1st week of Human Development (Days 1–7)

- The following events take place during the 1st week of development

I. Fertilization
II. Cleavage and Blastocyst Formation
III. Implantation

➢ **Fertilization**

- *The usual site of fertilization is the ampulla of the uterine tube*
- The fertilization process takes approximately 24 hours
- It is a sequence of coordinated events which include the following stages

I Passage of a sperm through the corona radiata:

- For sperms to pass through the corona radiata, they must have been capacitated (removal of the glycoprotein coat and seminal plasma proteins from the plasma membrane that overlies the acrosomal region of the spermatozoa)

Note:

- *Only capacitated sperms can pass freely through the corona radiata*

II. Penetration of the zona pellucida:

- The zona is a glycoprotein shell surrounding the egg that facilitates and maintains sperm binding and induces the acrosome reaction
- The intact acrosome of the sperm **binds** with a *zona glycoprotein (ZP3/ zona protein 3)* on the zona pellucida
- Release of acrosomal enzymes (acrosin) allows sperm to penetrate the zona pellucida, thereby coming in contact with the plasma membrane of the oocyte
- As soon as the head of a sperm comes in contact with the oocyte surface, *the permeability of the zona pellucida changes*
- When a sperm comes in contact with the oocyte surface, lysosomal enzymes are released from *cortical granules lining the plasma membrane of the oocyte*

- In turn, these enzymes alter properties of the zona pellucida to :
  - ✓ prevent sperm penetration and
  - ✓ inactivate binding sites for spermatozoa on the zona pellicida surface
- only one sperm seems to be able to penetrate the oocyte

III. Fusion of plasma membranes of the oocyte and sperm

- The plasma or cell membranes of the oocyte and sperm fuse and break down at the area of fusion
- The head and tail of the sperm enter the cytoplasm of the oocyte, but the sperm's plasma membrane remains behind

IV. Completion of the second meiotic division of oocyte and formation of female pronucleus

- Penetration of the oocyte by a sperm activates the oocyte into completing the second meiotic division and forming a **mature oocyte** and a second polar body
- The nucleus of the mature ovum/oocyte is now called the female pronucleus

V. Formation of the male pronucleus

- Within the cytoplasm of the oocyte, the nucleus of the sperm enlarges to form the male pronucleus and the tail of the sperm degenerates

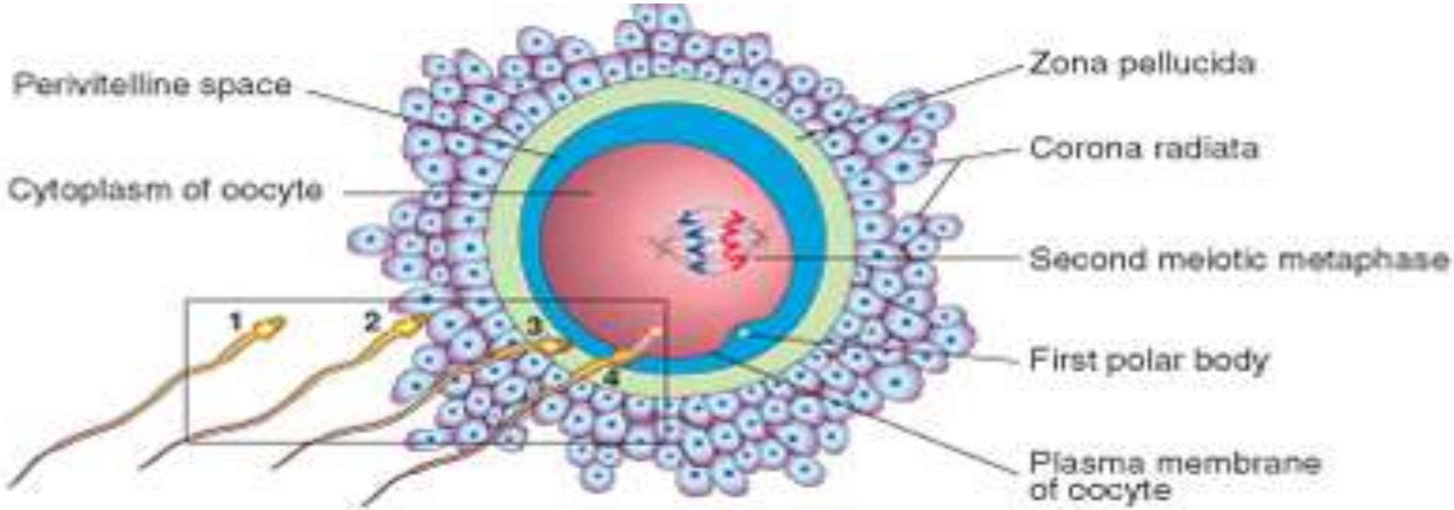
Note

❖ Since all sperm mitochondria degenerate, all mitochondria within the zygote are of maternal origin (i.e., all mitochondrial DNA is of maternal origin)

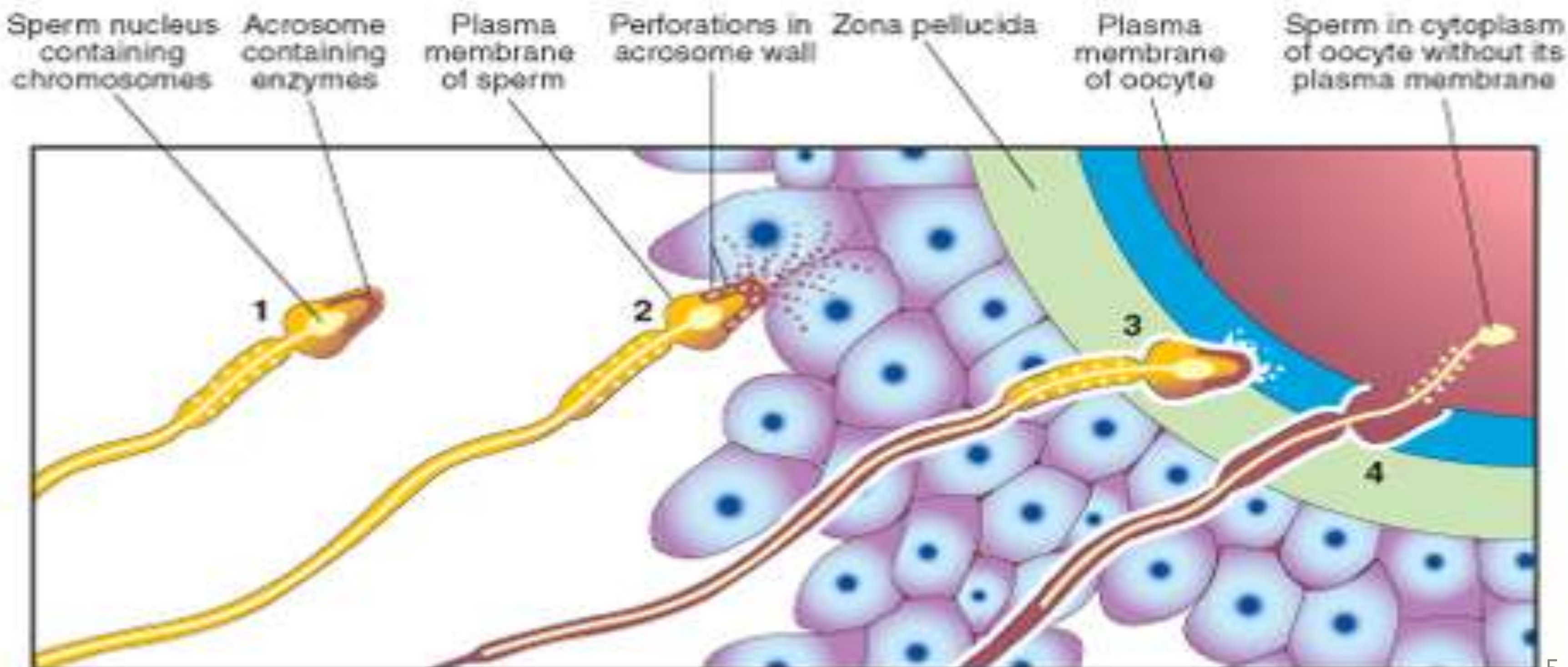
- *Morphologically, the male and female pronuclei are indistinguishable*
- *The oocyte now contains 2 pronuclei, each having haploid number of chromosomes(23)*
- The oocyte containing two haploid pronuclei is called an ***ootid***

VI. The 2 pronuclei fuse into a single diploid aggregation of chromosomes, the ootid becomes a zygote

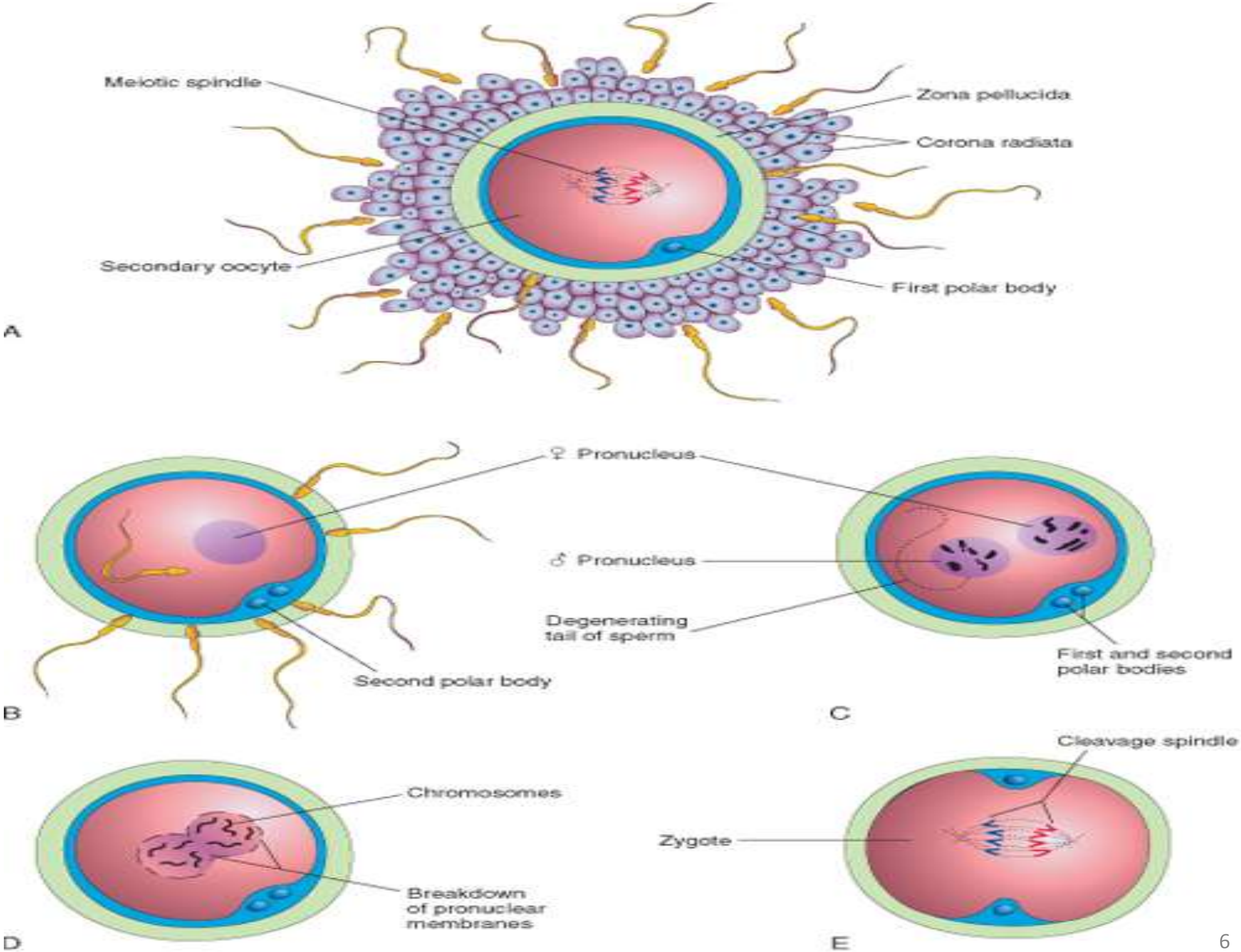
➢ The chromosomes in the zygote become arranged on a **cleavage spindle** in preparation for cleavage of the zygote


Perivitelline space
Cytoplasm of oocyte
Zona pellucida
Corona radiata
Second meiotic metaphase
First polar body
Plasma membrane of oocyte
1
2
3
4

A


Sperm nucleus containing chromosomes
Acrosome containing enzymes
Plasma membrane of sperm
Perforations in acrosome wall
Zona pellucida
Plasma membrane of oocyte
Sperm in cytoplasm of oocyte without its plasma membrane
1
2
3
4

B

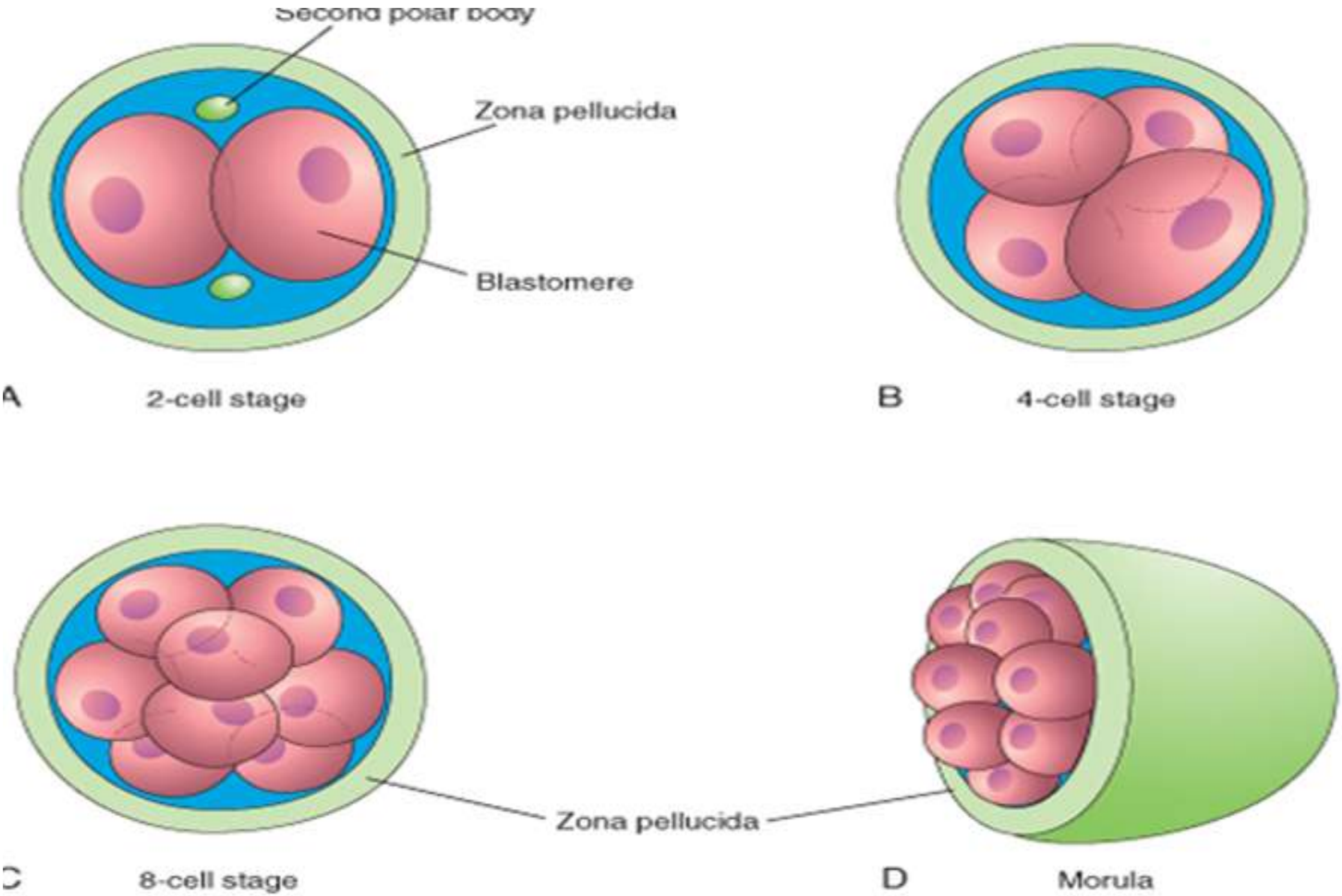


Meiotic spindle
Zona pellucida
Corona radiata
Secondary oocyte
First polar body
A
♀ Pronucleus
♂ Pronucleus
Degenerating tail of sperm
First and second polar bodies
Second polar body
B
C
Cleavage spindle
Chromosomes
Zygote
Breakdown of pronuclear membranes
D
E

Cleavage and Blastocyst Formation

Cleavage:

- Cleavage is a series of repeated mitotic divisions of the zygote resulting in a rapid increase in the number of cells(embryonic cells)
- These embryonic cells are called **blastomeres**
- **Blastomeres** become smaller with each successive cleavage division
- Cleavage normally occurs as the zygote passes along the uterine tube toward the uterus
- Division of the zygote into blastomeres begins approximately 30 hours after fertilization (day 2)
- the 1st cleavage is the division of the zygote into a two-cell stage
- the 2nd cleavage is from the two -cell stage into a four-cell stage
- the 3rd cleavage is from the four -cell stage into an eight-cell stage


Second polar body
Zona pellucida
Blastomere
A
2-cell stage
B
4-cell stage
Zona pellucida
C
8-cell stage
D
Morula

- After the eight-cell stage, the blastomeres change their shape and tightly align themselves against each other to form a compact ball of cells
- This process is called **compaction**
- This phenomenon, **compaction,** is probably mediated by cell surface adhesion glycoproteins
- Approximately 3 days after fertilization, cells of the compacted embryo divide again to form a 16-cell stage called **morula stage**

note

- ❖ When there are 16 to 32 blastomeres, the developing human is called a **morula**

Blastocyst formation

- Shortly after the morula enters the uterus (approx. 4 days after fertilization), a fluid-filled space called the **blastocystic cavity** appears inside the morula
- The fluid passes from the uterine cavity through the zona pellucida to form this space

- As fluid <u>increases</u> in the blastocystic cavity, it separates the blastomeres into <u>two parts</u>

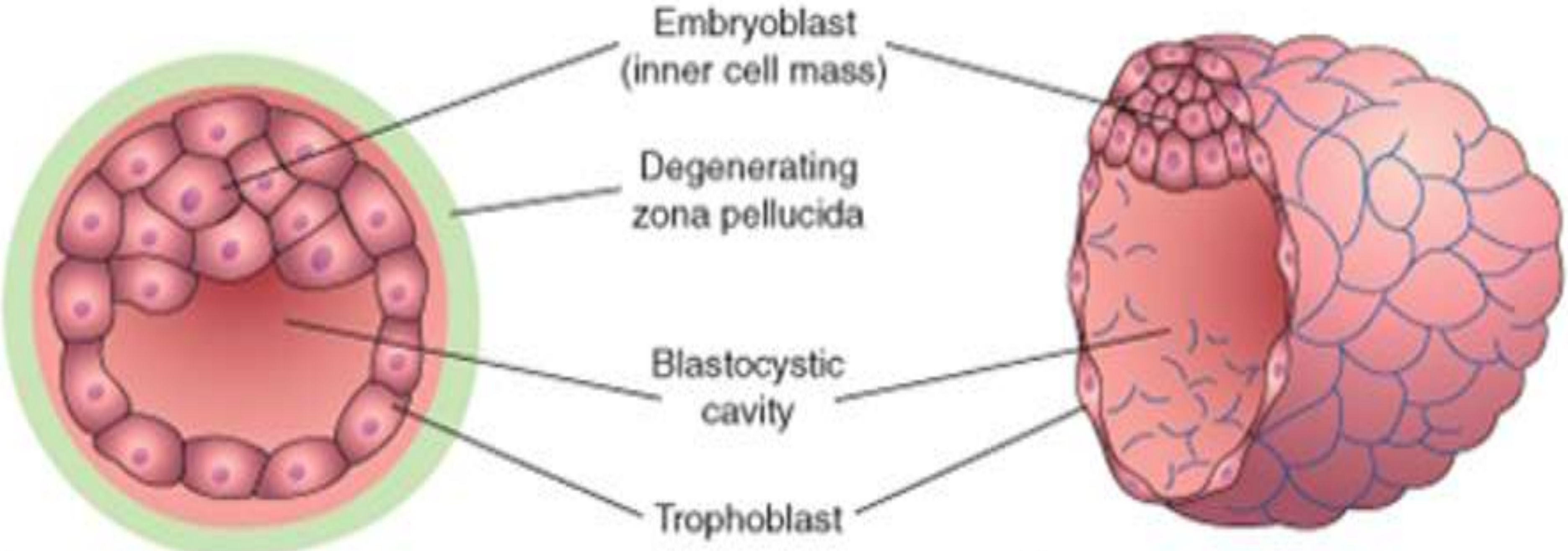
✓ An inner cell mass of cells called the **embryoblast**, which is surrounded by ⬇

✓ an outer cell mass of cells called the **trophoblast**

Note:

❖ By the late blastocyst stage (5th day; the stage where both embryoblast and trophoblast are present), <u>the zona pellucida has degenerated</u>

- *Although cleavage increases the number of blastomeres, note that each of the daughter cells is smaller than the parent cells*
- *As a result, there is no increase in the size of the developing embryo until the zona pellucida degenerates*
- *The blastocyst then enlarges considerably after the degeneration of the zona pellucida*
- <u>*The zona pellucida must degenerate for implantation to occur*</u>



E Early blastocyst

F Late blastocyst

Implantation

- The wall of the uterus consists of 3 layers:

(*a*) ***endometrium or mucosa*** lining the inside wall

(*b*) ***myometrium,*** *a thick layer of smooth muscle;*and

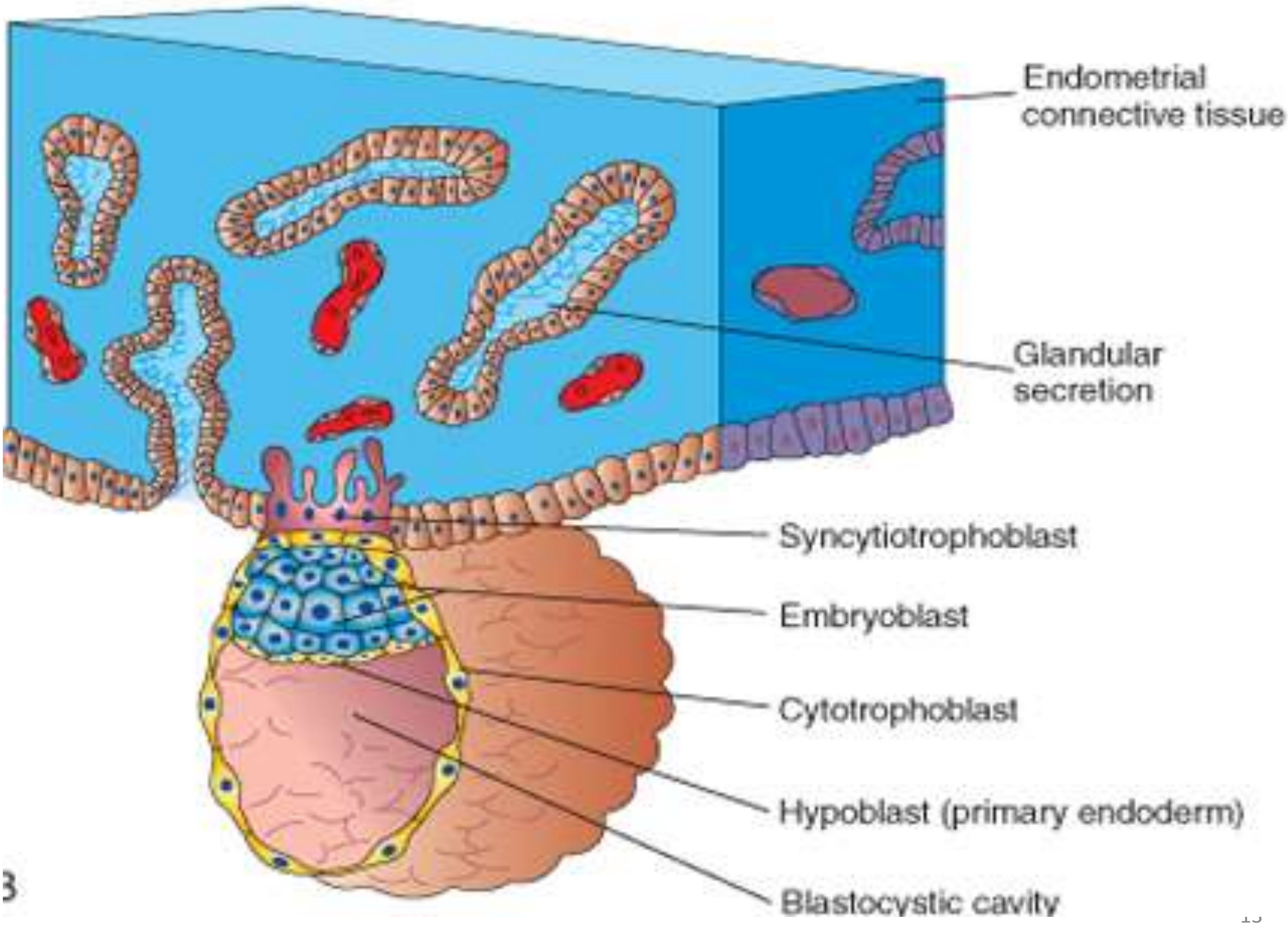
(*c*) ***perimetrium,*** *the peritoneal covering lining the outside wall*

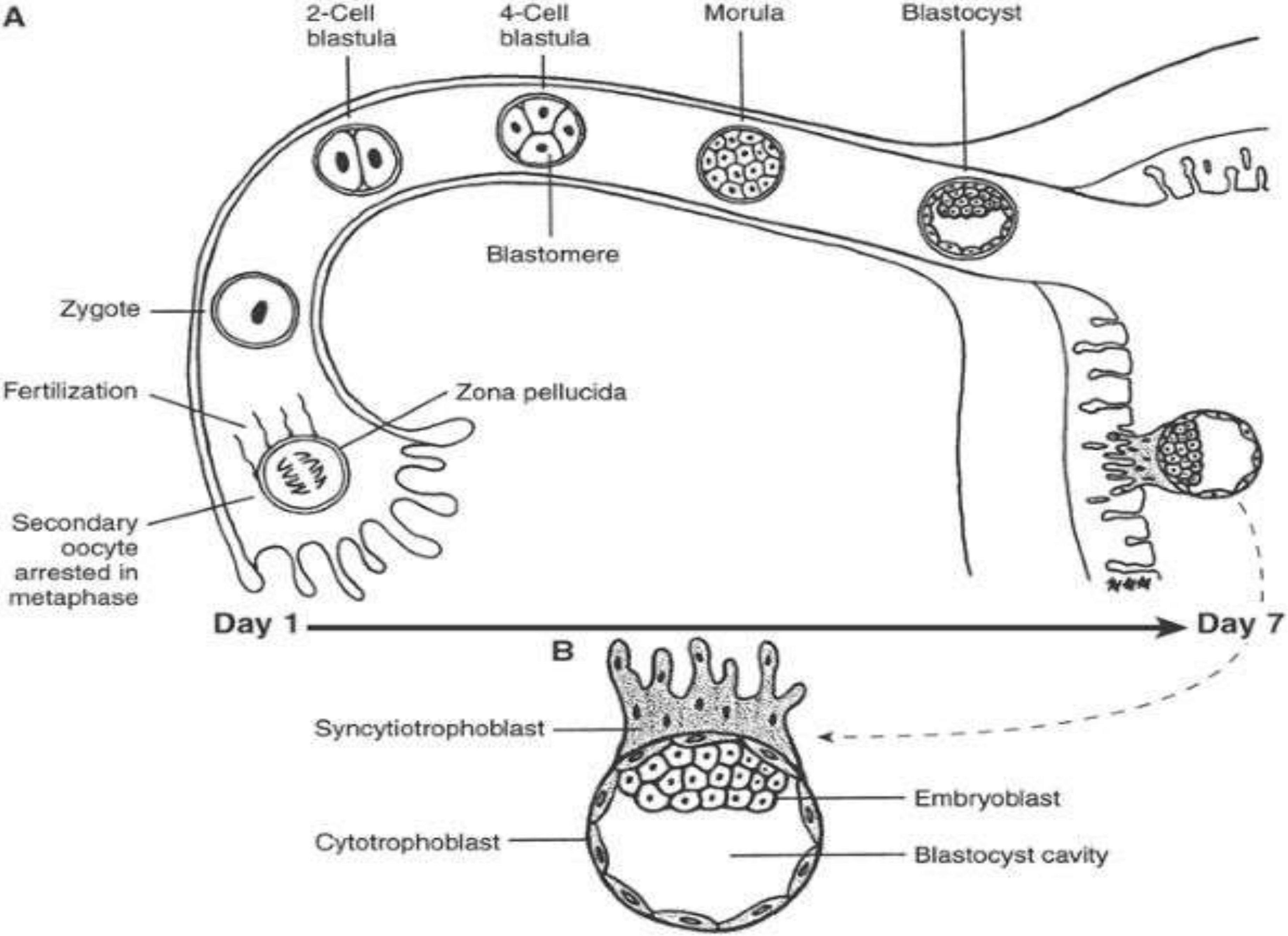
- *Approximately 6 days after fertilization* (day 20 of a 28-day menstrual cycle), the blastocyst attaches to the endometrial epithelium
- As soon as it attaches to the endometrial epithelium, the trophoblast starts to proliferate rapidly and gradually differentiates into 2 layers :

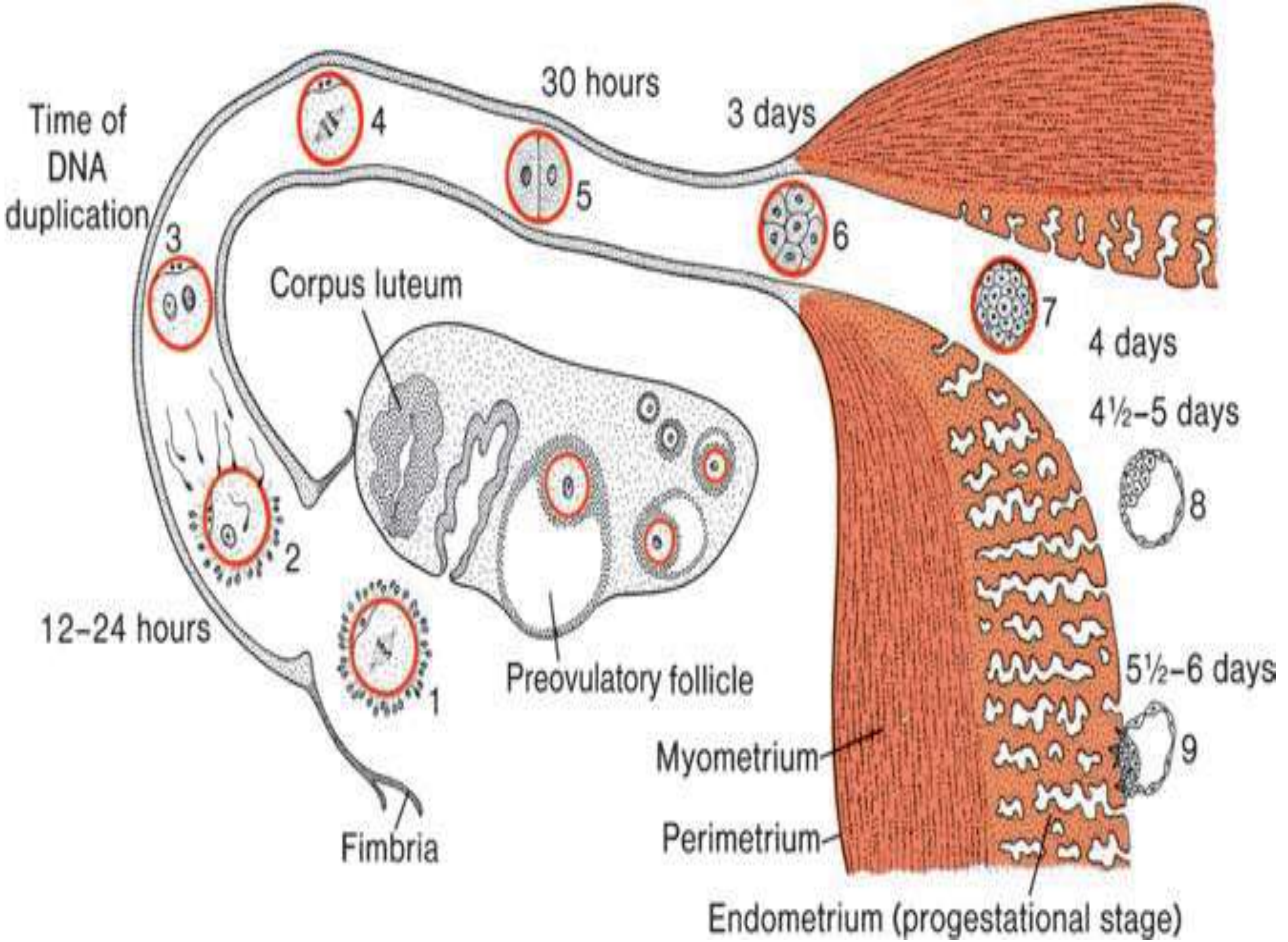
✓ An inner layer of **cytotrophoblast**

✓ An outer layer of **syncytiotrophoblast**

- *At approximately 7 days*, a layer of cells, a layer called **hypoblast** (primary endoderm), appears on the surface of the embryoblast facing the blastocystic cavity


Endometrial
connective tissue
Glandular
secretion
Syncytiotrophoblast
Embryoblast
Cytotrophoblast
Hypoblast (primary endoderm)
Blastocystic cavity


A
2-Cell blastula
4-Cell blastula
Morula
Blastocyst
Blastomere
Zygote
Fertilization
Zona pellucida
Secondary oocyte arrested in metaphase
Day 1
Day 7
B
Syncytiotrophoblast
Embryoblast
Cytotrophoblast
Blastocyst cavity



Time of
DNA
duplication
30 hours
3 days
4
5
6
3
7
Corpus luteum
4 days
4½–5 days
8
2
12–24 hours
Preovulatory follicle
5½–6 days
1
9
Myometrium
Perimetrium
Fimbria
Endometrium (progestational stage)

Clinical correlates

- **Ectopic tubal pregnancy (ETP)**

- ETP occurs when the blastocyst implants within the uterine tube due to delayed transport
- The ampulla of the uterine tube is the most common site of an ectopic pregnancy

- **Assisted Reproductive Technologies**

In Vitro Fertilization and Embryo Transfer

- In vitro fertilization (IVF) of oocytes and transfer of the cleaving zygotes into the uterus have provided an opportunity for many women who are sterile (e.g., owing to tubal occlusion) to bear children

Intracytoplasmic Sperm Injection

- A sperm can be injected directly into the cytoplasm of a mature oocyte
- This technique has been successfully used for the treatment of couples for whom in vitro fertilization failed or in cases where there are too few sperms available for in vitro insemination

Cryopreservation of Embryos

- Early embryos resulting from in vitro fertilization can be preserved for long periods by freezing them with a cryoprotectant (e.g., glycerol)
- Successful transfer of four- to eight-cell embryos and blastocysts to the uterus after thawing is now a common practice

Surrogate Mothers

- Some women produce mature oocytes but are unable to become pregnant, for example, a woman who has had her uterus excised (hysterectomy)
- In these cases, in vitro fertilization may be performed and the embryos transferred to another woman's uterus for development and delivery

2nd week of development

The following events take place during the 2nd week of development:

I. Completion of implantation of the blastocyst
II. Formation of bilaminar embryonic disc(epiblast and hypoblast)
III. Formation of extraembryonic structures(amniotic cavity, amnion, umbilical vesicle [yolk sac], connecting stalk, and chorionic sac)

Day 8

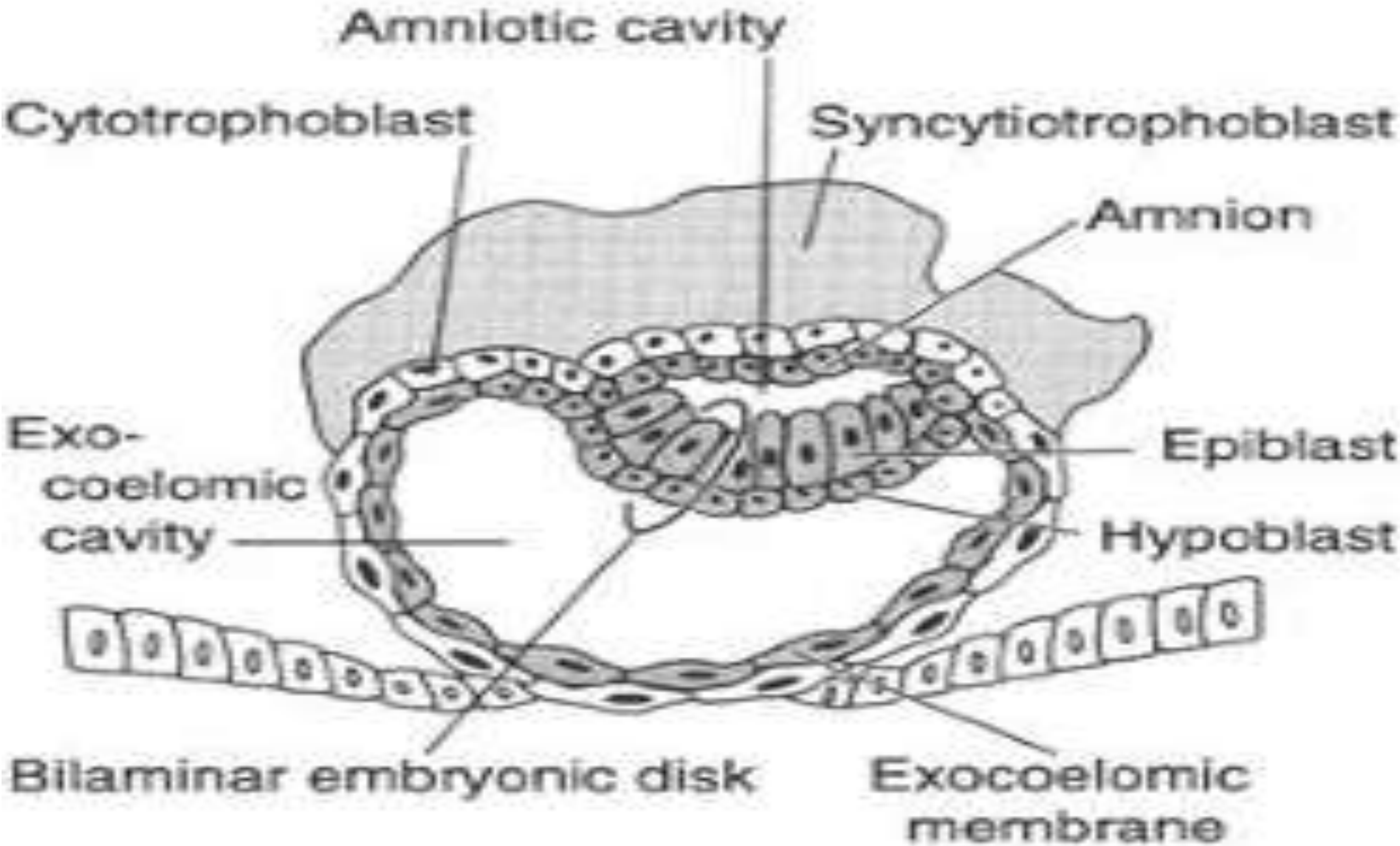
- At the eighth day of development, the blastocyst is partially (slowly) embedded in the endometrium
- the syncytiotrophoblast continues its invasion of the endometrium, thereby eroding endometrial blood vessels and endometrial glands
- More cells in the cytotrophoblast divide and migrate into the syncytiotrophoblast, where they fuse and lose their individual cell membranes

- Cells of the inner cell mass or embryoblast also differentiate into 2 layers:

I. the **hypoblast** layer, which is made up of small cuboidal cells, and it is adjacent(nearer) to the blastocyst cavity

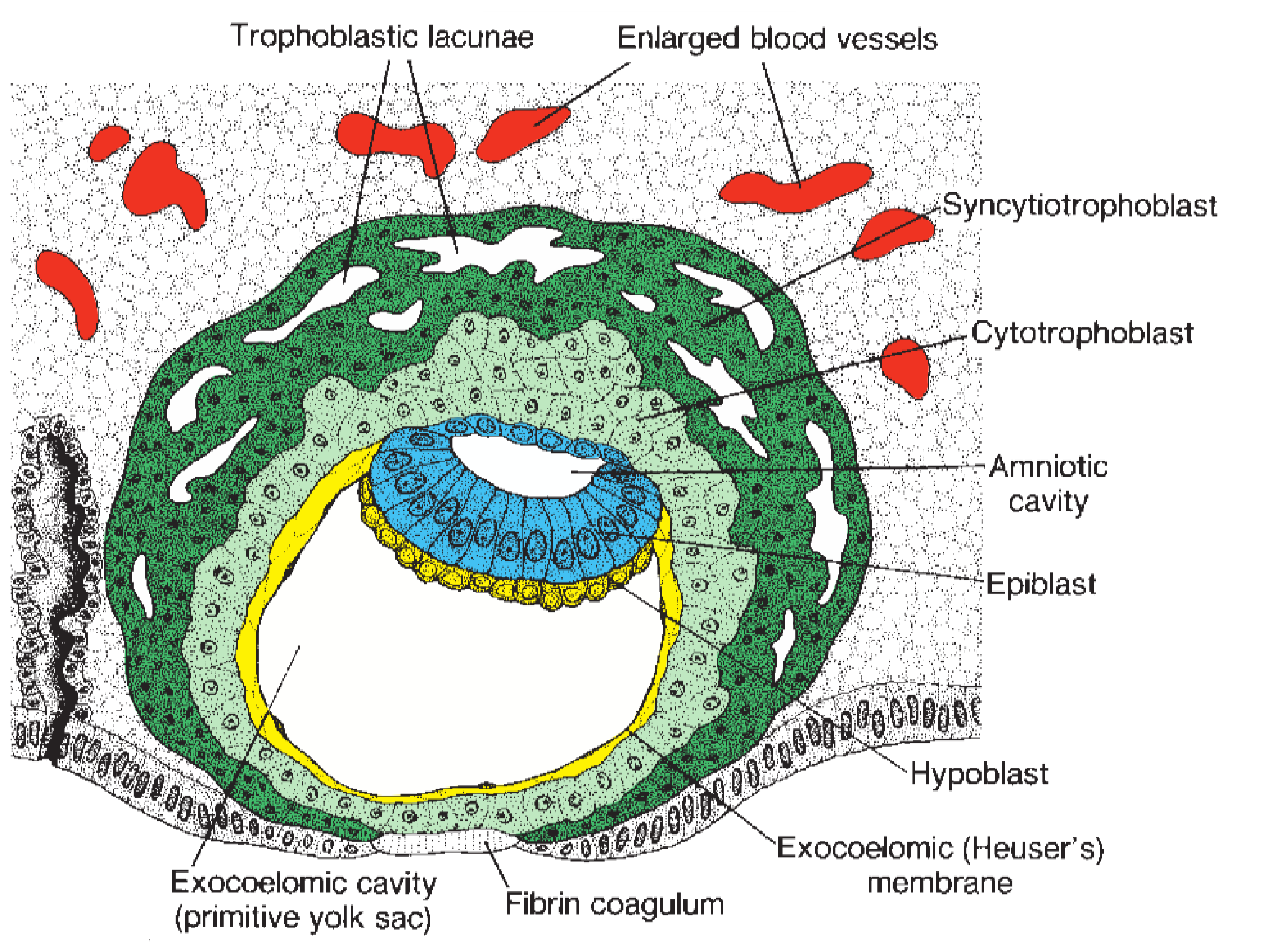
II. the **epiblast** layer which is made up of high columnar cells, and it adjacent to the amniotic cavity

- The hypoblast and epiblast layers ***together*** form a flat ovoid shaped disc called the **bilaminar embryonic disc**
- At the same time, a small cavity appears within the epiblast which enlarges to form the amniotic cavity
- Epiblast cells adjacent to the cytotrophoblast are called **amnioblasts**
- **Amnioblasts** together with the rest of the epiblast, line the amniotic cavity
- The endometrium adjacent to the implantation site is edematous and highly vascular

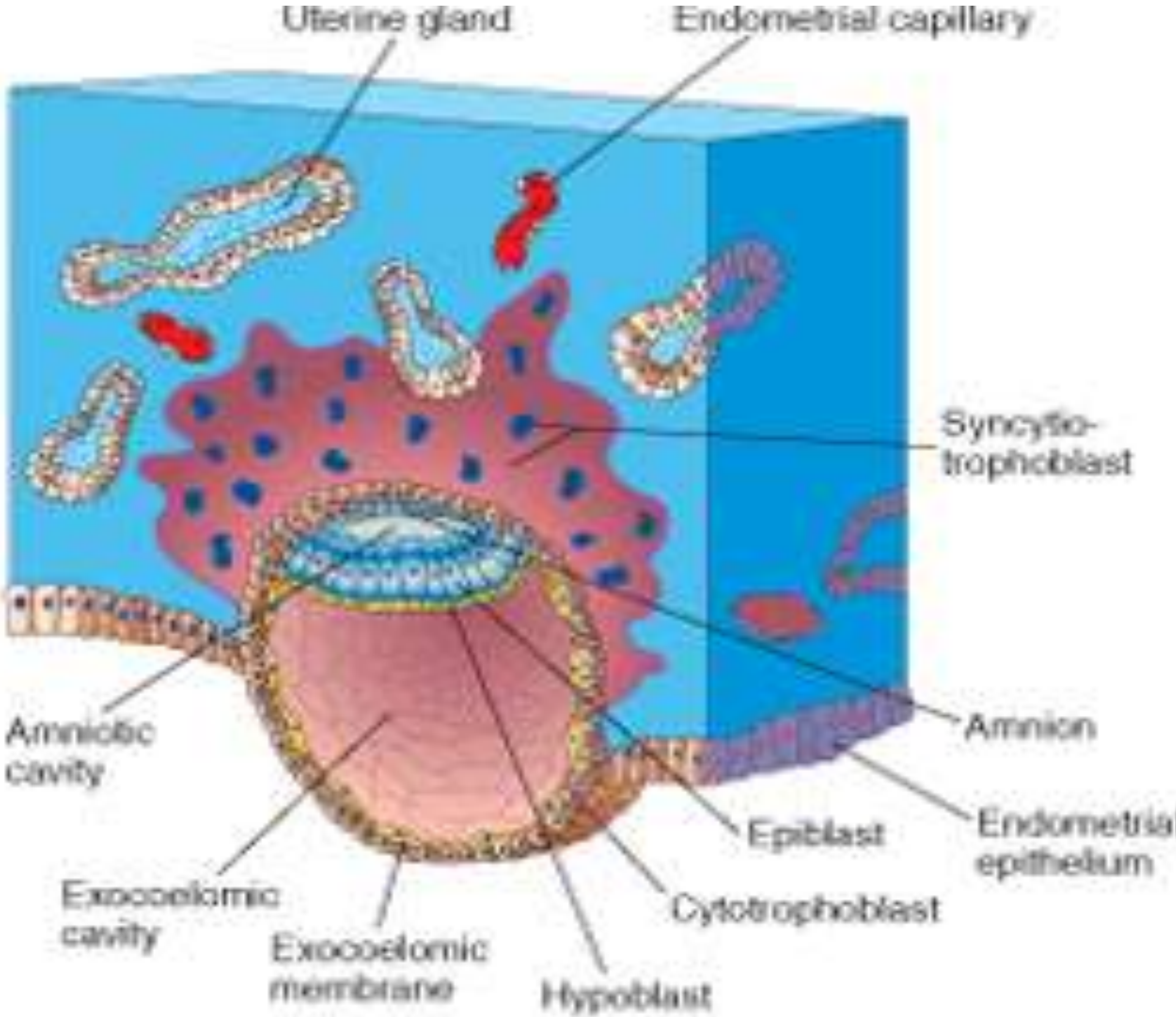

Amniotic cavity
Cytotrophoblast
Syncytiotrophoblast
Amnion
Exo-
coelomic
cavity
Epiblast
Hypoblast
Bilaminar embryonic disk
Exocoelomic
membrane

Day 9

- The blastocyst is more deeply embedded in the endometrium, and the penetration defect in the surface epithelium is closed by a coagulum called **fibrin**
- Vacuoles appear at the region of the trophoblast and they fuse to form lager lacunae
- this phase of trophoblast development is known as the **lacunar stage**
- the cells of the hypoblast adjacent to the cytotrophoblast form a thin membrane called the **exocoelomic (Heuser's) membrane**
- this membrane lines the inner surface of the cytotrophoblast
- the **exocoelomic (Heuser's) membrane** together with the hypoblast forms the lining of the **exocoelomic cavity,** or **primitive yolk sac** or **primary umbilical vesicle**



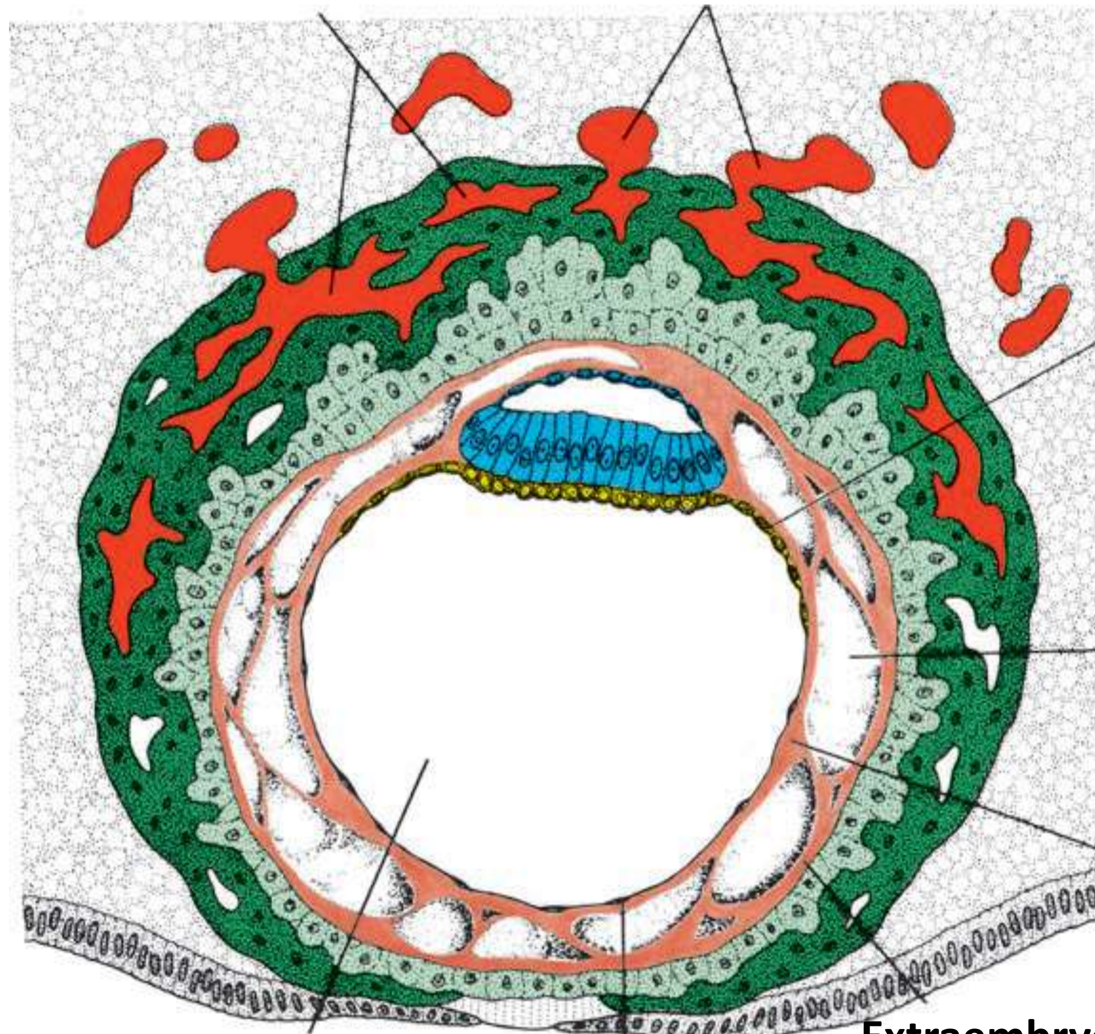
Trophoblastic lacunae
Enlarged blood vessels
Syncytiotrophoblast
Cytotrophoblast
Amniotic cavity
Epiblast
Hypoblast
Exocoelomic (Heuser's) membrane
Fibrin coagulum
Exocoelomic cavity (primitive yolk sac)



Uterine gland
Endometrial capillary
Syncytio-
trophoblast
Amniotic
cavity
Amnion
Epiblast
Endometrial
epithelium
Exocoelomic
cavity
Cytotrophoblast
Exocoelomic
membrane
Hypoblast

11^{th} - 12^{th} day of development

- The blastocyst is completely embedded in the endometrium,
- and the surface epithelium almost entirely covers the original defect in the uterine wall
- The blastocyst now produces a slight protrusion into the lumen of the uterus
- cells of the syncytiotrophoblast penetrate deeper into the stroma(tissue) and erode the endothelial lining of the endometrial capillaries
- These ruptured endometrial capillaries are called **sinusoids**
- The lacunae then begin to communicate with the sinusoids, and <u>maternal blood enters the lacunar system</u>
- The communication of the eroded endometrial capillaries with the lacunae establishes the **primordial uteroplacental circulation**
- When maternal blood flows into the lacunae, <u>oxygen and nutritive substances are available to the embryo</u>


Trophoblastic
lacunae
Maternal
sinusoids
Endoderm
cells
Extraembryonic
cavity
Extraembryonic
splanchnic
mesoderm
Exocoelomic cavity
(primitive yolk sac)
Exocoelomic
somatic
mesoderm
Extraembryonic
somatic
mesoderm

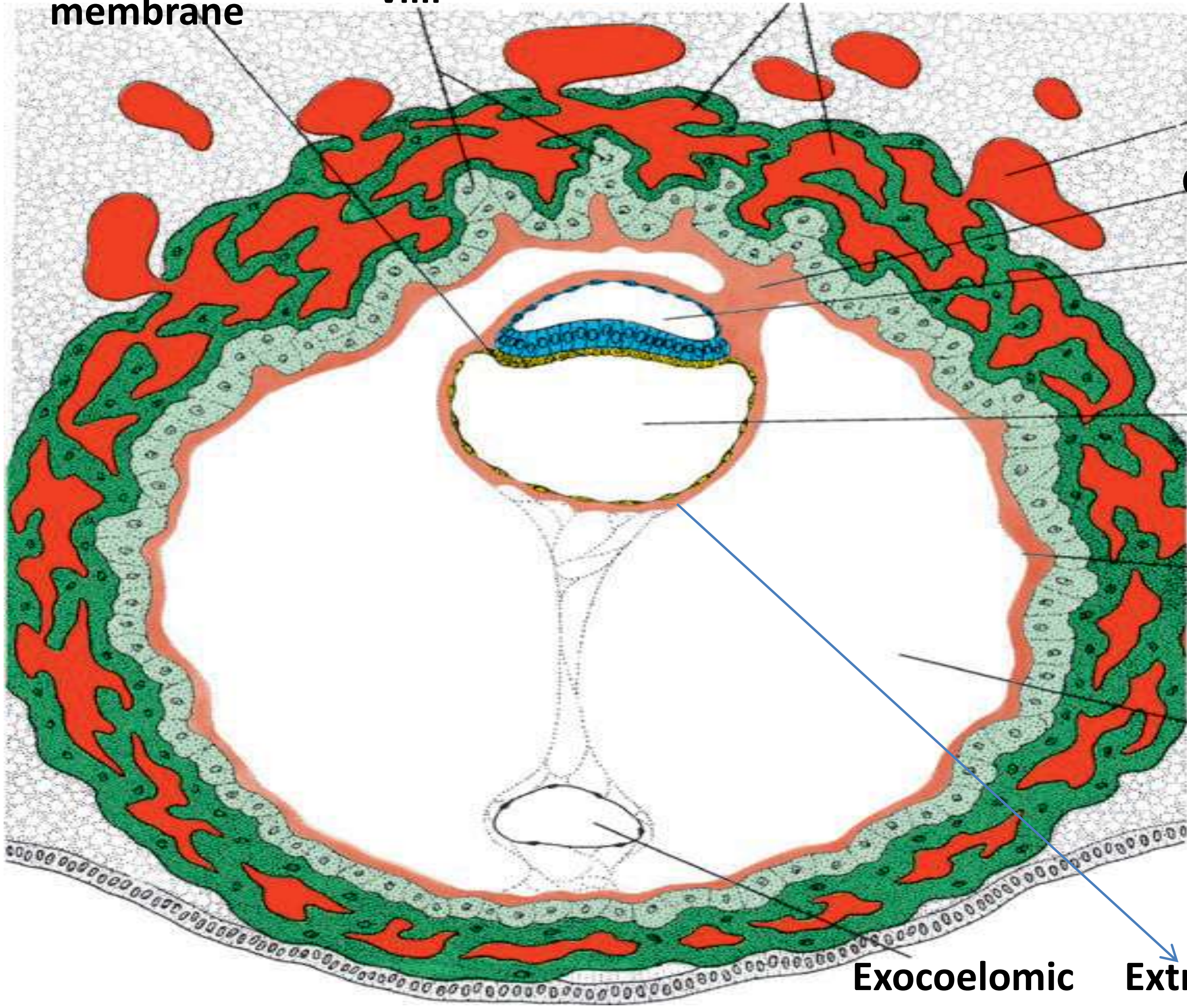
- a new population of cells appears between the inner surface of the cytotrophoblast and the outer surface of the exocoelomic cavity
- These cells which are derived from yolk sac cells form a fine, loose connective tissue called the **extraembryonic mesoderm**
- Soon, large cavities develop in the extraembryonic mesoderm, and when these become confluent, they form a new space known as the **extraembryonic cavity,** or **chorionic cavity** or **extraembryonic coelom**
- This space surrounds the primitive yolk sac and amniotic cavity, except where the germ disc is connected to the trophoblast by the connecting stalk
- The extraembryonic mesoderm lining the cytotrophoblast and amnion is called the **extraembryonic somatic mesoderm**
- the lining covering the yolk sac is known as the **extraembryonic splanchnic mesoderm**

- As the conceptus implants, the endometrial connective tissue cells undergo a transformation, called **decidual reaction**
- During this transformation, the cells of the endometrium swell because of the accumulation of glycogen and lipid in their cytoplasm, and they are known as **decidual cells**
- The primary function of the decidual reaction is to provide nutrition for the early embryo and an immunologically privileged site for the conceptus

13th day of development

- The surface defect in the endometrium has been completely covered by the surface epithelium
- Occasionally bleeding occurs at the implantation site as a result of increased blood flow into the lacunar spaces

- Cells of the cytotrophoblast proliferate locally and penetrate into the syncytiotrophoblast, forming cellular columns surrounded by syncytium
- Cellular columns with the syncytial covering are known as **primary villi**
- In the meantime, the <u>hypoblast produces additional cells that migrate along the inside of the exocoelomic membrane</u>
- These cells proliferate and gradually form a new cavity within the exocoelomic cavity
- This new cavity is known as the <u>**secondary yolk sac**</u> or <u>**definitive yolk sac**</u> or the <u>**secondary umbilical vesicle**</u>
- This yolk sac is much smaller than the original exocoelomic cavity or primitive yolk sac
- During its formation, large portions of the exocoelomic cavity are pinched off to form **exocoelomic cysts**


Oropharyngeal membrane
Primary villi
Trophoblastic lacunae
Maternal sinusoid
Connecting stalk
Amniontic cavity
Secondary yolk sac
Extraembryonic somatic mesoderm (chorionic plate)
Extraembryonic cavity (chorionic cavity)
Exocoelomic cyst
Extraembryonic splanchnic mesoderm

- **Exocoelomic cysts** are often found in the extraembryonic cavity or chorionic cavity or extraembryonic coelom
- Meanwhile, the extraembryonic coelom expands and forms a large cavity, the **chorionic cavity**
- The extraembryonic mesoderm lining the inside of the cytotrophoblast is then known as the chorionic plate
- The only place where extraembryonic mesoderm traverses the chorionic cavity is in the **connecting stalk**
- With development of blood vessels, the connecting stalk becomes the **umbilical cord**

3^{rd} week of embryonic development

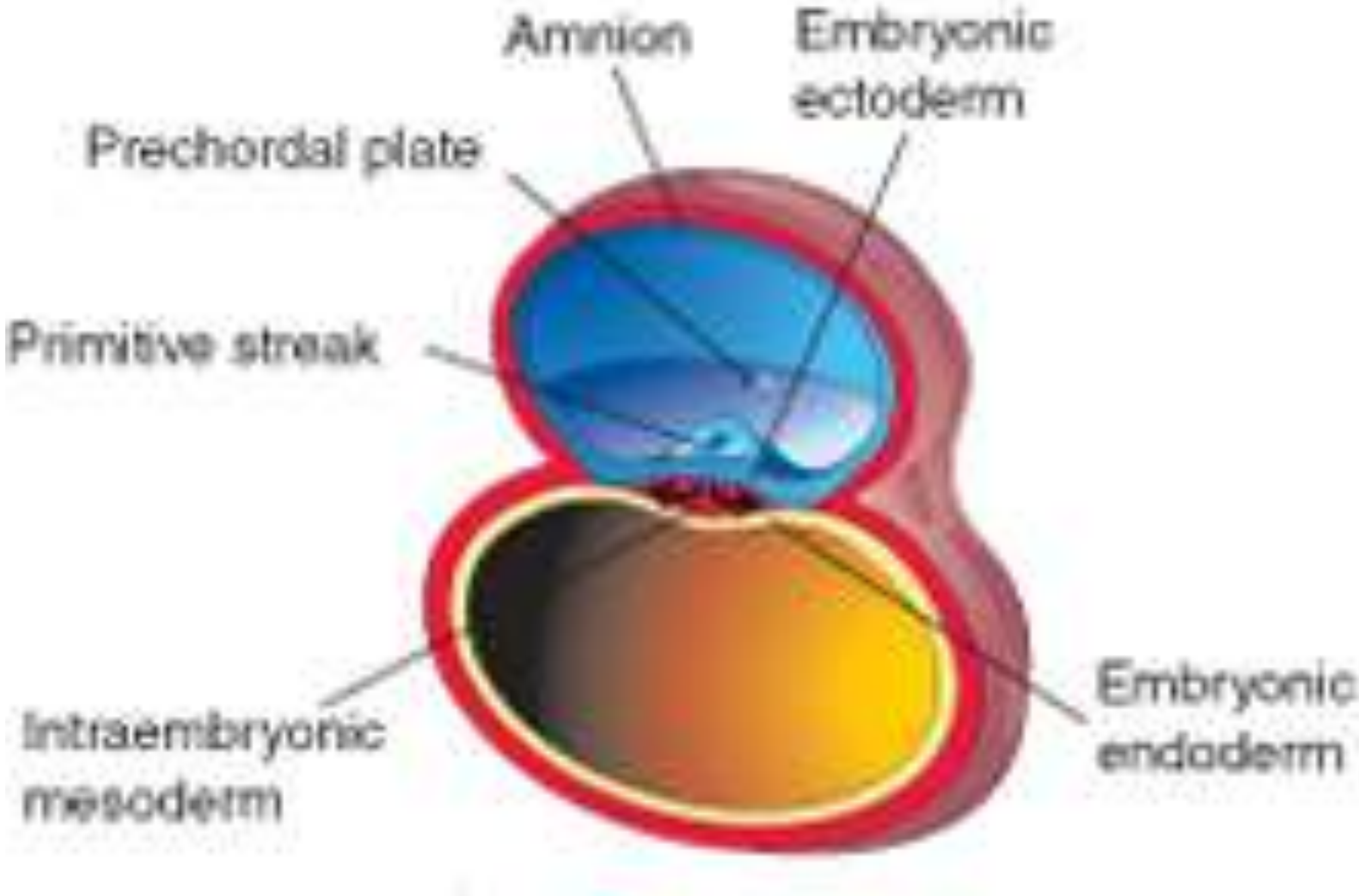
- The 3rd week of embryonic development is characterized by
- Appearance of primitive streak
- Development of notochord
- Differentiation of three germ layers

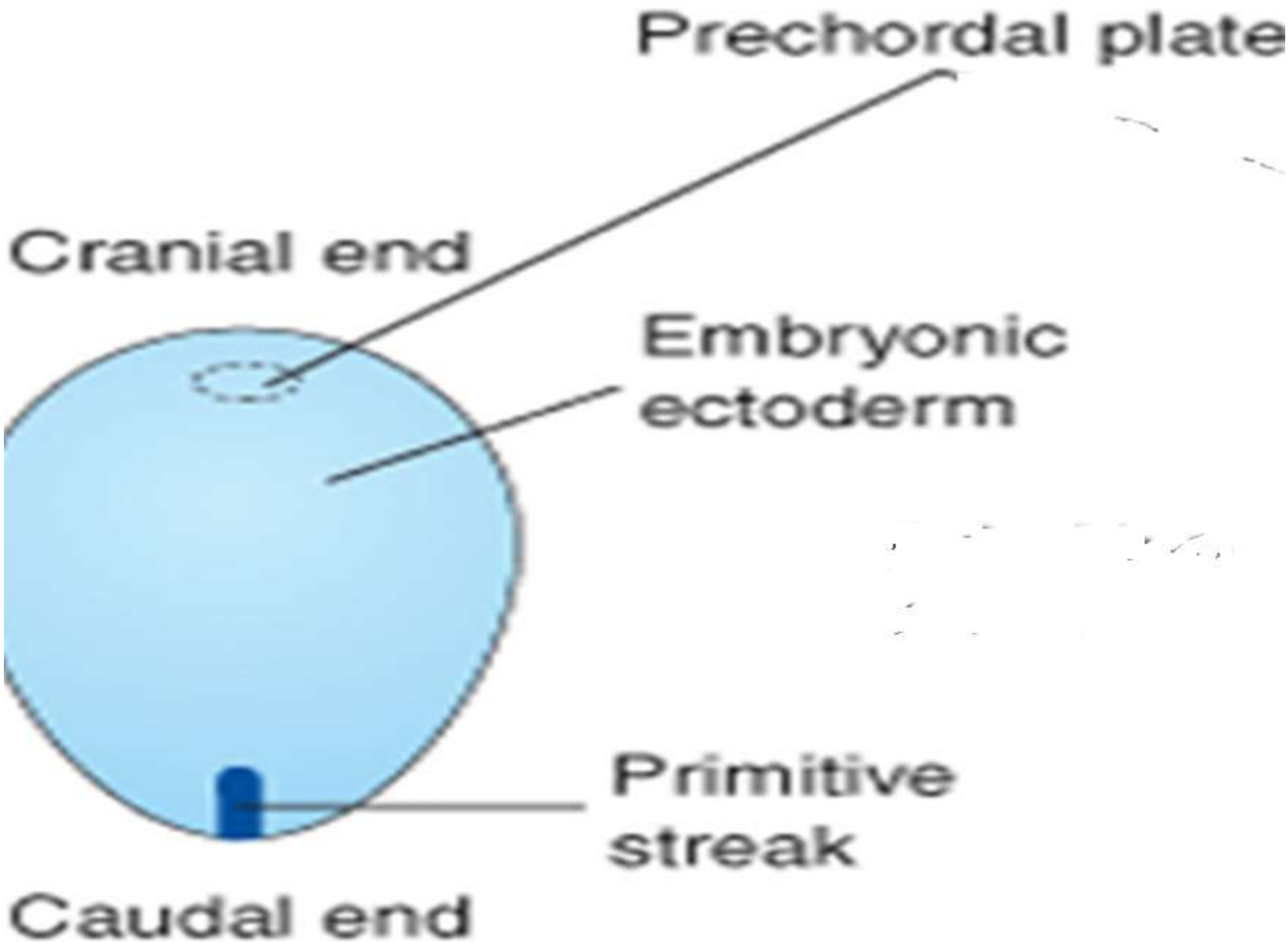
- **Gastrulation**
- This is the formation of 3 germ layers in embryos
- During gastrulation, the bilaminar embryonic disc is converted into a trilaminar embryonic disc
- Extensive cell shape changes, rearrangement, movement, and changes in adhesive properties contribute to the process of gastrulation
- Gastrulation is the beginning of **morphogenesis** (development of body form) and is the significant event occurring during the 3rd week

- The 1st morphologic sign of gastrulation begins with formation of the ***primitive streak*** on the surface of the epiblast of the embryonic disc
- During this period, the embryo may be referred to as a **gastrula**
- the 3 germ layers are
- ✓ Ectoderm
- ✓ Mesoderm
- ✓ and endoderm
- Each of these layers gives rise to specific tissues and organs
- **Embryonic ectoderm:** gives rise to the epidermis, central and peripheral nervous systems(CNS & PNS), the eye, and inner ear, neural crest cells
- **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

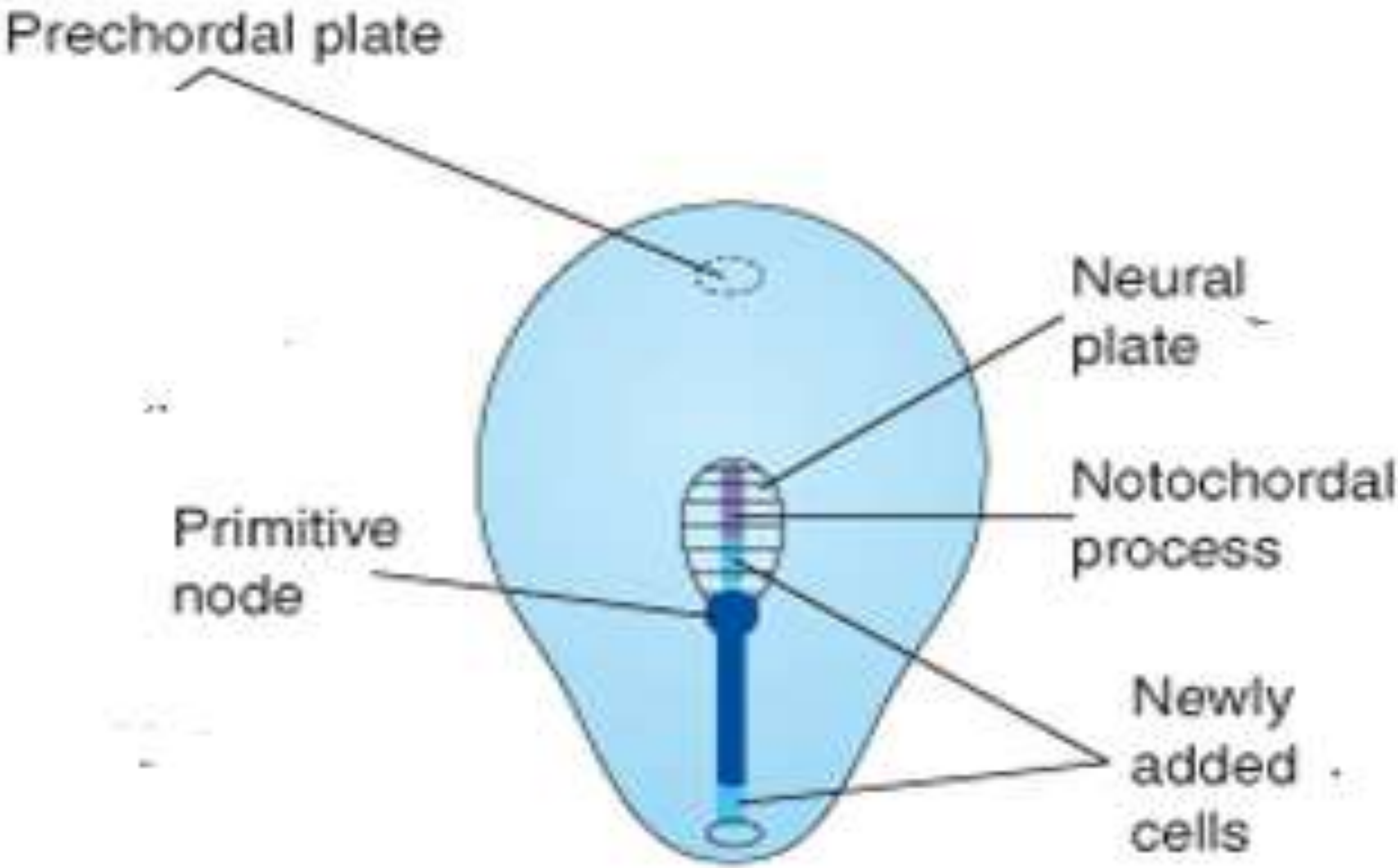
- In the trunk, it is the source of all connective tissues, including cartilage, bones, tendons, ligaments, dermis, and stroma of internal organs
- **Embryonic endoderm** gives rise to the epithelial linings of the respiratory and alimentary (digestive) tracts, including the glands opening into the gastrointestinal tract and the glandular cells of associated organs such as the liver and pancreas

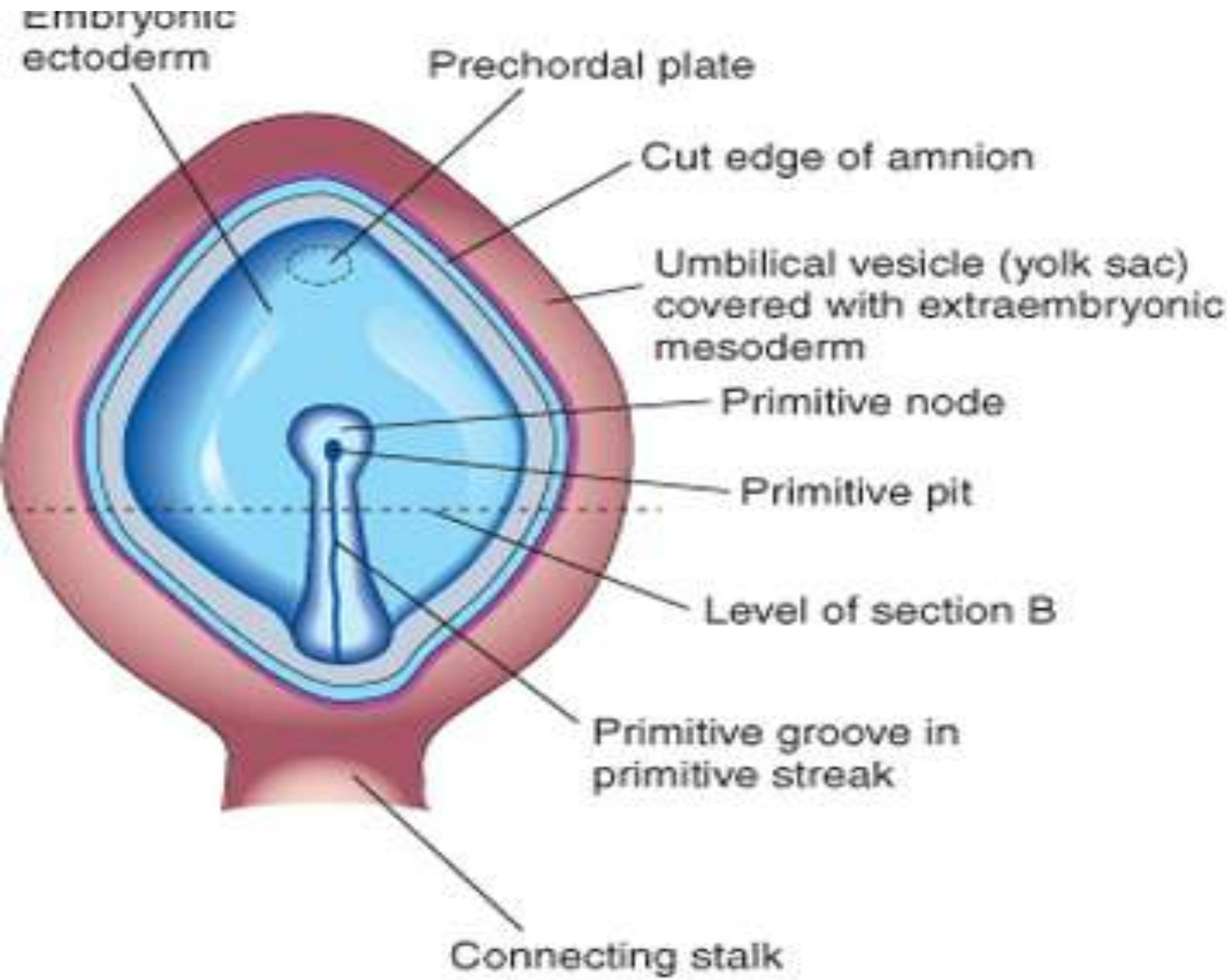
- **Primitive streak**
- The first sign of gastrulation is the *appearance of the primitive streak*
- The primitive streak results from the proliferation and movement of cells of the epiblast to the median plane of the embryonic disc
- At the beginning of the 3rd week, the **primitive streak** appears caudally (tail end) in the median plane of the dorsal (posterior) aspect of the embryonic disc


Amnion
Embryonic ectoderm
Prechordal plate
Primitive streak
Intraembryonic mesoderm
Embryonic endoderm

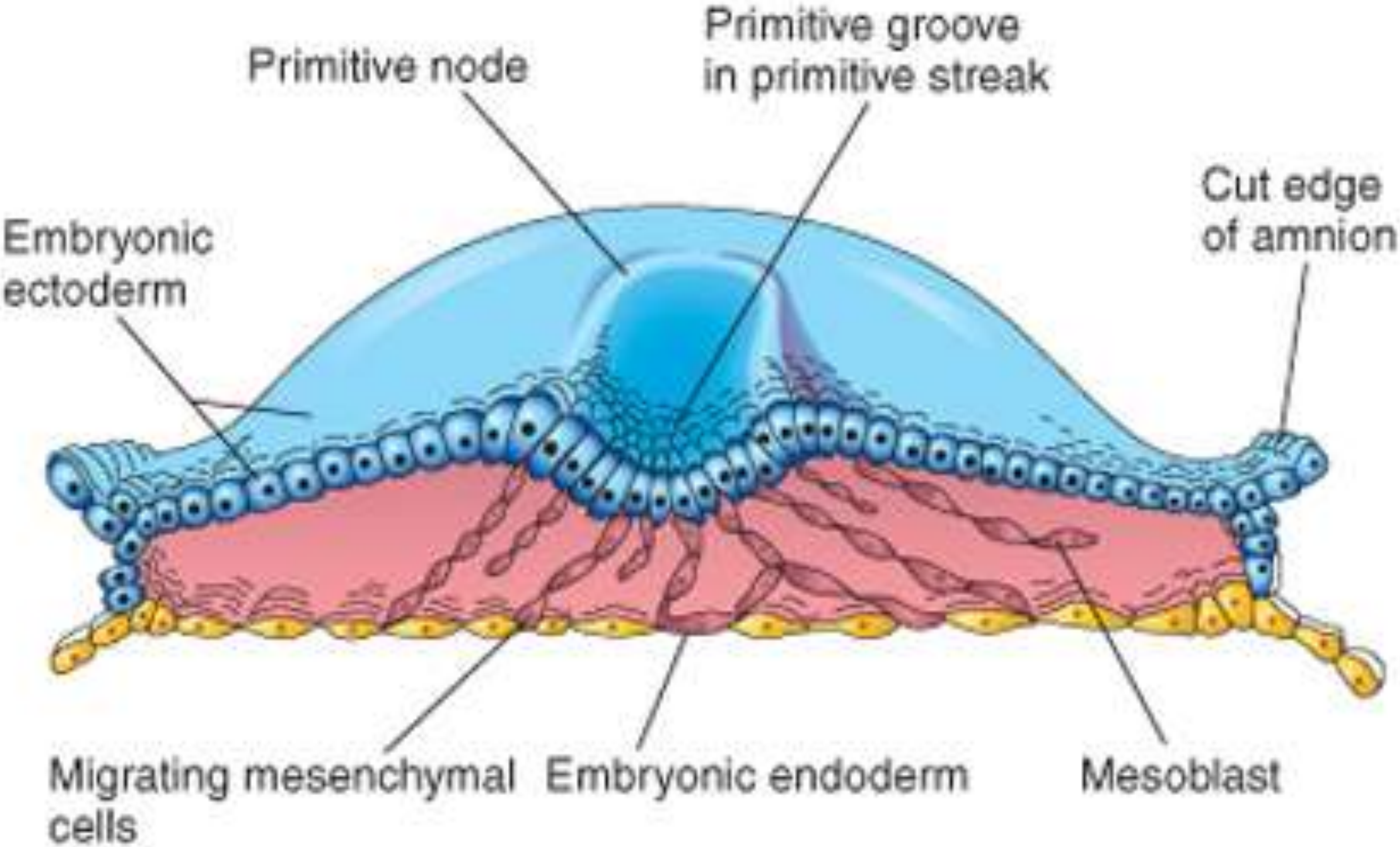


Prechordal plate
Cranial end
Embryonic
ectoderm
Primitive
streak
Caudal end


Prechordal plate
Neural plate
Notochordal process
Primitive node
Newly added cells


ectoderm
Prechordal plate
Cut edge of amnion
Umbilical vesicle (yolk sac) covered with extraembryonic mesoderm
Primitive node
Primitive pit
Level of section B
Primitive groove in primitive streak
Connecting stalk

- As the primitive streak elongates by addition of cells to its caudal end, its cranial end proliferates to form a **primitive node**
- Concurrently, a narrow groove called the **primitive groove** develops in the primitive streak
- This narrow groove '<u>primitive groove</u>' is continuous with a small depression in the primitive node called the **primitive pit**
- Shortly after the primitive streak appears, cells leave its deep surface and form **mesenchyme** (a tissue consisting of loosely arranged cells suspended in a gelatinous matrix)
- **Mesenchymal cells** are ameboid and actively phagocytic
- Mesenchyme forms the supporting tissues of the embryo, such as most of the connective tissues of the body and the connective tissue framework of glands


Primitive node
Primitive groove
in primitive streak
Cut edge
of amnion
Embryonic
ectoderm
Migrating mesenchymal
cells
Embryonic endoderm
Mesoblast

- Some mesenchyme forms **mesoblast** (undifferentiated mesoderm), which forms the ***intraembryonic or embryonic mesoderm***
- Cells from the epiblast, as well as from the primitive node and other parts of the primitive streak migrate inorder to displace the hypoblast
- This inward movement is known as **invagination**
- Cell migration and specification are controlled by fibroblast growth factor 8 (FGF8), which is synthesized by streak cells themselves
- Once the cells have invaginated, some displace the hypoblast, creating the embryonic **endoderm,**
- and others come to lie between the epiblast and newly created endoderm to form **mesoderm**
- Cells remaining in the epiblast then form **ectoderm**
- *In summary, cells of the epiblast, through the process of gastrulation, give rise to all 3 germ layers in the embryo, the primordia of all its tissues and organs*

Fate of the Primitive Streak

- The primitive streak actively forms mesoderm by the ingression of cells until the early part of the fourth week; thereafter, production of mesoderm slows down
- The primitive streak diminishes in relative size and becomes an insignificant structure in the sacrococcygeal region of the embryo
- Normally the primitive streak undergoes degenerative changes and disappears by the end of the 4th week

Clinical correlate

Sacrococcygeal Teratoma

- Remnants of the primitive streak may persist and give rise to a **sacrococcygeal teratoma**
- Because they are derived from pluripotent primitive streak cells, these tumors contain tissues derived from all three germ layers in incomplete stages of differentiation
- Sacrococcygeal teratomas are the most common tumor in newborns and have an incidence of approximately one in 35,000

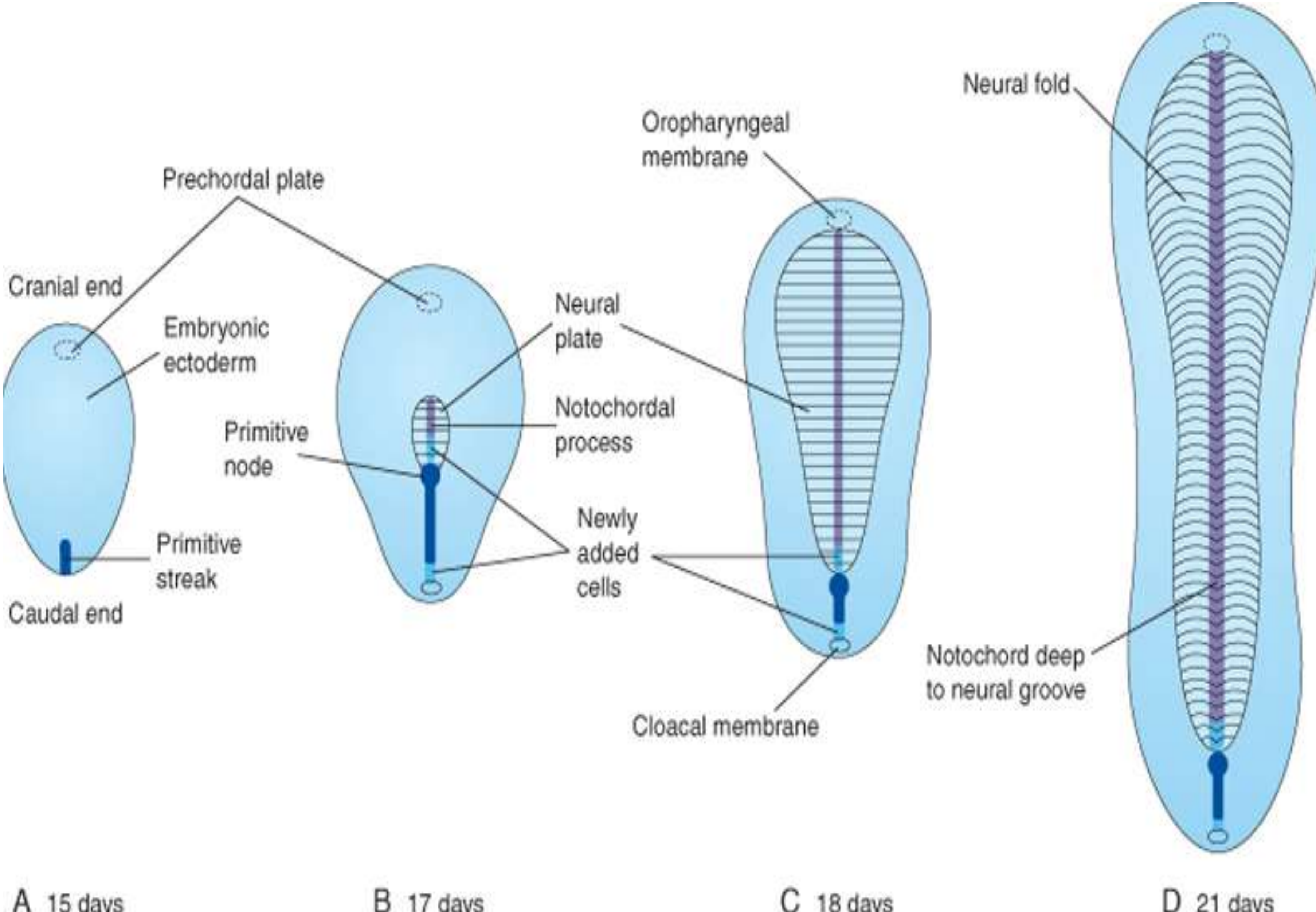
- most affected infants (80%) are female
- Sacrococcygeal teratomas are usually diagnosed on routine antenatal ultrasonography, and most tumors are mild
- These tumors are usually surgically excised promptly, and the prognosis is good

Notochordal process and notochord

Notochordal process

- Some mesenchymal cells that have ingressed through the streak, acquired mesodermal cell and migrate cranially from the primitive node and pit, forming a median cellular cord, the **notochordal process**

- This process soon acquires a lumen, the **notochordal canal**.
- The notochordal process grows cranially between the ectoderm and endoderm until it reaches the **prechordal plate**, a small circular area of columnar endodermal cells where the ectoderm and endoderm are in contact
- The prechordal plate is the primordium of the **oropharyngeal membrane**, located at the future site of the oral cavity
- Caudal to the primitive streak there is a circular area-the **cloacal membrane**, which indicates the future site of the anus



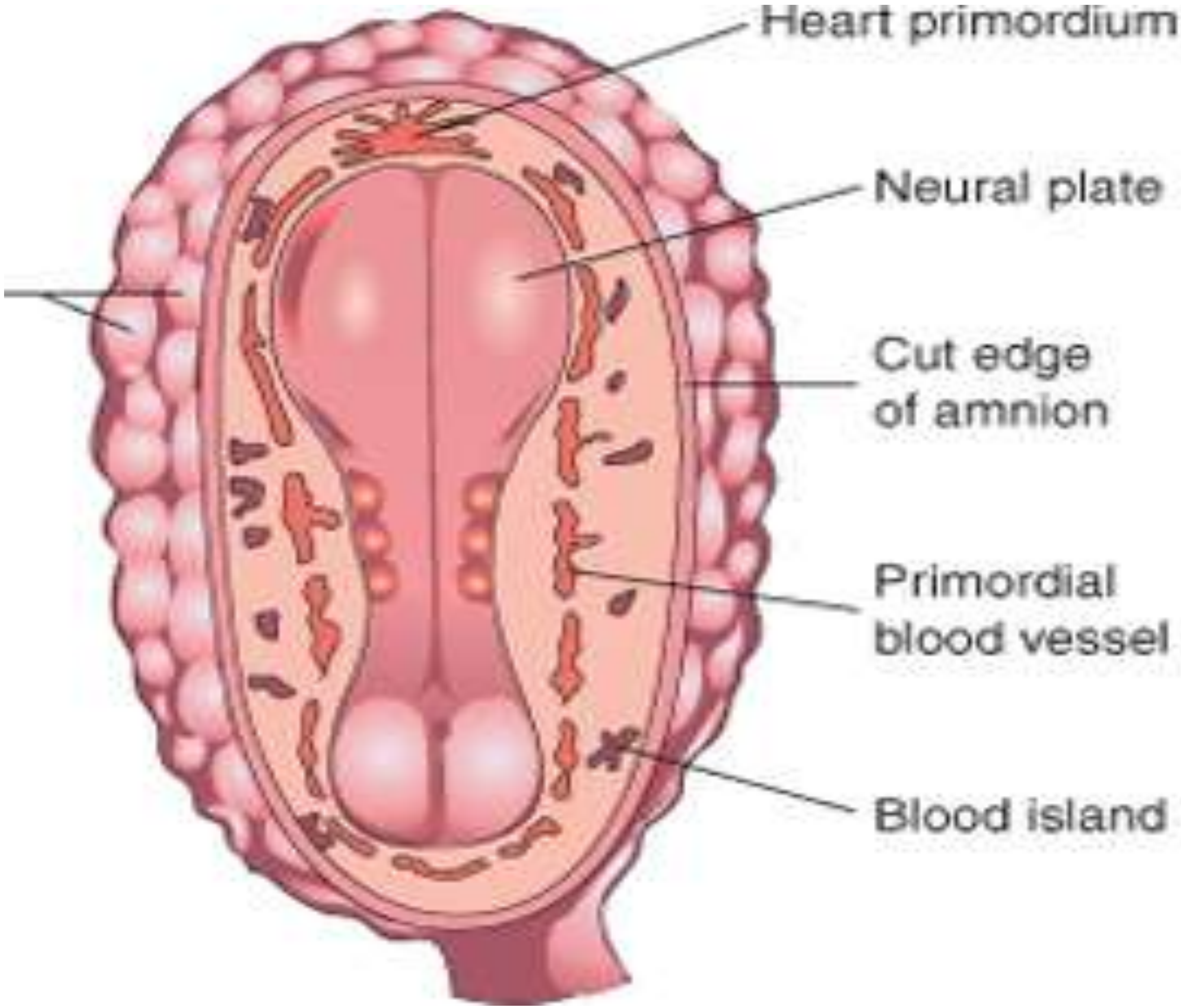
Prechordal plate
Cranial end
Embryonic ectoderm
Primitive streak
Caudal end
Primitive node
Neural plate
Notochordal process
Newly added cells
Oropharyngeal membrane
Cloacal membrane
Neural fold
Notochord deep to neural groove
A 15 days
B 17 days
C 18 days
D 21 days

- cranially on each side of the notochordal process is a region of mesoderm called the cardiogenic region(area)
- This region lies **<u>rostral</u>**<u>(*anterior/cranial)*</u> to the prochordal plate, and it is where the primordium heart begins to develop at the end of the third week
- The embryonic disc remains **bilaminar** at the <u>cloaca</u> and <u>oropharyngeal membrane</u>
- This is because the embryonic ectoderm and endoderm are <u>fused</u> at these sites, thereby preventing migration of mesenchymal cells (which form mesoderm) between them
- By the middle of the 3rd week, intraembryonic mesoderm separates the ectoderm and endoderm everywhere except

I. at the oropharyngeal membrane cranially

II. In the median plane cranial to the primitive node, where the notochordal process is located

III. at the cloacal membrane caudally

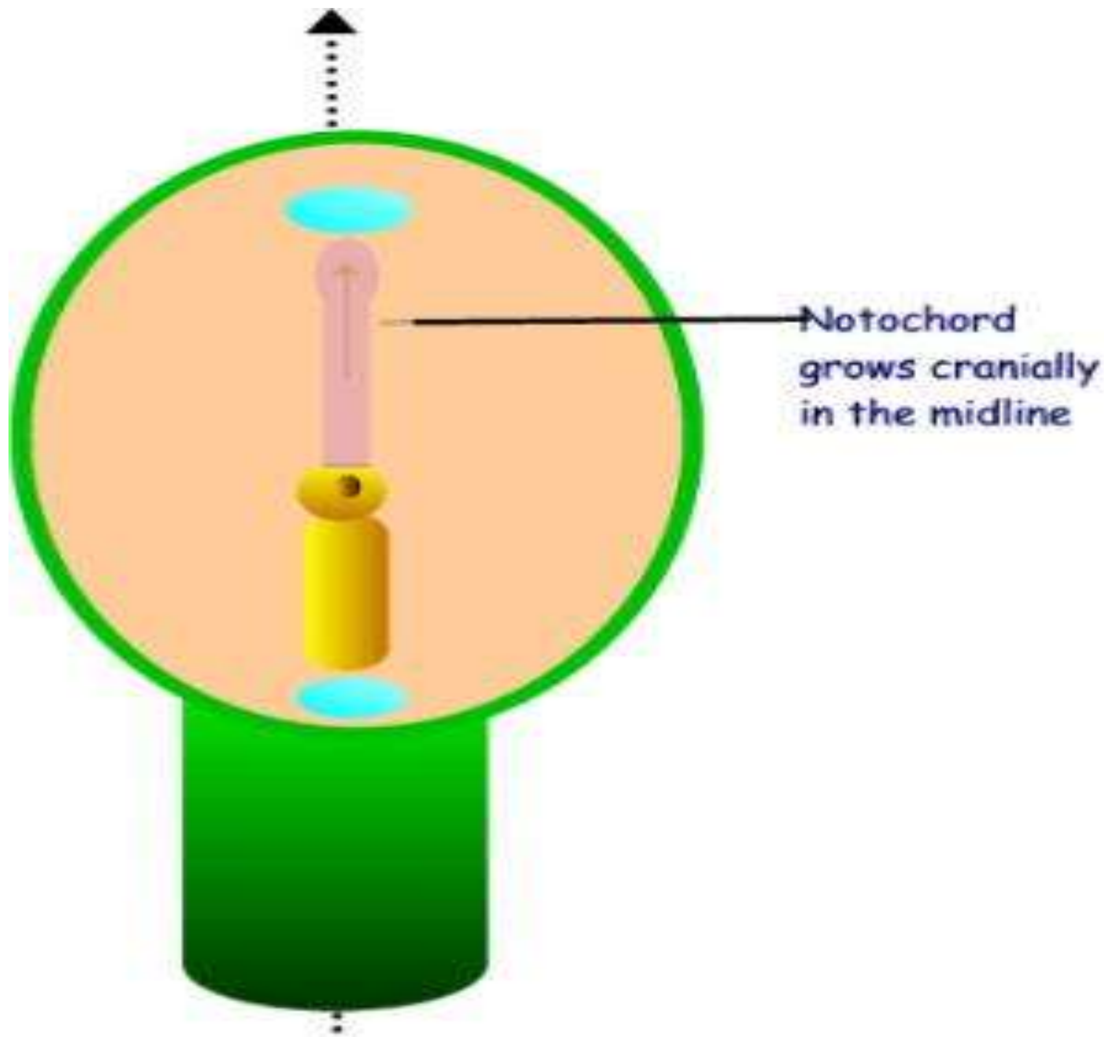

Heart primordium
Neural plate
Cut edge
of amnion
Primordial
blood vessel
Blood island

Notochord

- Notochord is a rod of mesenchymal cells

✓located in the midline

✓extending *cranially* from the **primitive node** to the **buccopharyngeal membrane**



Formation of the notochord

1. The **notochordal process** elongates by invagination of cells from the primitive pit **(fig 1a & b)**

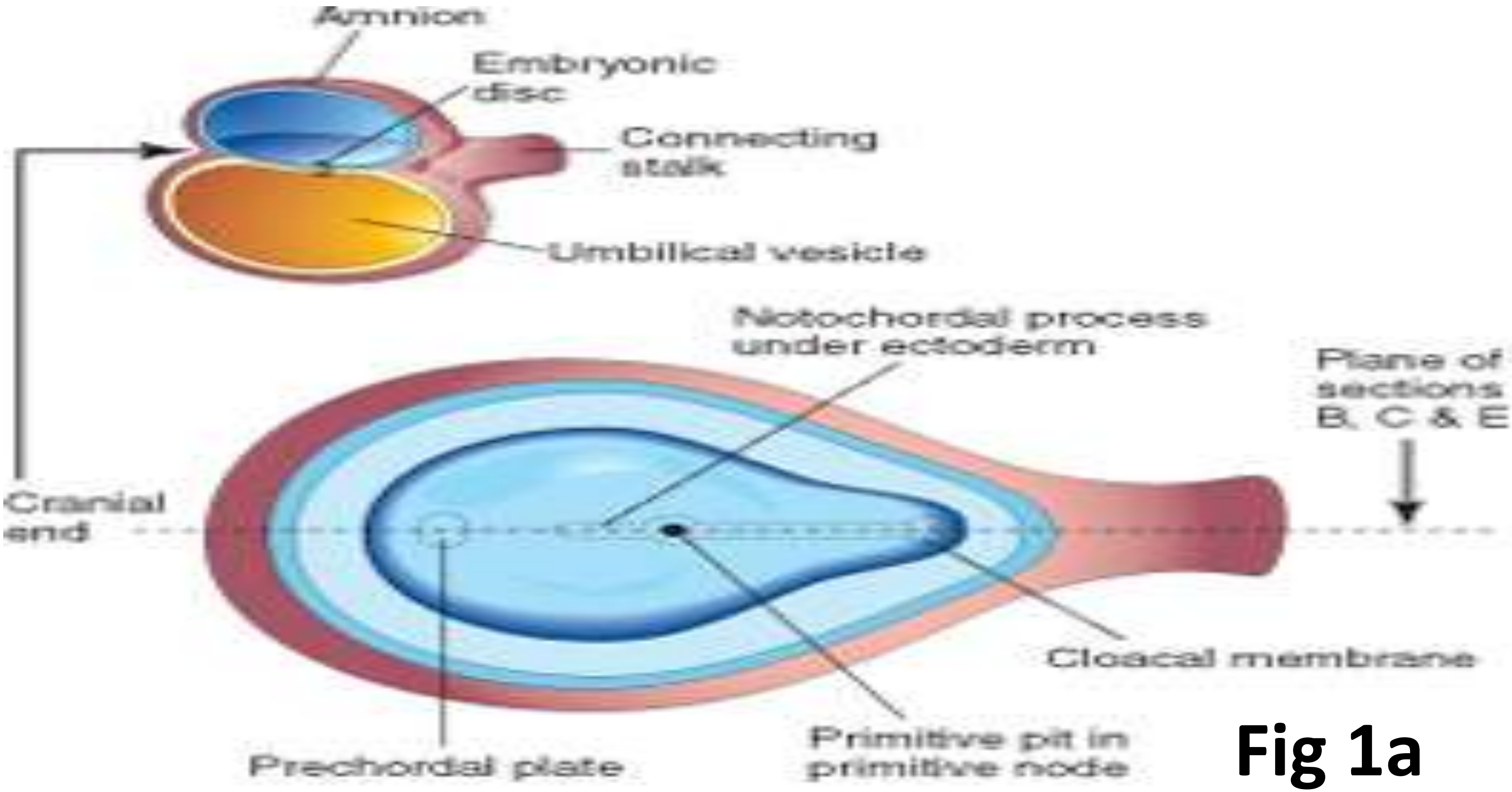


Fig 1a

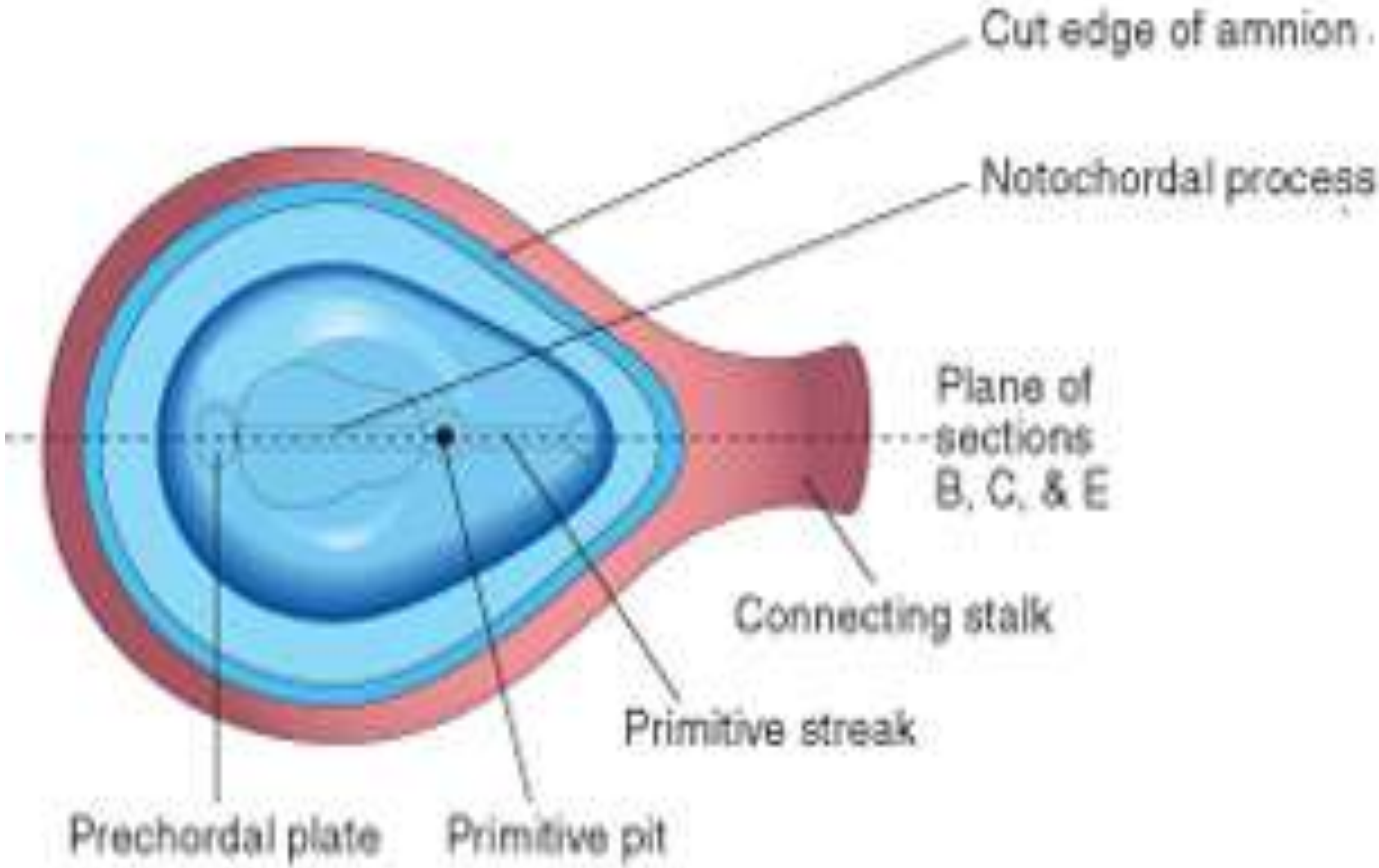

Cut edge of amnion
Notochordal process
Plane of sections B, C, & E
Connecting stalk
Primitive streak
Prechordal plate
Primitive pit

Fig 1b

2. The primitive pit extends into the notochordal process, forming a **notochordal canal (fig 2a & b)**

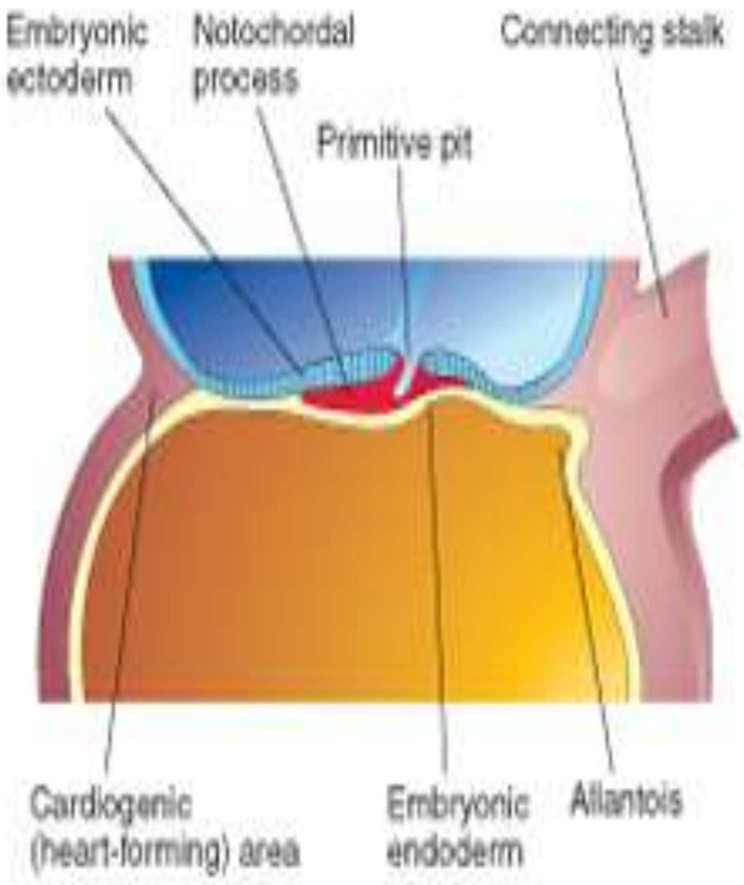


Fig 2a

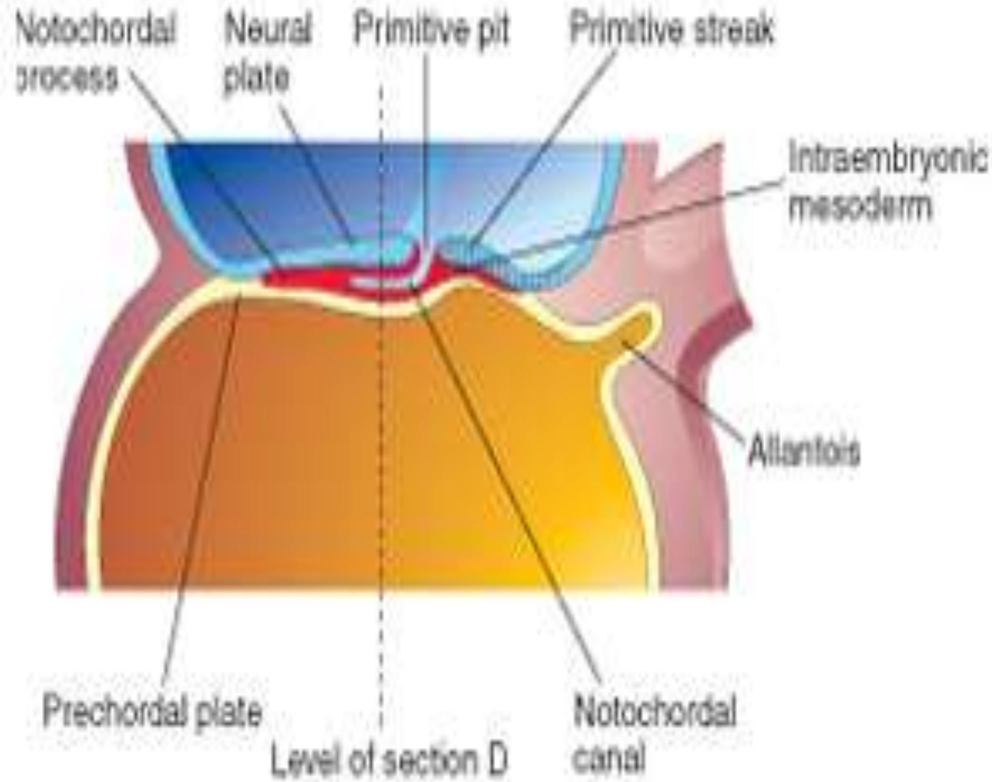


Fig 2b

3 The floor of the notochordal process fuses with the underlying embryonic endoderm (**fig 3a)**

- The fused layers gradually undergo degeneration, resulting in the formation of openings in the floor of the notochordal process, which brings the notochordal canal into communication with the umbilical vesicle (**fig 3b)**

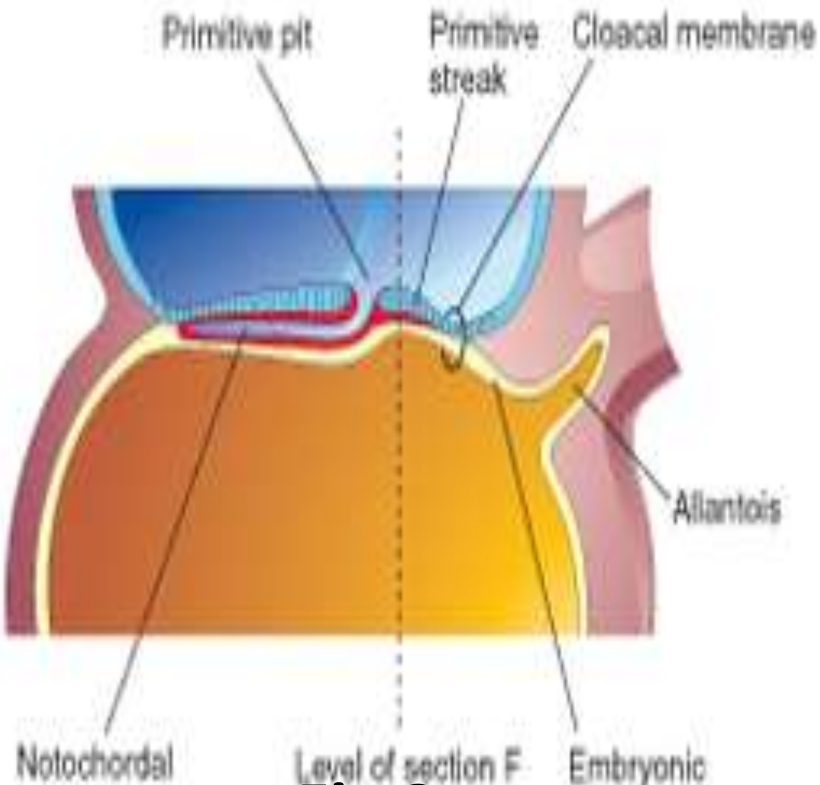


Fig 3a

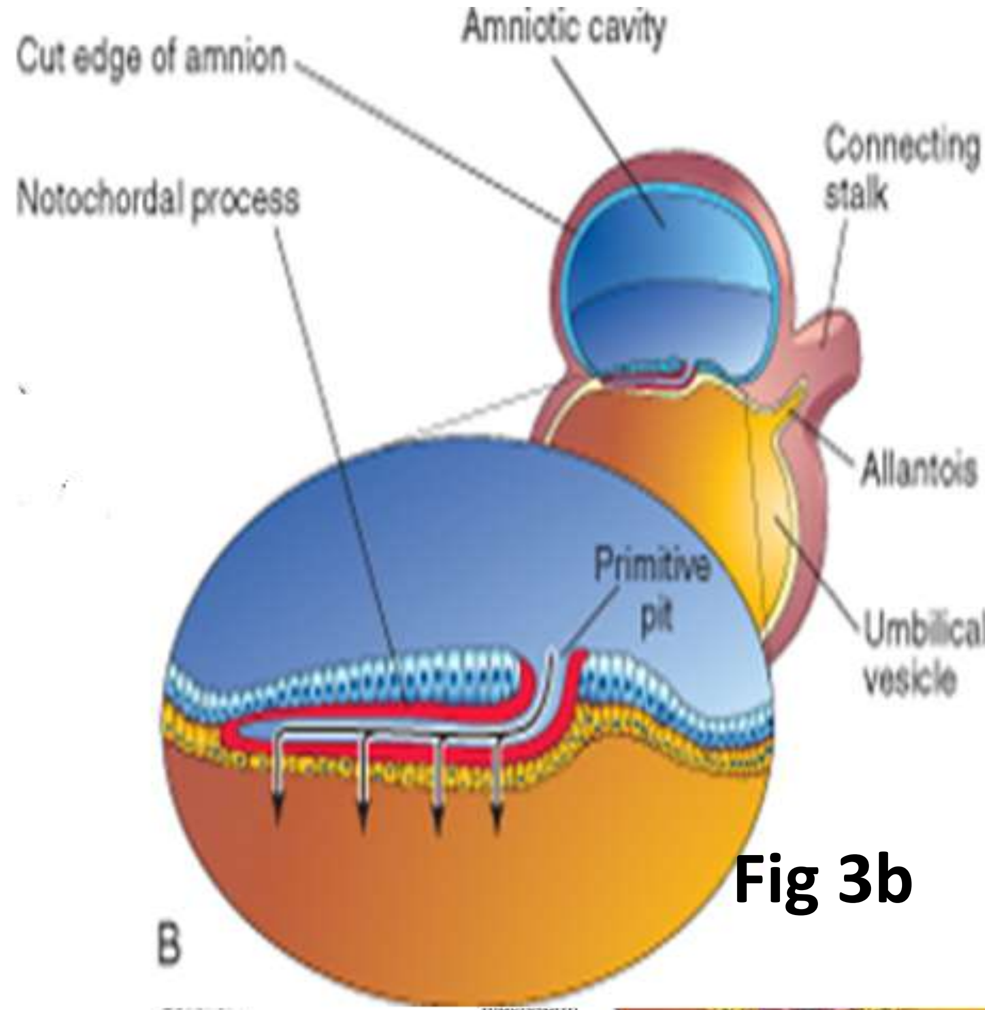


Fig 3b

4. The openings rapidly become confluent and the floor of the notochordal canal disappears (**fig 4)**

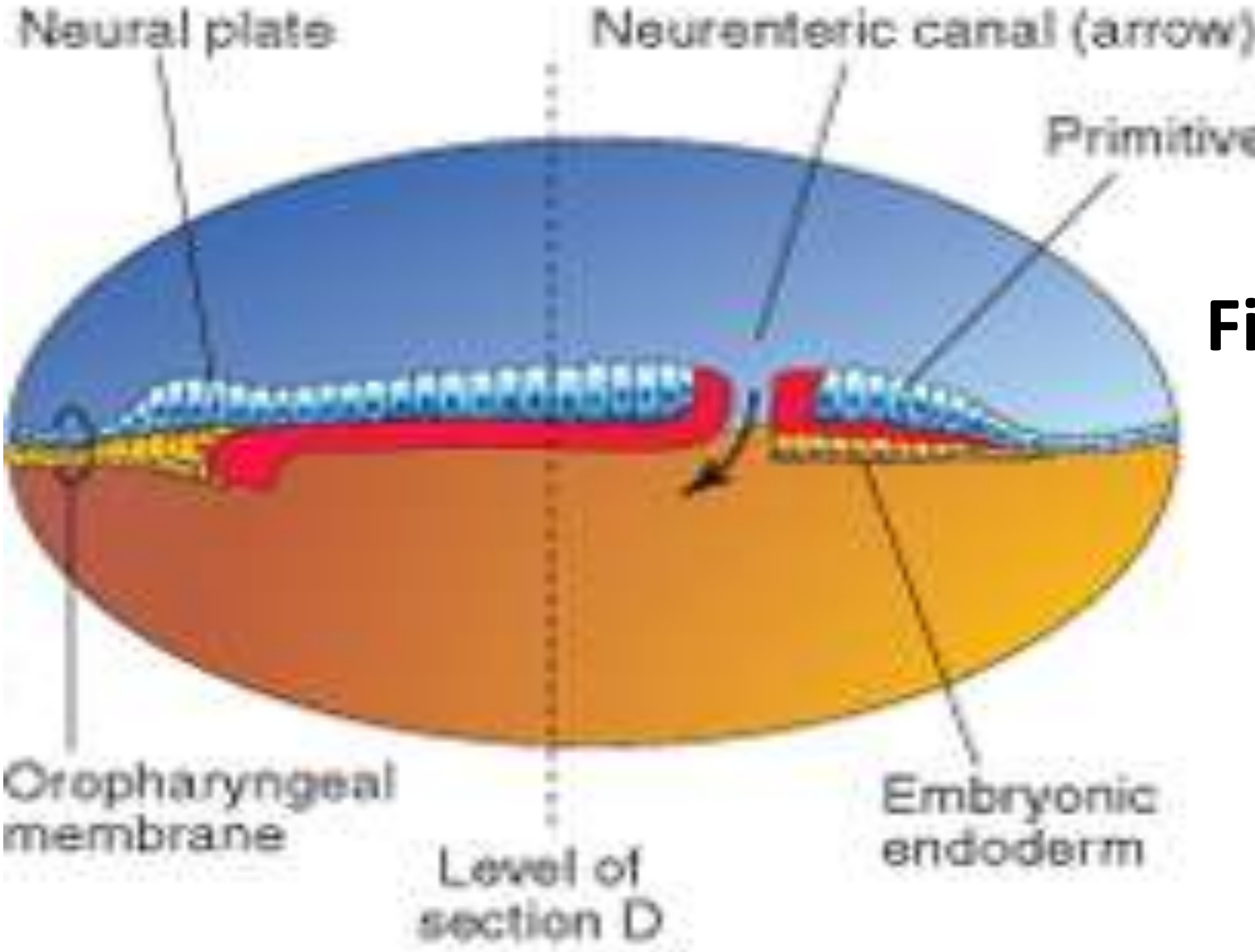
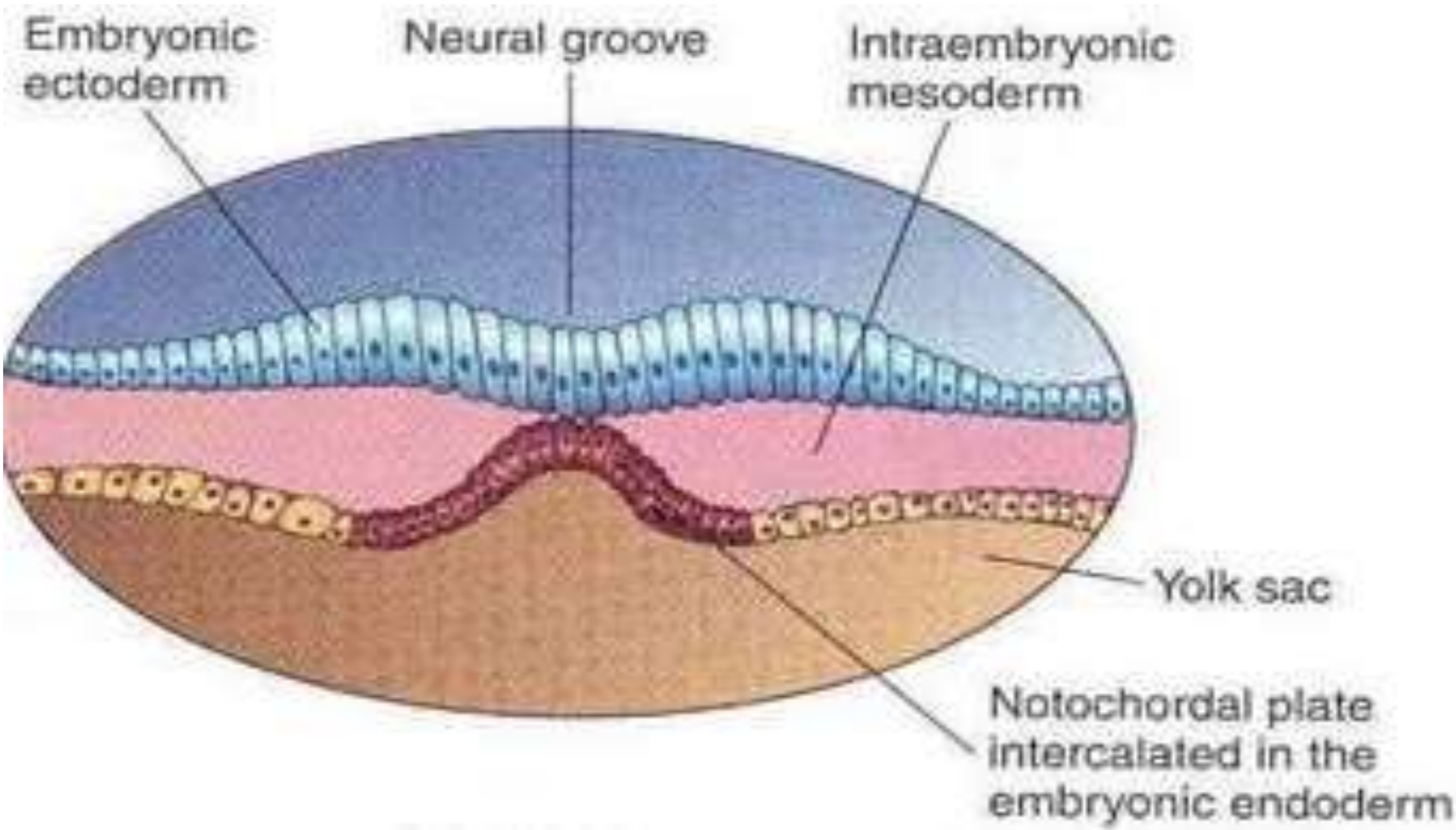


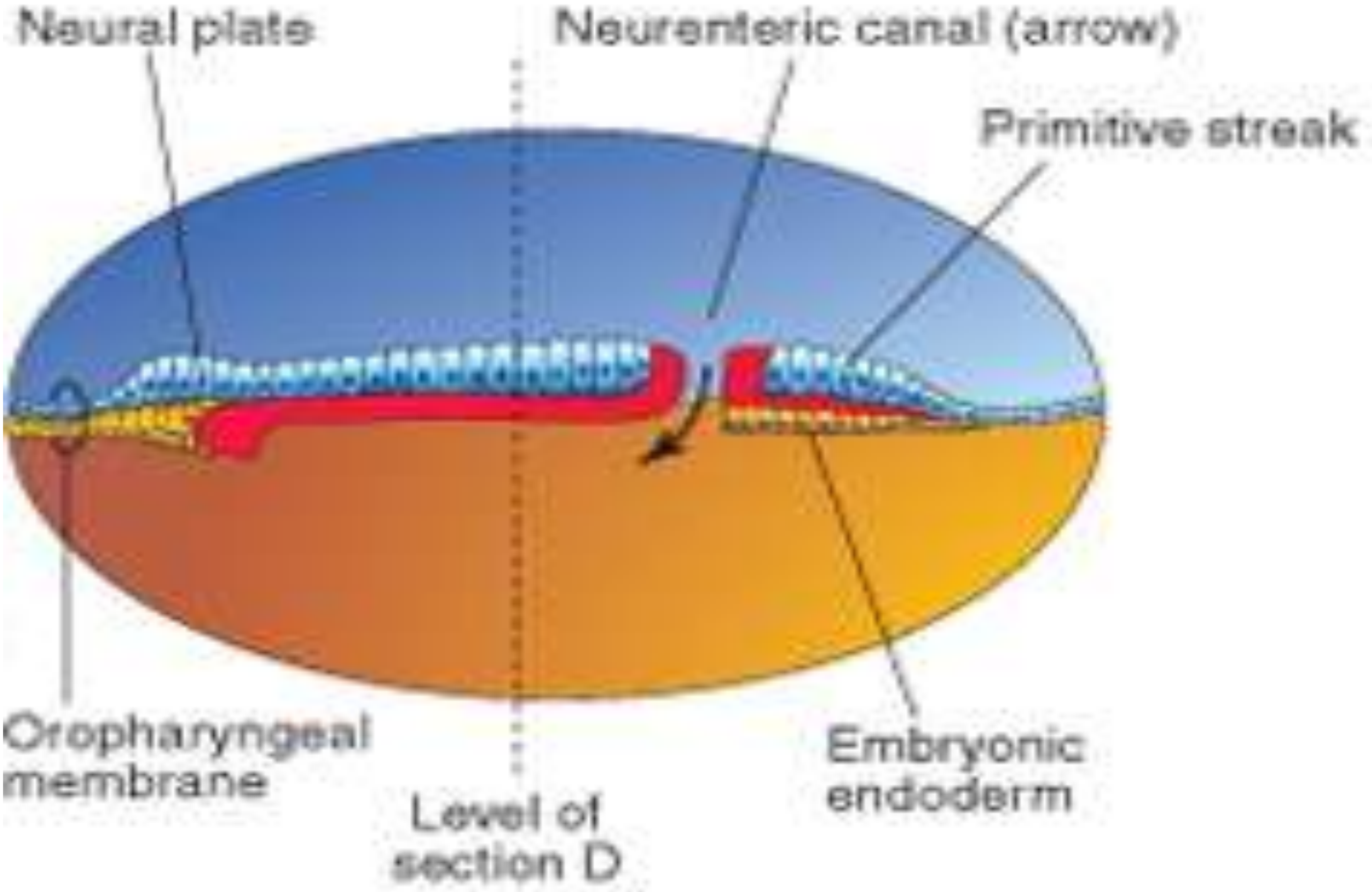
Fig 4

6. The floor of the tube and the underlying endoderm fuse and then break down, forming a **notochordal plate**

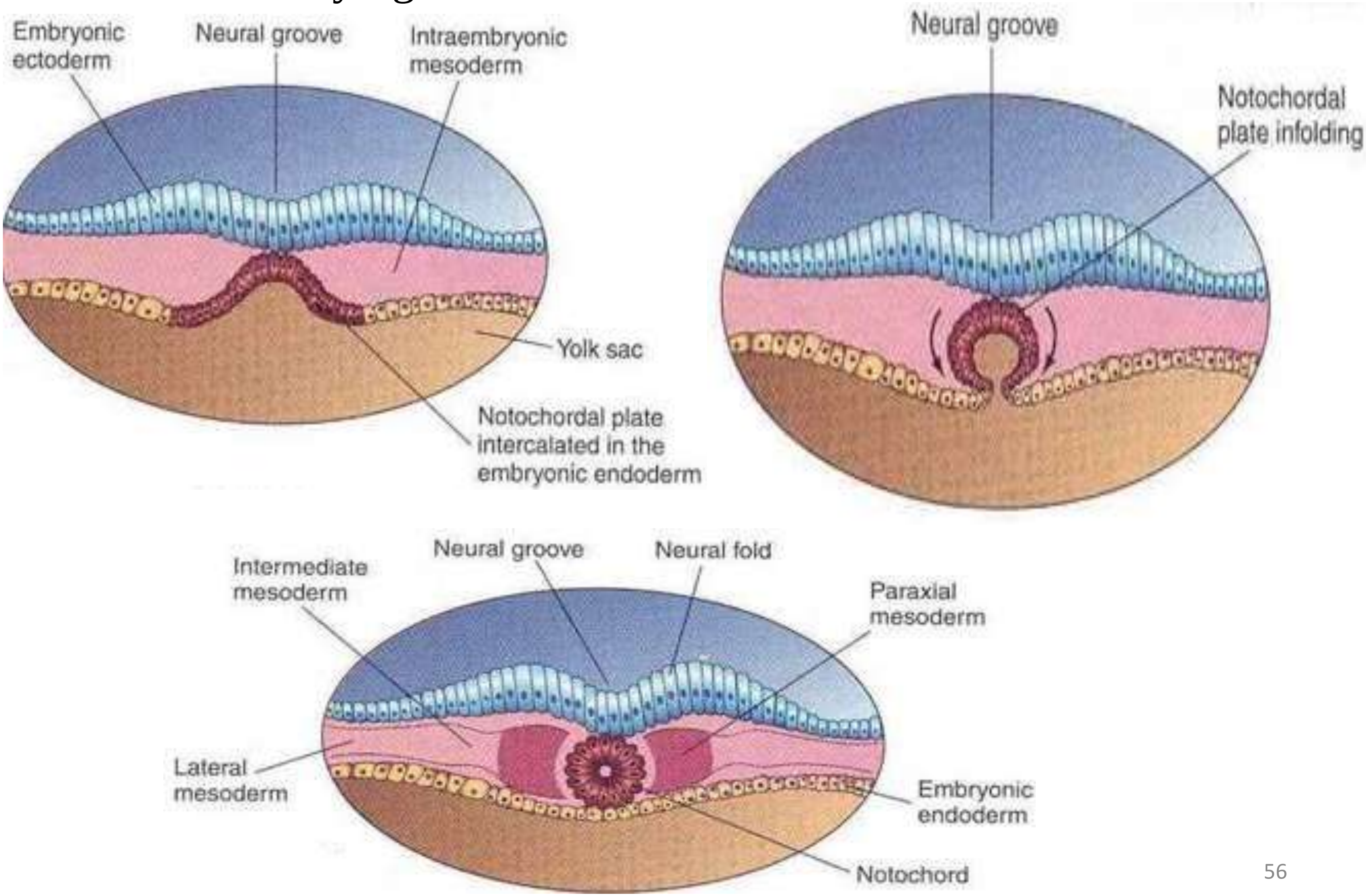
- The notochordal plate becomes continuous with the endodermal layer



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



- Notochordal plate folds to form the **notochord**,which gets separated from the underlying endoderm



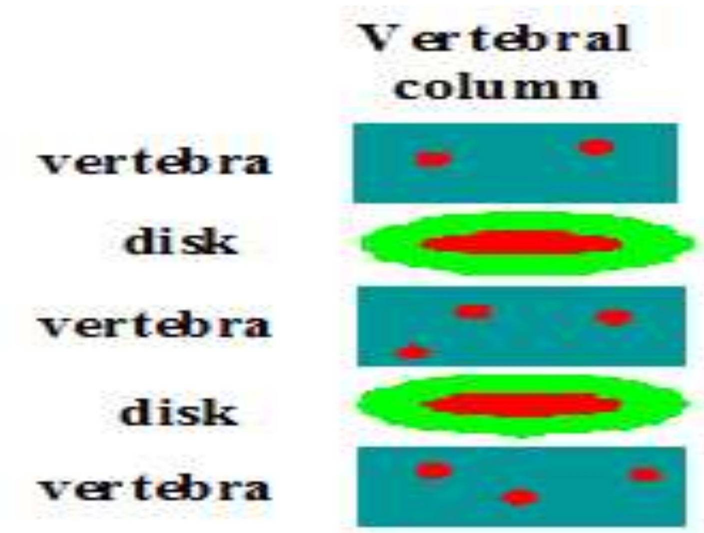
Functions of Notochord

- Defines primordial axis of the embryo
- Provides rigidity to the embryo
- Serves as a basis for the development of the axial skeleton
- Contributes to the intervertebral discs
- Regulates differentiation of surrounding structures including the overlying ectoderm and the mesoderm

Fate of notochord

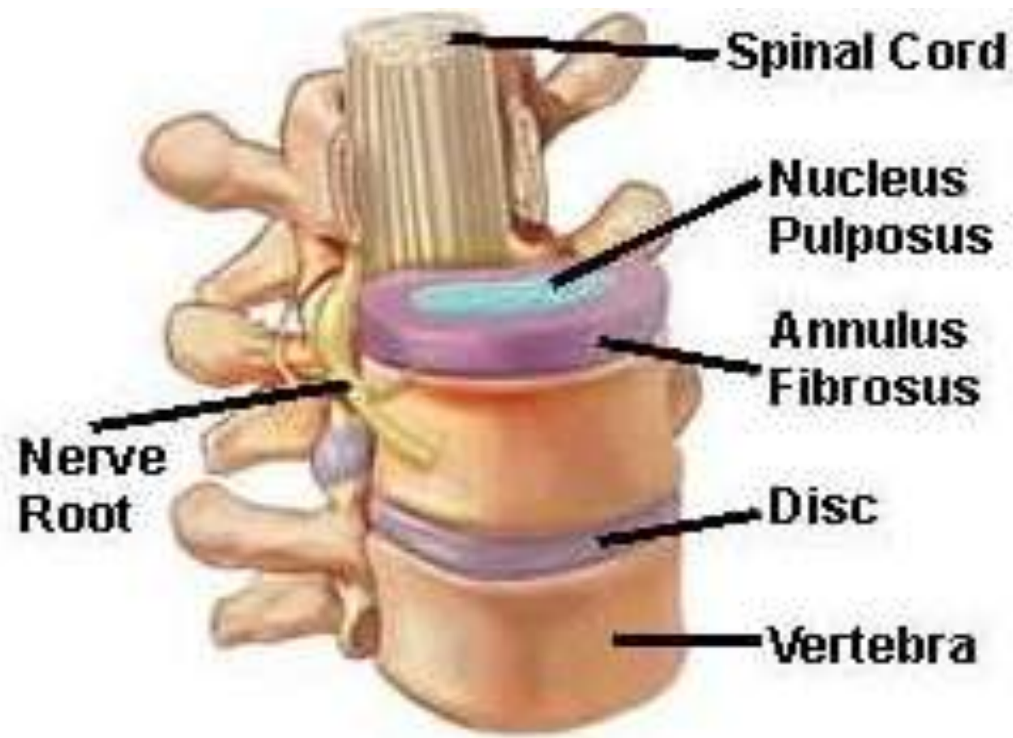
•Degenerates and disappears as the bodies of the vertebrae develop

•The part that lies between the vertebral bodies persists as the nucleus pulposus of each intervertebral disc



•Remnants of notochordal tissue give rise to tumors called Chordomas

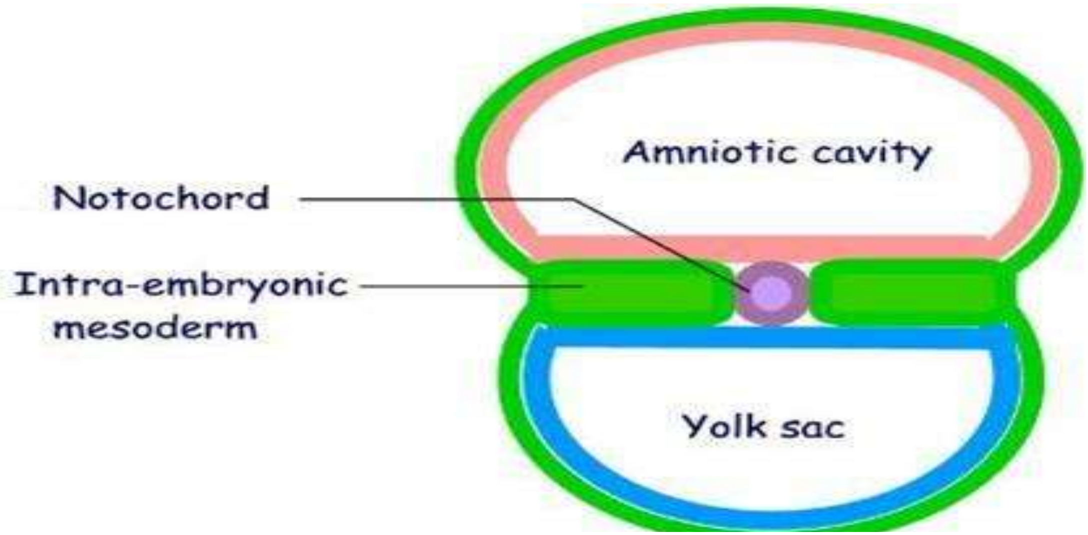
•Approximately one third of chordomas occur at the base of the cranium and extend to the nasopharynx.

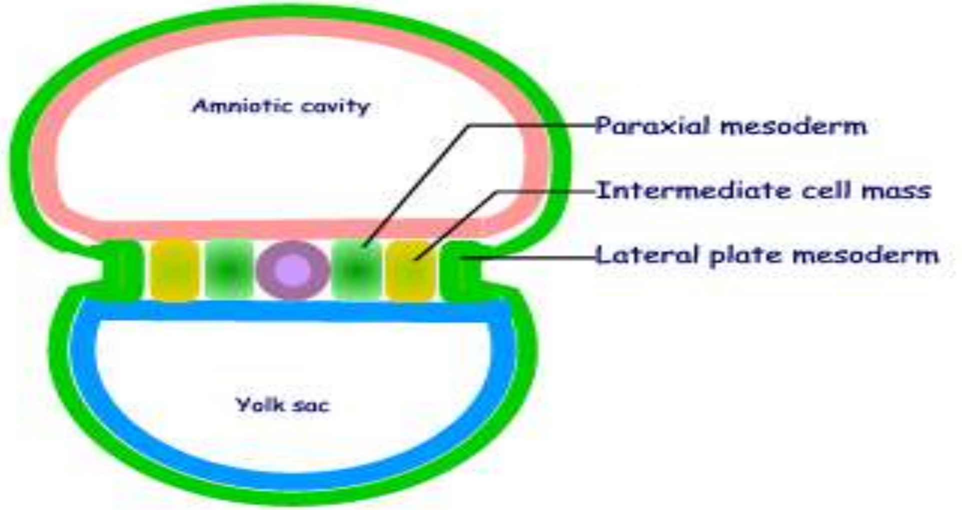


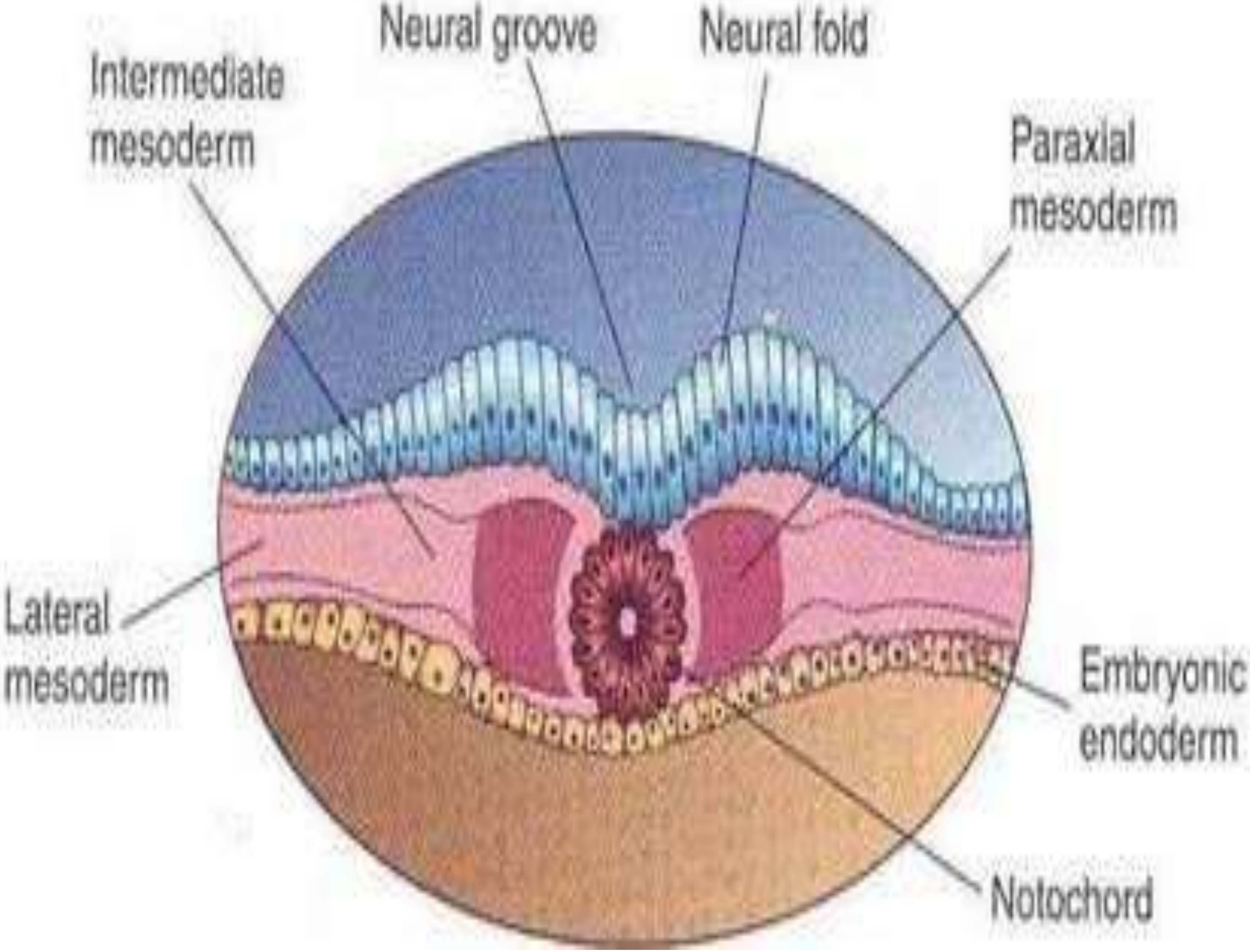
Differentiation of the Intraembryonic Mesoderm

- Induced by the notochord

- Differentiates into the:
  - ✓Paraxial mesoderm
  - ✓Intermediate cell mass
  - ✓Lateral plate mesoderm






Neural groove
Neural fold
Intermediate mesoderm
Paraxial mesoderm
Lateral mesoderm
Embryonic endoderm
Notochord

Note:

- *The **embryonic period**, or **period of organogenesis**, occurs from the third to the eighth weeks of development and is the time when each of the three germ layers, ectoderm, mesoderm, and endoderm, gives rise to a number of specific tissues and organs*

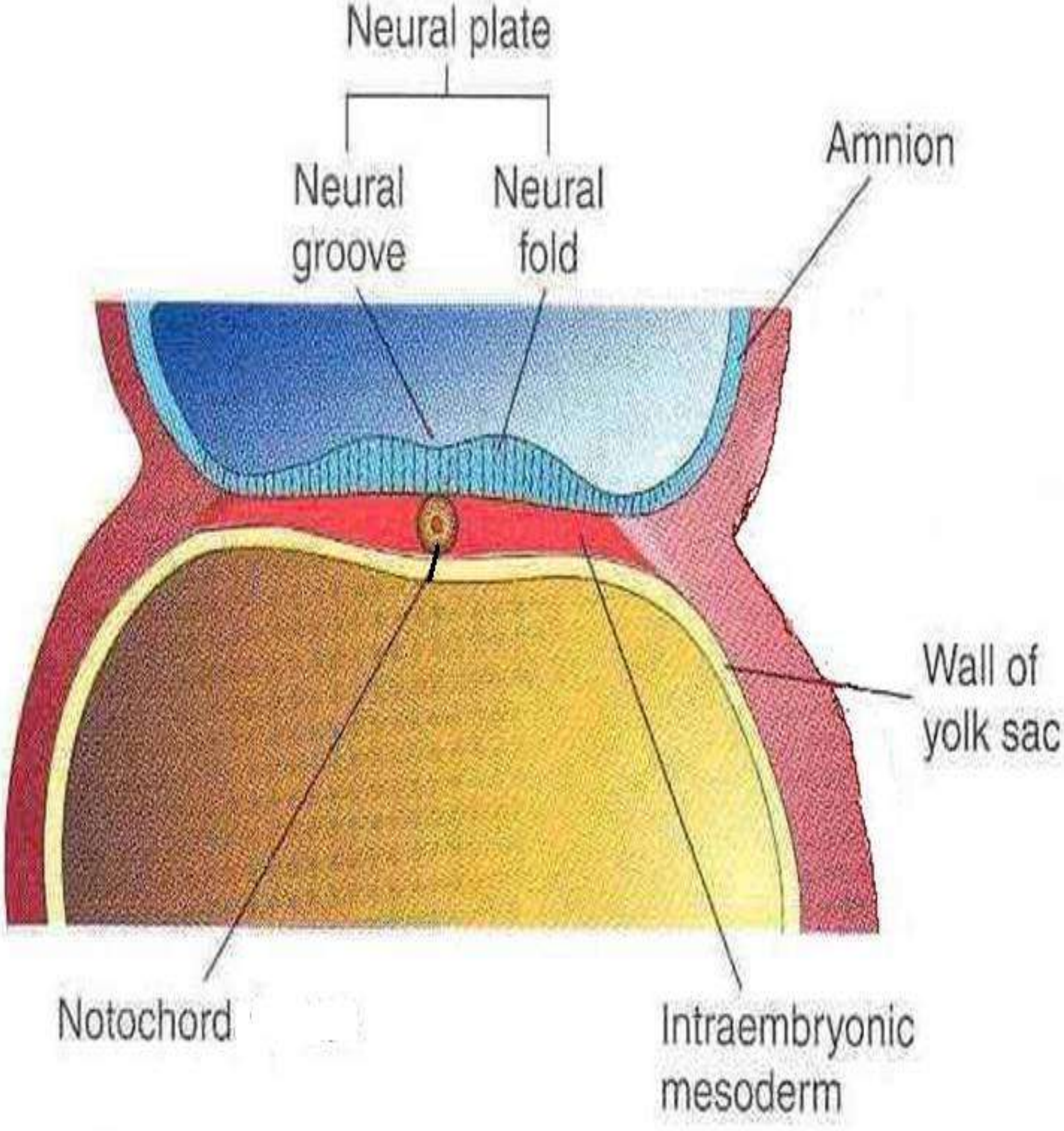
- *By the end of the embryonic period, the main organ systems have been established, rendering the major features of the external body form recognizable by the end of the second month*

Neurulation

- *It is the process by which the* <u>*neural tube*</u> *is formed*
- *During neurulation, the embryo may be referred to as a* ***neurula***
- *The stages of neurulation include the formation of:*
    - ✓*Neural plate*
    - ✓*Neural groove*
    - ✓*Neural folds & their fusion*
    - ✓*Neural crest cells*
    - ✓*Neural tube*

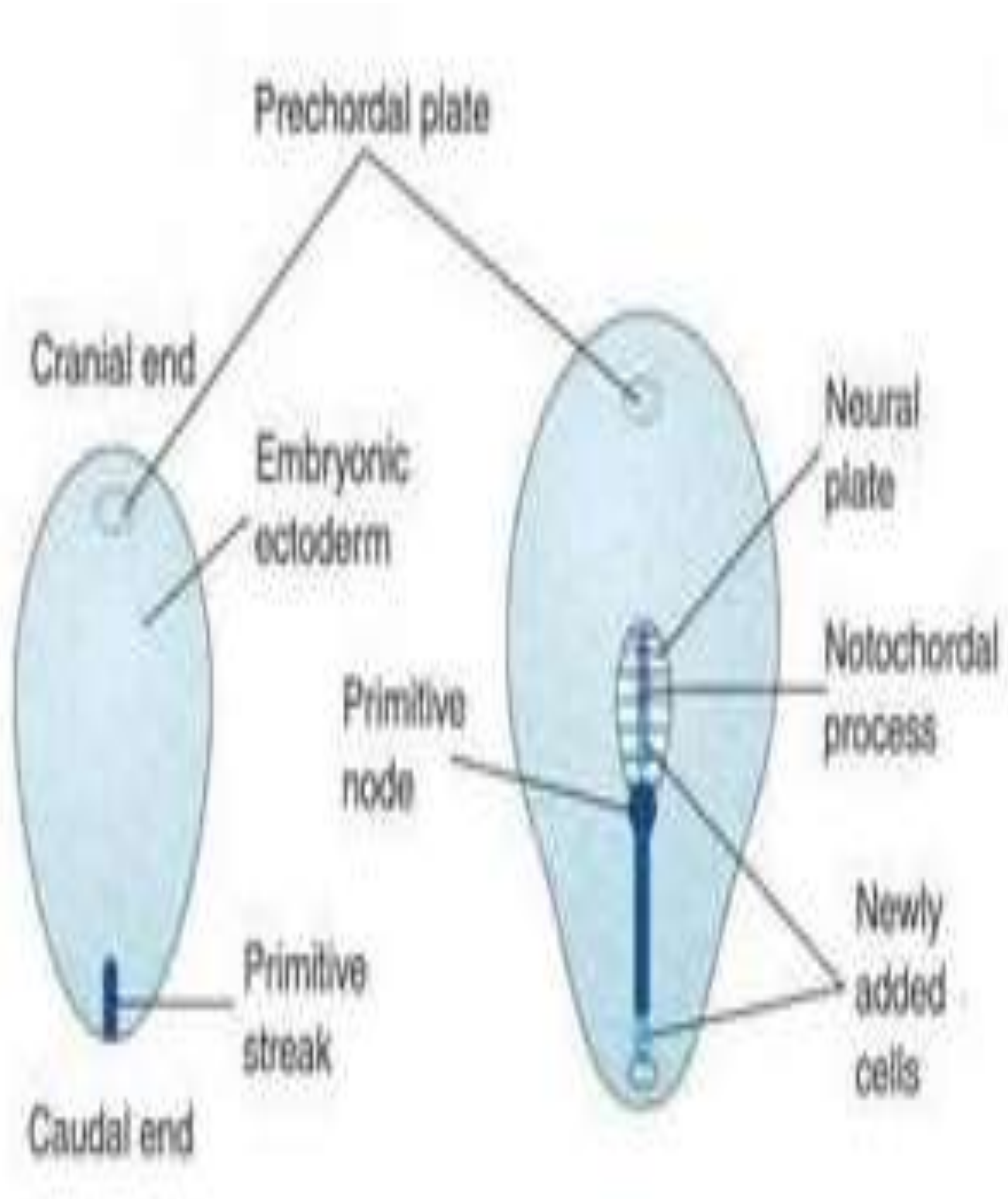
Formation

Under the inducing effect of the developing notochord, the overlying ectodermal cells thickens to form the neural plate



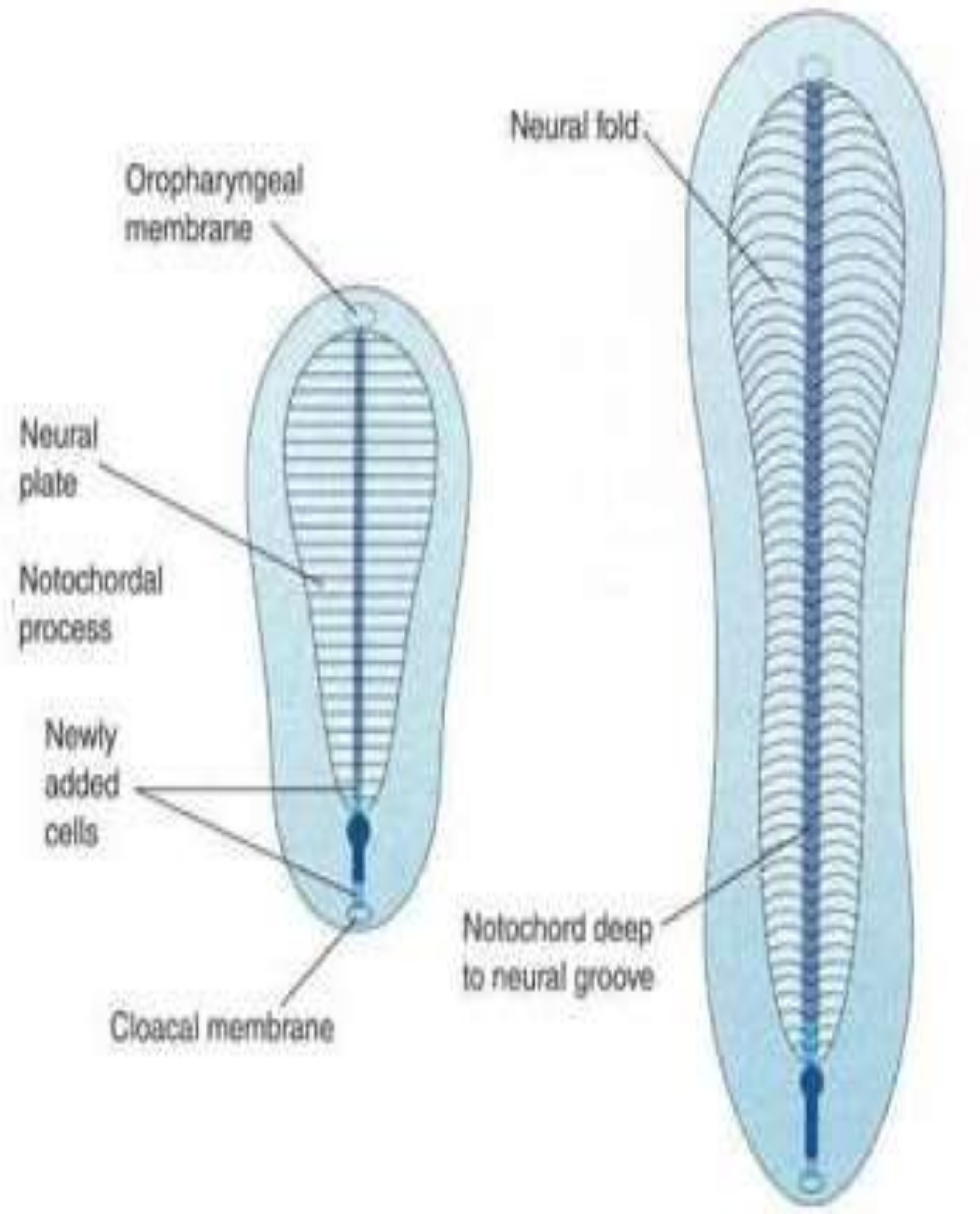
<u>At first the neural plate</u>:

- ✓ *cranial to the primitive node*
- ✓*dorsal(posterior) to the developing notochord & the mesoderm adjacent to it*
- ✓ *corresponds in length to the underlying notochord*

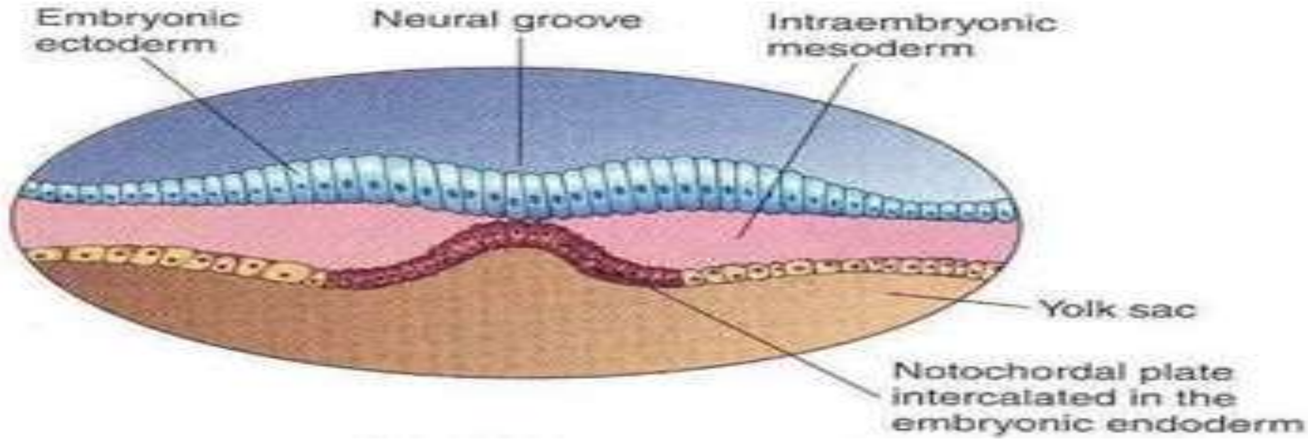


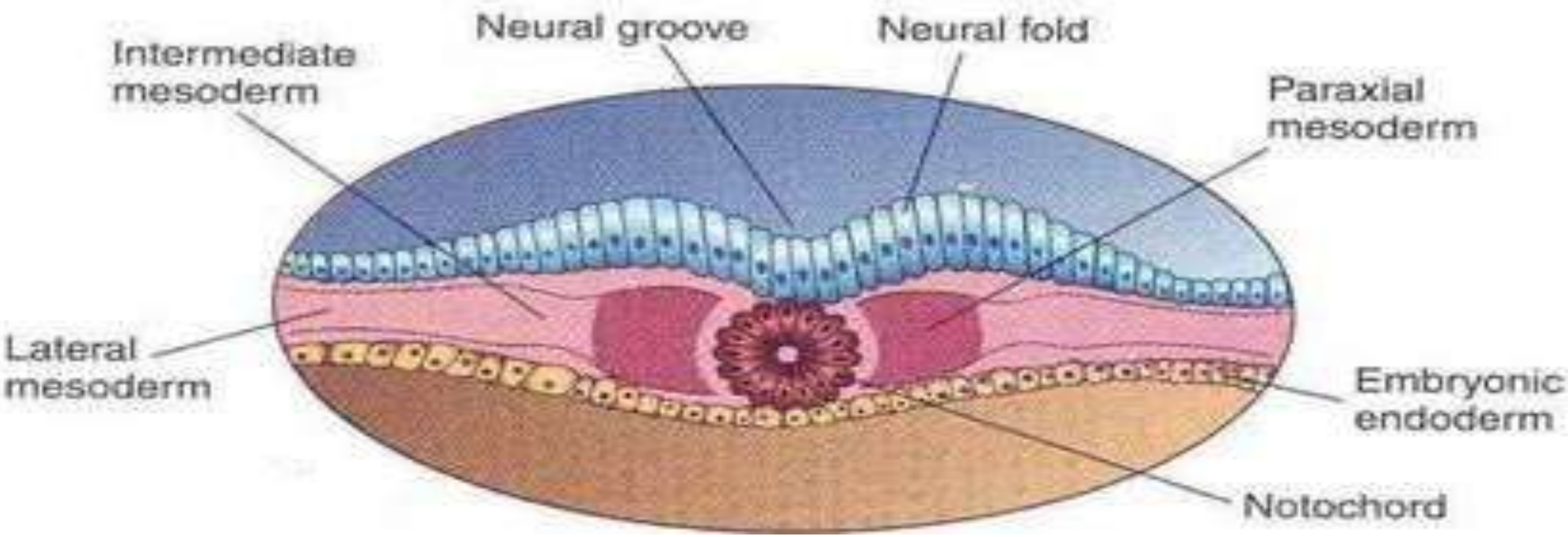
<u>As the notochord forms & elongates</u>:

- ✓*The embryonic disc elongates and becomes club-shaped*
- ✓*The neural plate broadens and extends cranially as far as the buccopharyngeal membrane,*
- ✓ *later on grows beyond the notochord*



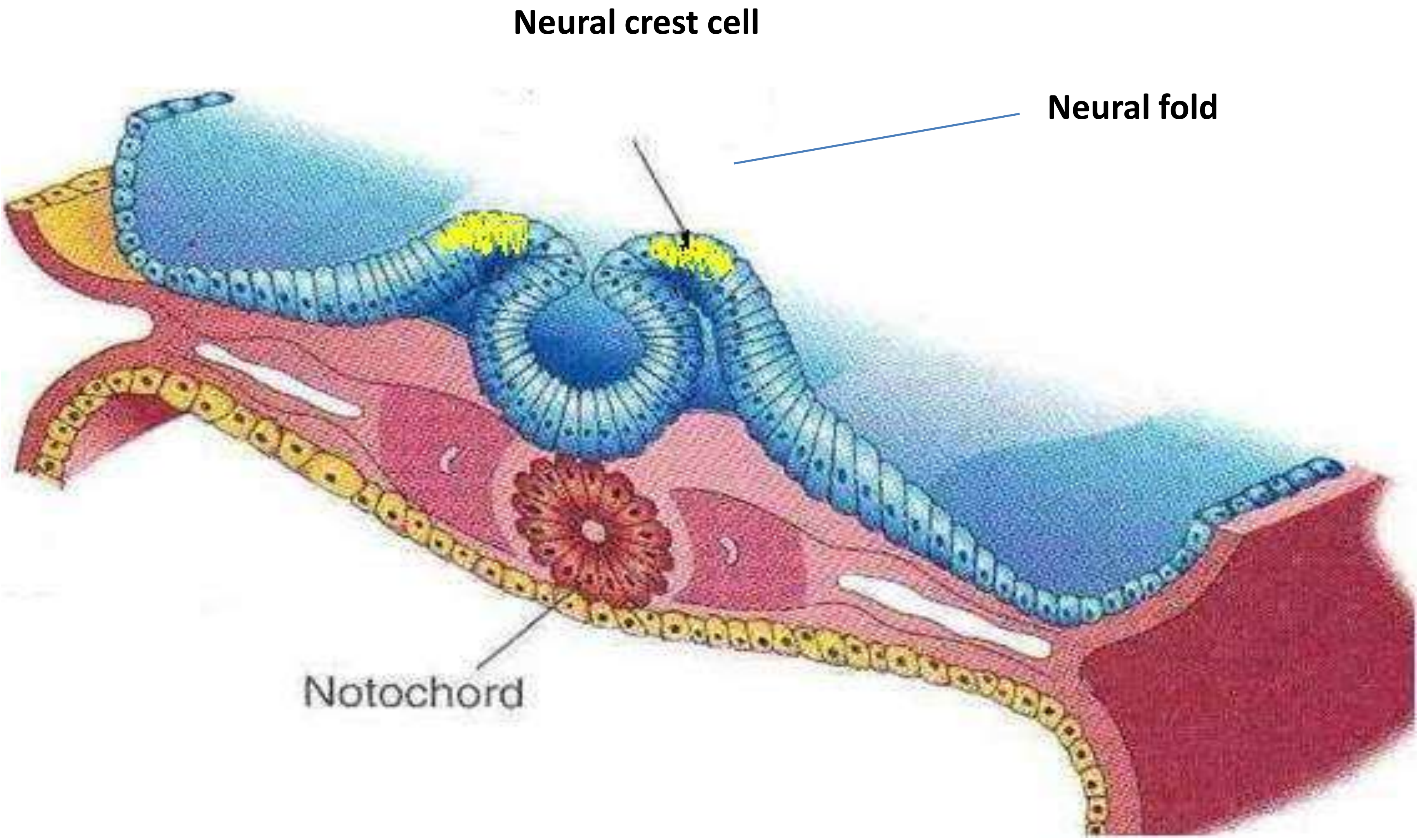
On 18th day: the neural plate invaginates to form <u>neural groove & neural folds</u>



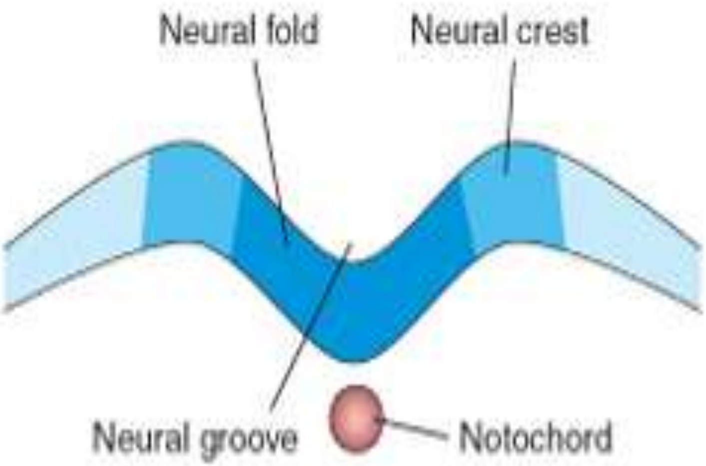


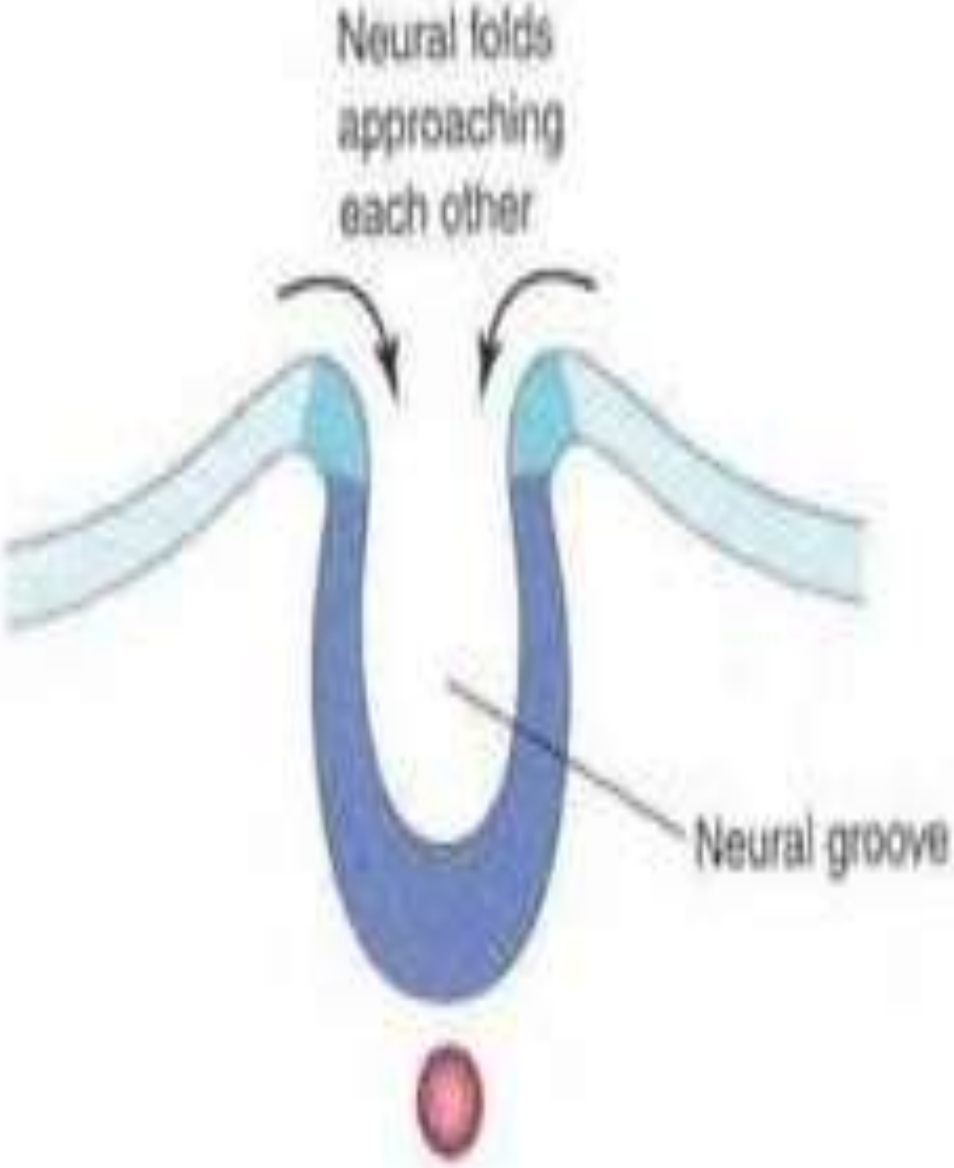
- Some neuroectodermal cells along the crest of the neural fold differentiate as the neural crest cells

❖ ***Note***: *(neuroectoderm: the ectoderm of the neural plate)*

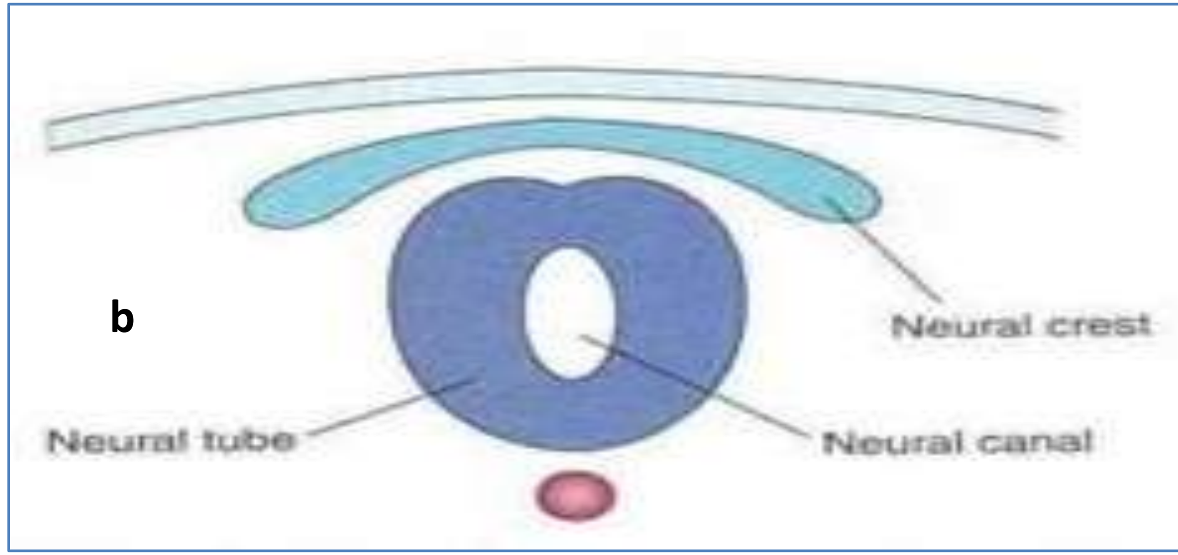


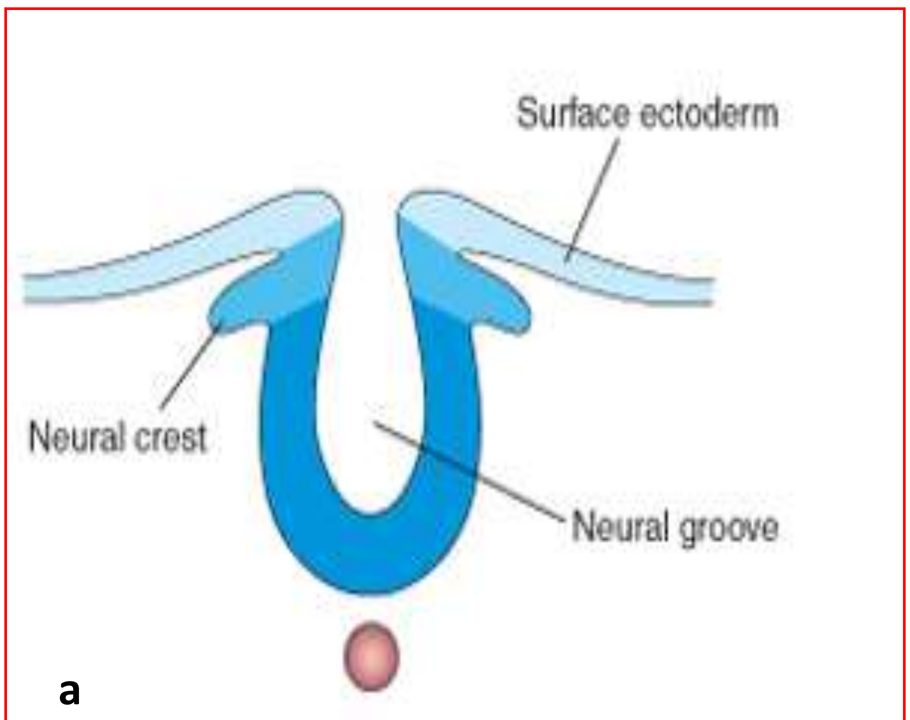
By the end of 3rd week, the neural folds move to the midline and <u>fuse</u> to form the ***neural tube***

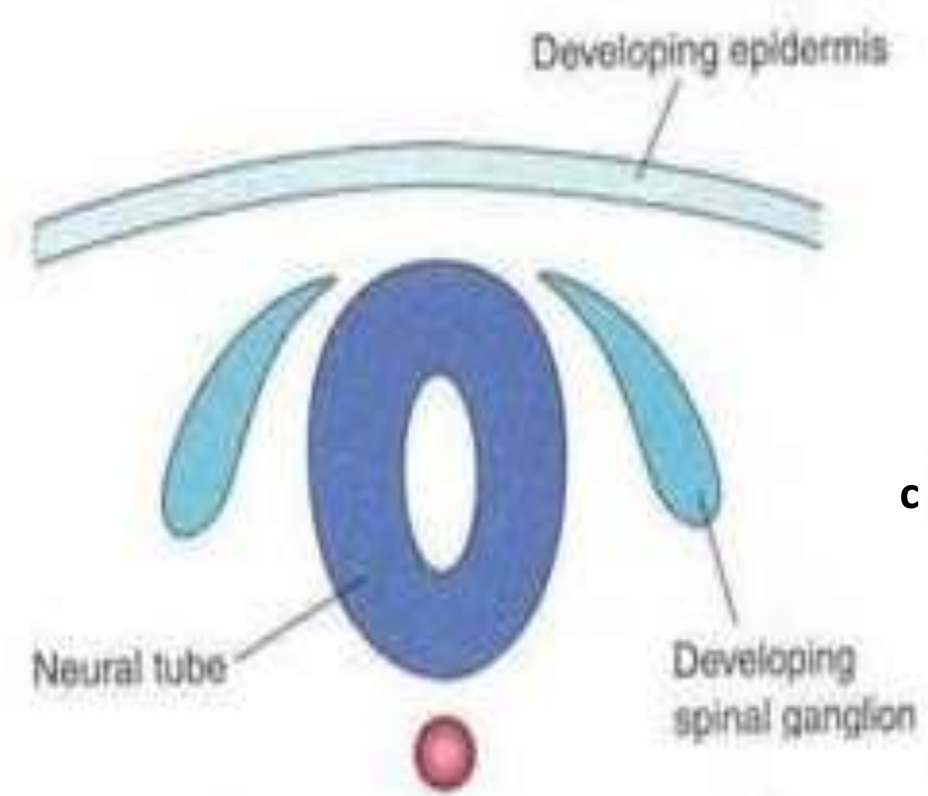




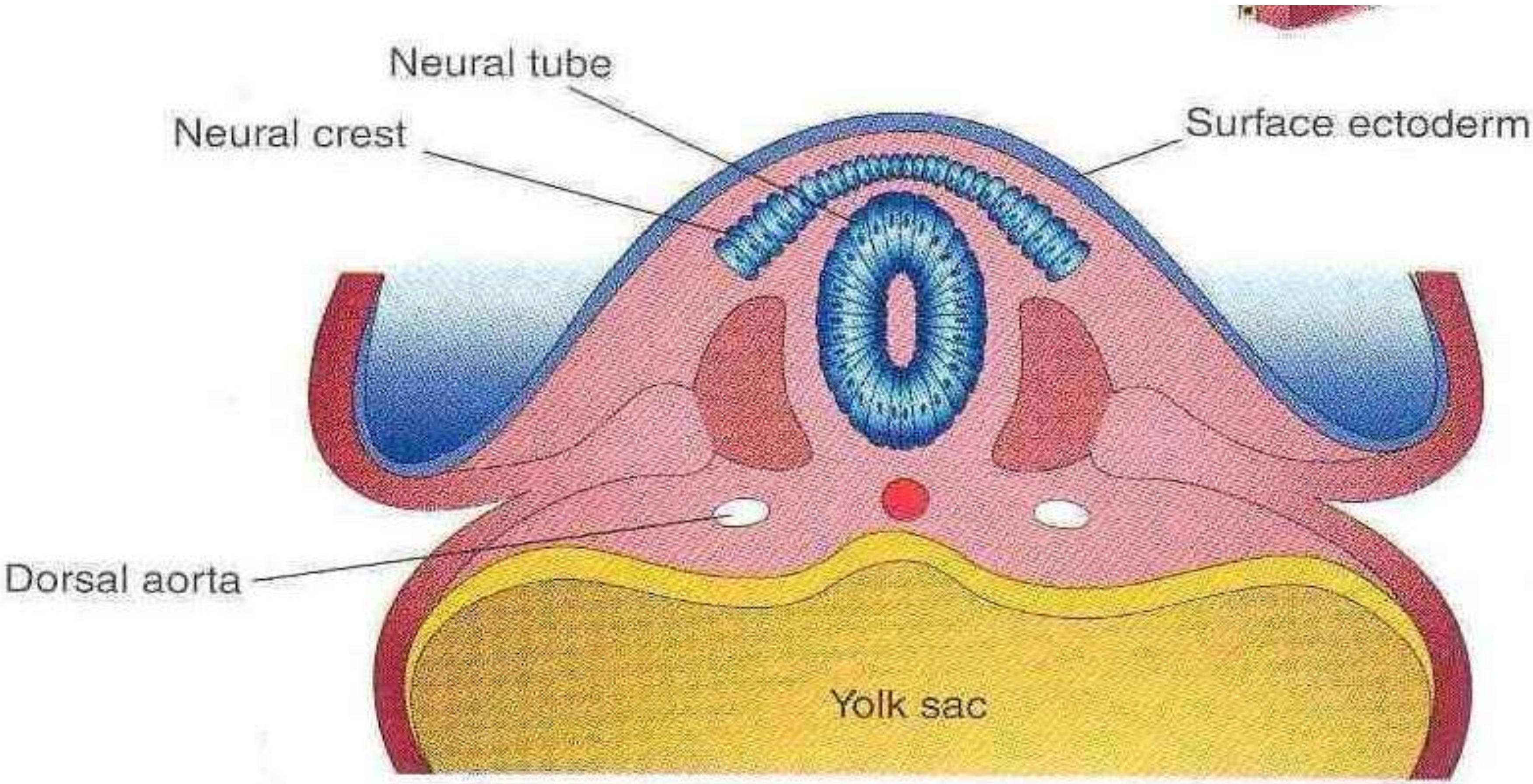
Following fusion of the neural folds, the neural crest cells become separated and move laterally to form the ***<u>sensory neurons of the spinal (dorsal root) ganglia</u>***



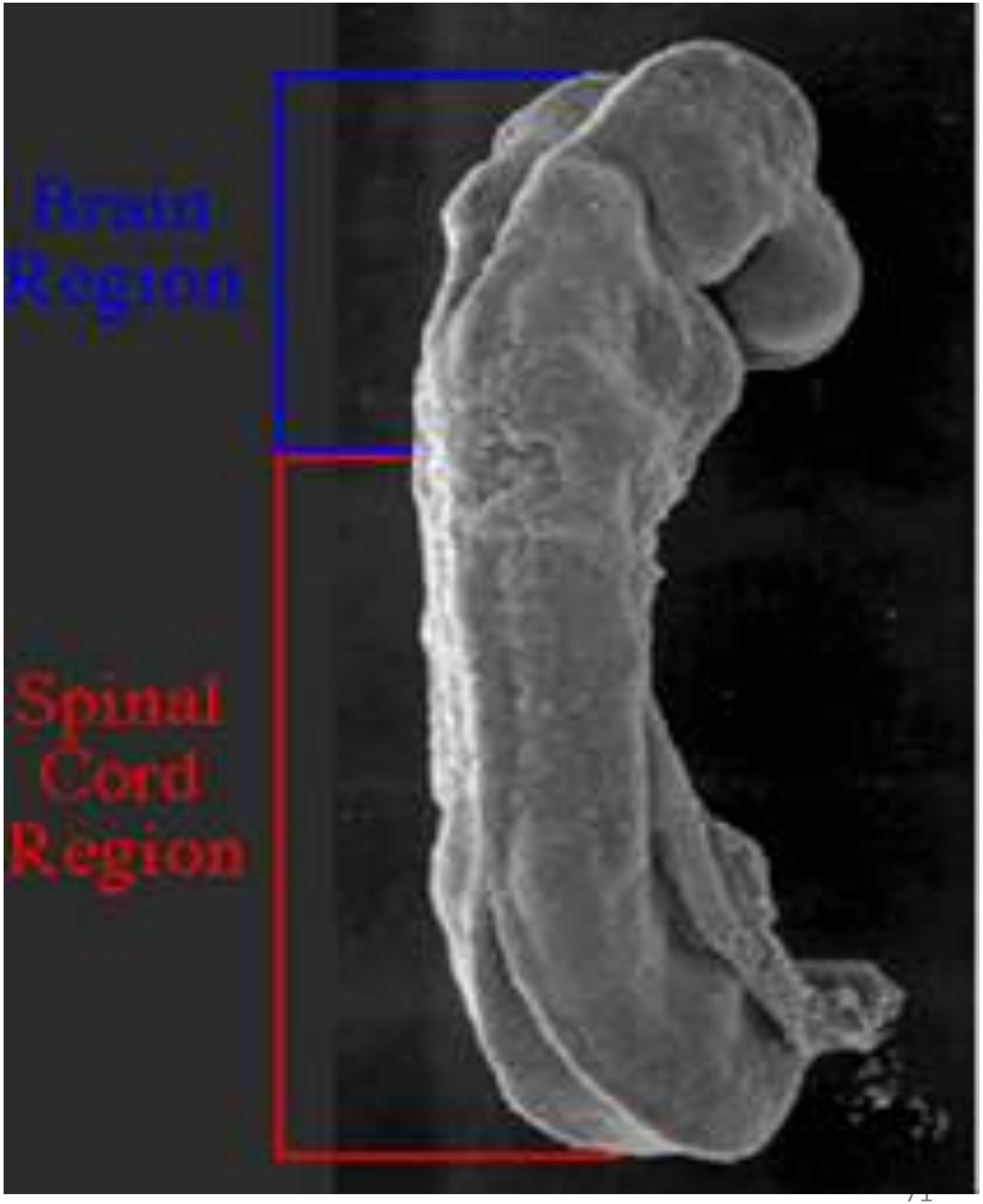




- By the end of 3rd week, the neural folds move to the midline and fuse to form the **neural tube**
- The *<u>neural tube separates from the surface ectoderm</u>*, lies in the midline, dorsal to the notochord

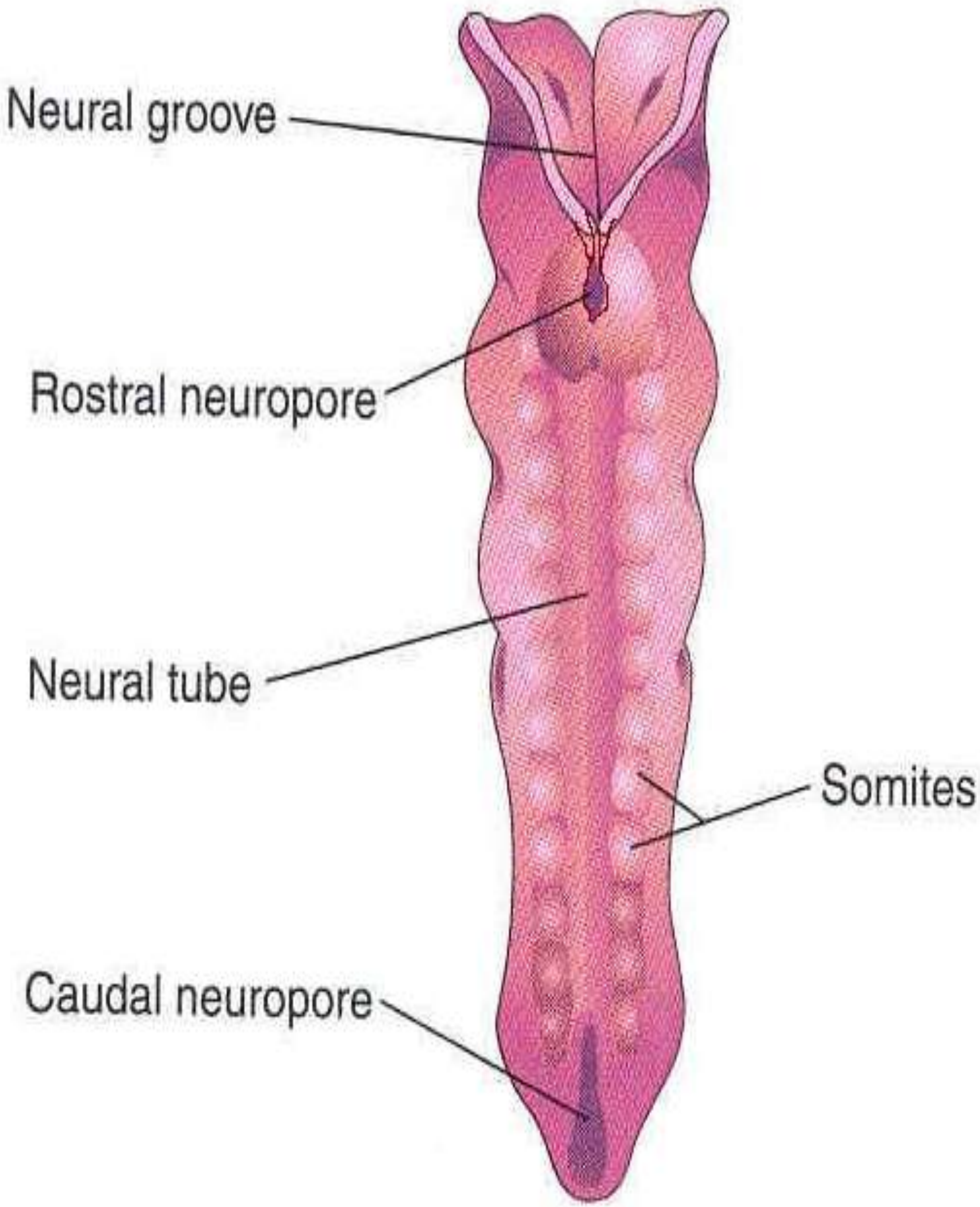


- ✓*The cranial ⅓ of the neural tube represent the future brain*
- ✓*The caudal ⅔ represents the future spinal cord*



✓*Neural tube is open at both ends, communicating freely with the amniotic cavity*

✓*The cranial opening, the <u>rostral neuropore closes</u> at about 25th day while the caudal neuropore closes at about the 27th day(2 days after)*

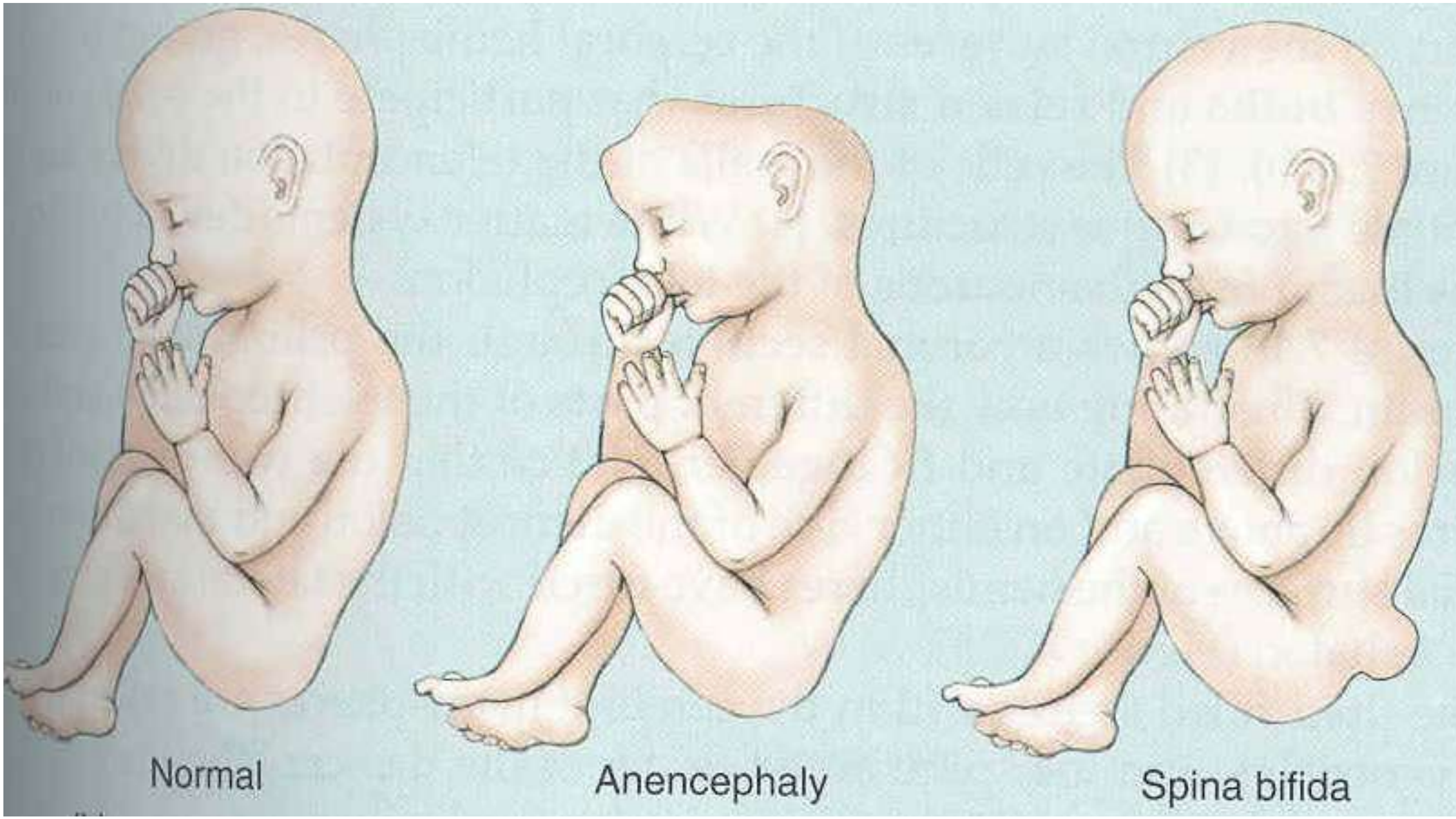


Congenital anomalies

- Disturbance of neurulation may result in severe abnormalities of the brain and the spinal cord
- Most defects are the result of non-closure or defective closure of the neural tube:
    - In the brain region (e.g. anencephaly: total absence of the brain

    Meroencephaly (partial absence of the brain) is the most severe neural tube defect and is also the most common anomaly affecting the CNS

    - In the spinal cord regions (e.g. spina bifida)


Normal
Anencephaly
Spina bifida

Spinal bifida

Ectoderm

- *Surface ectoderm*
- *Neuroectoderm*

Surface Ectoderm Derivatives

- Epidermis of the skin
- Hair
- Nail
- Sweat & Sebaceous glands
- Mammary glands
- Enamel of the teeth
- Lens of eye
- Internal ear
- Anterior lobe of the pituitary gland

Neuroectoderm

- Neural Tube
- Neural Crest Cells

Neural Tube Derivatives

- Central nervous system
- Peripheral nervous system
- Retina
- Sensory epithelia of nose & ear
- Pineal gland
- Posterior lobe of the pituitary gland

Neural Crest Cells Derivatives

- Sensory ganglia (cranial & spinal)
- Autonomic ganglia
- Meninges (Pia mater & Arachnoid mater) of the brain & spinal cord
- Schwann cells
- Satellite cells
- Melanoblasts
- Suprarenal medulla (chromaffin cells)
- Several skeletal & muscular components in the head (derived from pharyngeal arches)

<u>Derivatives of mesodermal germ layer</u>

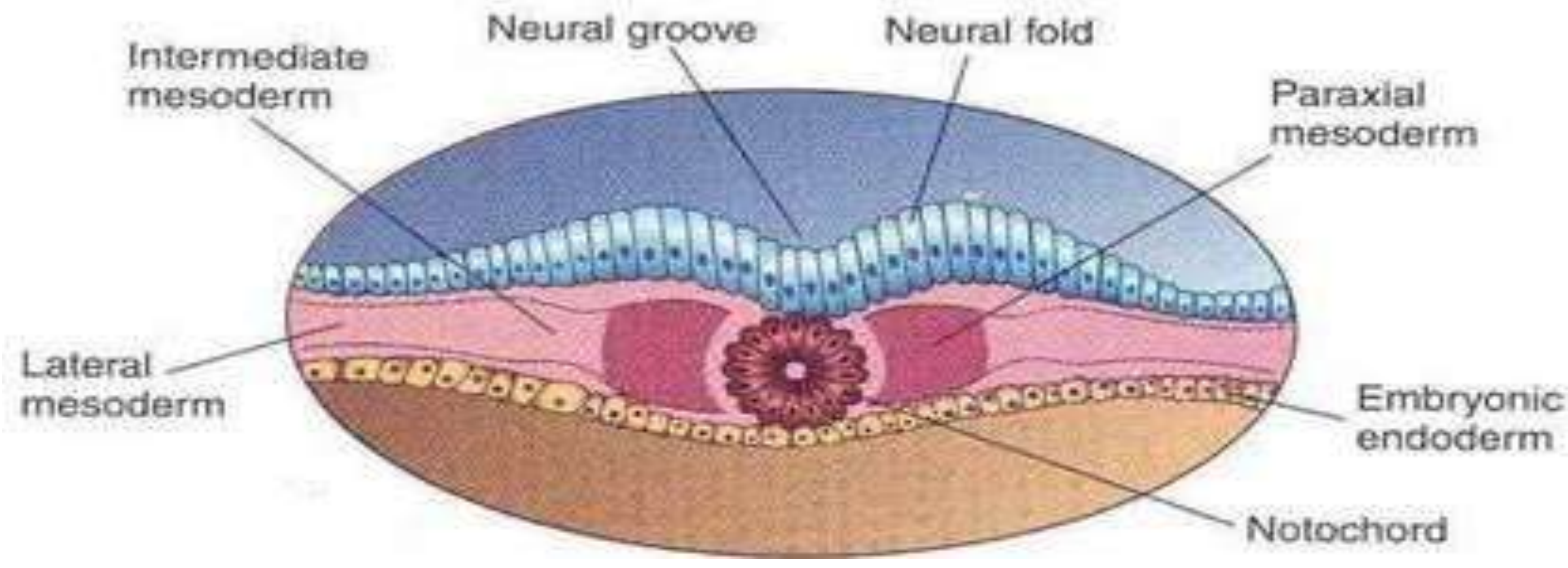
- As the notochord & neural tube form, the ***intraembryonic mesoderm*** on each side of them proliferates to form:

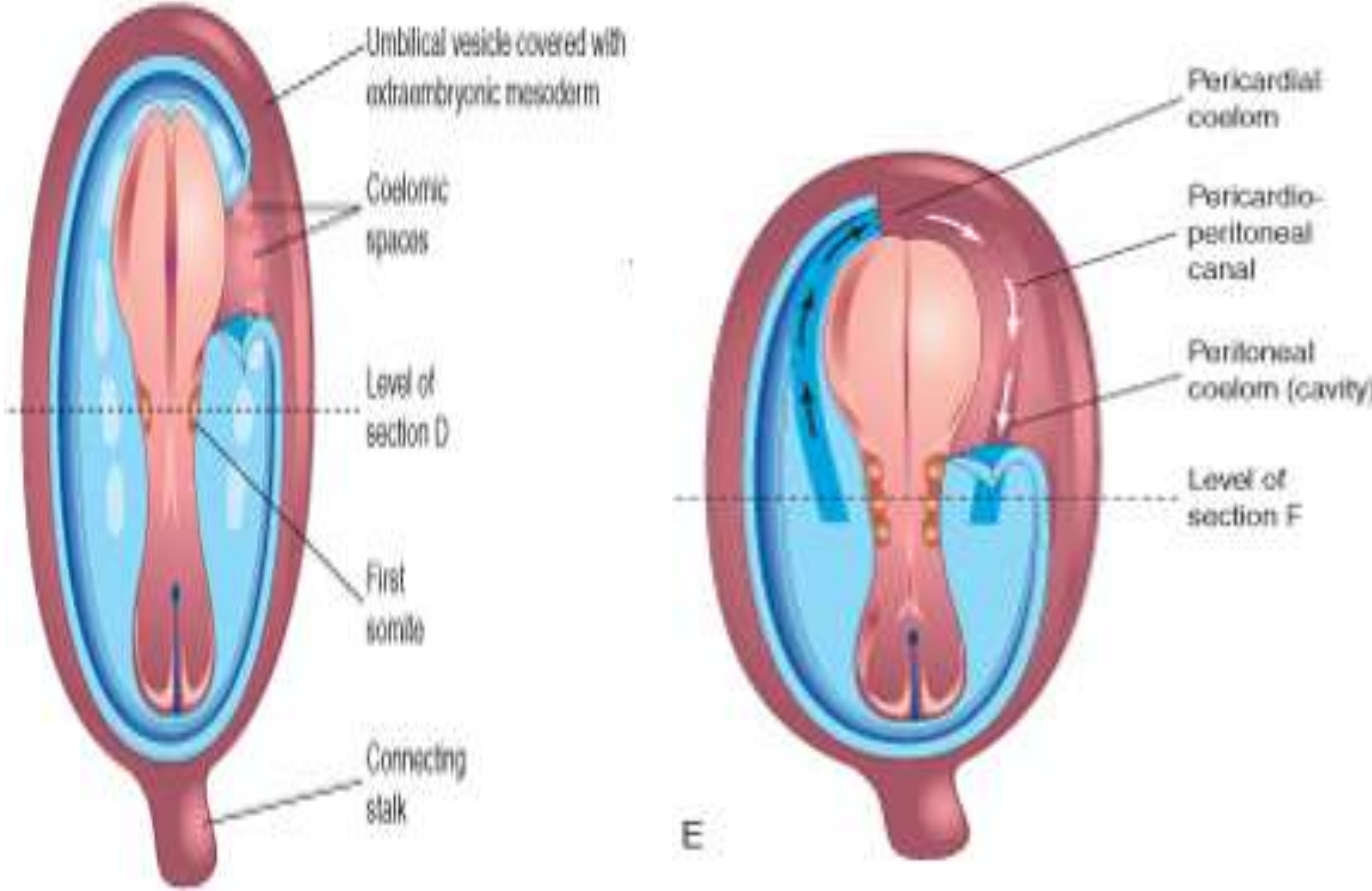
I. a thick, longitudinal column of <u>*paraxial mesoderm*</u>

II. which is continuous with <u>*intermediate mesoderm*</u> which gradually thins into

III. <u>*lateral mesoderm*</u>

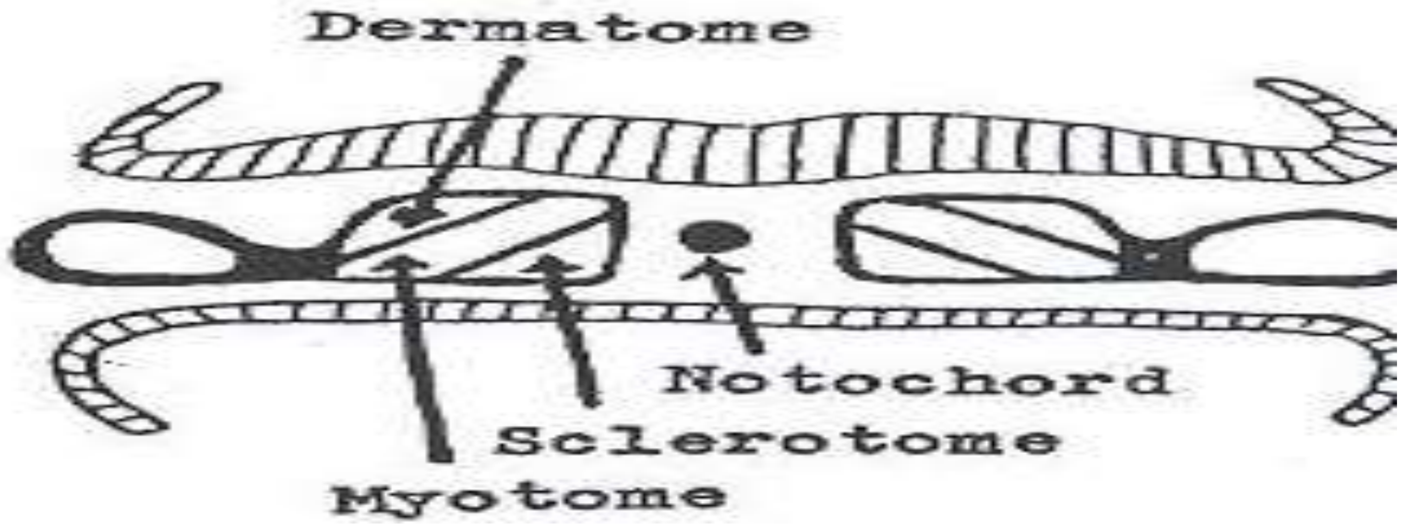
❖ The lateral mesoderm is continuous with the <u>*extraembryonic mesoderm*</u> covering the yolk sac & amnion.




Umbilical vesicle covered with extraembryonic mesoderm
Coelomic spaces
Level of section D
First somite
Connecting stalk
Pericardial coelom
Pericardio-peritoneal canal
Peritoneal coelom (cavity)
Level of section F
E

- ***Paraxial mesoderm***:
- By the beginning of the 3rd week, paraxial mesoderm is organized into segments called ***somitomeres***
- Somitomeres appear first in the cephalic region of the embryo, and their formation proceeds cephalocaudally (extends cranially and caudally /from head to tail or crown to rump)
- From the occipital region caudally, *somitomeres* further organize into *somites*
- Toward the end of the 3rd week (at approximately the 20th day of development), the 1st pair of somites arises in the occipital region
- From here, new somites appear in craniocaudal sequence at a rate of approximately 3 pairs per day
- The somite period of human embryo development is from days 20 – 30
- About *38 pairs of somites* are present on *day 30*
- By the end of the 5th week, *42 to 44 pairs of somites are present*

- There are
- ✓ 4 occipital,
- ✓ 8 cervical,
- ✓ 12 thoracic,
- ✓ 5 lumbar,
- ✓ 5 sacral,
- ✓ and 8 to 10 coccygeal pairs



- ➢ The 1st occipital and the last 5-7 coccygeal somites later disappear
- The remaining somites divide into:

a. ventromedial part called ***sclerotome***

sclerotome gives rise to the bones, cartilages and ligaments of the vertebral column & ribs

So, the somites give rise to most of the axial skeleton

b. Middle part called ***myotome***

myotome gives rise to skeletal muscles of the chest and abdomen

c. Dorsolateral part called ***dermatome***

It gives rise to dermis and subcutaneous tissue of the skin

- Because the somites are so prominent during the 4th and 5th weeks, they are used as one of several criteria for *determining an embryo's age*

Intermediate mesoderm

- connects paraxial mesoderm with the lateral plate *differentiates into urogenital* structures
- Excretory units of the urinary system (kidney) and the gonads (testis and ovary) develop from the intermediate mesodern

Lateral mesoderm

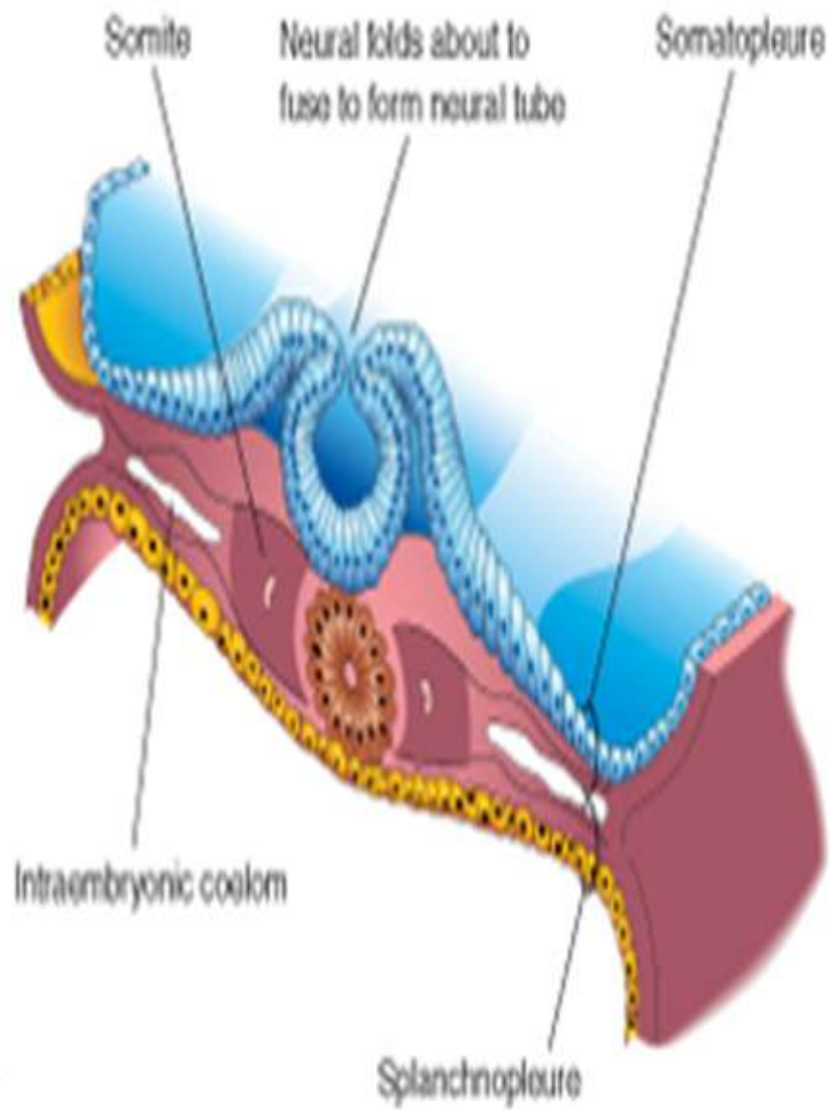
- is a thin plate of mesoderm located along the lateral sides of the embryo
- Large spaces develop in the lateral mesoderm and coalesce to from the *intraembryonic coelom*

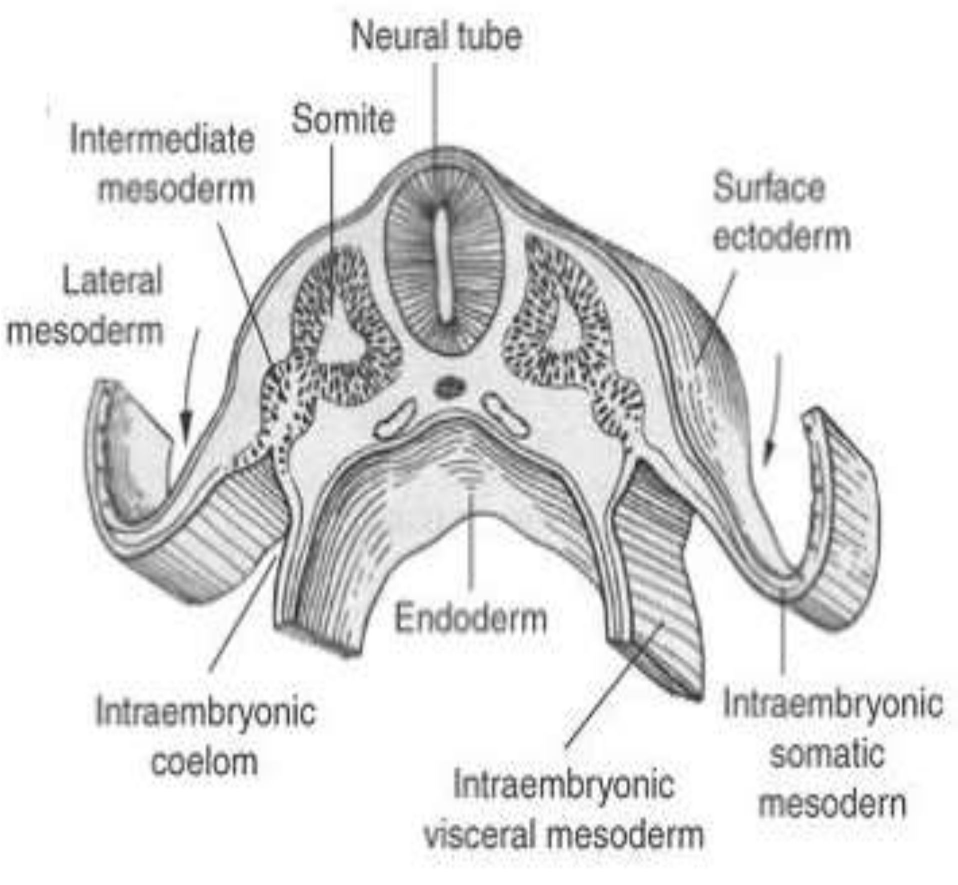
The intraembryonic coelom divides the lateral mesoderm into 2 layers:

- ✓ somatic/ parietal layer of lateral mesoderm
- ✓ splanchnic or *visceral layer* of lateral mesoderm

- ➢ somatic/*parietal layer* : is located beneath the ectodermal epithelium and continuous with the extraembryonic mesoderm covering the amnion
- ➢ splanchnic or *visceral layer*: is located adjacent to the endoderm and continuous with the extraembryonic mesoderm covering the umbilical vesicle (yolk sac)
  - The somatic mesoderm and overlying embryonic ectoderm form the embryonic body wall or **somatopleure**
  - whereas the splanchnic mesoderm and underlying embryonic endoderm form the embryonic gut or **splanchnopleure**

- During the second month, the intraembryonic coelom is divided into three body cavities:
- Pericardial cavity
- Pleural cavities
- Peritoneal cavity





Blood and Blood Vessels

- Blood cells and blood vessels also arise from mesoderm

➢ Blood vessels form in two ways:

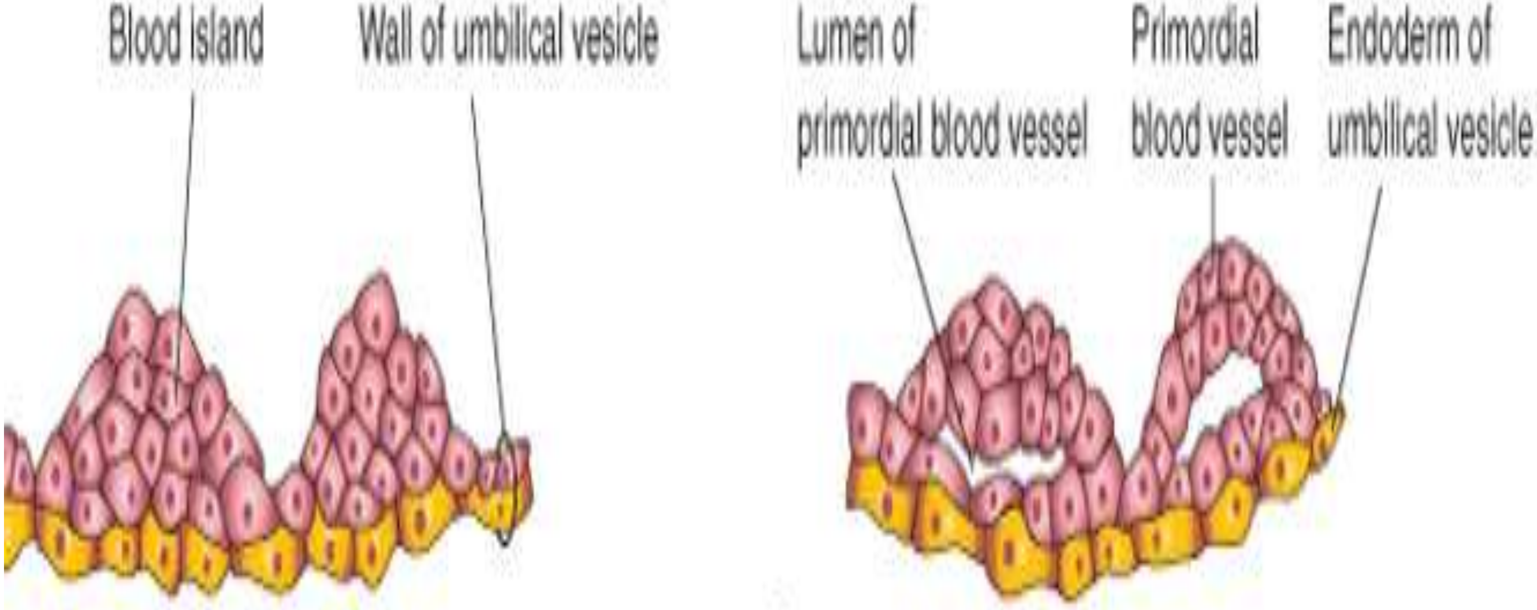
✓ vasculogenesis: whereby vessels arise from blood islands and

✓ angiogenesis, which entails sprouting from existing vessels

A) Vasculogenesis (blood vessels)

- Mesenchymal cells differentiate into endothelial precursors called angioblasts (vessel-forming cells)
- Angioblasts aggregate to form blood islands
- Small cavities appear within the blood islands
- Angioblasts flatten and arrange themselves around the cavities to form endothelial cells of blood vessels
- These endothelium – lined cavities soon fuse to form networks of endothelial channels

B : Angiogenesis: entails sprouting from existing vessels



Blood island
Wall of umbilical vesicle
Lumen of
primordial blood vessel
Primordial
blood vessel
Endoderm of
umbilical vesicle

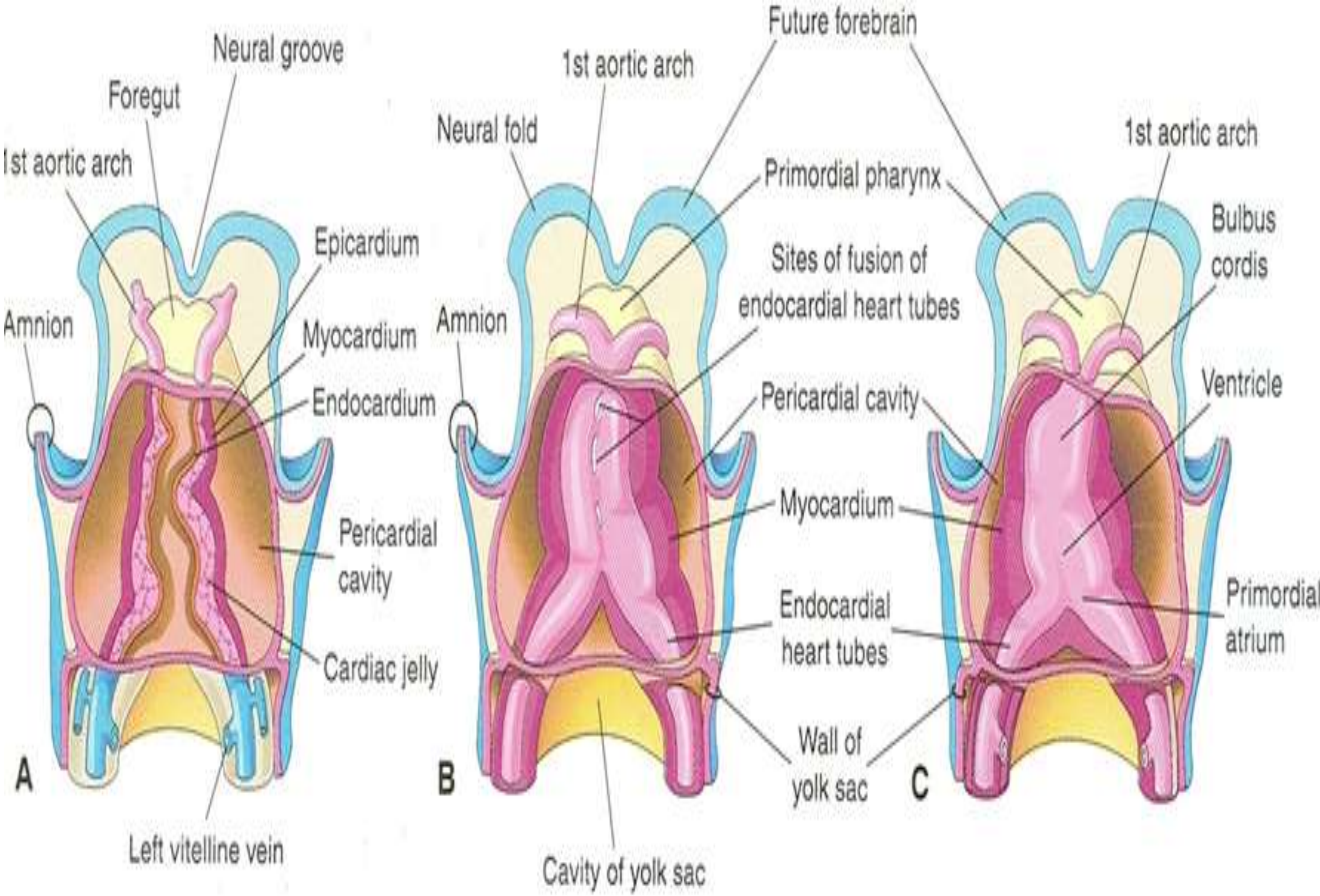
D

Blood cells formation

- blood cells(hamatoblasts) develop from the endothelial cells of vessels
- develop on the umbilical vesicle(yolk sac) and allantois at the end of the 3rd week
- Blood formation (**hematogenesis**) does not begin in the embryo until the fifth week.
- It occurs first along the aorta and then in various parts of the embryonic mesenchyme, mainly, the liver, and later in the spleen, bone marrow, and lymph nodes.

Primodial cardiovascular system

- Heart & great vessels develop from mesenchymal cells in the cardiogenic area
- Paired longitudinal endothelial lined channels or endocardial heart tubes develop during the 3rd week
- These tubes fuse to form the heart tube
- The tubular heart joins with blood vessels in the embryo, connecting stalk, chorion and yolk sac to form a *primordial cardiovascular system*
- Heart begins to beat on 21-22 days and blood circulates
- CVS is the first organ system to reach a functional state



Neural groove
Foregut
1st aortic arch
Epicardium
Amnion
Myocardium
Endocardium
Pericardial cavity
Cardiac jelly
A
Left vitelline vein
1st aortic arch
Neural fold
Amnion
B
Cavity of yolk sac
Future forebrain
Primordial pharynx
Sites of fusion of endocardial heart tubes
Pericardial cavity
Myocardium
Endocardial heart tubes
Wall of yolk sac
C
1st aortic arch
Bulbus cordis
Ventricle
Primordial atrium

- **Endoderm** gives rise to the epithelial lining of the gastrointestinal and respiratory tracts, parenchyma of the tonsils, thyroid and parathyroid glands, thymus, liver, and pancreas, epithelial lining of the urinary bladder and most of the urethra, and the epithelial lining of the tympanic cavity, tympanic antrum, and pharyngotympanic (auditory) tube

Major derivatives of the embryonic germ layers