Third Week of Development: Trilaminar Germ Disc

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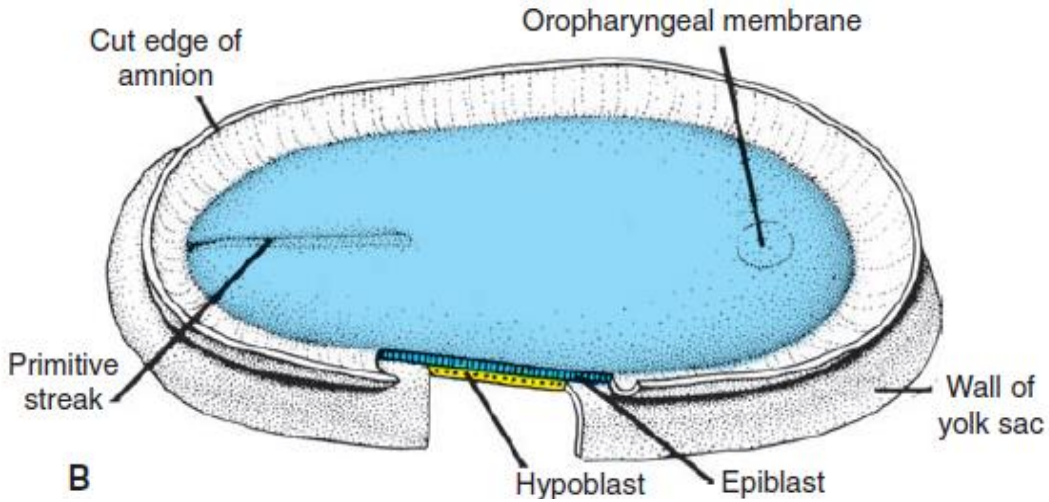
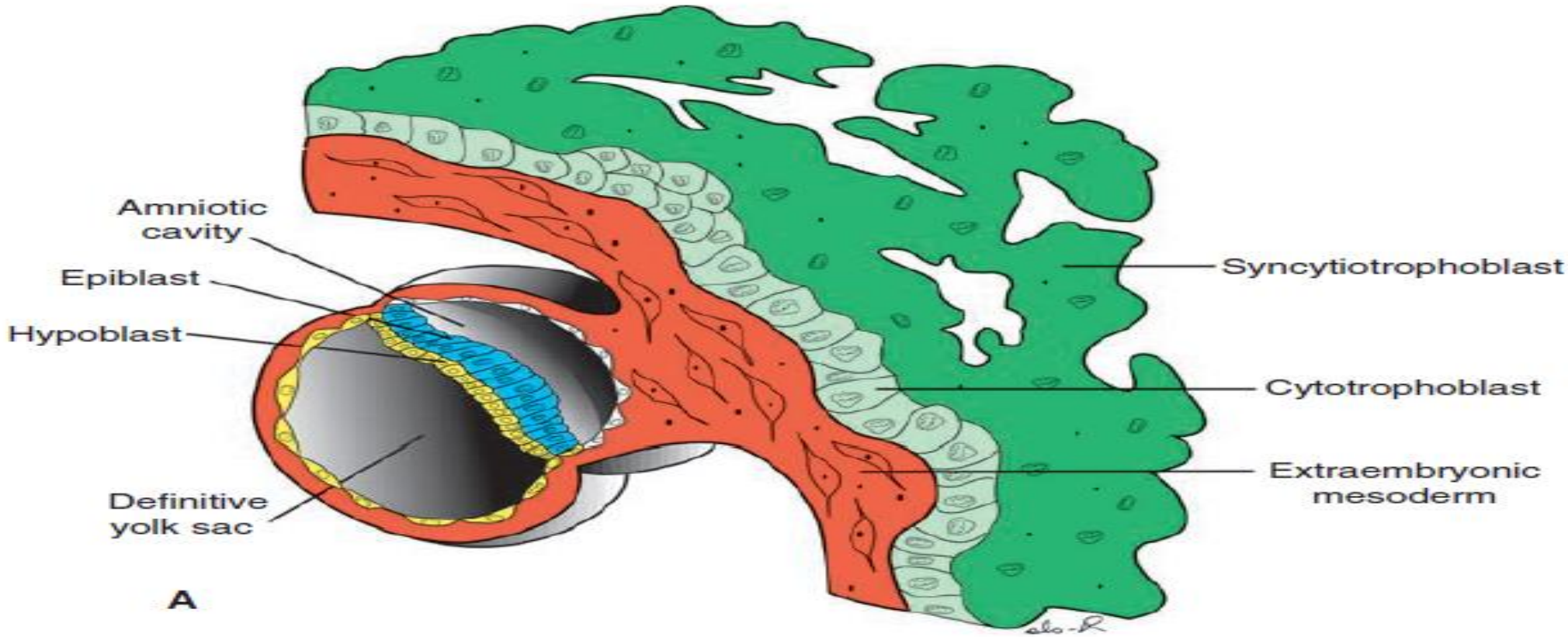
- 3rd embryonic week begins a six-week period of rapid development & differentiation
- During the 3rd week, the 3 primary germ layers are established, which lays the groundwork for organ development in weeks 4 through 8

- **Gastrulation**
- The most characteristic event occurring during the 3rd week of gestation is **gastrulation**, occurs about 15 days after fertilization
- In this process, the bilaminar (two-layered) embryonic disc, consisting of epiblast & hypoblast, is transformed into a **trilaminar** (three-layered) **embryonic disc** consisting of 3 primary germ layers: the ectoderm, mesoderm, and endoderm
- The **primary germ layers** are the major embryonic tissues from which the various tissues and organs of the body develop
- Axial orientation of the embryo is established

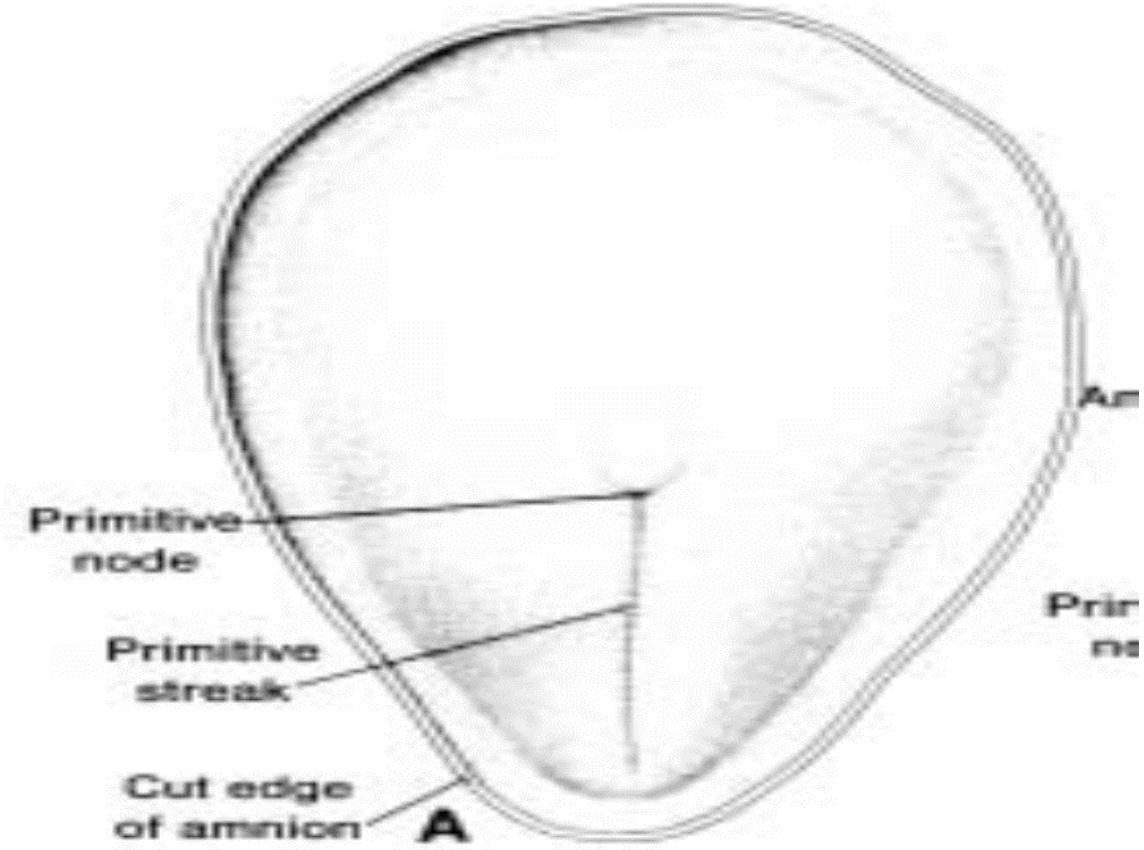
- Gastrulation involves the well-coordinated & important rearrangement & migration of cells from the epiblast to set the stage for the important interactions of the newly positioned cells
- It is the beginning of morphogenesis (formation of body form)
- ***Bone morphogenetic proteins*** and other **signaling molecules** such as ***FGFs*** and ***Wnts*** play an essential role in this process
- Consists of formation of the primitive streak, the 3 germ layers & the notochord
- Embryo is referred to as a **Gastrula**

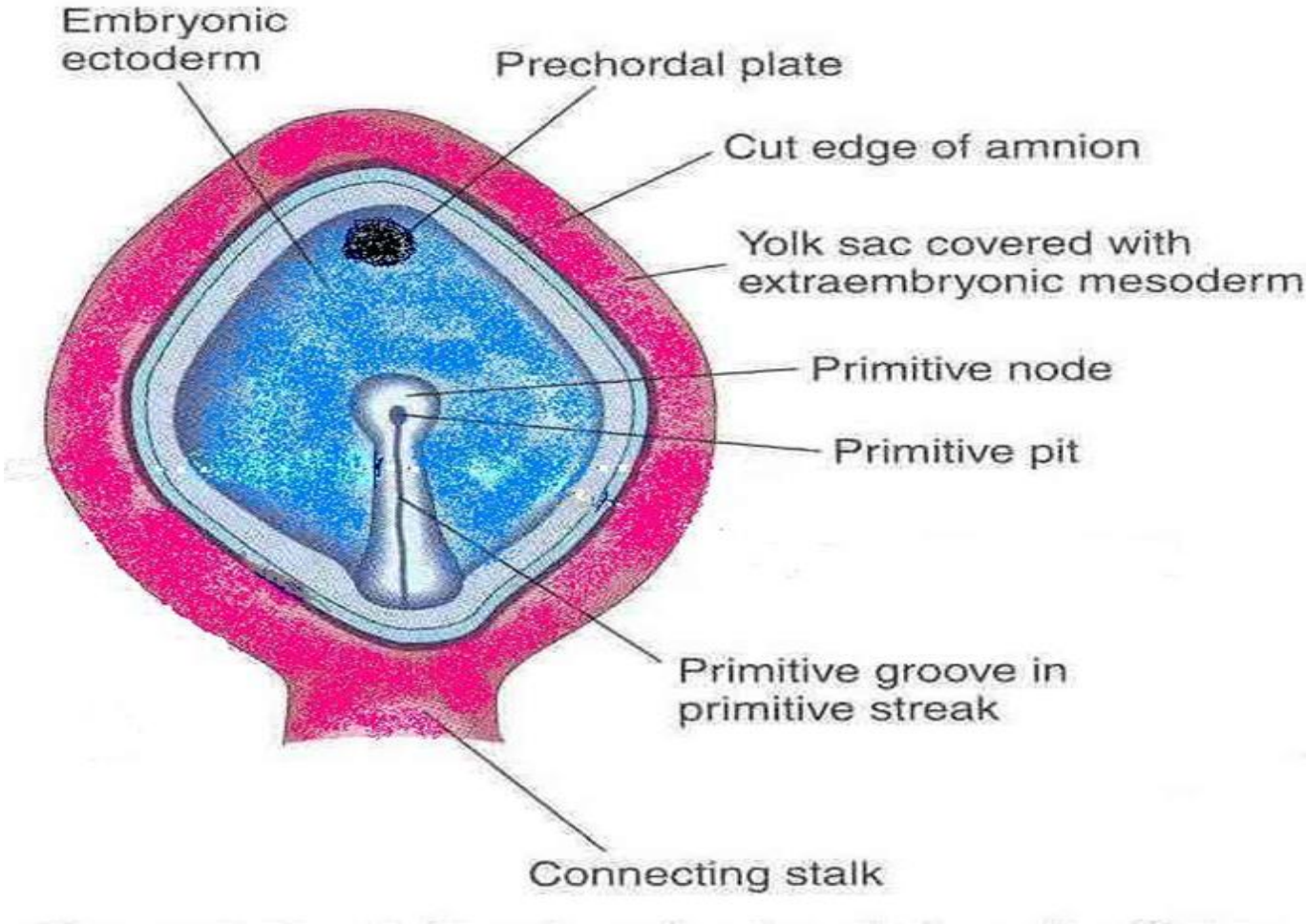
- **Formation of the Primitive Streak**
- first evidence of gastrulation is the formation of the **primitive streak**
- Primitive streak appears caudally in the median plane of the dorsal aspect of the embryonic disc
- primitive streak results from proliferation of the epiblastic cells in the median plane, in the caudal half of the epiblast & lies along the cranio-caudal axis.
- Its cranial end forms **primitive node**
- A groove, **primitive groove**, appears in the primitive streak, which continues with a small depression, **primitive pit**, in the primitive node

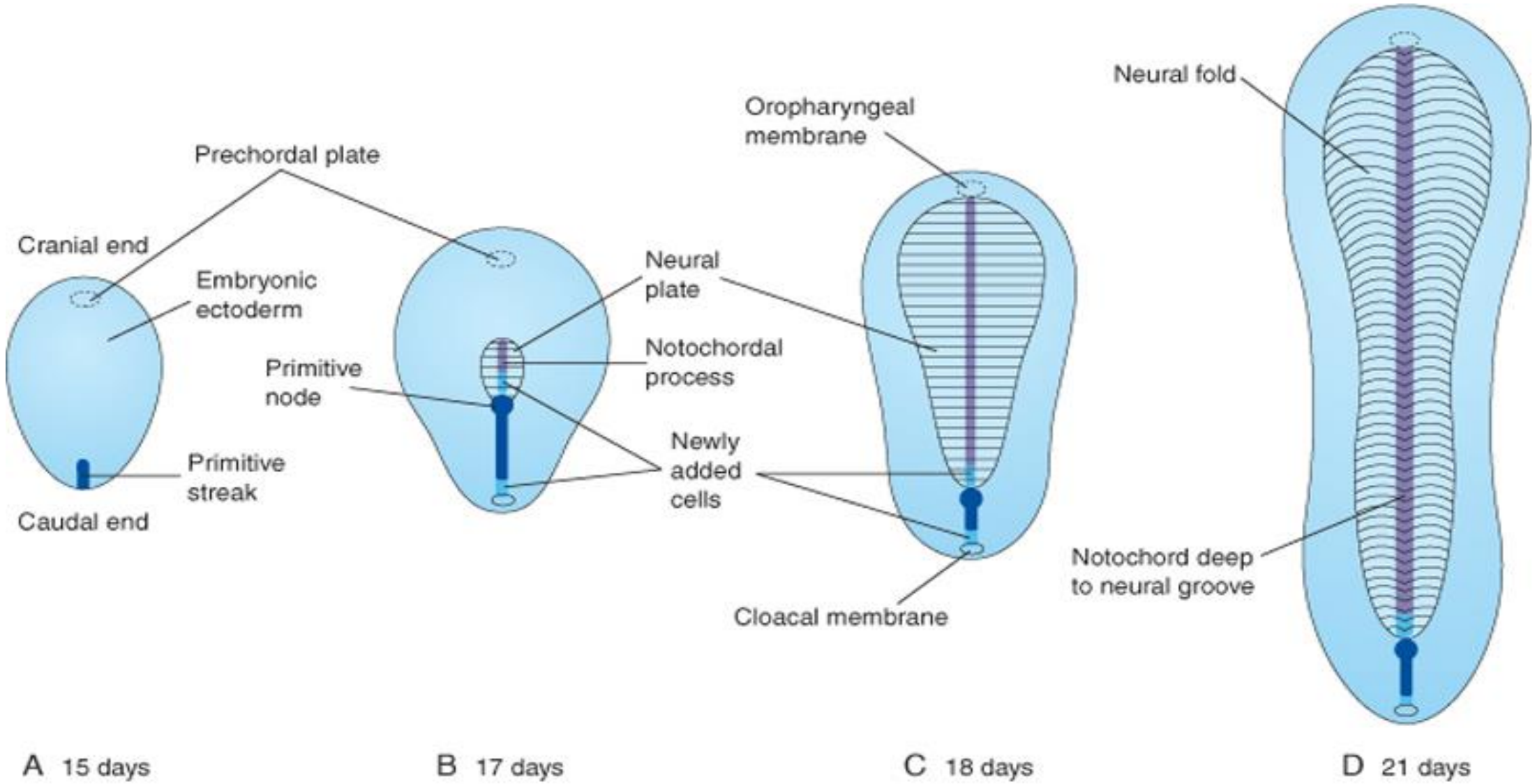

Cut edge of amnion
Oropharyngeal membrane
Primitive streak
Wall of yolk sac
Hypoblast
Epiblast
B


Amniotic cavity
Epiblast
Hypoblast
Definitive yolk sac
Syncytiotrophoblast
Cytotrophoblast
Extraembryonic mesoderm
A

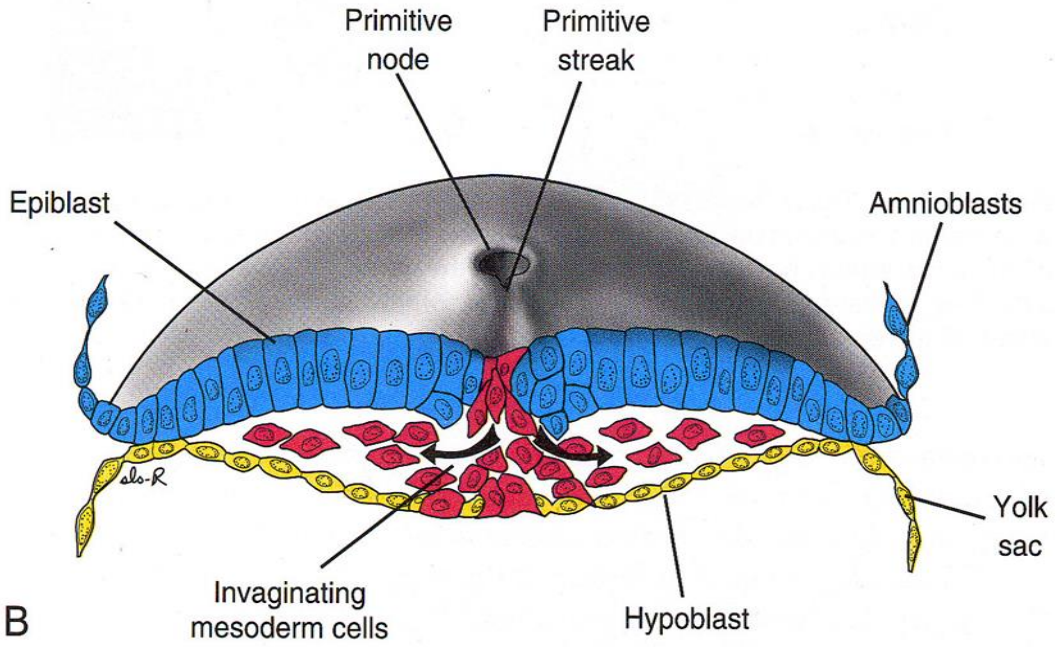
- By this stage of development, it is possible to identify the embryo's:
  - ❖craniocaudal axis
  - ❖cranial and caudal ends
  - ❖dorsal and ventral surfaces

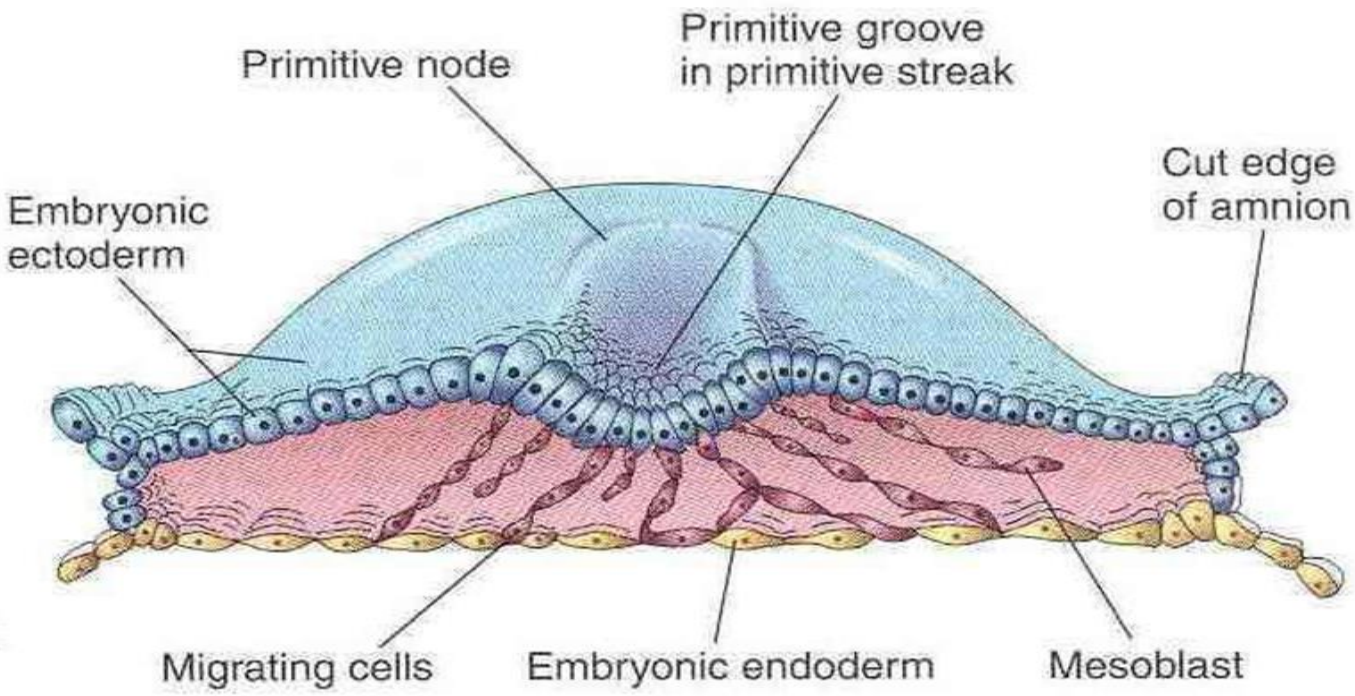




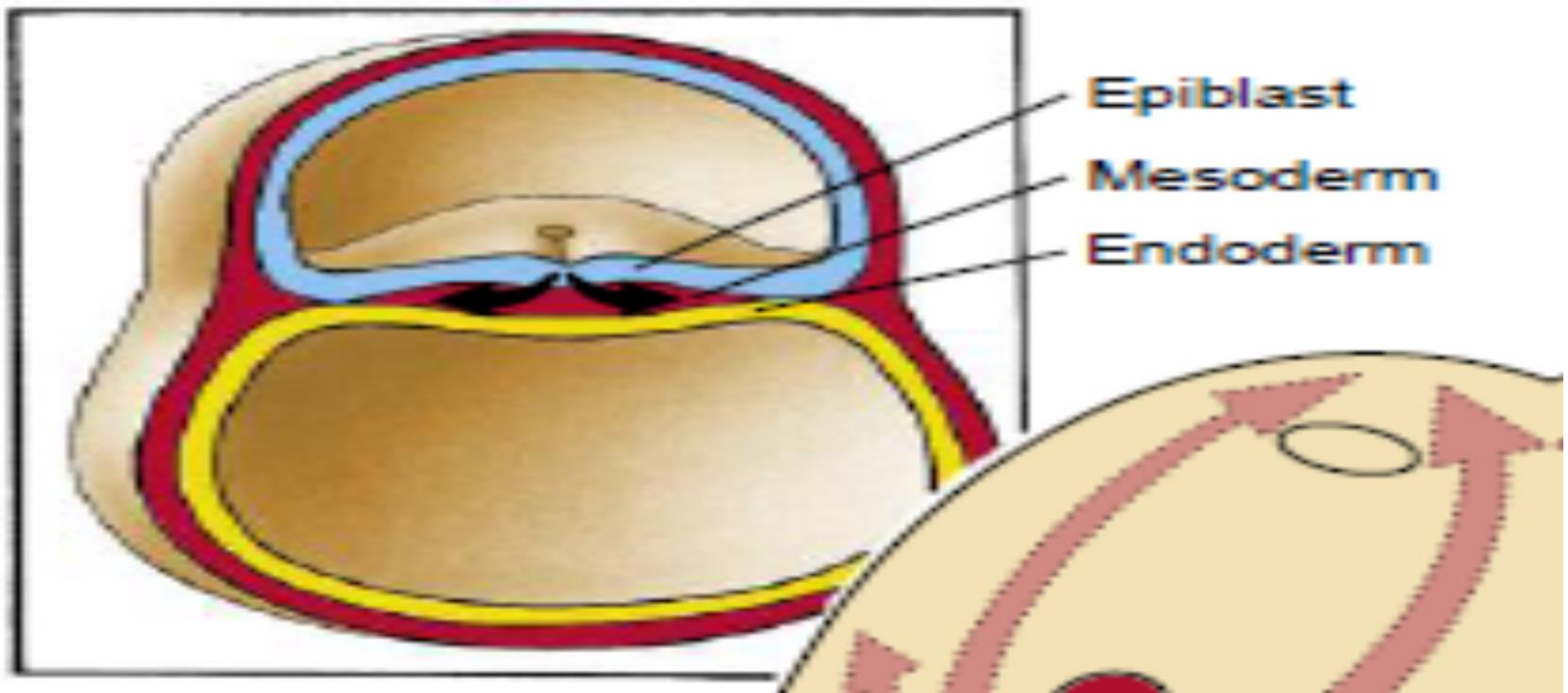


- after the primitive streak appears, cells leave its deep surface & form **mesenchyme**
- a tissue consisting of loosely arranged cells suspended in a gelatinous matrix
- Mesenchyme forms the supporting tissues of the embryo, such as most of the connective tissues of the body and the connective tissue framework of Organs and glands
- Some mesenchyme forms **mesoblast** (undifferentiated mesoderm), which forms the **intraembryonic, or embryonic, mesoderm**

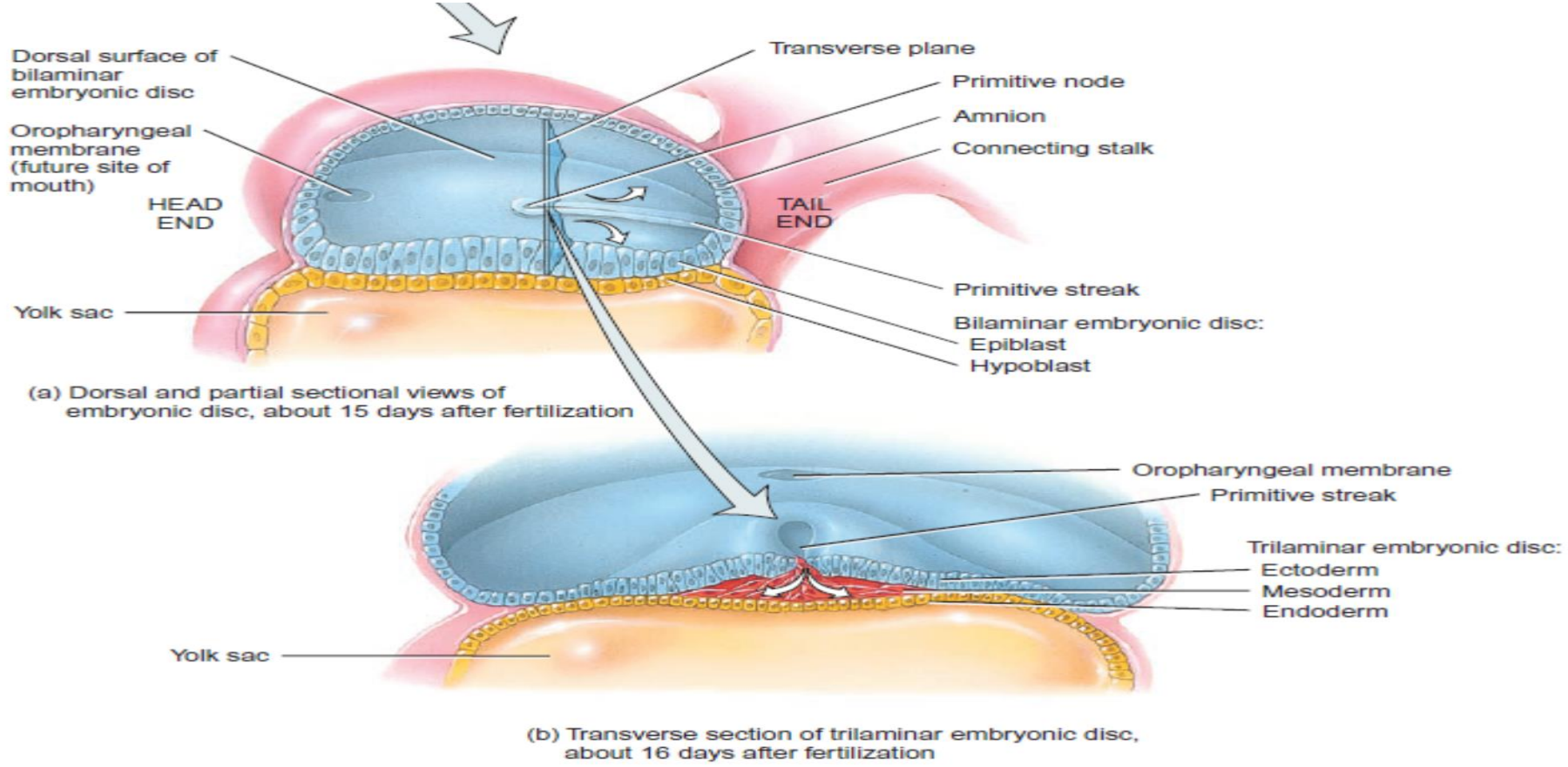


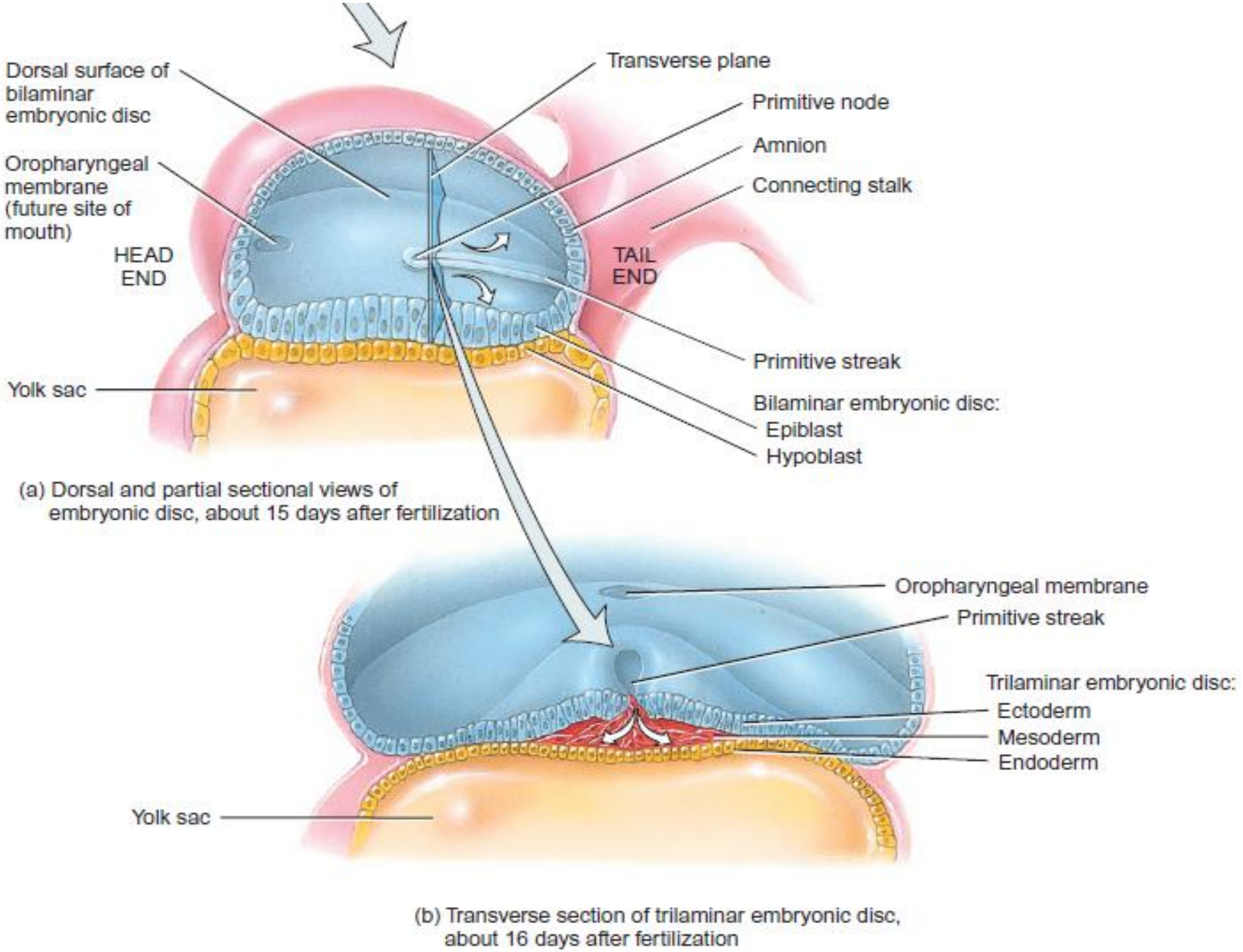


- Cells from the epiblast, the primitive node & other parts of the primitive streak displace the hypoblast, forming the **embryonic endoderm** in the roof of the umbilical vesicle
- Cells remaining in the epiblast then form the **ectoderm**
- The epiblast through the process of gastrulation, is the source of all of the germ layers
- Cells in these layers will give rise to all of the tissues and organs in the embryo



- *signaling molecules* (***nodal factors***) of the *transforming growth factor* Î² superfamily induce formation of mesoderm
- concerted action of other signaling molecules (e.g., *FGFs*) also participates in specifying germ cell layer fates
- transforming growth factor Î² (***nodal***), a ***T-box* transcription factor (*veg T*)**, and the ***Wnt* signaling pathway** appear to be involved in specification of the endoderm



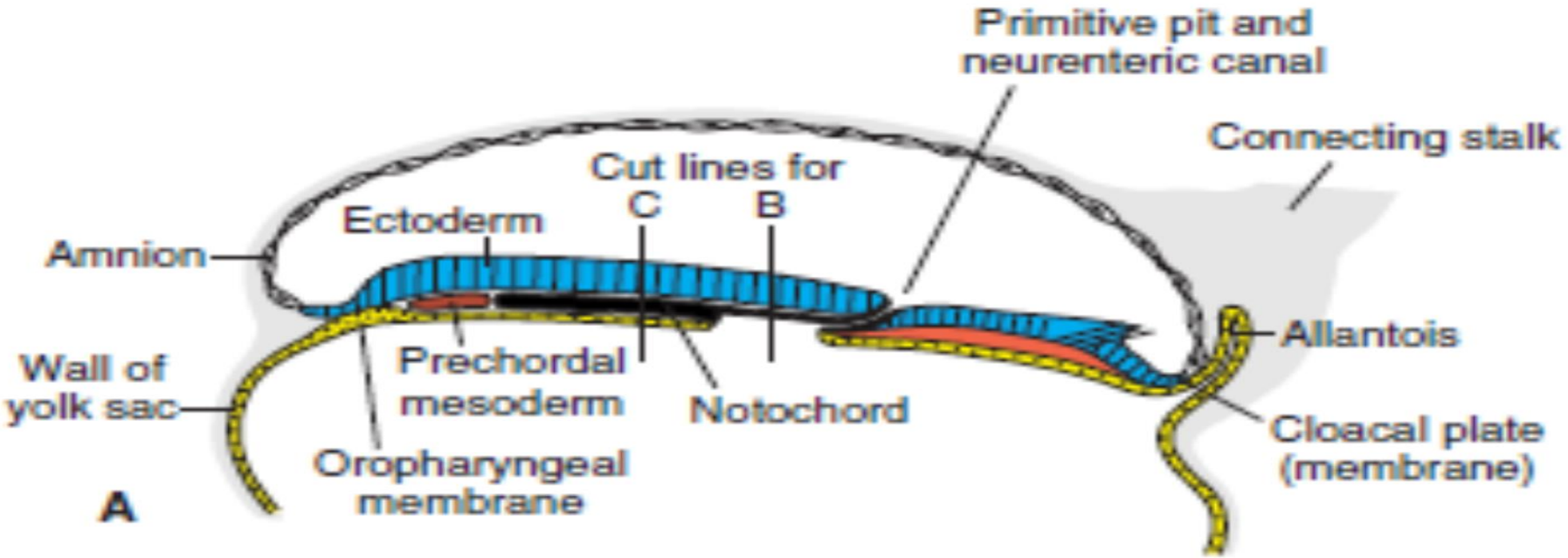

Dorsal surface of bilaminar embryonic disc
Oropharyngeal membrane (future site of mouth)
HEAD END
Transverse plane
Primitive node
Amnion
Connecting stalk
TAIL END
Primitive streak
Yolk sac
Bilaminar embryonic disc:
Epiblast
Hypoblast
(a) Dorsal and partial sectional views of embryonic disc, about 15 days after fertilization
Oropharyngeal membrane
Primitive streak
Trilaminar embryonic disc:
Ectoderm
Mesoderm
Endoderm
Yolk sac
(b) Transverse section of trilaminar embryonic disc, about 16 days after fertilization

- **Embryonic ectoderm** gives rise to the epidermis, central and peripheral nervous systems, the eye, and inner ear, and, as neural crest cells, to many connective tissues of the head
- **Embryonic endoderm** is the source of the epithelial linings of the respiratory and alimentary (digestive) tracts, including the glands opening into the gastrointestinal tract and the glandular cells of associated organs such as the liver and pancreas
- **Embryonic mesoderm** gives rise to all skeletal muscles, blood cells and the lining of blood vessels, all visceral smooth muscular coats, the serosal linings of all body cavities, the ducts and organs of the reproductive and excretory systems, and most of the cardiovascular system.
- In the trunk, it is the source of all connective tissues, including cartilage, bones, tendons, ligaments, dermis, and stroma of internal organs

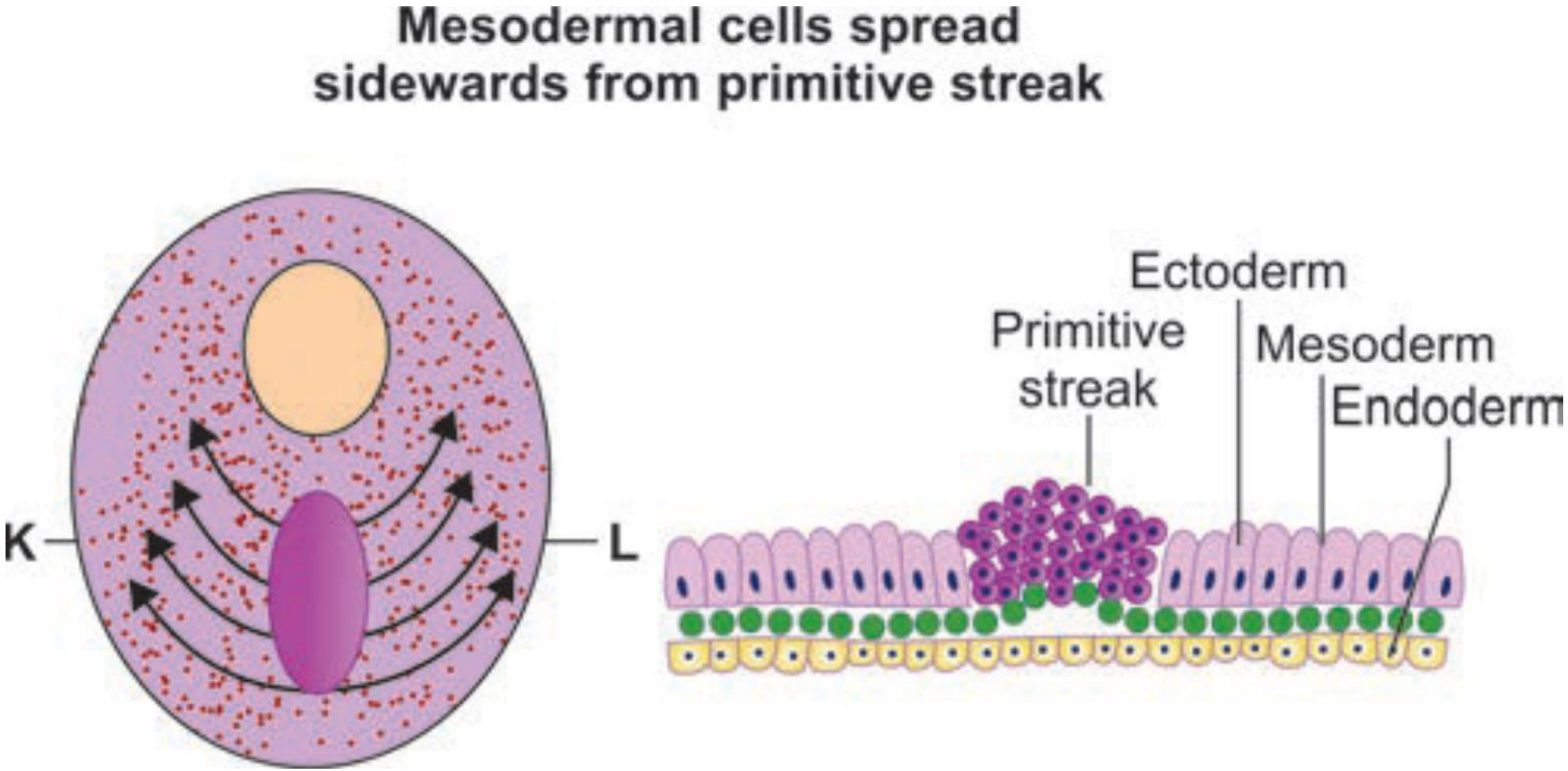
- **Fate of Primitive Streak**
- Actively forms mesoderm until the early part of 4th week
- starts regressing & becomes an insignificant structure in sacrococcygeal regions
- Normally it degenerates & disappears by the end of 4th week
- Remnants may persist & give rise to a large tumor - **Sacrococcygeal Teratomas**
- they are derived from pluripotent primitive streak cells, these tumors contain tissues derived from all 3 germ layers in incomplete stages of differentiation

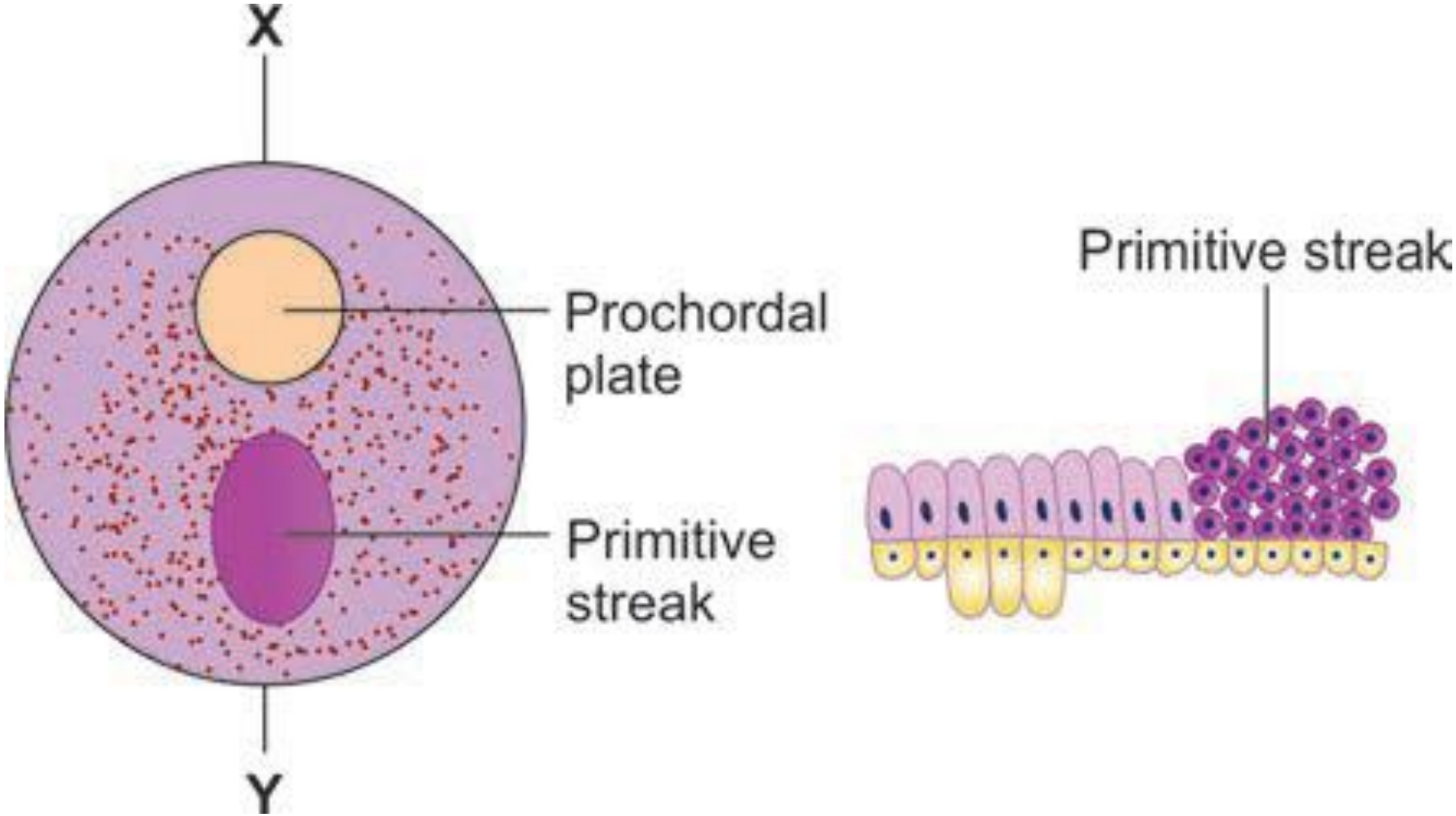
Figure 5.9 Sacrococcygeal teratoma probably resulting from remnants of the primitive streak. These tumors may become malignant and are most common in female fetuses.

- ***Extensions of intraembryonic mesoderm*:**
- intraembryonic mesoderm spreads throughout the disc except in the region of the **prochordal plate**
- region of the **prochordal plate**, ectoderm & endoderm remain in contact
- Prechordal plate have a role as a signaling center for controlling development of cranial structures
- Prechordal mesoderm is a mesenchymal population rostral to the notochord & essential in forebrain & eye induction

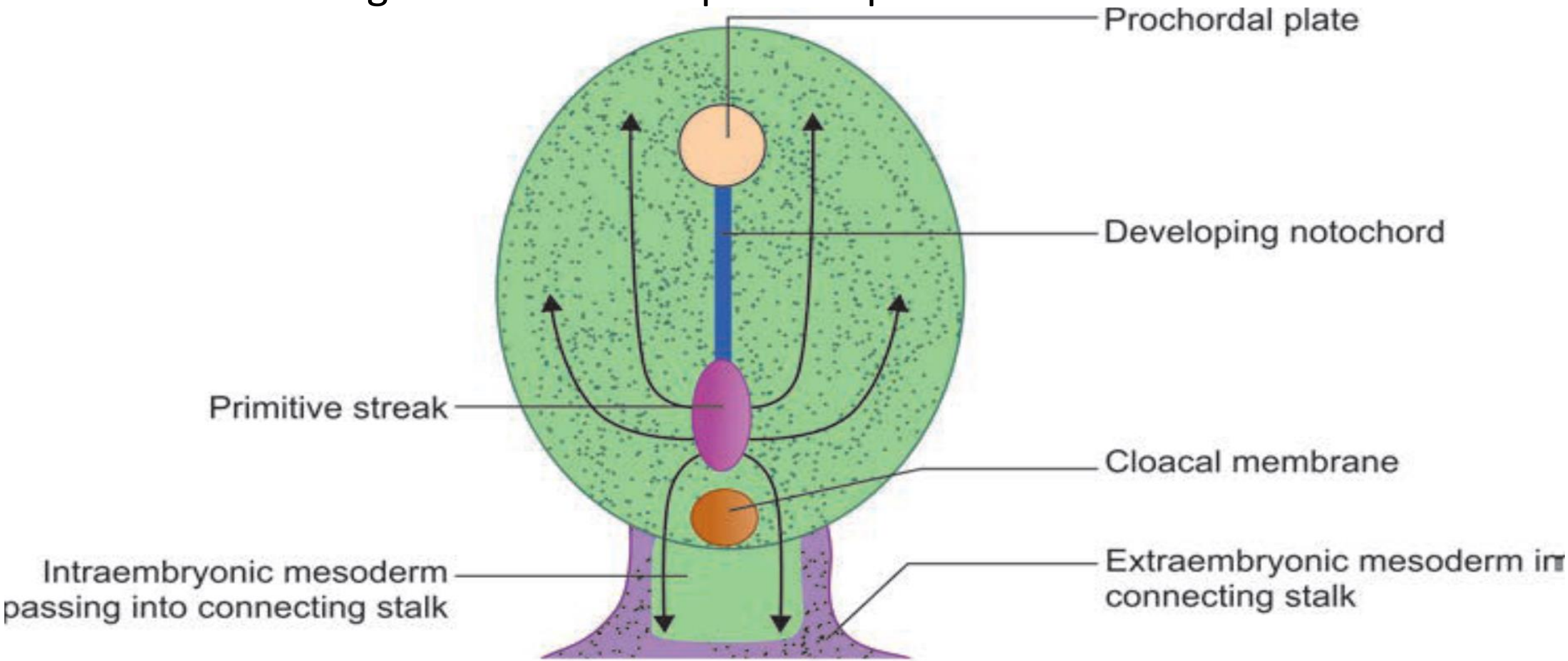


- mesoderm extends cranial to the prochordal plate & here mesoderm from the 2 sides becomes continuous across the midline
- meet cranially to form cardiogenic mesoderm in the **cardiogenic area** where the **heart primordium** begins to develop at the end of the 3rd week

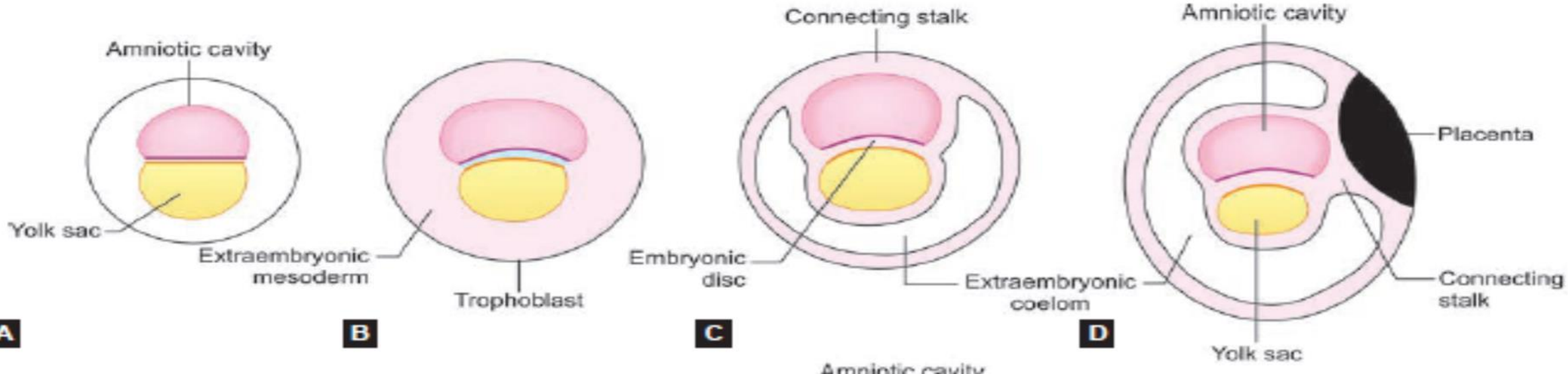


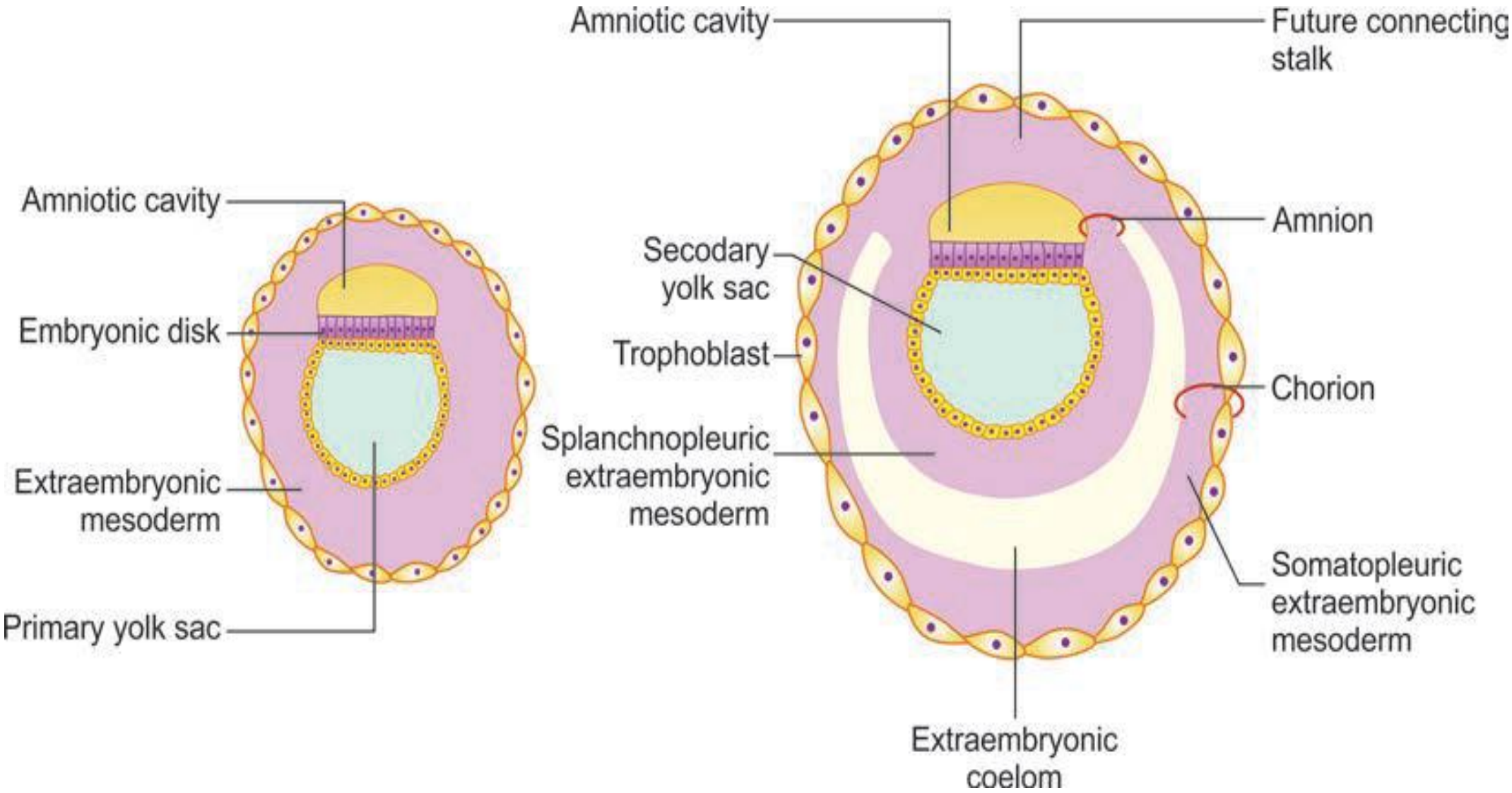

X
Prochordal plate
Primitive streak
Y
Primitive streak

- later development, ectoderm & endoderm mostly persist as a lining epithelium
- there is no mesoderm in the prochordal plate, this region remains relatively thin, & later forms the ***buccopharyngeal membrane***
- The disc also elongates & becomes pear-shaped

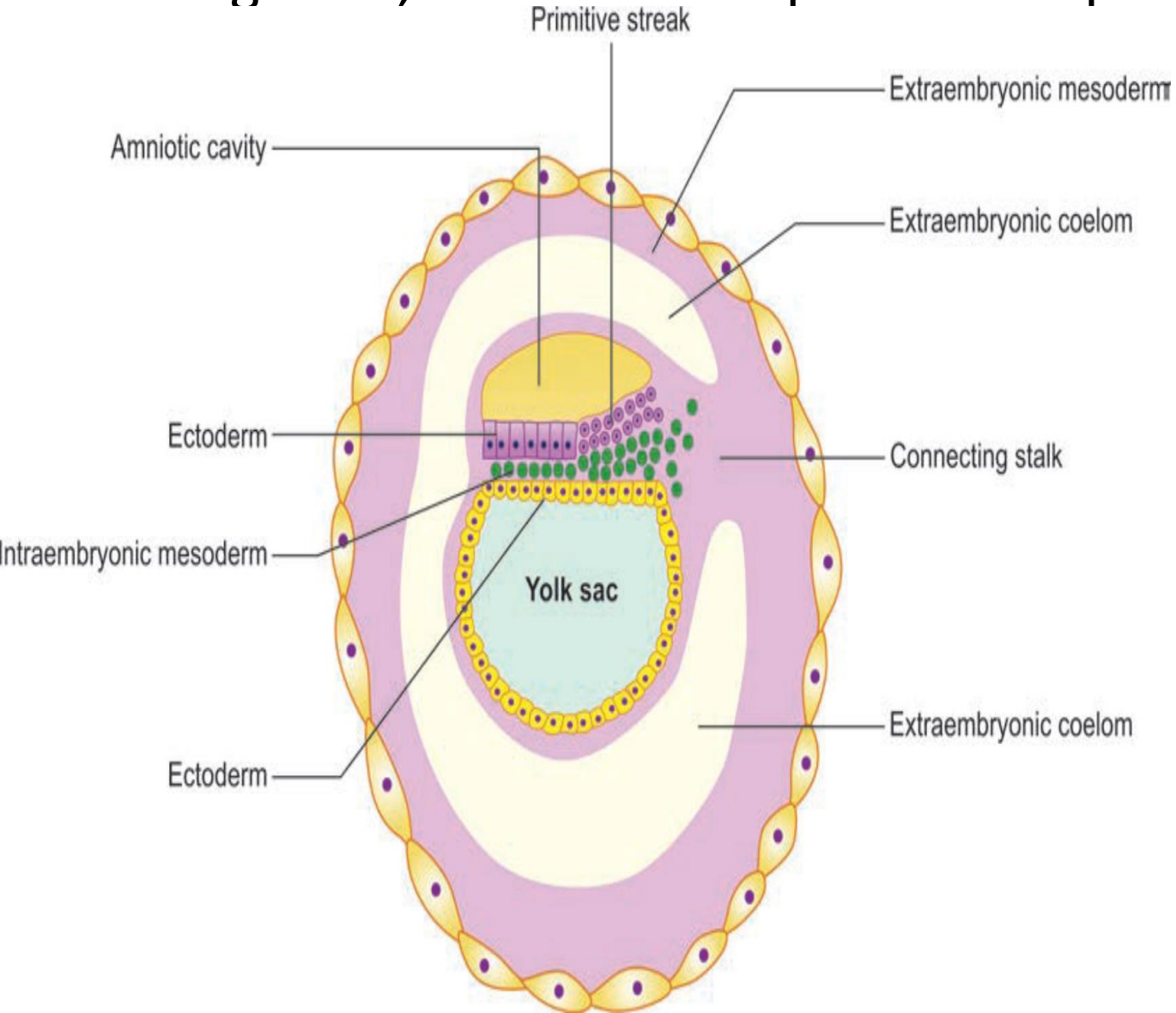


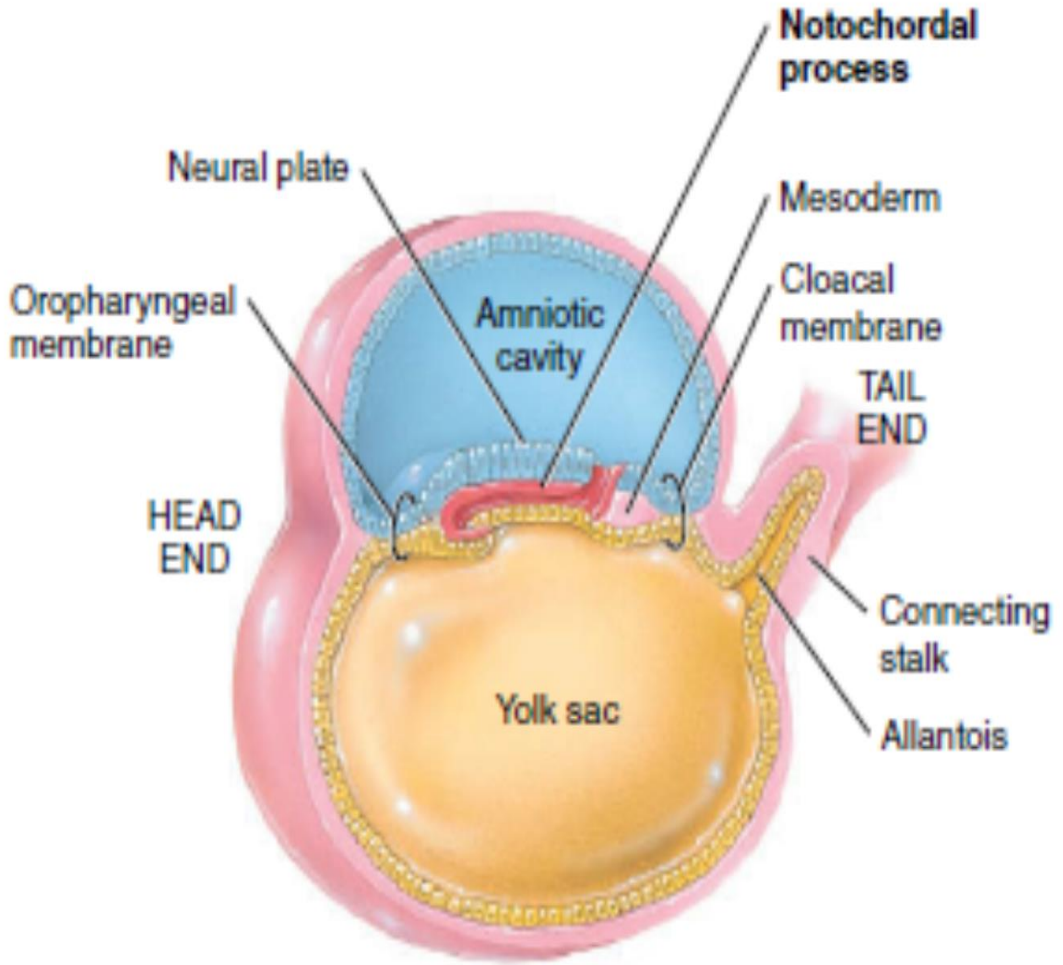
- ***Connecting stalk*:**
- When the embryonic disc is first formed, it is suspended (along with amniotic cavity and yolk sac) from the trophoblast by the connecting stalk
- Initially the connecting stalk is very broad compared to the size of the embryo
- As the embryonic disc enlarges in size, elongates,
- connecting stalk becomes relatively small & its attachment becomes confined to the region of the tail end of the embryonic disc
- Some intraembryonic mesoderm arising from the primitive streak passes backward into the connecting stalk




Amniotic cavity
Embryonic disk
Extraembryonic mesoderm
Primary yolk sac
Amniotic cavity
Future connecting stalk
Amnion
Secodary yolk sac
Trophoblast
Chorion
Splanchnopleuric extraembryonic mesoderm
Somatopleuric extraembryonic mesoderm
Extraembryonic coelom

- As it does so, it leaves an area caudal to the primitive streak, where ectoderm & endoderm remain in contact (i.e. mesoderm does not separate them)
- This region is, similar to the prochordal plate & forms the ***cloacal membrane***



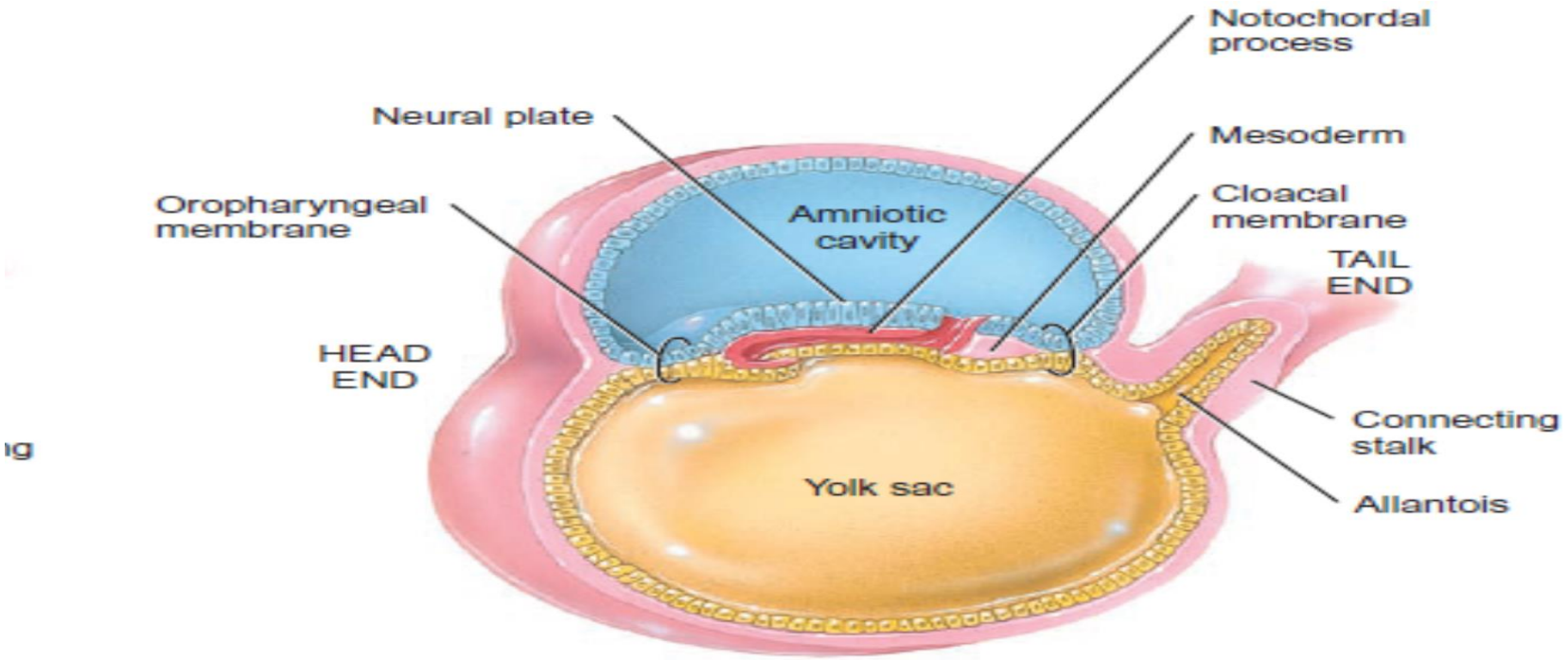


(b) Sagittal section of trilaminar embryonic disc, about 16 days after fertilization

- 2 faint depressions appear on the dorsal surface of the embryo where the ectoderm & endoderm make contact but lack mesoderm between them

1. **Buccopharyngeal membrane** at the cranial end of the disc consists of a small region of tightly adherent ectoderm & endoderm cells

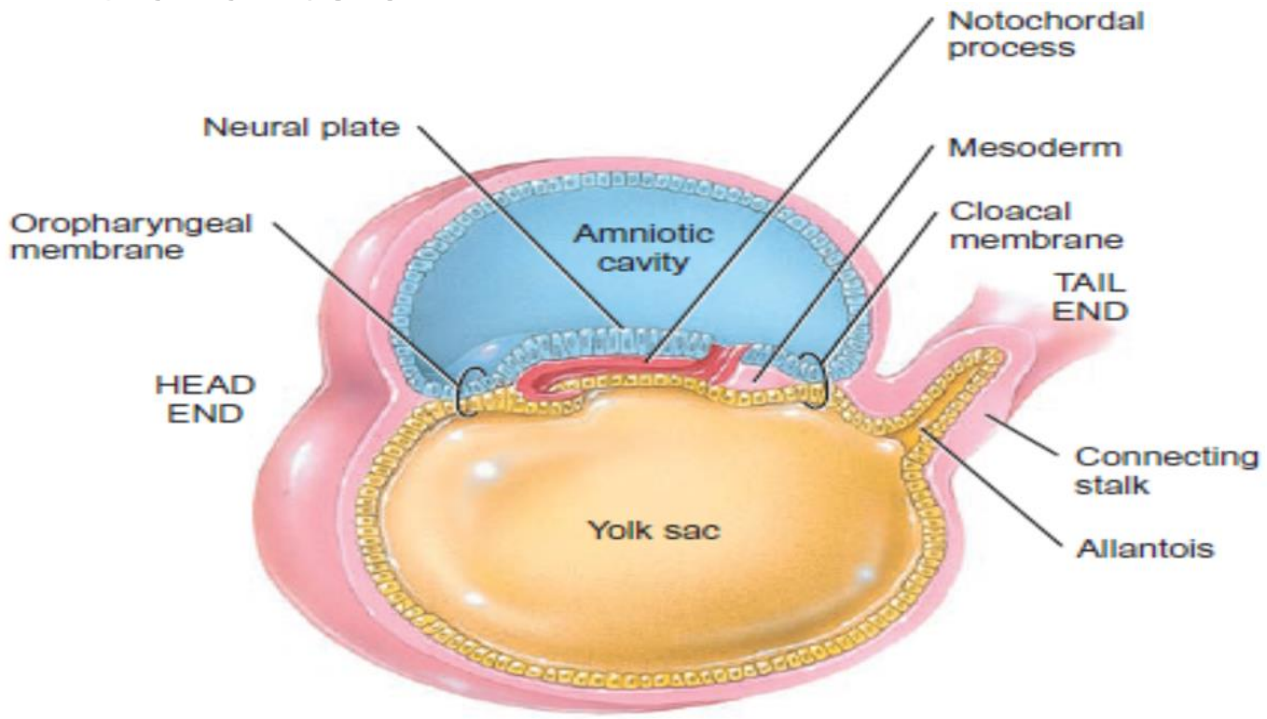
- It represents the future opening of the oral cavity
- It breaks down during the 4th week to connect the mouth cavity to the pharynx (throat) & the remainder of the gastrointestinal tract



(b) Sagittal section of trilaminar embryonic disc, about 16 days after fertilization

2.The cloacal membrane is formed at the caudal end of the embryonic disc

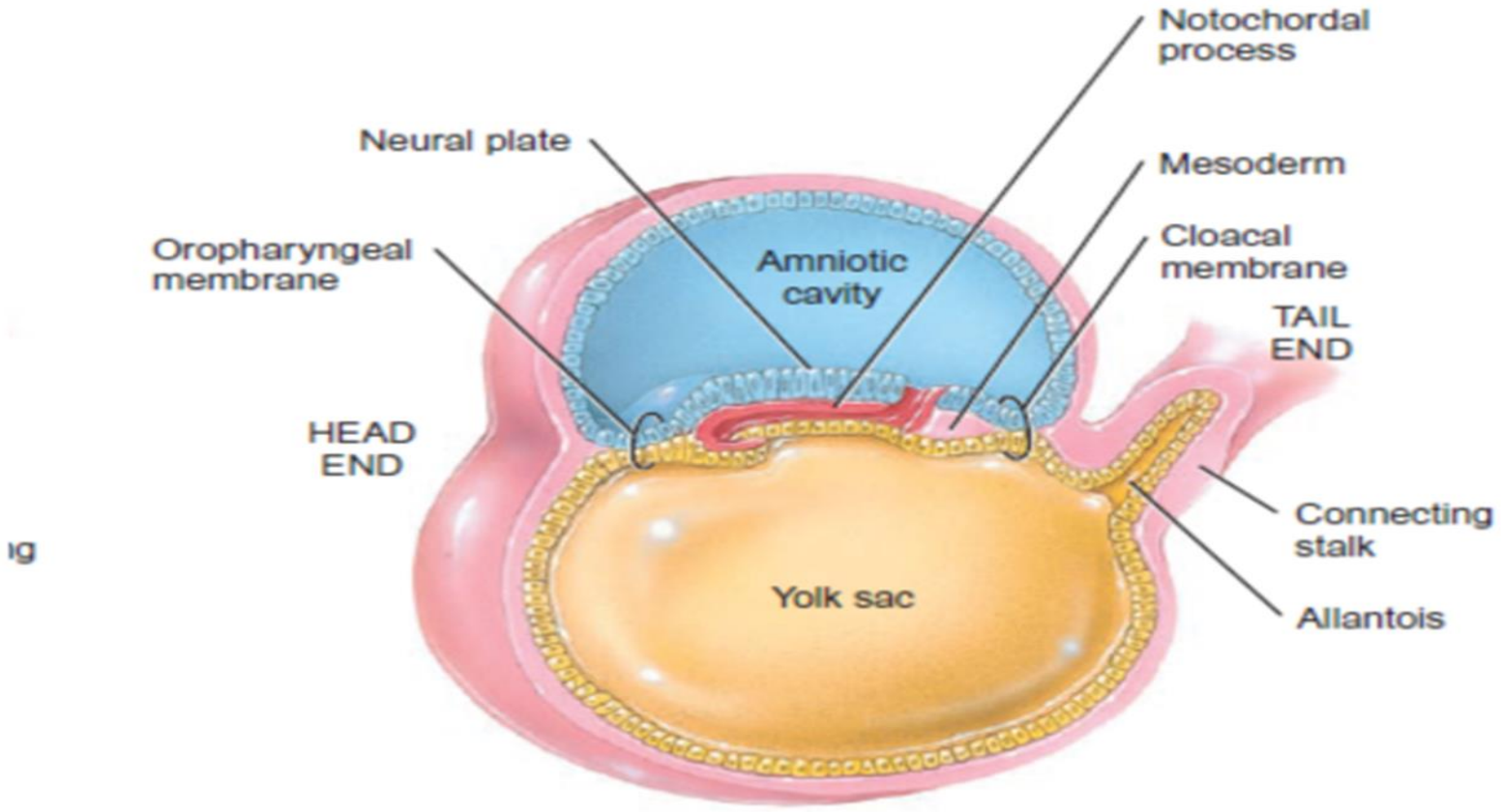
- membrane consists of tightly adherent ectoderm & endoderm cells with no intervening mesoderm
- Degenerates in the 7th week to form the openings of the anus & urinary & reproductive tracts
- When the cloacal membrane appears the posterior wall of the yolk sac forms a small vascularized outpouching called the **allantois**
- extends into the connecting stalk



(b) Sagittal section of trilaminar embryonic disc, about 16 days after fertilization

- **THE ALLANTOIS**
- appears on approximately day 16
- as a small, sausage-shaped diverticulum (outpouching) from the caudal wall of the umbilical vesicle that extends into the connecting stalk
- In humans, the allantoic sac remains very small
- but allantoic mesoderm expands beneath the chorion and forms blood vessels that will serve the placenta
- The blood vessels of the allantoic stalk become the umbilical arteries

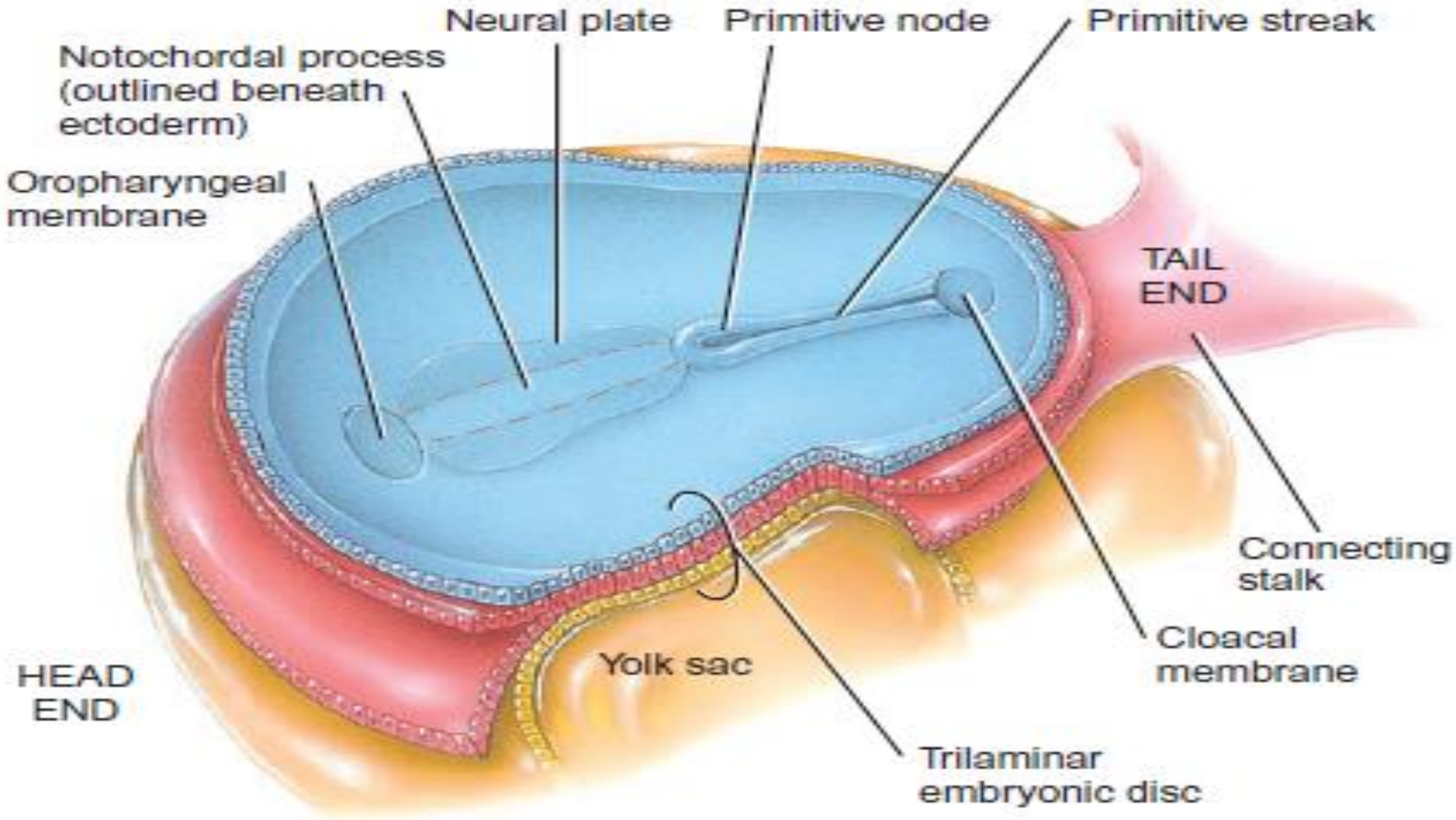
- The proximal part of the original allantoic diverticulum persists throughout much of development as a stalk called the **urachus**,
- which extends from the bladder to the umbilical region
- The urachus is represented in adults by the **median umbilical ligament**



(b) Sagittal section of trilaminar embryonic disc, about 16 days after fertilization

- **Allantoic Cysts**
- remnants of the extraembryonic portion of the allantois, are usually found between the fetal umbilical vessels and can be detected by ultrasonography
- detected in the proximal part of the umbilical cord, near its attachment to the anterior abdominal wall
- are generally asymptomatic until childhood or adolescence, when they may present with infection and inflammation

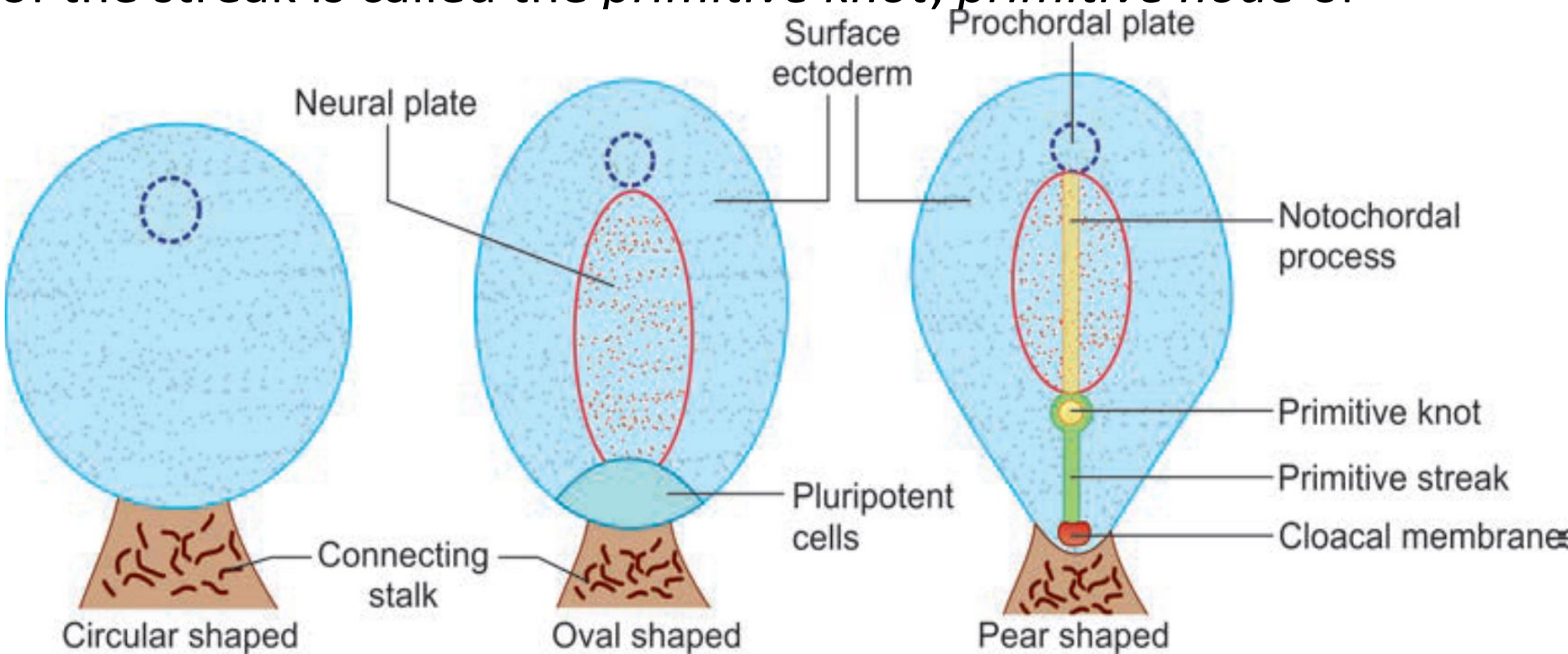
- **FORMATION OF THE NOTOCHORD**
- 16 days after fertilization mesodermal cells from the primitive node migrate toward the head end of the embryo
- form a hollow tube of cells in the midline called the **notochordal process**
- notochordal process becomes a solid cylinder of cells called the **notochord**
- plays an extremely important role in **induction**
- a process in which one tissue (*inducing tissue*) stimulates the specialization of an adjacent tissue



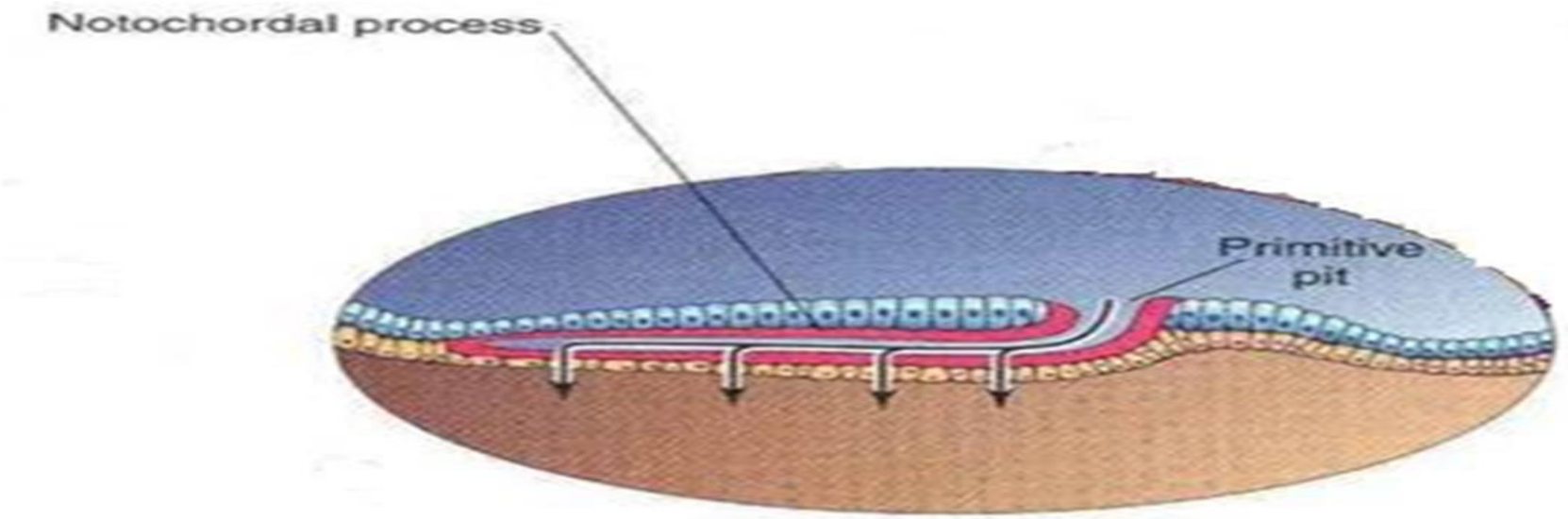
(a) Dorsal and partial sectional views of trilaminar embryonic disc, about 16 days after fertilization

- Instructive signals from the primitive streak region induce notochordal precursor cells to form the **notochord**
- molecular mechanism that induces these cells involves (at least) Shh signaling from the floor plate of the neural tube

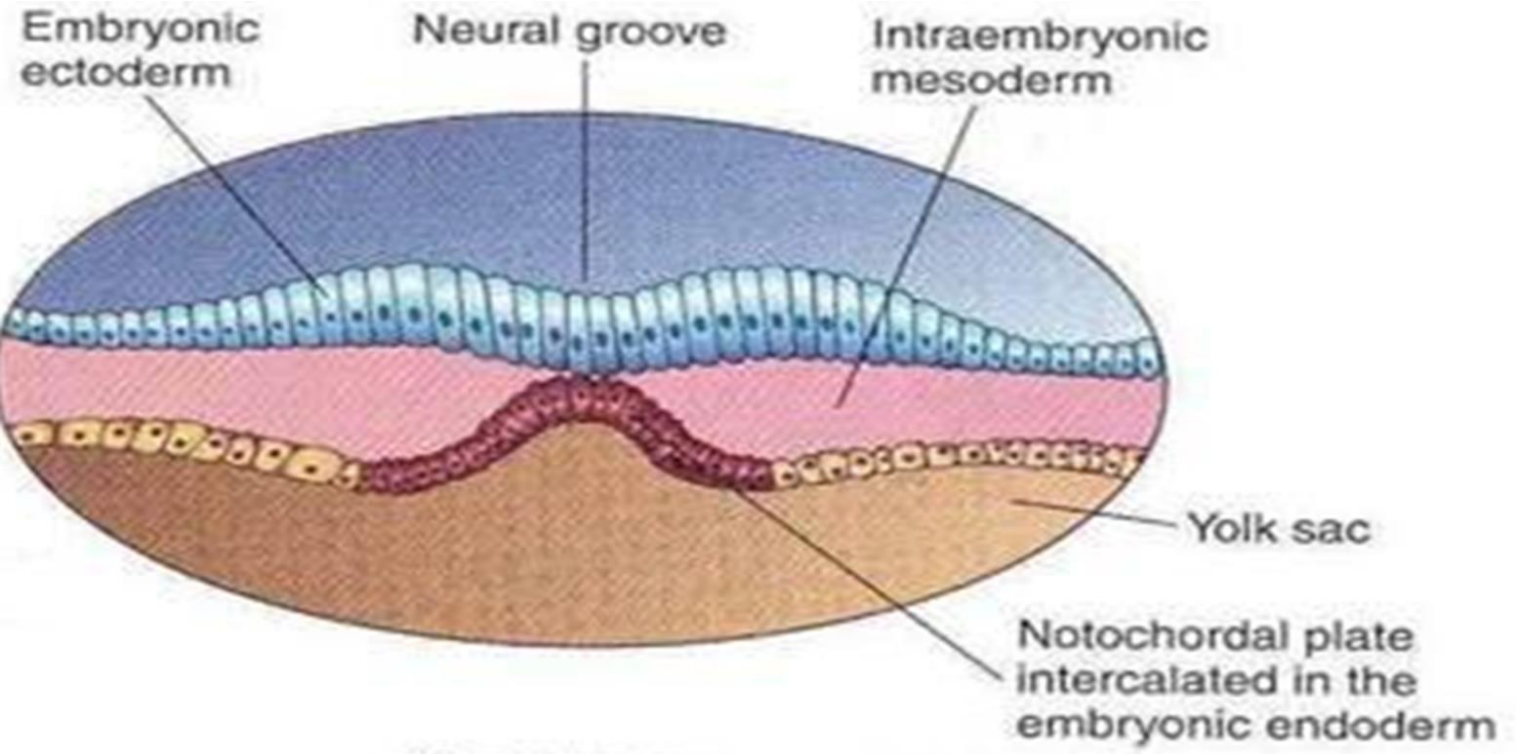
- notochord is a midline structure
- develops in the region lying between the cranial end of the primitive streak & caudal end of the prochordal plate
- During its development passes through several stages that are as follows:-
- cranial end of the primitive streak becomes thickened
- thickened part of the streak is called the *primitive knot*, *primitive node* or *Henson's node*

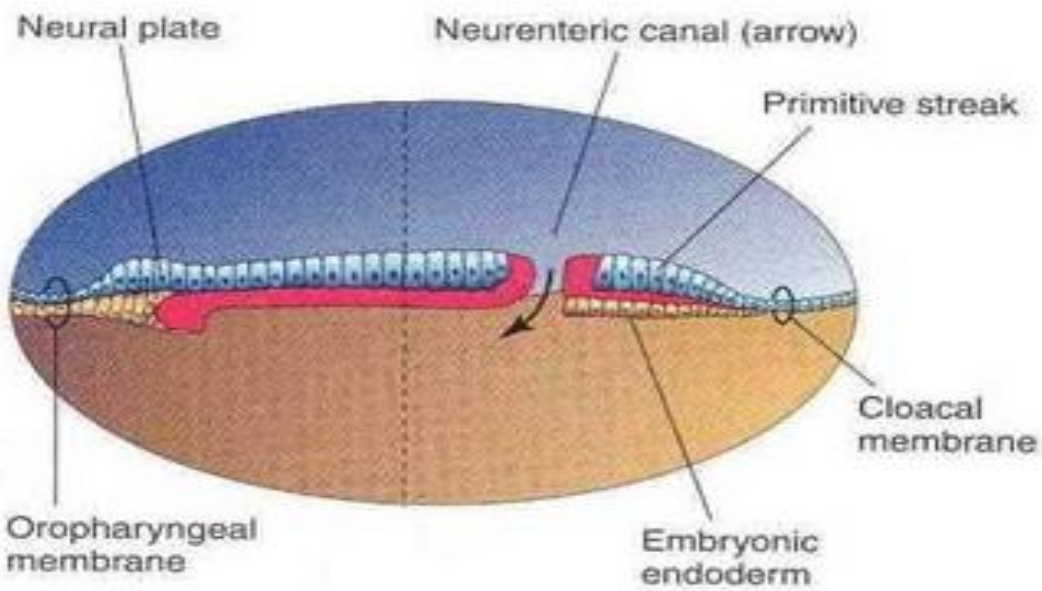


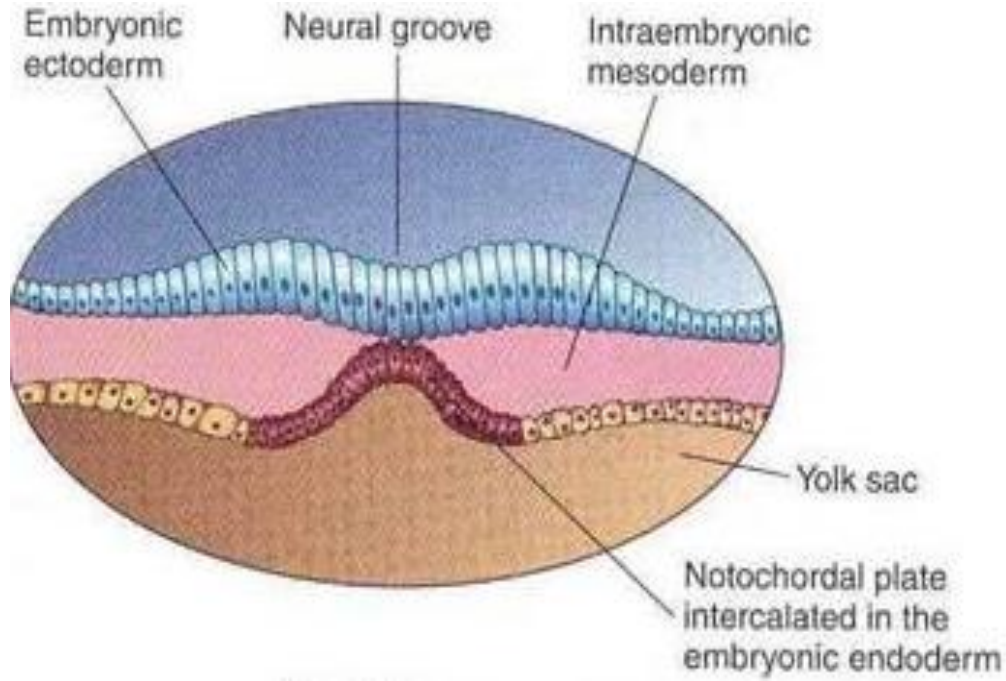
- depression appears in the center of the primitive knot
- depression is called the *blastopore/primitive pit*
- Cells in the primitive knot multiply
- pass cranially in the middle line, between the ectoderm and endoderm, reaching up to the caudal margin of the prochordal plate
- These cells form a solid cord called the ***notochordal process*** or *head process*



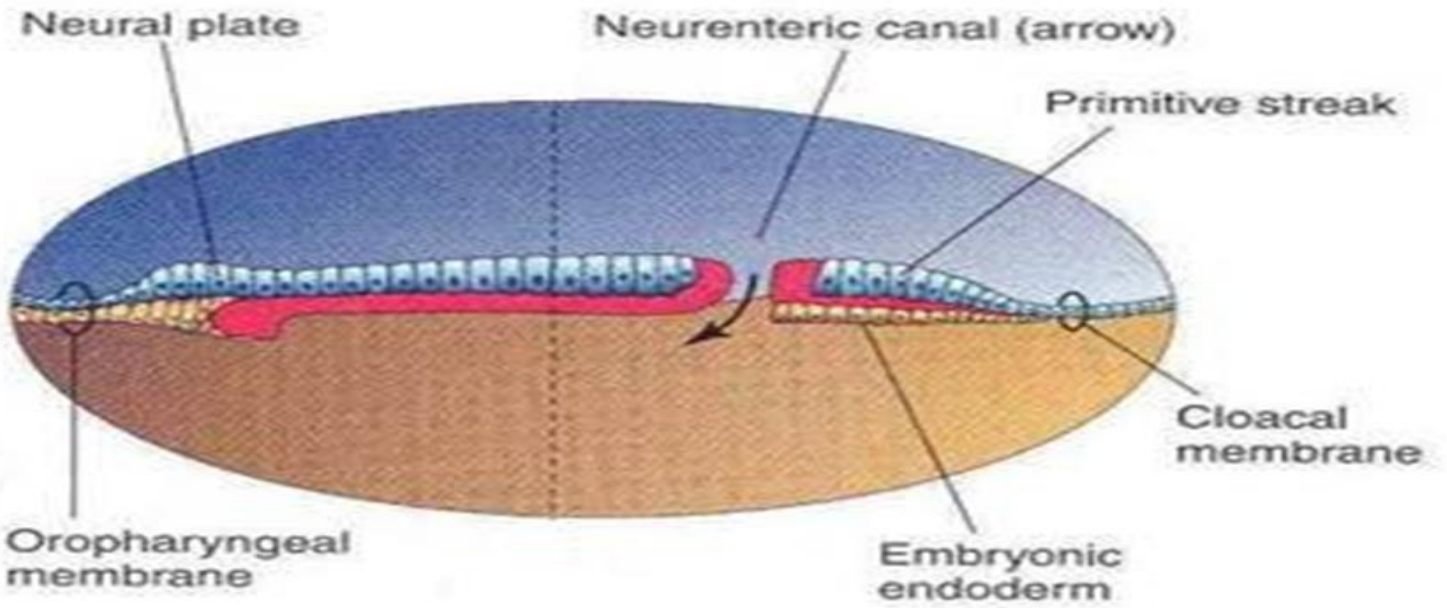
- cavity of blastopore extends into the notochordal process and converts it into a tube called the ***notochordal canal***
- cells forming the floor of notochordal canal become intercalated in (i.e. become mixed up with) the cells of the endoderm
- The cells forming the floor of the notochordal canal now separate the canal from the cavity of the yolk sac
- floor of the notochordal canal begins to break down




Neural plate
Neurenteric canal (arrow)
Primitive streak
Cloacal membrane
Oropharyngeal membrane
Embryonic endoderm

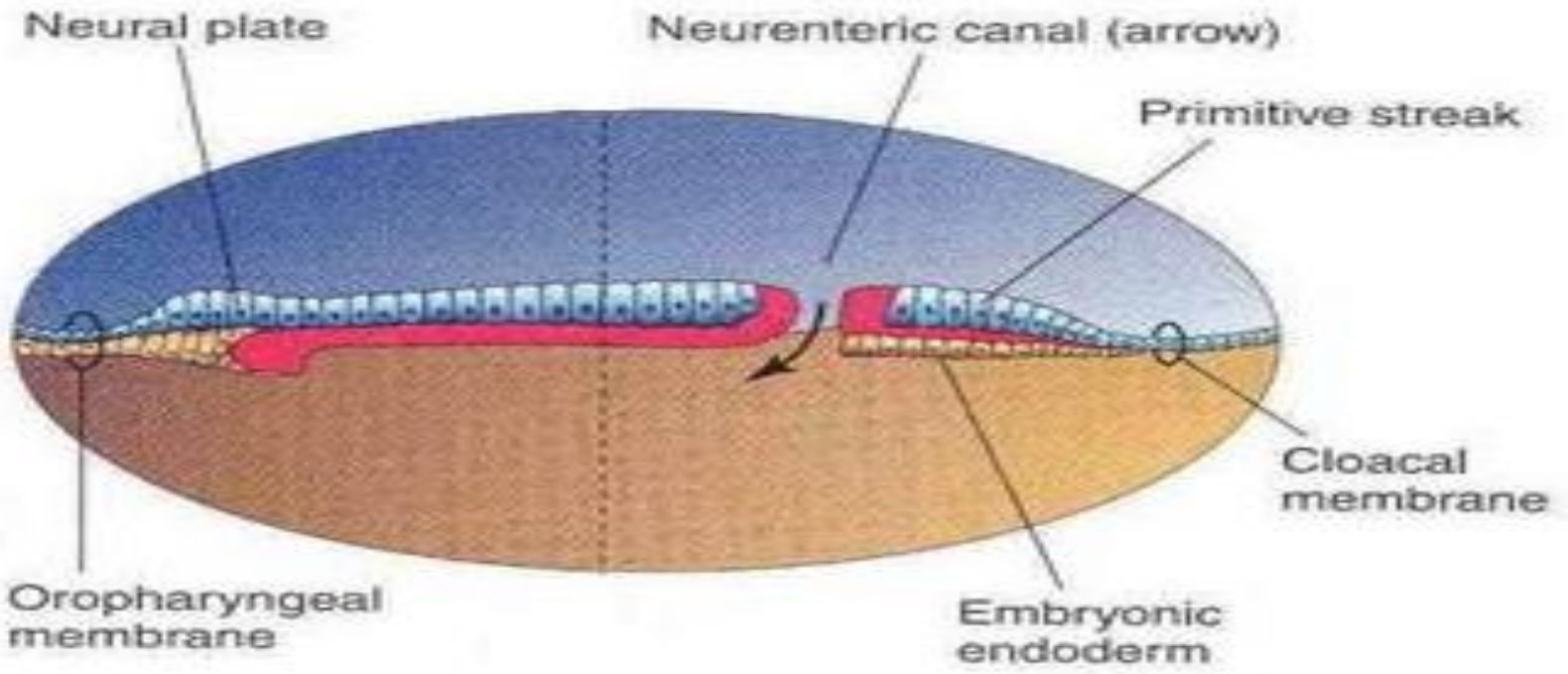

Embryonic ectoderm
Neural groove
Intraembryonic mesoderm
Yolk sac
Notochordal plate intercalated in the embryonic endoderm

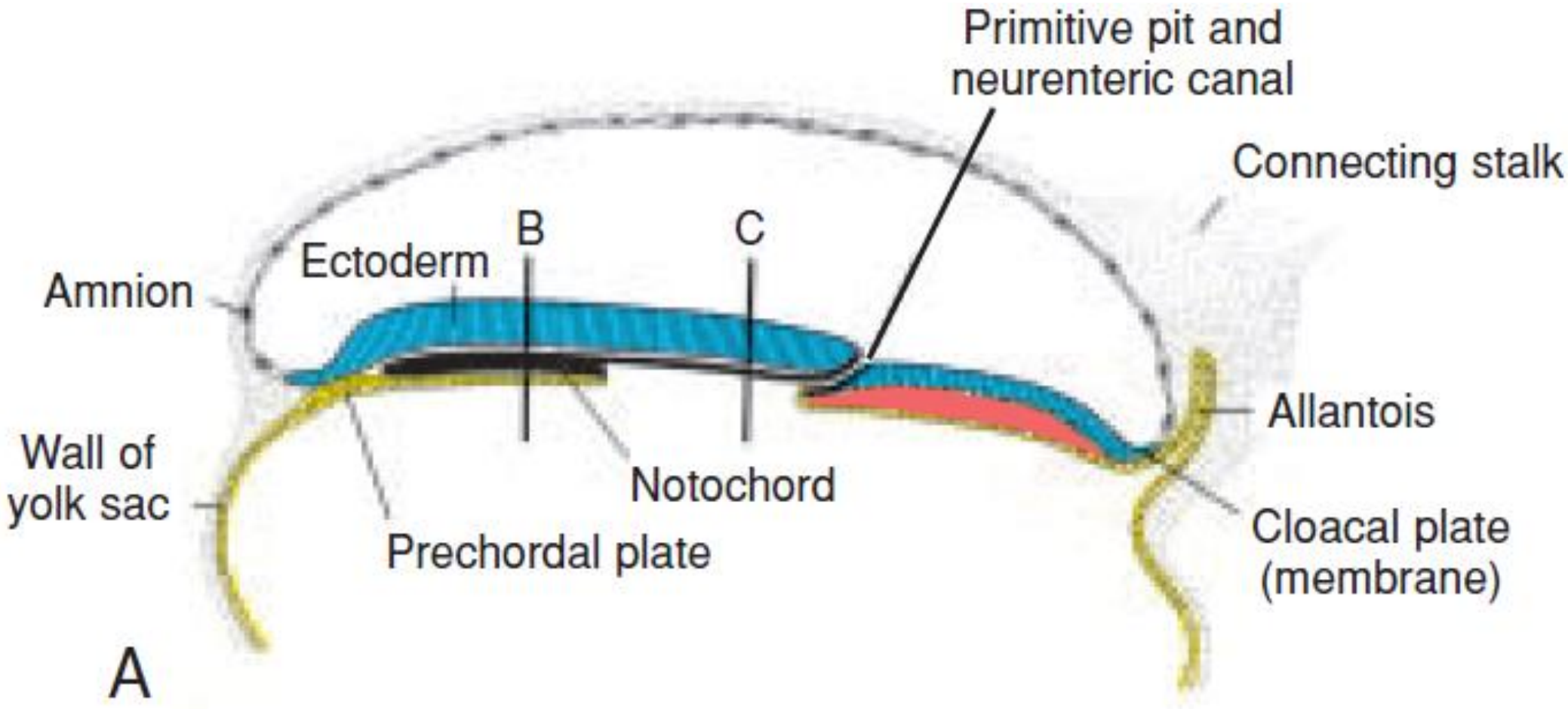
- First, there are small openings formed in it, but gradually the whole canal comes to communicate with the yolk sac
- notochordal canal also communicates with the amniotic cavity through the blastopore or ***neurenteric canal***
- At this stage, amniotic cavity & yolk sac are in communication with each other
- Gradually the walls of the canal become flattened so that instead of a rounded canal we have a flat plate of cells called the ***notochordal plate***



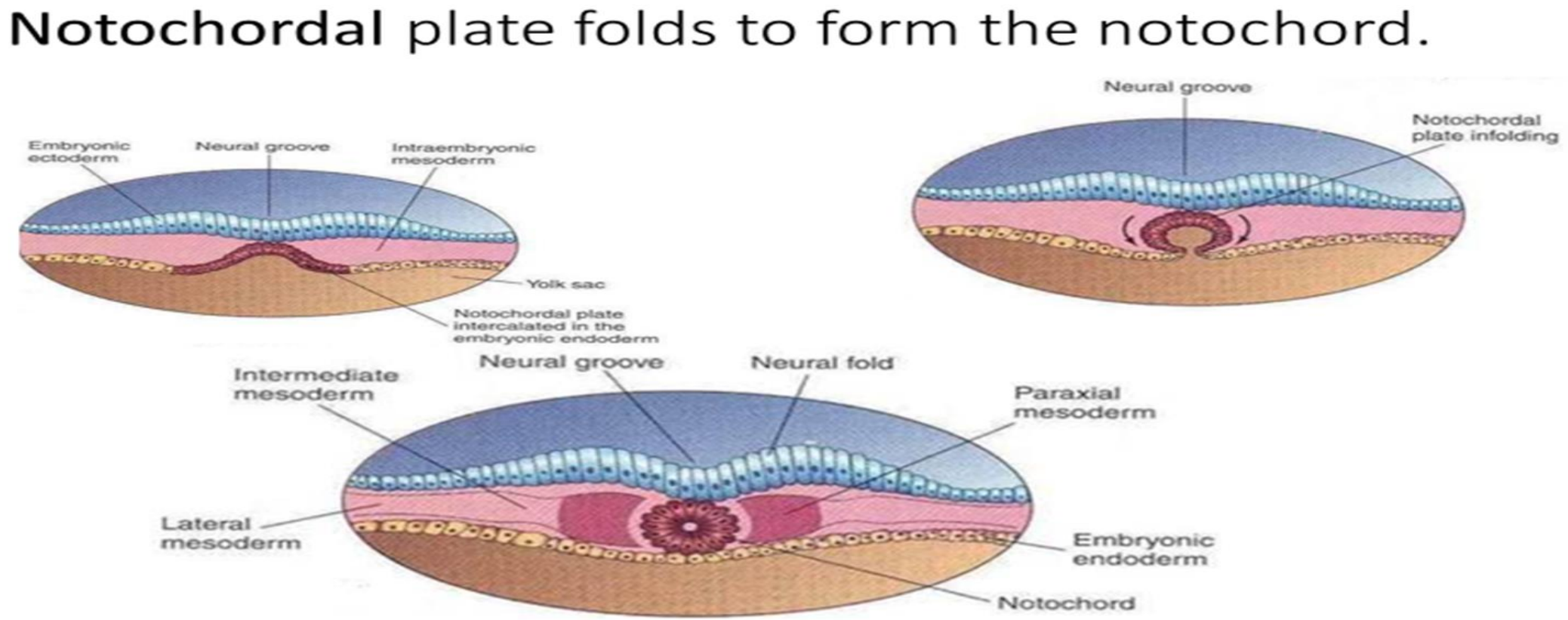
Formation of Notochord cont'd

- A temporary communication is established between the amniotic cavity and the yolk sac, termed the neurenteric canal.

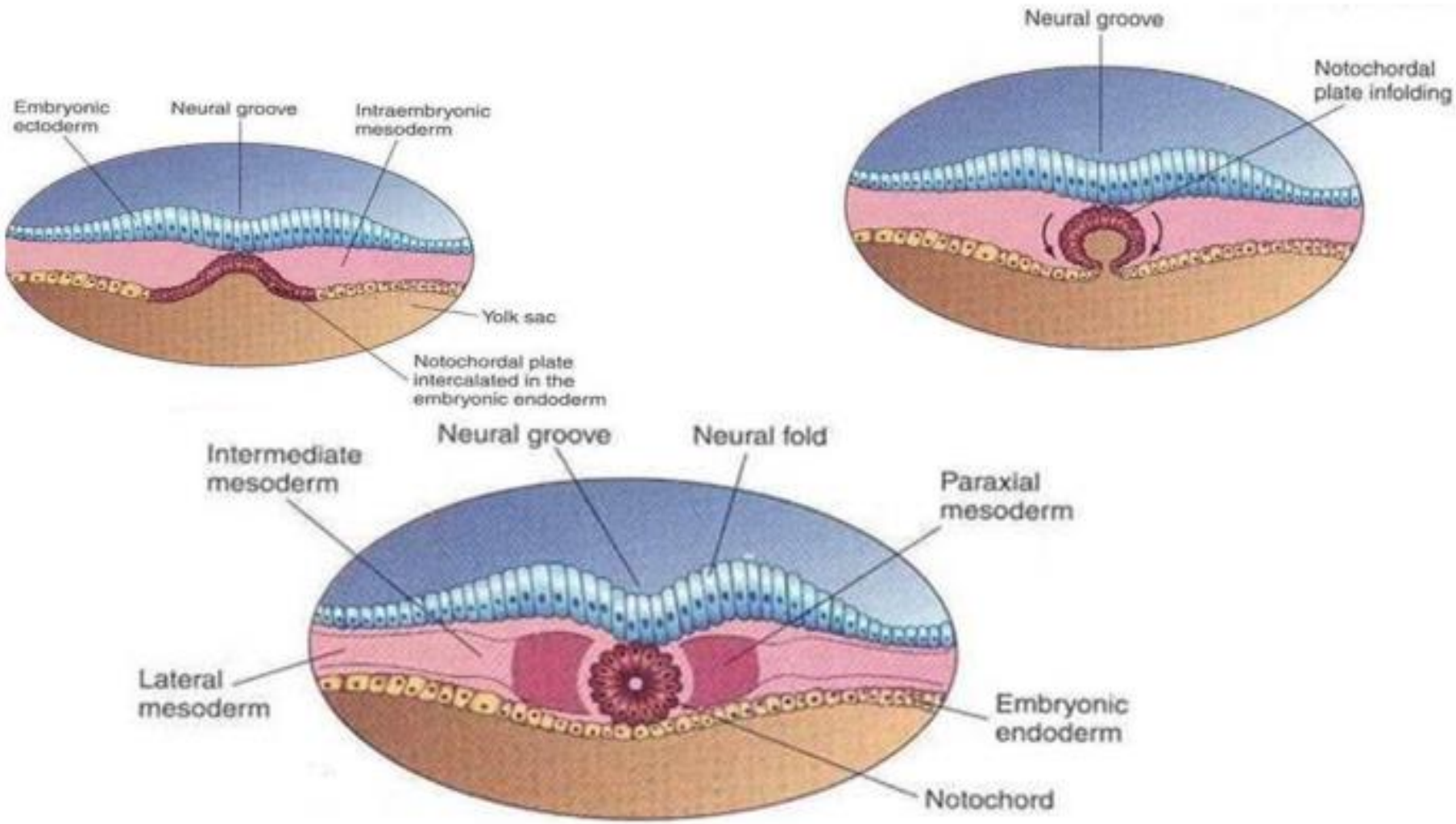



Primitive pit and
neurenteric canal
Connecting stalk
B
C
Ectoderm
Amnion
Allantois
Wall of
yolk sac
Notochord
Cloacal plate
(membrane)
Prechordal plate
A

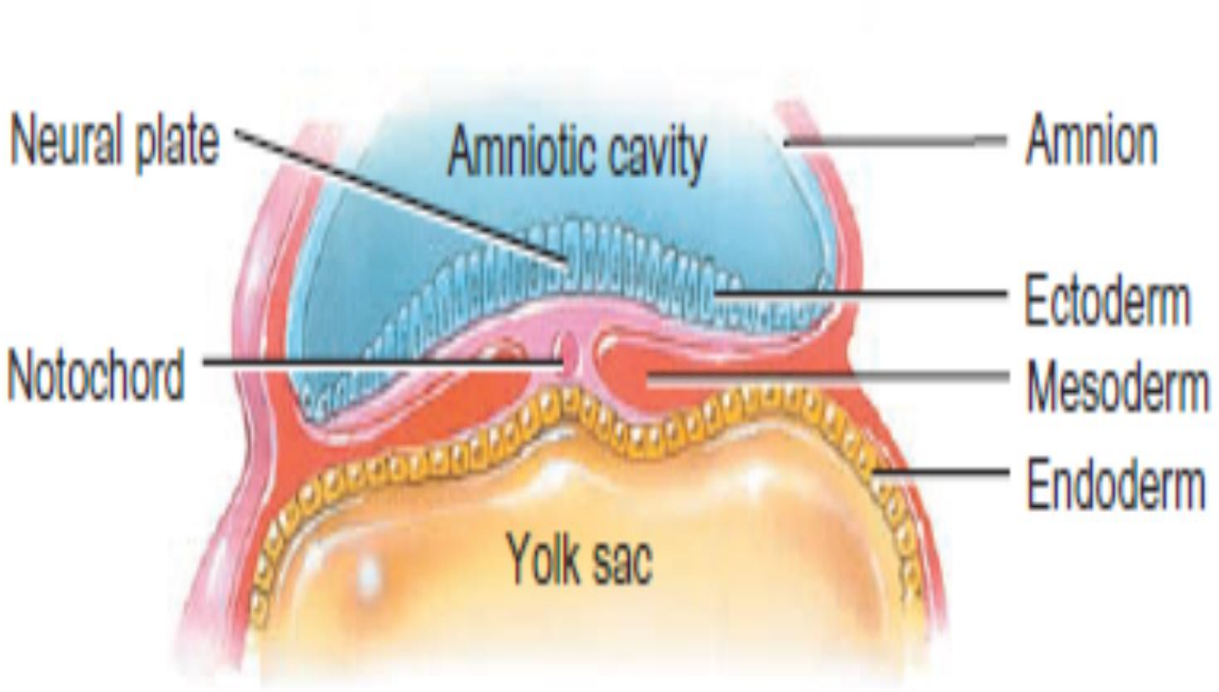
- Proliferation of cells of this tube converts it into a solid rod of cells
- This rod is the ***definitive notochord***
- gets completely separated from the endoderm
- As the embryo enlarges, the notochord elongates and lies in the midline, in the position to be later occupied by the vertebral column



Notochordal plate folds to form the notochord.



- **The notochord**
- induces certain neighboring mesodermal cells(somites) to develop into parts of vertebrae (back bones)
- induces the overlying ectoderm to fold inward to form the nervous system
- contributes to the formation of intervertebral discs between vertebrae (nucleus pulposus)
- Defines primordial longitudinal axis of the embryo cranio-caudal axis and right and left sides of embryo
- Provides rigidity to the embryo

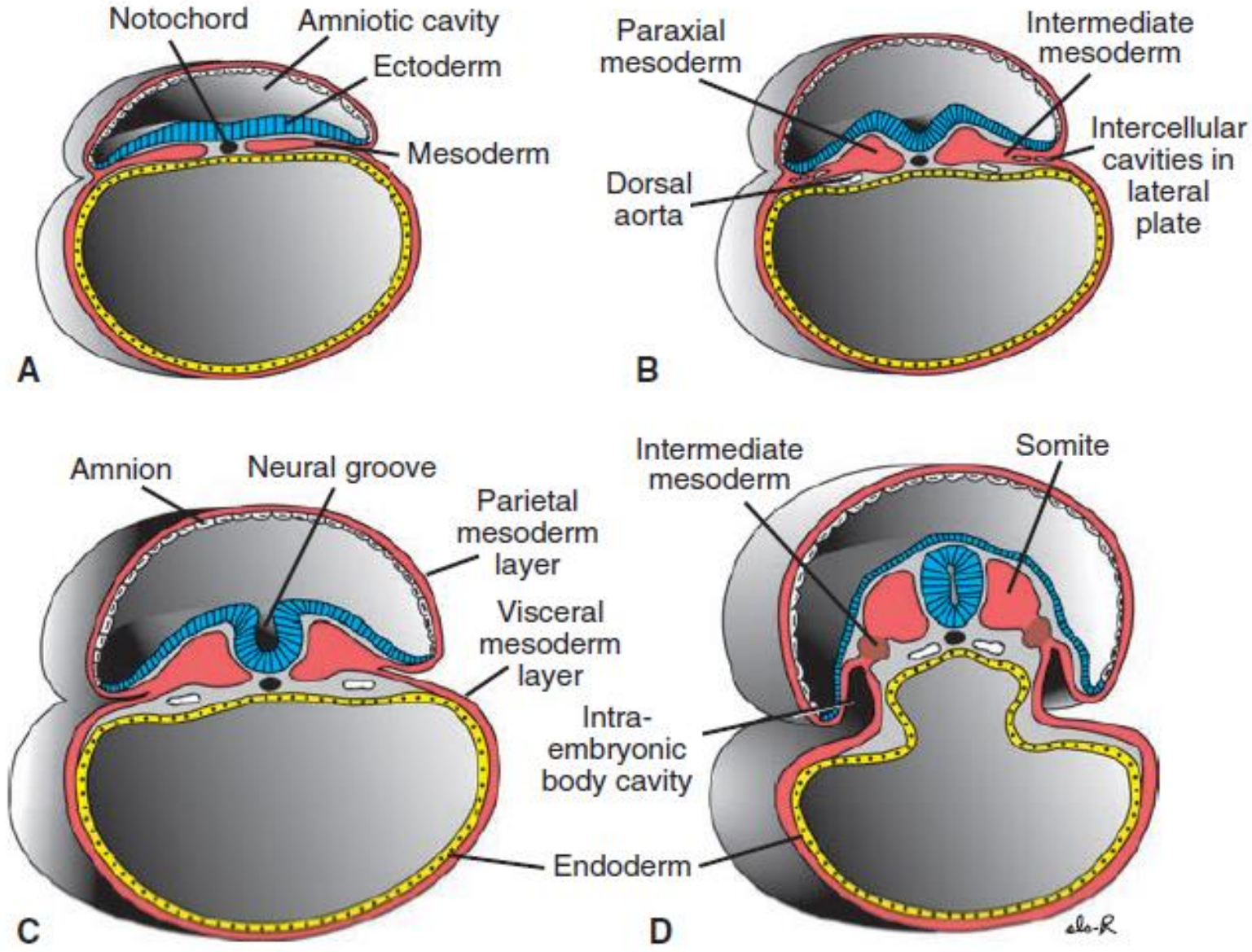


Fate of Notochord

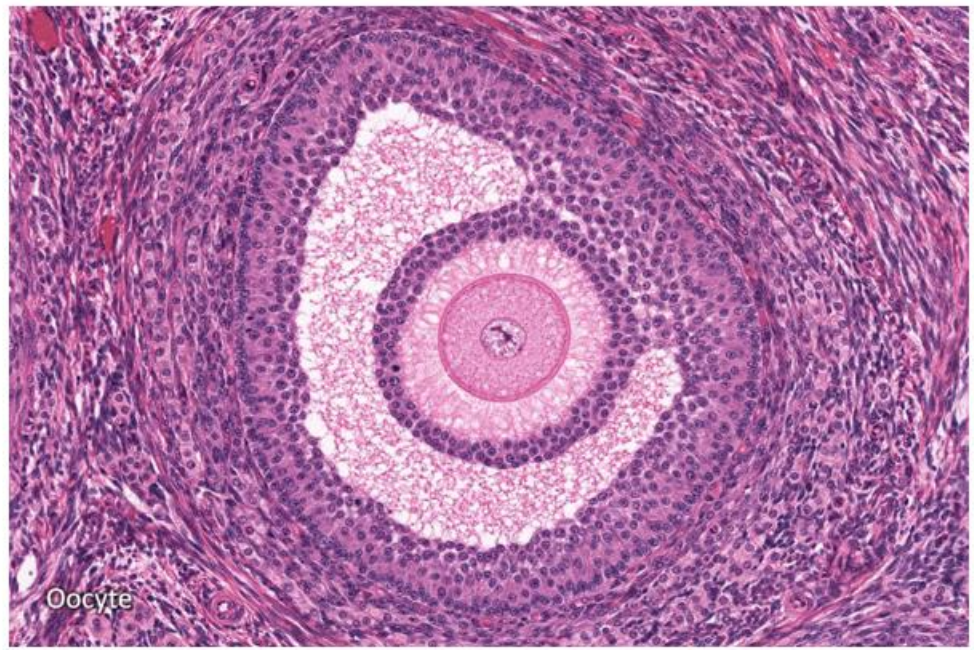
- Degenerates and disappears as the bodies of the vertebrae develop, but it persists as the nucleus pulposus of each intervertebral disc and its cranial continuation the *apical ligament of dens of axis vertebra*
- Remnants of notochordal tissue give rise to both benign and malignant tumors called Chordomas

Differentiation of the Intraembryonic Mesoderm

- Induced by the notochord
- Differentiates (in the region of notochord) into:
  - Paraxial mesoderm
  - Intermediate cell mass
  - Lateral plate mesoderm



gure 6.8 Transverse sections showing development of the mesodermal germ layer. **A.** Day 17. **B.** Day 19. **C.** Day 20. . Day 21. The thin mesodermal sheet gives rise to paraxial mesoderm (future somites), intermediate mesoderm (future :cretory units), and the lateral plate, which is split into parietal and visceral mesoderm layers lining the intraembryonic cavity.


Oocyte