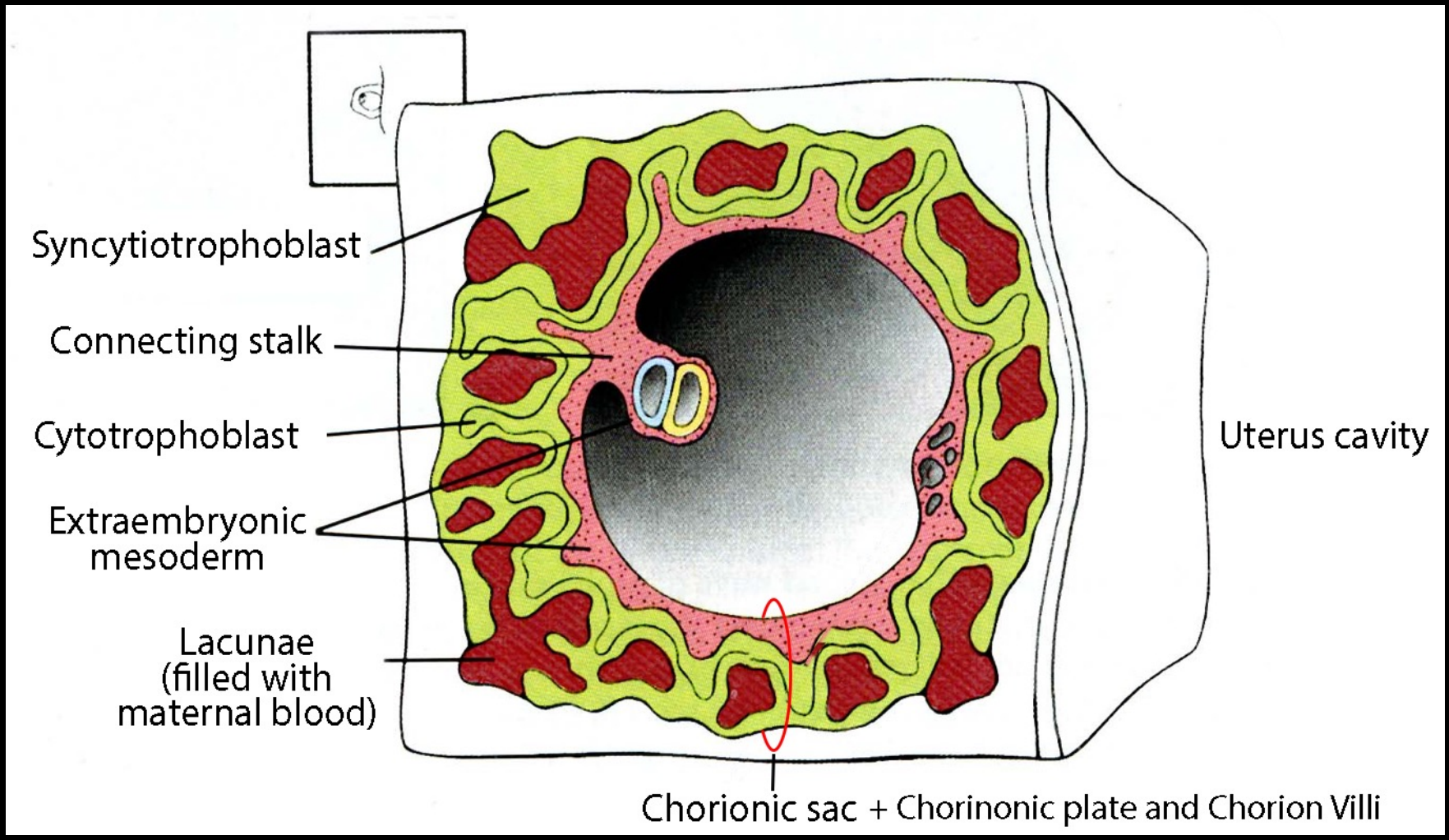
- Formation of Chorionic cavity
- Extrusion of hypoblastic cell layer to extend the yolk sac
- Decrease in invasion capacity of syncytiotrophoblasts

Days 13-14



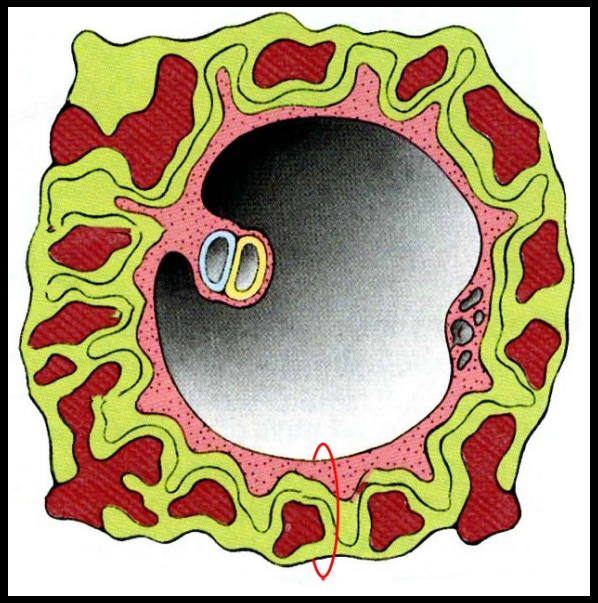
- Formation of Definitive Yolk Sac (secondary umbilical vesicle) while remnants of primitive yolk sac (primary umbilical vesicle) protrudes towards abembryonic pole.
- The umbilical vesicle in humans contains no yolk; however, it has important functions-for example, it is the site of origin of primordial germ cells (PGCs).

Days 14-15

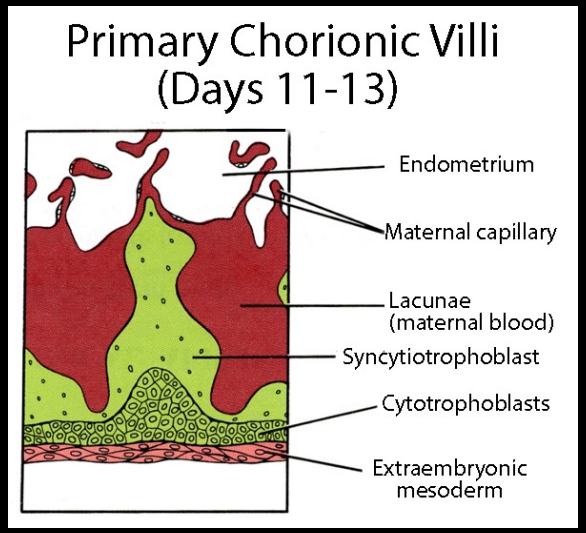


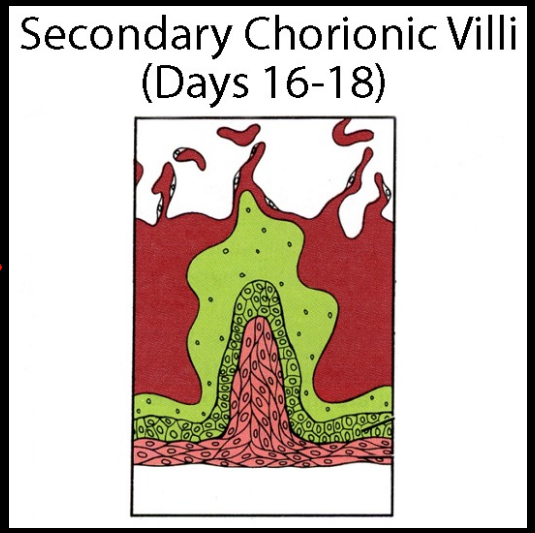
- Definitive yolk sac gets disconnected with the primitive yolk sac remnants
- Bilaminar embryonic disc is covered with two sacs (amnion and yolk sac)
- Embryonic disc is connected to outer cell layers with connecting stalk

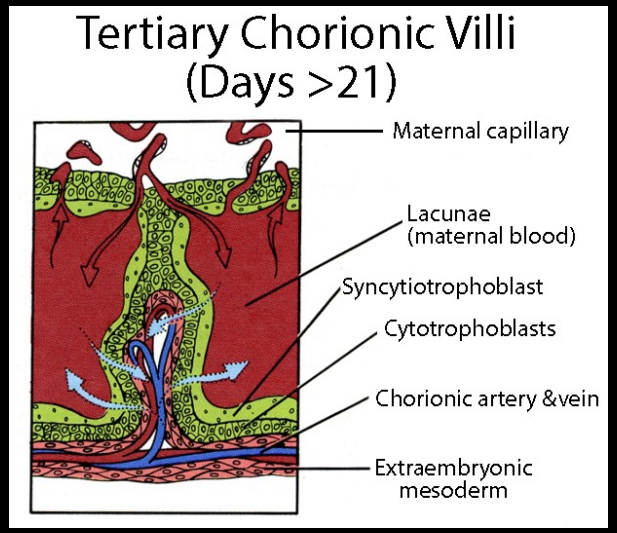
Chorionic Villi



Terminology Note
Villus: Finger-shape protrusions
Villi (plural)
Villus (singular)







Summary of Second Week

- Following implantation, bilaminar embryo disc is formed composed of epiblast and hypoblast.
- Extraembryonic structures are formed
  - Amniotic cavity
  - Amnion
  - Extraembryonic mesoderm
  - Umbilical vesicle
  - Connecting stalk
  - Chorionic sac and primary chorionic villi

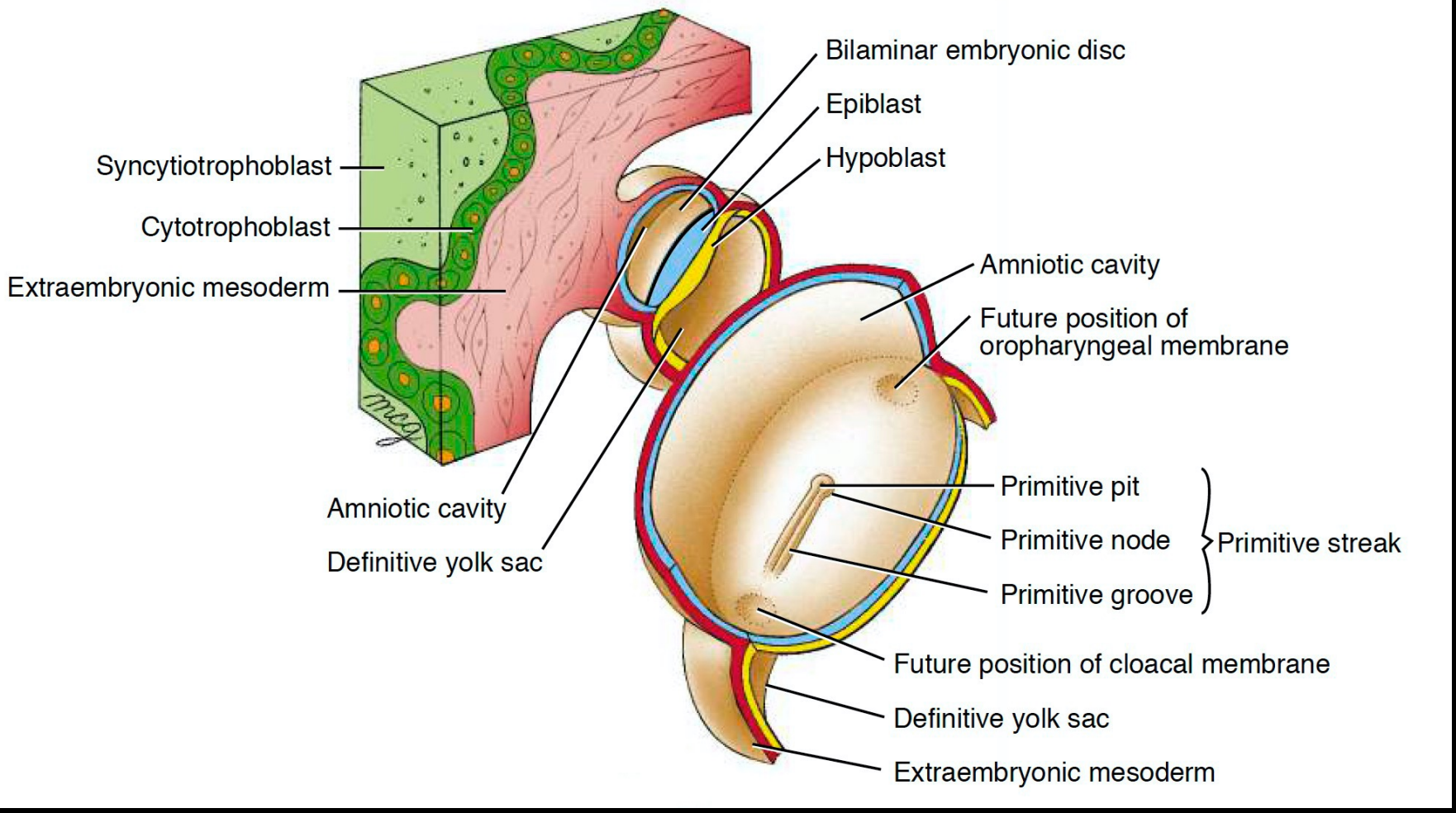
Third Week of Life

Two-Layer Embryo Disc (Blastula)

Three-Layer Embryo Proper (Gastrula)

- Gastrulation (formation of three germ layers)
- Determination of cranio-caudal axis
- Formation of somitomeres, somites, and neural plate
- Onset of tissue organization
- Organogenesis

Day 15

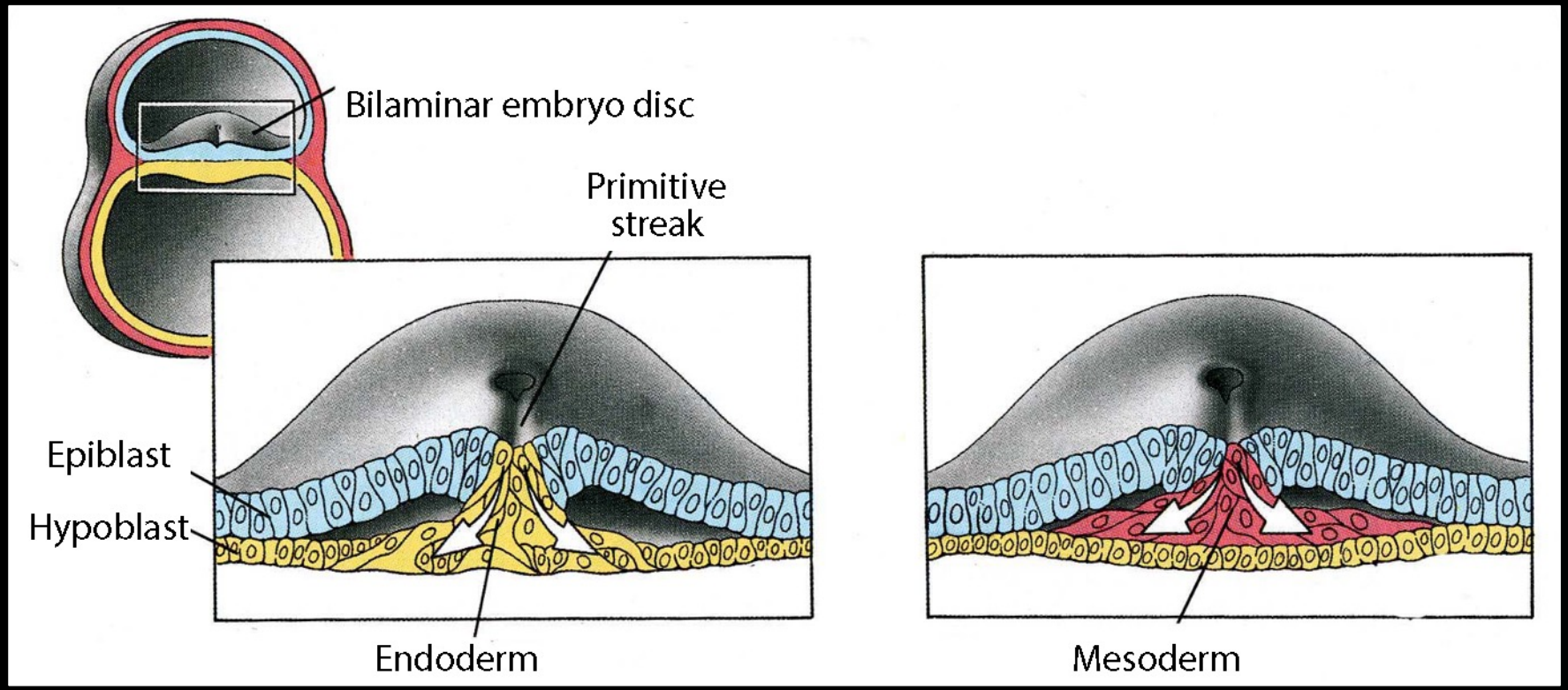


Anterior-posterior, left-right and dorsal-ventral axis are determined by the formation of primitive streak

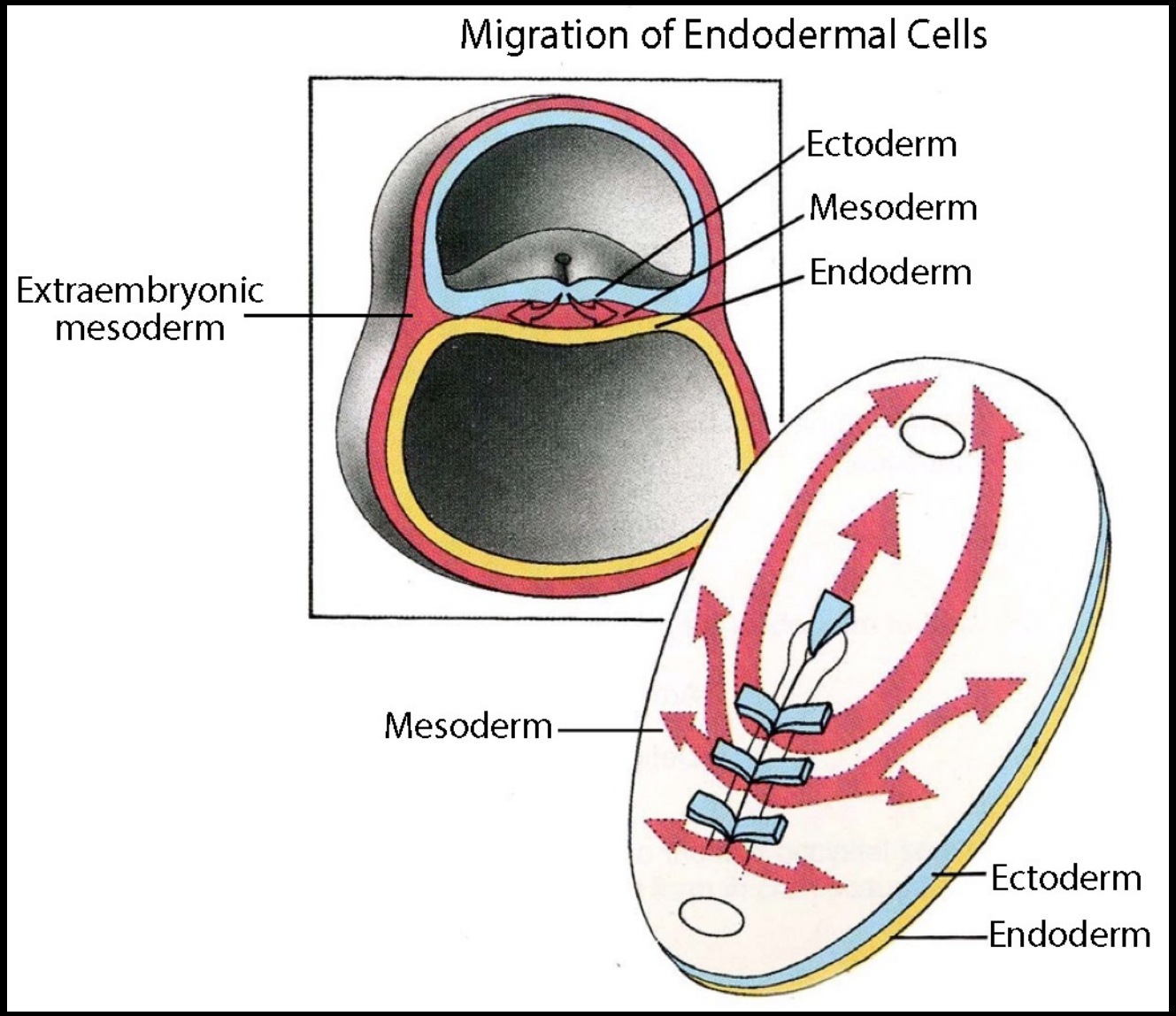
Gastrulation

Days 14-15

Days 16



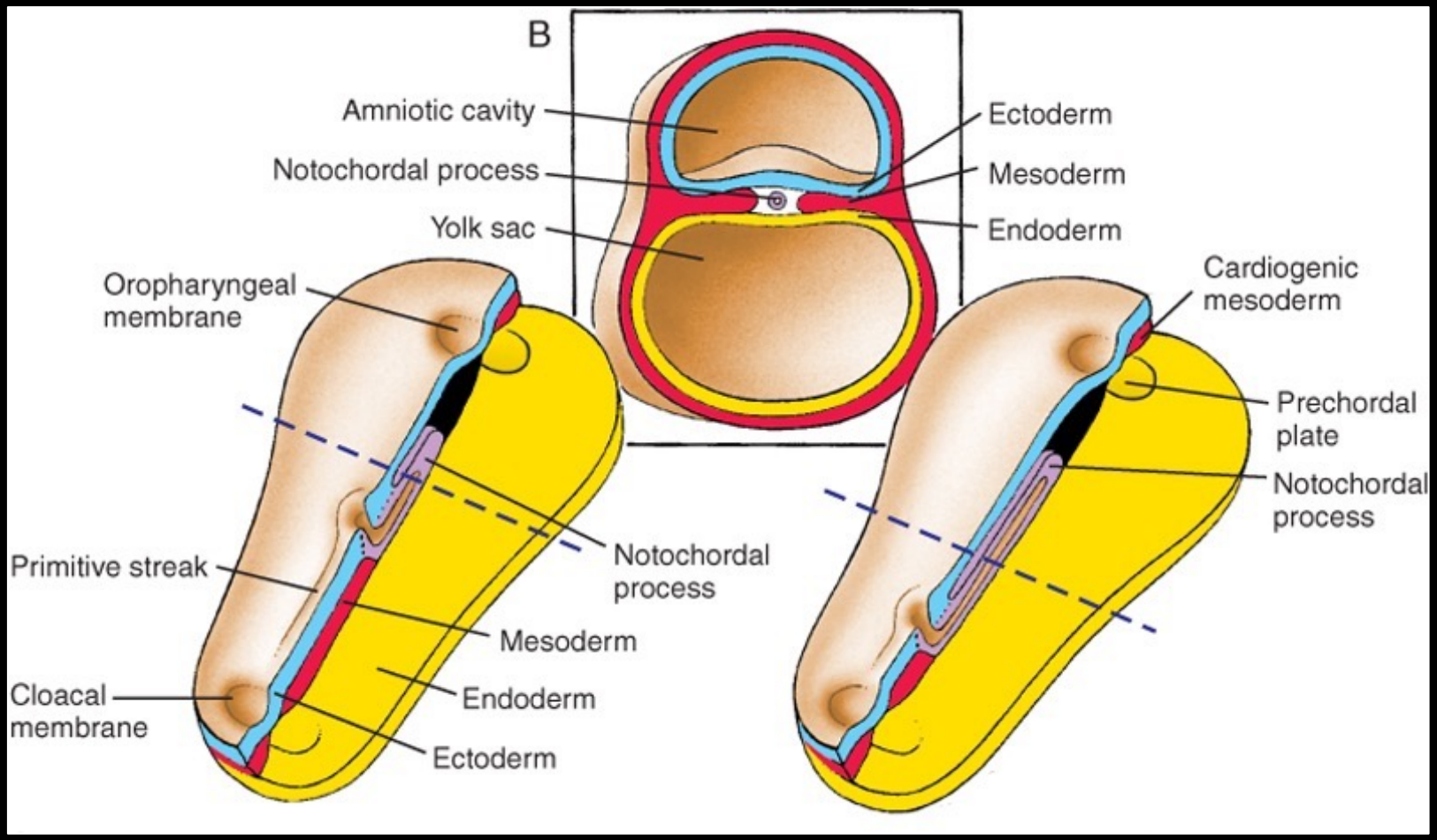
Day 16


Migration of Endodermal Cells
Ectoderm
Mesoderm
Endoderm
Extraembryonic mesoderm
Mesoderm
Ectoderm
Endoderm

Formation of Notochord

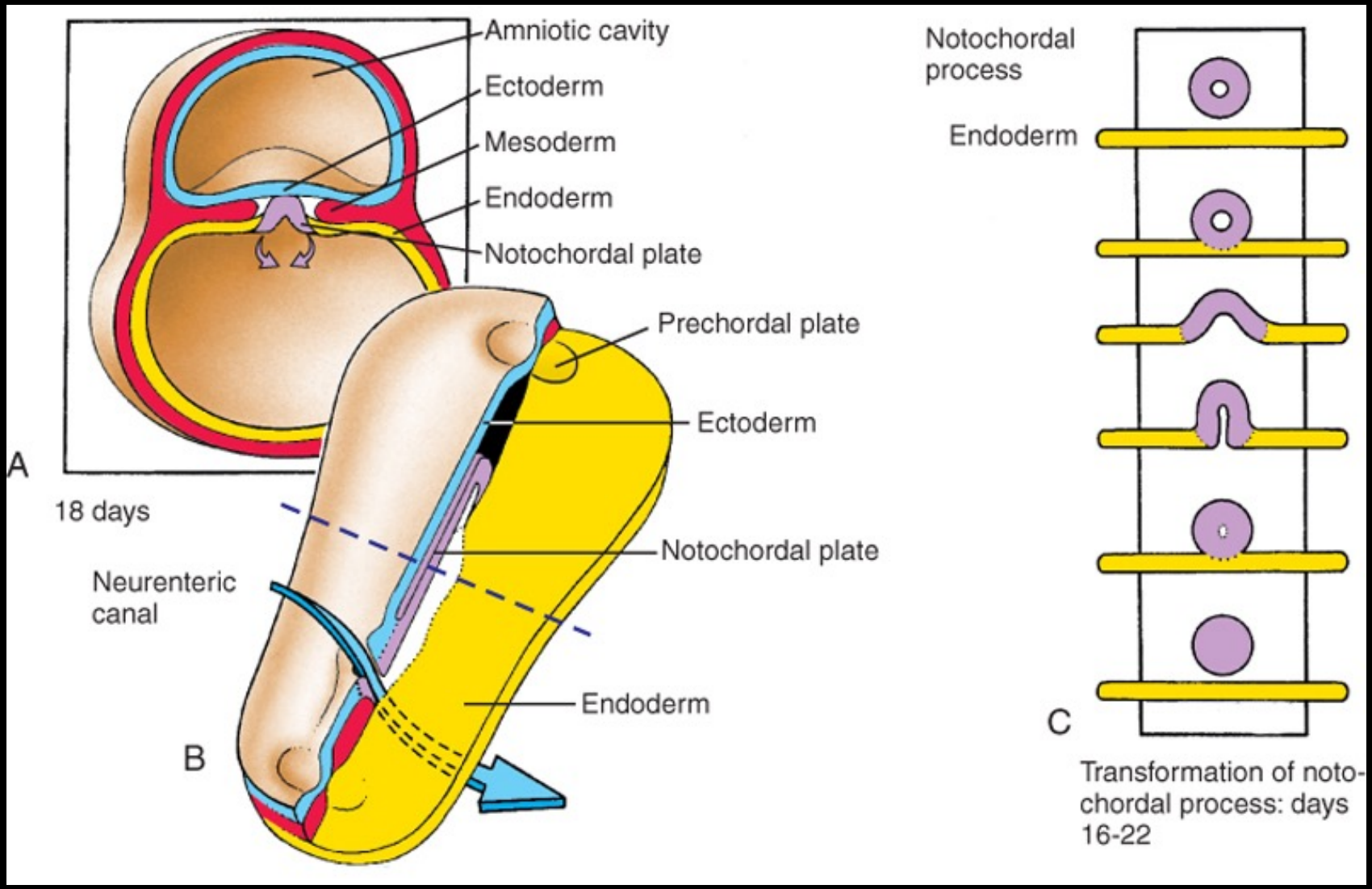
Early Day 17

Late Day 17



Primitive streak begins to regress

Days 16-22



Tube

Day 16

Day 17

Day 18

Day 19

Day 20

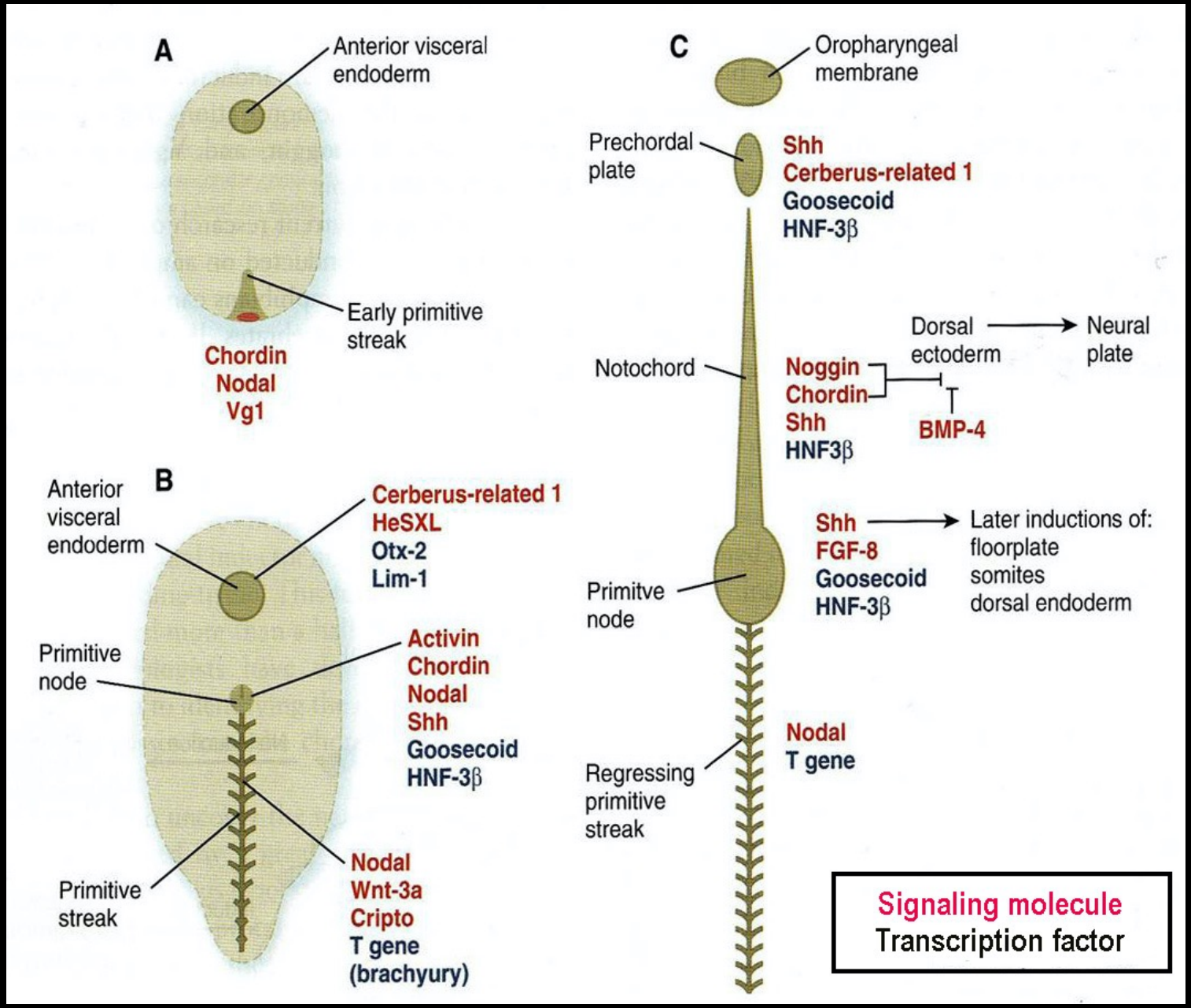
Day 22

Cord

Functions of Notochord

1. Provides rigidity and determines longitudinal axis of the developing embryo
2. Induces the development of vertebral column and nucleus pulposus.
3. Induces the overlying ectoderm, which is differentiated into neural plate that forms the central nervous system (CNS).

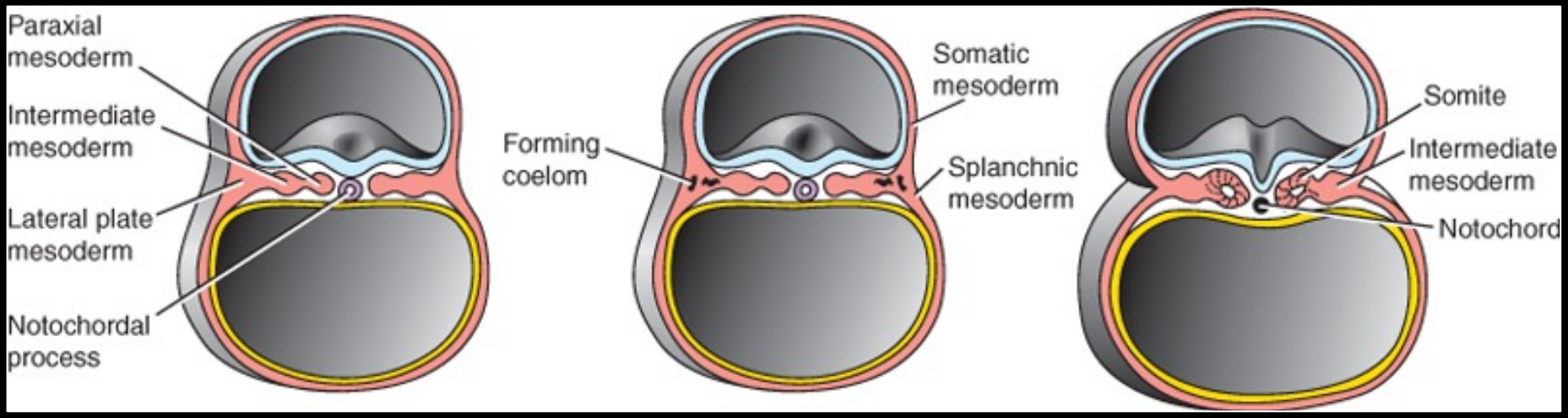
Modulatory Effects of Notochord



Day 17

Day 18

Day 21

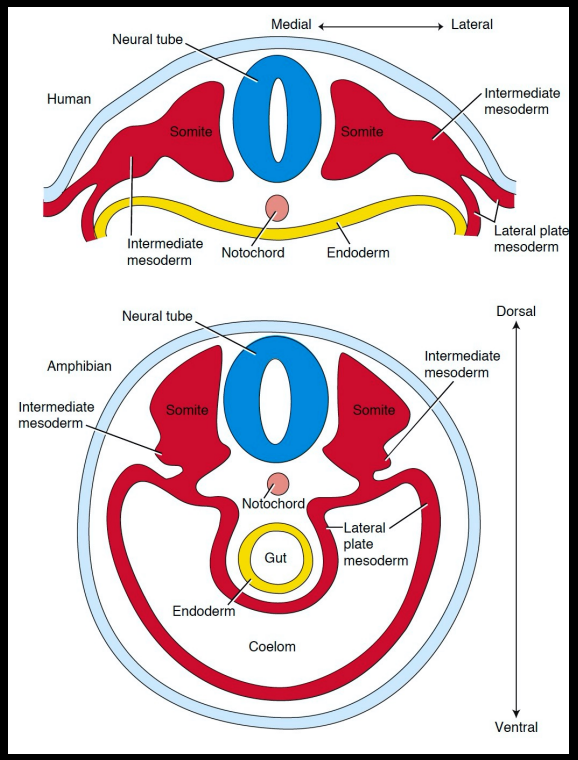


Paraxial Mesoderm

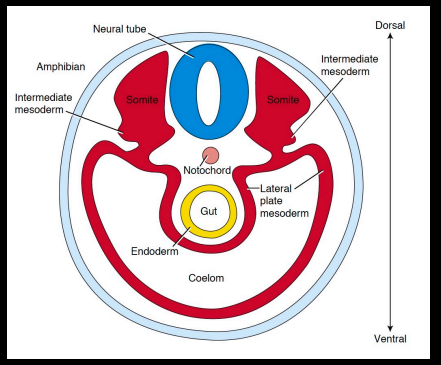
- Skeleton & connective tissue of body
- Skeletal muscles
- Portion of dermis

Intermediate Mesoderm

- Urinary tract
- Portion of genital tract



Lateral Mesoderm



- Parietal mesoderm (Somatic mesoderm)

  (Upper layer - adjacent to ectoderm)

  – Covers the body wall cavities (pleura, peritoneum etc.) with overlying ectoderm
  – Major portion of dermis
  – Bones and connective tissue of the limbs, and the sternum
  – Costal cartilages, limb muscles, most of body wall muscles

- Visceral mesoderm (Splanchnic mesoderm)

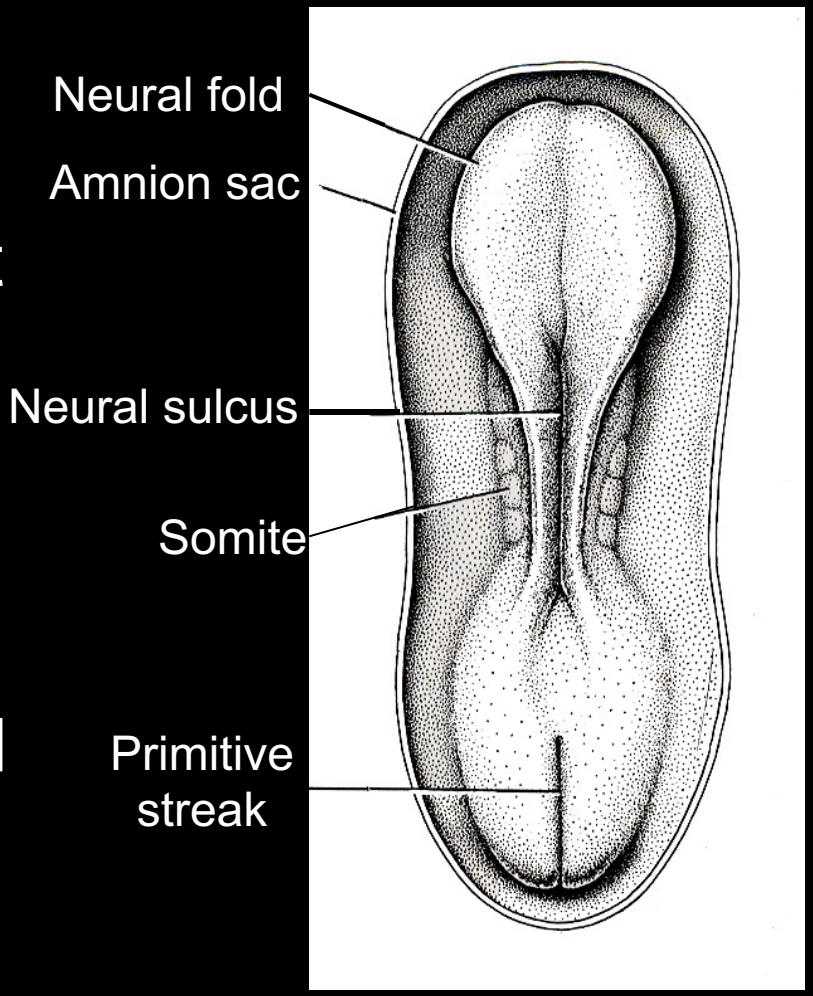
  (Lower Layer - adjacent to endoderm)

  – Wall of the gut tube
  – Serous membranes of visceral organs

Differentiation of Ectoderm (Neural Development)

Towards end of 3rd Week

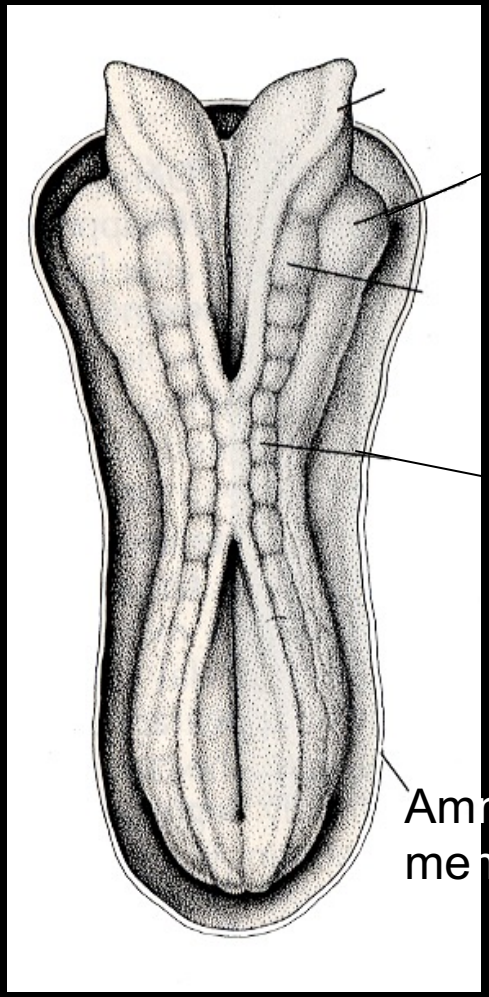
- Primitive streak becomes relatively short
- Ectoderm turns to neural plate which enlarges and begin to fold (neural folds)
- Midline groove is named as neural sulcus.



Top view

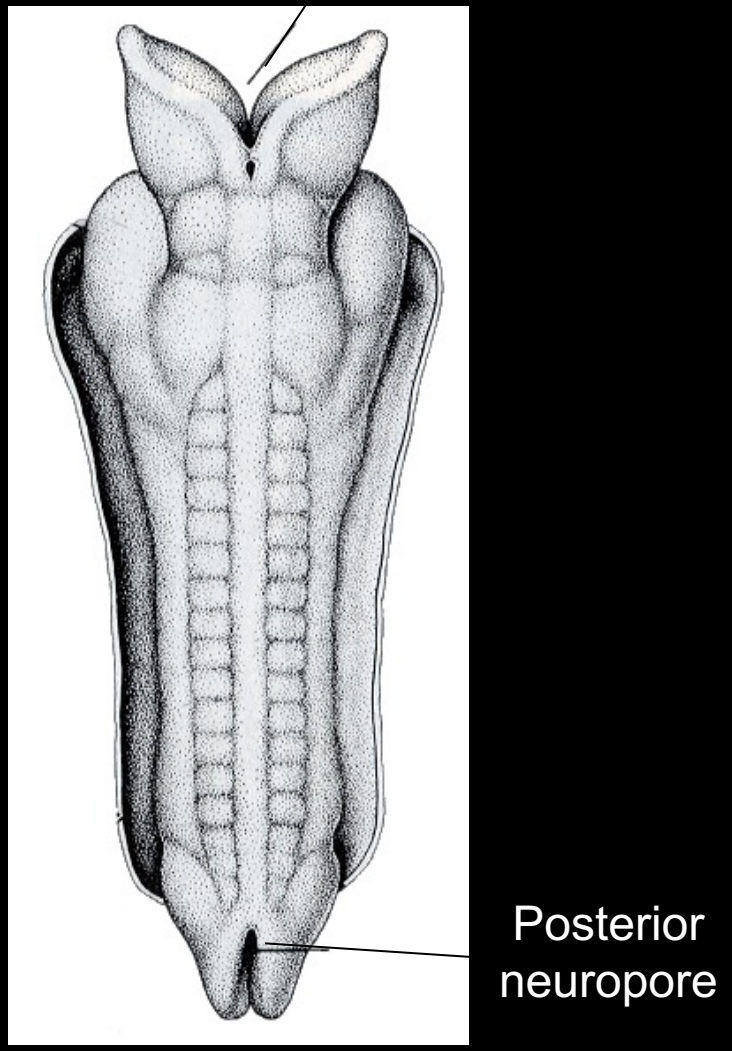
Day 20

- Neural folds enlarges and fuse in the midline
- This fusion happens at the 4th somite level in the cervical region and gradually extends to cranial and caudal regions



End of day 23

- Fusion is completed when all somite levels fuse together and to form a neural tube.
- Neural tube is open at the cephalic and caudal regions namely anterior neuropore and posterior neuropore respectively.

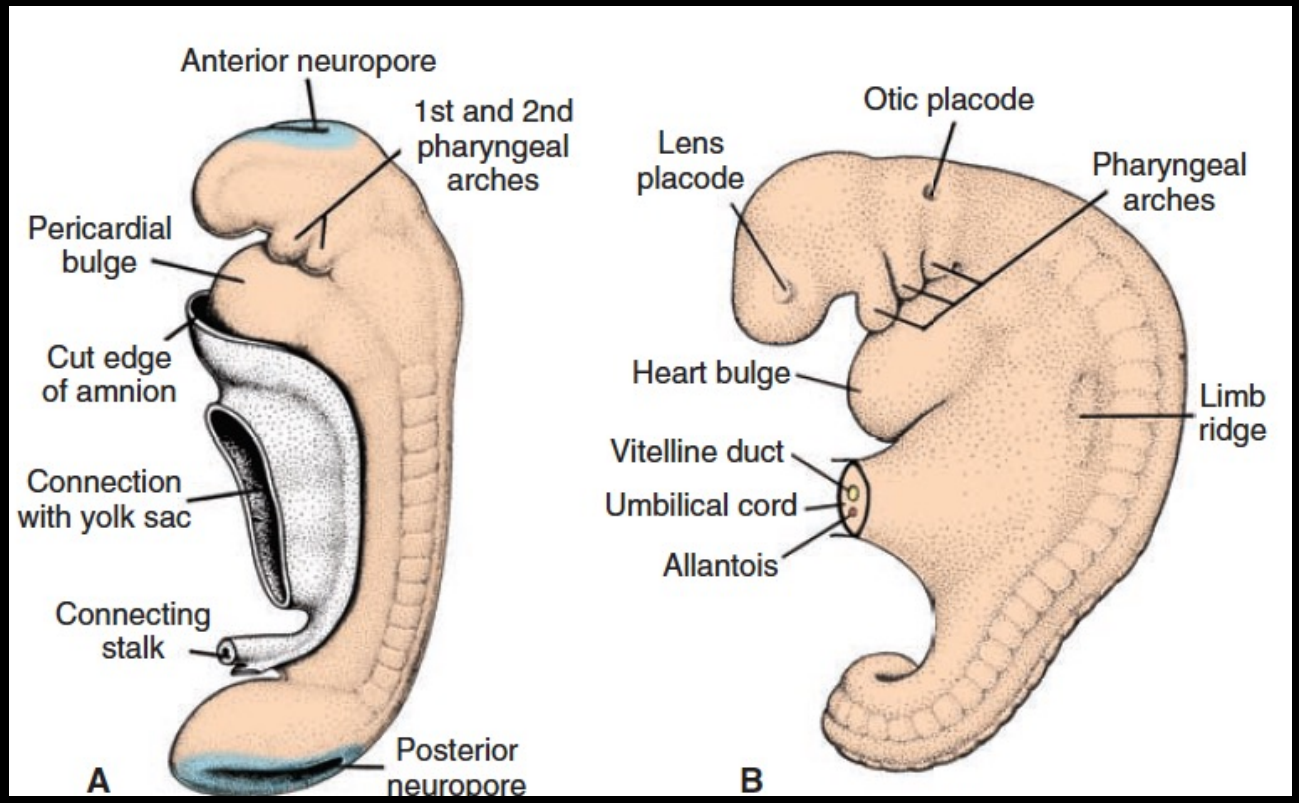


Closure of Anterior Neuropore

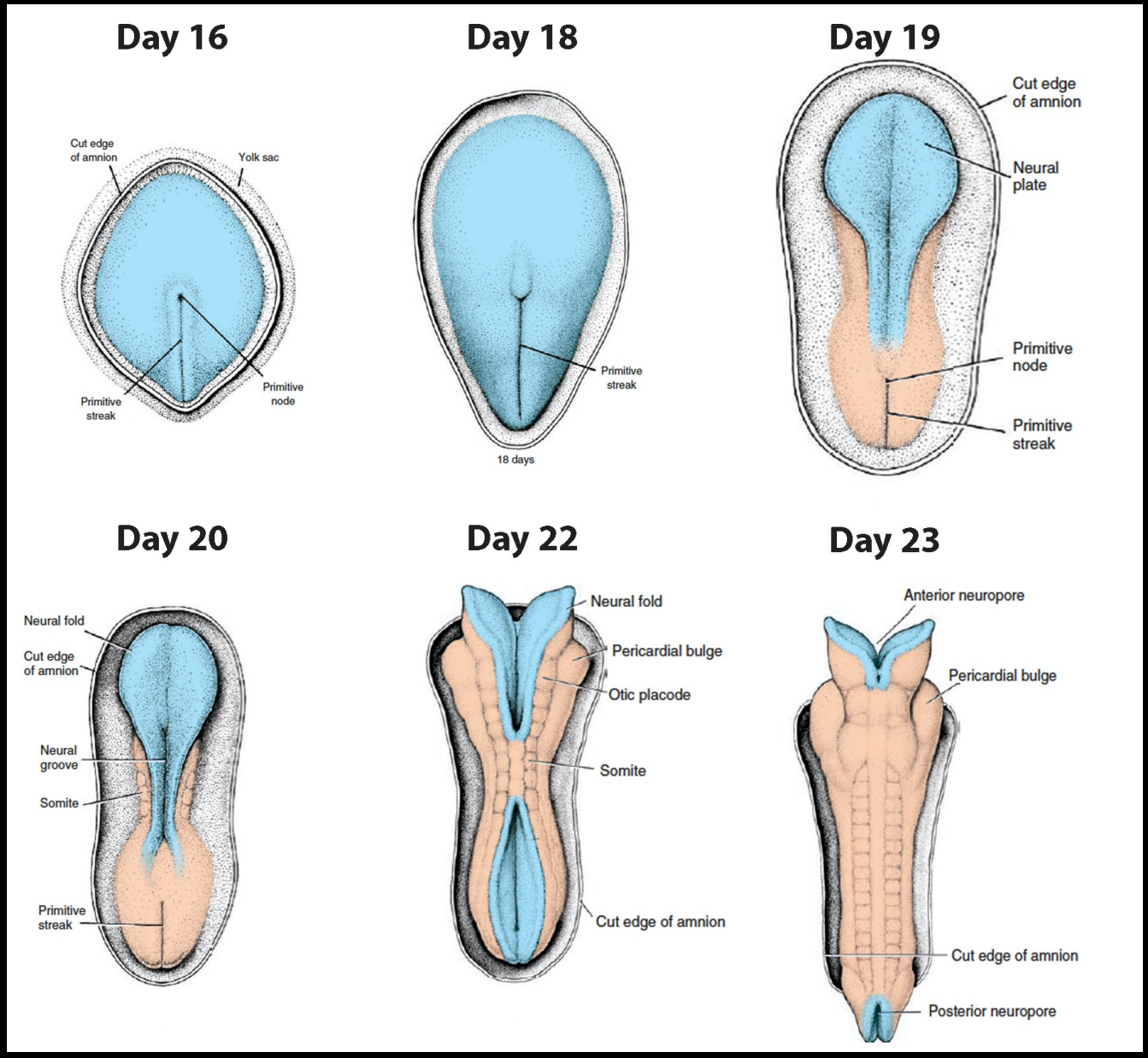
- By the end of Day 25
- This is 18-20-somite period

Closure of Posterior Neuropore

- By the end of Day 27
- This is 25-somite period

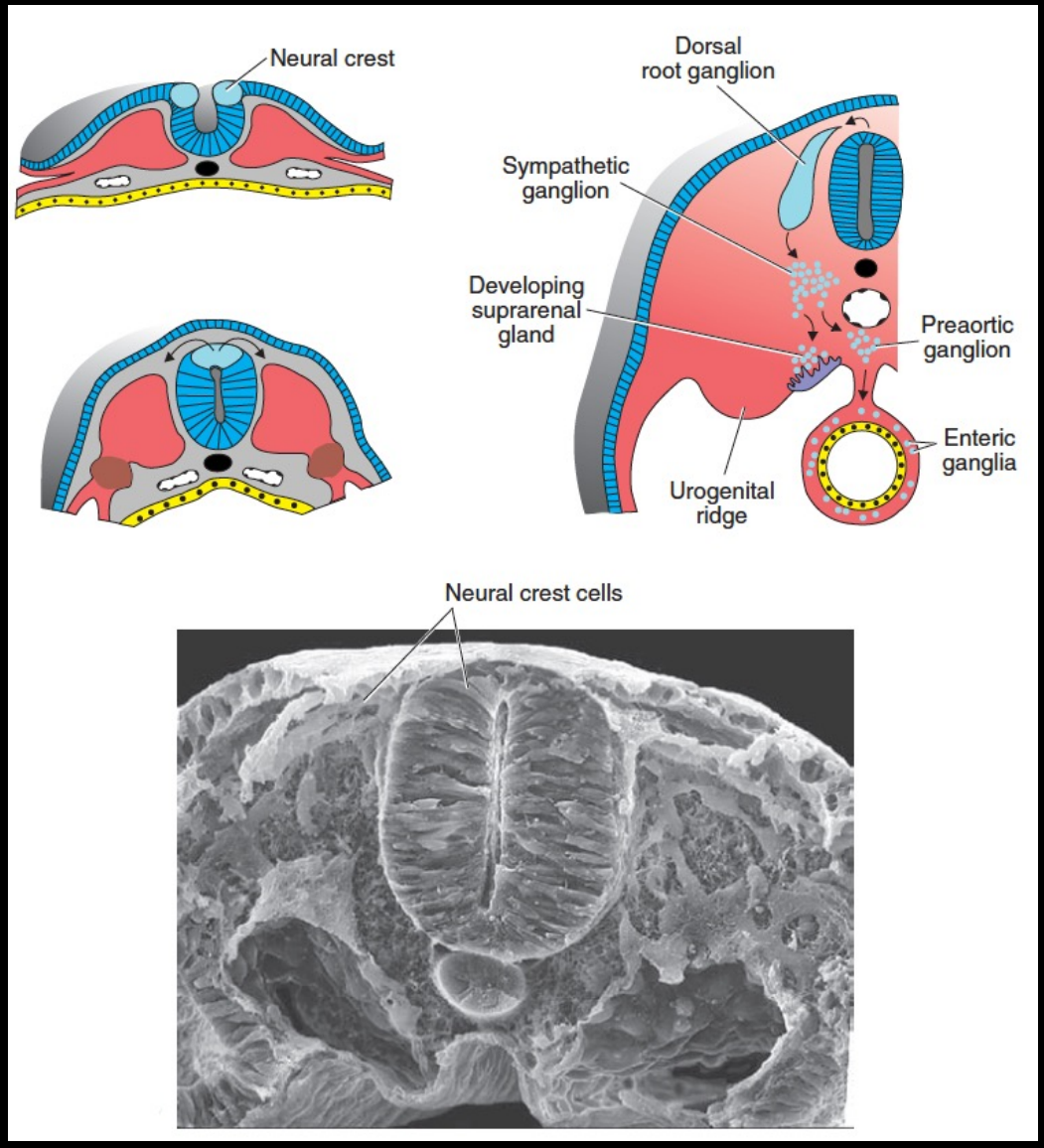


Summary of Neural Development During Days 16-23 (Third Week)



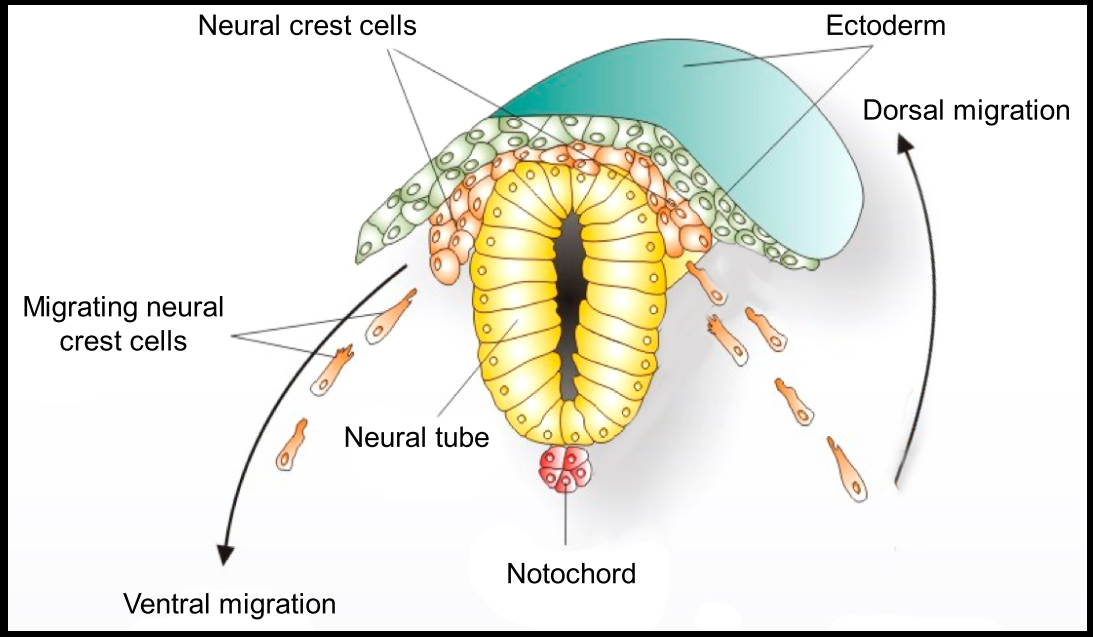
Neural Crest (Crista Neuralis)

- As the neural folds elevate and fuse, cells at the lateral border or crest of the neuroectoderm begin to dissociate from their neighbors.
- This cell population, the neural crest will undergo an epithelial-to-mesenchymal transition as it leaves the neuroectoderm by active migration and displacement to enter the underlying mesoderm.



Neural crest cells from the trunk region leave the neuroectoderm after the closure of the neural tube and migrate along one of two directions;

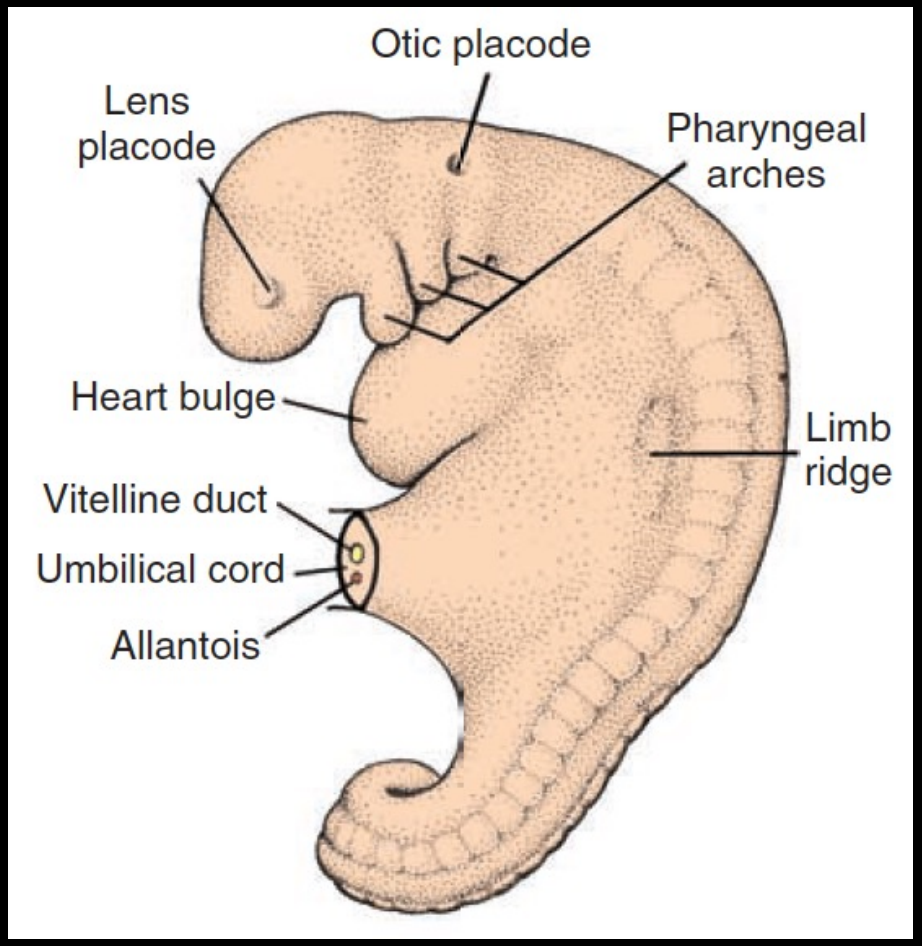
1. Dorsal migration through the dermis, where they will enter the ectoderm through holes in the basal lamina to form melanocytes in the skin and hair follicles.
2. Ventral migration through the anterior half of each somite to become sensory ganglia, sympathetic and enteric neurons, Schwann's cells, glial cells and cells of the adrenal medulla.



Derivatives of Neural Crest Cells
(by induction of Bone Morphogenetic Protein=BMP)

- Connective tissue and bones of the face and skull
- Cranial nerve ganglia
- C cells of the thyroid gland
- Conotruncal septum in the heart
- Odontoblasts
- Dermis in face and neck
- Spinal (dorsal root) ganglia
- Sympathetic chain and preaortic ganglia
- Parasympathetic ganglia of the gastrointestinal tract
- Adrenal medulla
- Schwann cells
- Glial cells
- Meninges (forebrain)
- Melanocytes
- Smooth muscle cells in blood vessels of face and forebrain

External View of Day 28 Human Embryo



- Otic placode (later otic vesicle)
- Lens placode (later eye lens)
- Pharyngeal arches (later many cranio-facial bones, glands etc.)
- Heart bulge (developing heart)
- Limb ridge (upper extremity)
- Vitellin duct (regressing)
- Umbilical cord (developing)
- Allantois (transitory endodermal sac)

Summary of Ectodermal Derivatives

- The central nervous system
- The peripheral nervous system
- The sensory epithelium of the ear, nose, and eye

- The epidermis, including the hair and nails

- Subcutaneous glands
- The mammary glands
- The pituitary gland

- Enamel of the teeth