

3rd week of development

RECAP

- Morula –12- 32 cell stage
- Inner cell mass – embryoblast
- Blastocoele
- Outer cell mass - trophoblast
- Embryolast divides in to epiblast and hypoblast
- Cavity within epiblast – amniotic cavity
- Cavity within hypoblast - primitive yolk sac
- Implantation 14th day after fertilization
- Extraembryonic mesoderm (EEM)– cavity within extraembryonic coelome
- EEM divides into somatopleuric and splanchnopleuric

Major events of the 3rd week of development

- Formation Of Germ Layers And Early Tissue And Organ Differentiation
- Gastrulation:
- Primitive Streak
- Notochordal Process And Notochord
- The Allantois
- Neurulation
- Development Of Somites
- Development Of The Intraembryonic Coelom
- Early Development Of The Cardiovascular System
- Development Of Chorionic Villi

Formation of Germ Layers and Early Tissue and Organ Differentiation: Third Week

- Rapid development of the embryo from the embryonic disc during the third week is characterized by
 - Appearance of primitive streak.
 - Development of notochord
 - Differentiation of three germ layers

Gastrula

- During this period, the embryo may be referred to as a gastrula.
 - Each of the three germ layers:
 - ▢ Embryonic ectoderm
 - ▢ Embryonic endoderm
 - ▢ Embryonic mesoderm
- gives rise to specific tissues and organs

GERM LAYER DERIVATIVES

- *The three germ layers (ectoderm, mesoderm, and endoderm) formed during gastrulation give rise to the primordia of all the tissues and organs.*
- *The specificity of the germ layers, however, is not rigidly fixed.*
- *The cells of each germ layer divide, migrate, aggregate, and differentiate in rather precise patterns as they form the various organ systems.*
- *The main germ layer derivatives are as follows :*

Ectoderm gives rise to the:

- central nervous system,
 - peripheral nervous system;
 - sensory epithelia of the eye, ear, and nose;
 - epidermis and its appendages (hair and nails);
 - mammary glands; pituitary gland;
 - subcutaneous glands; and
 - enamel of teeth.

Neural crest derivatives

- Neural crest cells give rise to the spinal ganglia (dorsal root ganglia) and the ganglia of the autonomic nervous system.
- The ganglia of cranial nerves V, VII, IX, and X are also partly derived from neural crest cells.
- In addition to forming ganglion cells, neural crest cells form the neurolemma sheaths of peripheral nerves and contribute to the formation of the leptomeninges .
- **Neural crest cells** also contribute to the formation of pigment cells, the suprarenal (adrenal) medulla, and many connective tissue components in the head .

Neural crest cells

- derived from neuroectoderm, give rise to the cells of the :
 - spinal, cranial (cranial nerves V, VII, IX, and X), and autonomic ganglia;
 - ensheathing cells of the peripheral nervous system;
 - pigment cells of the dermis;
 - muscle, connective tissues, and bone of pharyngeal arch origin;
 - suprarenal medulla; and
 - meninges (coverings) of the brain and spinal cord.

Mesoderm gives rise to :

■ connective tissue;

- cartilage;
- bone;
- striated and smooth muscles;
- heart, blood, and lymphatic vessels;
- kidneys; ovaries; testes; genital ducts;
- serous membranes lining the body cavities (pericardial, pleural, and peritoneal);
- spleen; and
- cortex of suprarenal glands.

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.

Endoderm gives rise to:

■ the epithelial lining of the:

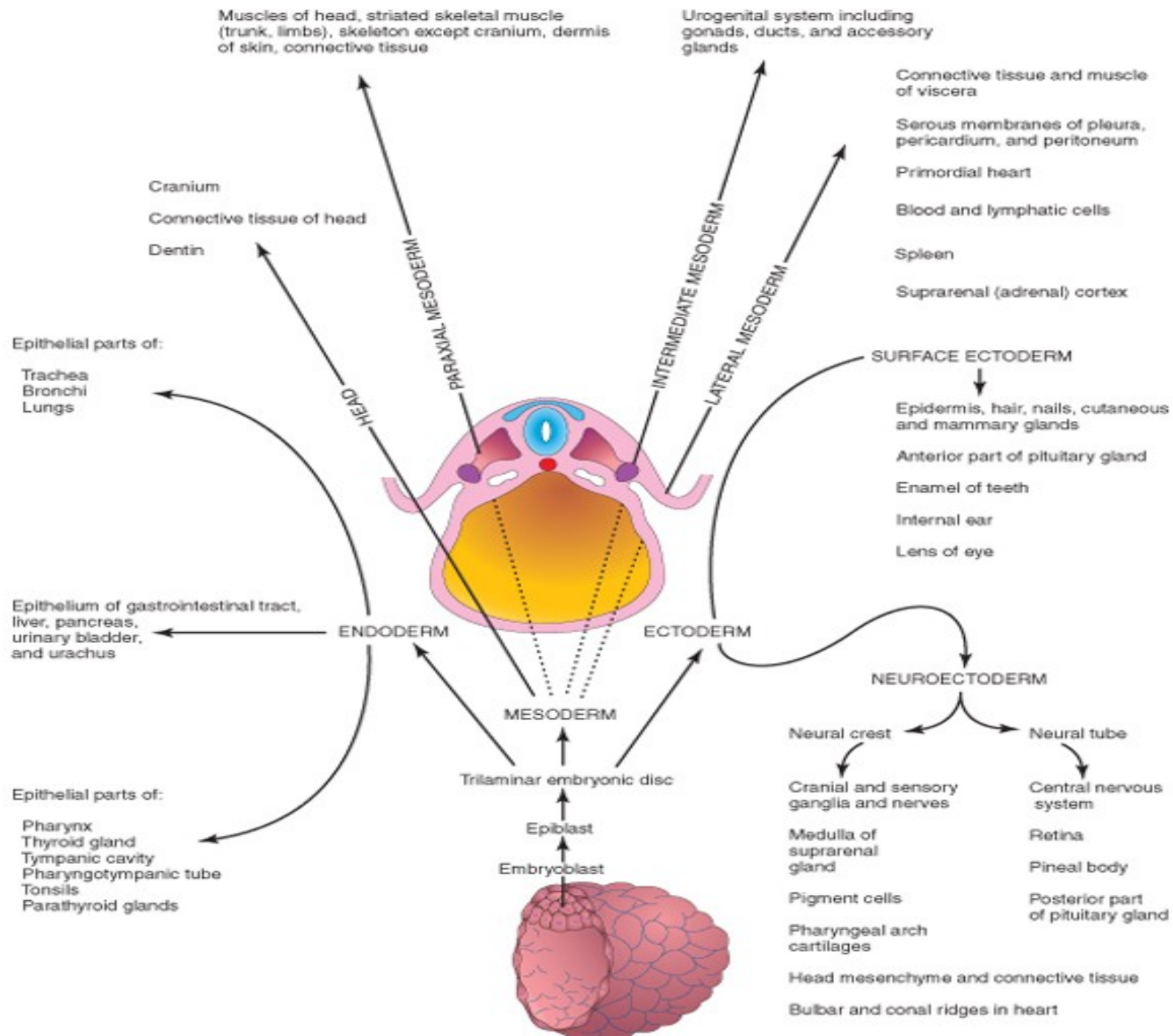
- gastrointestinal and
- respiratory tracts

■ epithelial lining of :

- the urinary bladder and most of the urethra, and
- the tympanic cavity, tympanic antrum, and pharyngotympanic (auditory) tube.

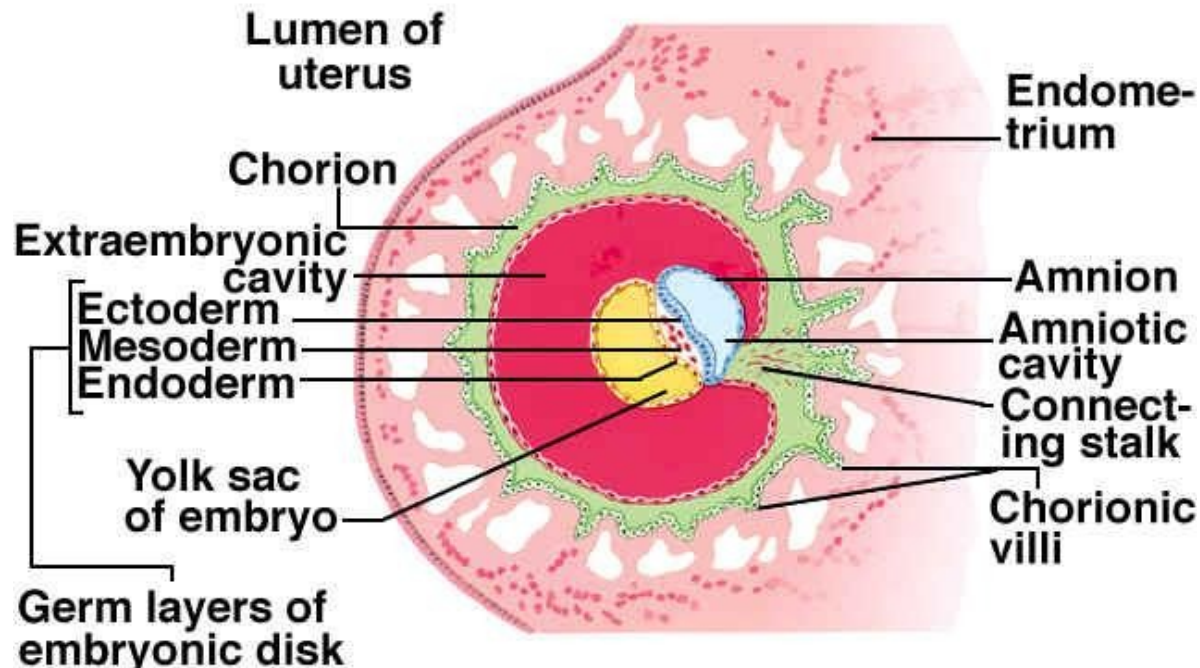
■ parenchyma of the:

- tonsils,
- thyroid and parathyroid glands,
- thymus,
- liver, and
- pancreas,

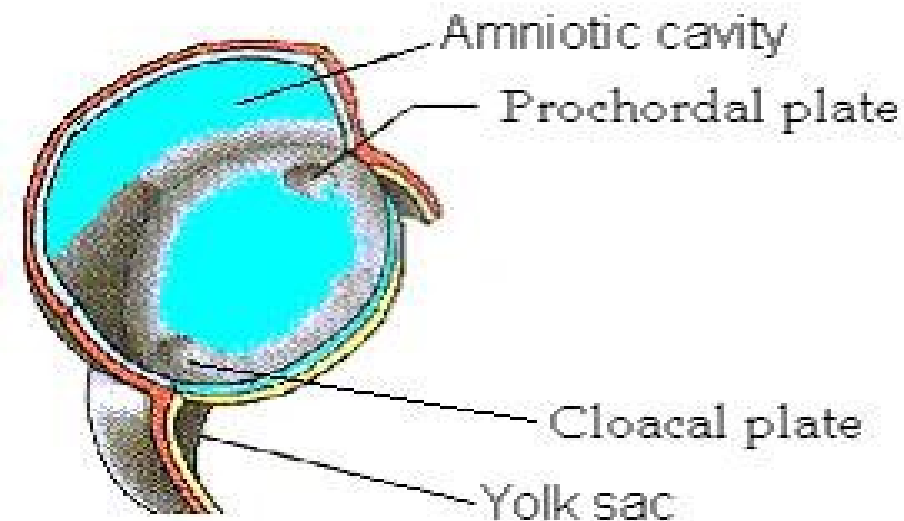
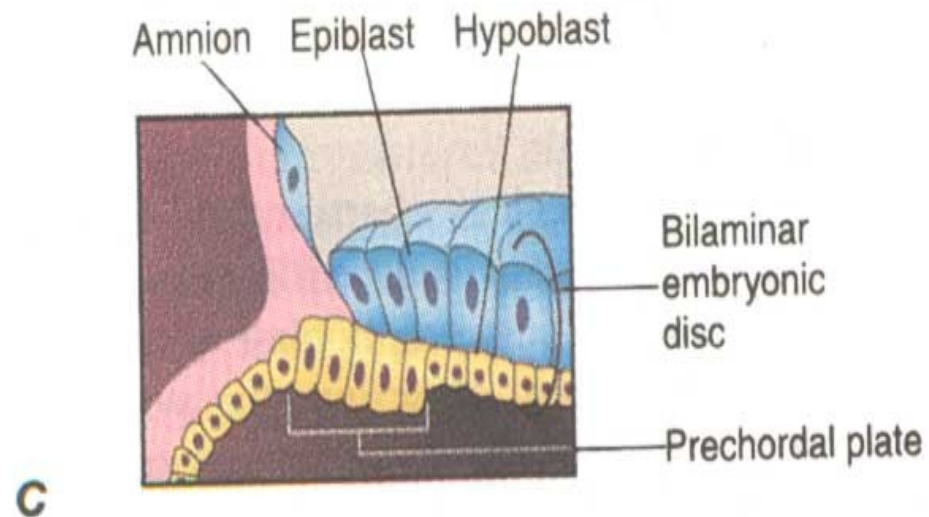


- At 14th day after fertilization the embryo is still in the form of bilaminar germ disc.
- Head end, tail end or sides could not be made out.
- At this stage the hypoblast cells become columnar from cuboidal at a localized area in the median plane.

Embryonic Primary Germ Layers



- This thickened circular area is called – **PRECHORDAL PLATE**
- Prechordal plate indicates the future head end of the embryo.
- It is also an important organizer of the head region.
- It determines the central axis of the embryo.



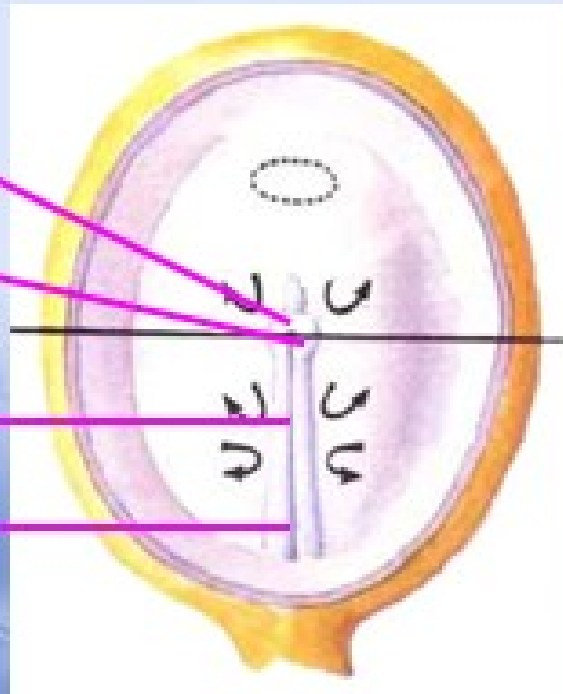
PRIMITIVE STREAK

Primitive
node

Primitive
pit

Primitive
groove

Primitive
streak



Significance of primitive streak

- Determine the direction of the embryo
- notochord

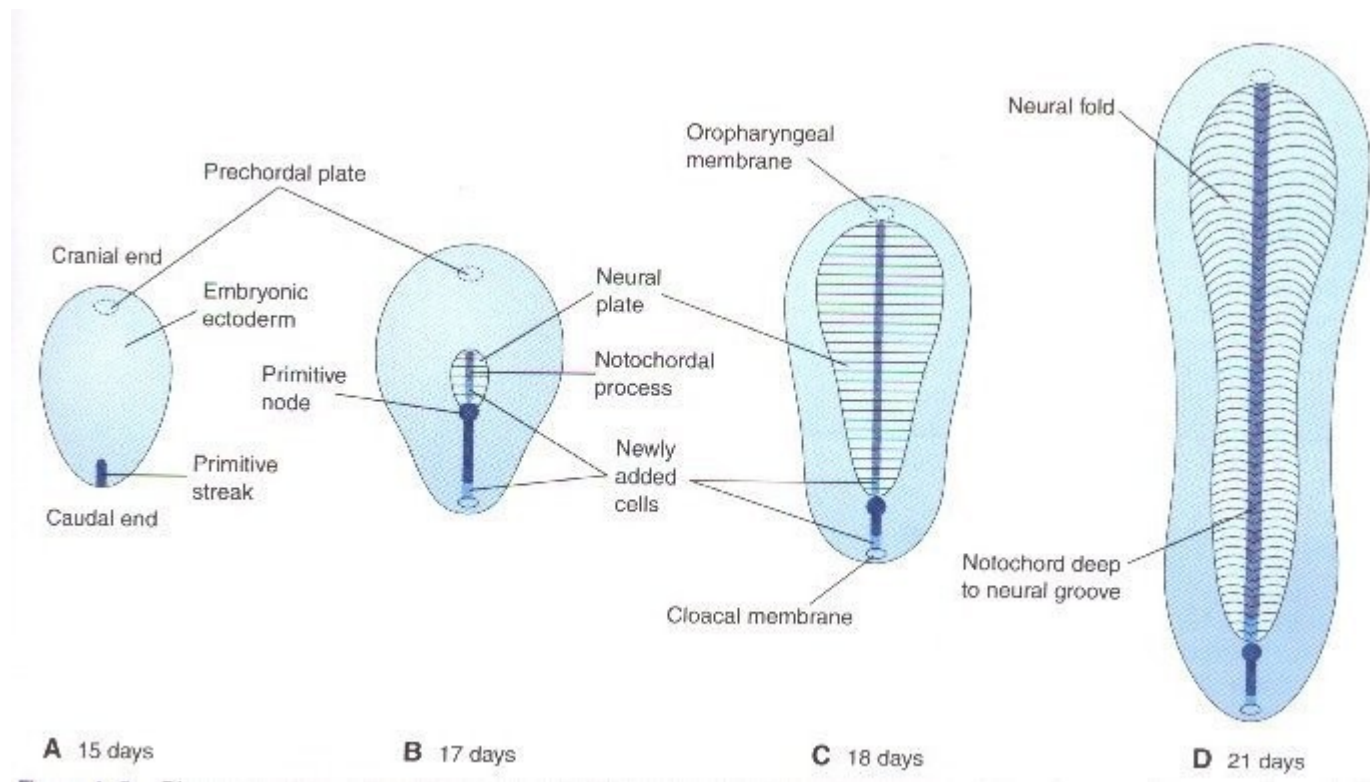
PRIMITIVE STREAK

- The first sign of gastrulation is the appearance of the primitive streak.
- At the beginning of the third week, an **opacity formed** by a thickened linear band of epiblast-the **primitive streak**-appears caudally in the median plane of the dorsal aspect of the embryonic disc.
- The primitive streak results from the **proliferation and** movement of cells of the **epiblast** to the median plane of the embryonic disc.
- As the streak elongates by addition of cells to its caudal end, its cranial end proliferates to form a **primitive node**.

PRIMITIVE STREAK

- Concurrently, a narrow groove-**primitive groove**-develops in the primitive streak
- As soon as the primitive streak appears, it is possible to identify the embryo's **craniocaudal axis, its cranial and caudal ends, its dorsal and ventral surfaces, and its right and left sides.**

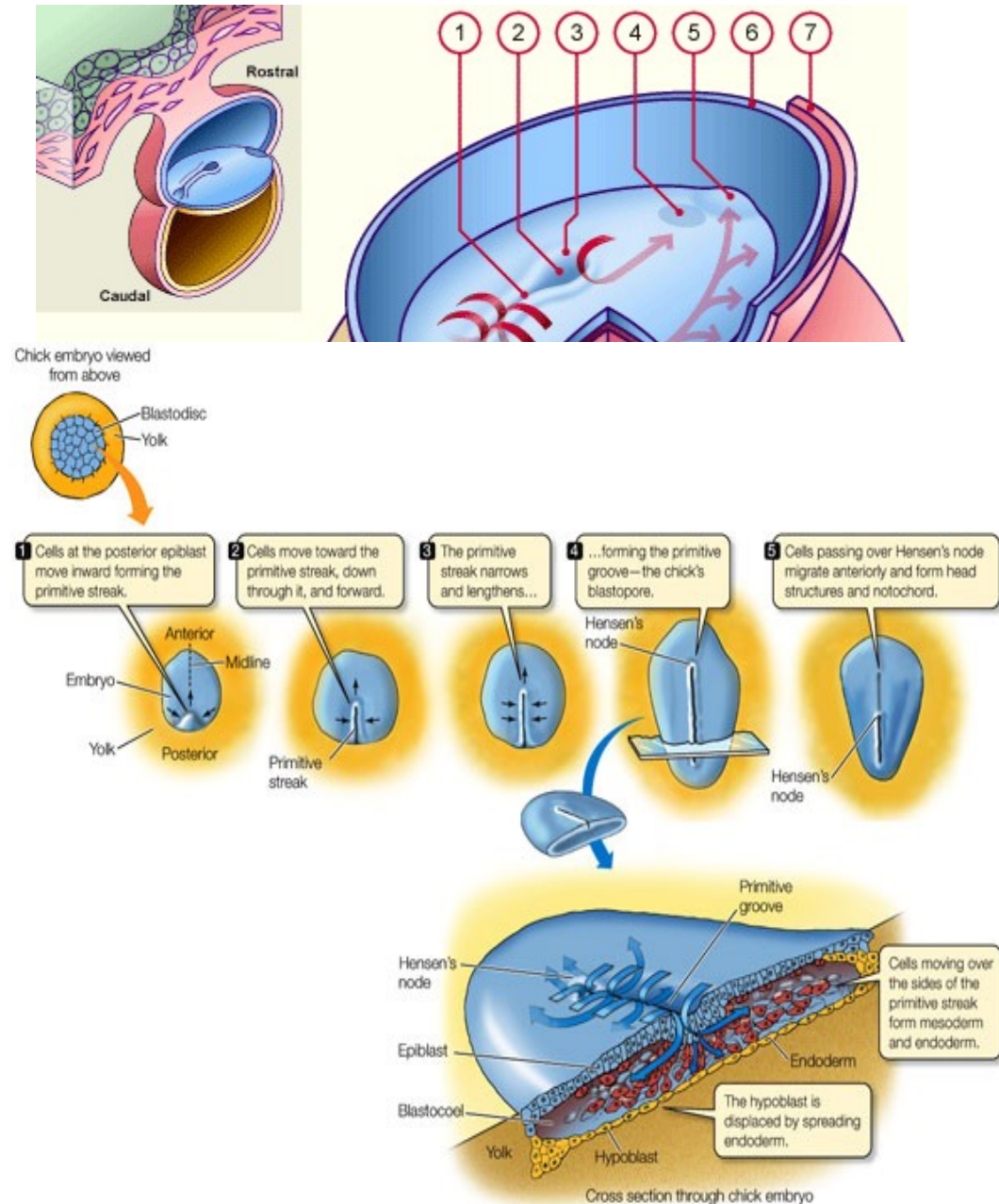
- At the tail end of the embryo the epiblastic cells proliferate & migrate towards the median plane.
- Forms a thickening at the caudal end – **PRIMITIVE STREAK**.
- At first it is very small & rounded.



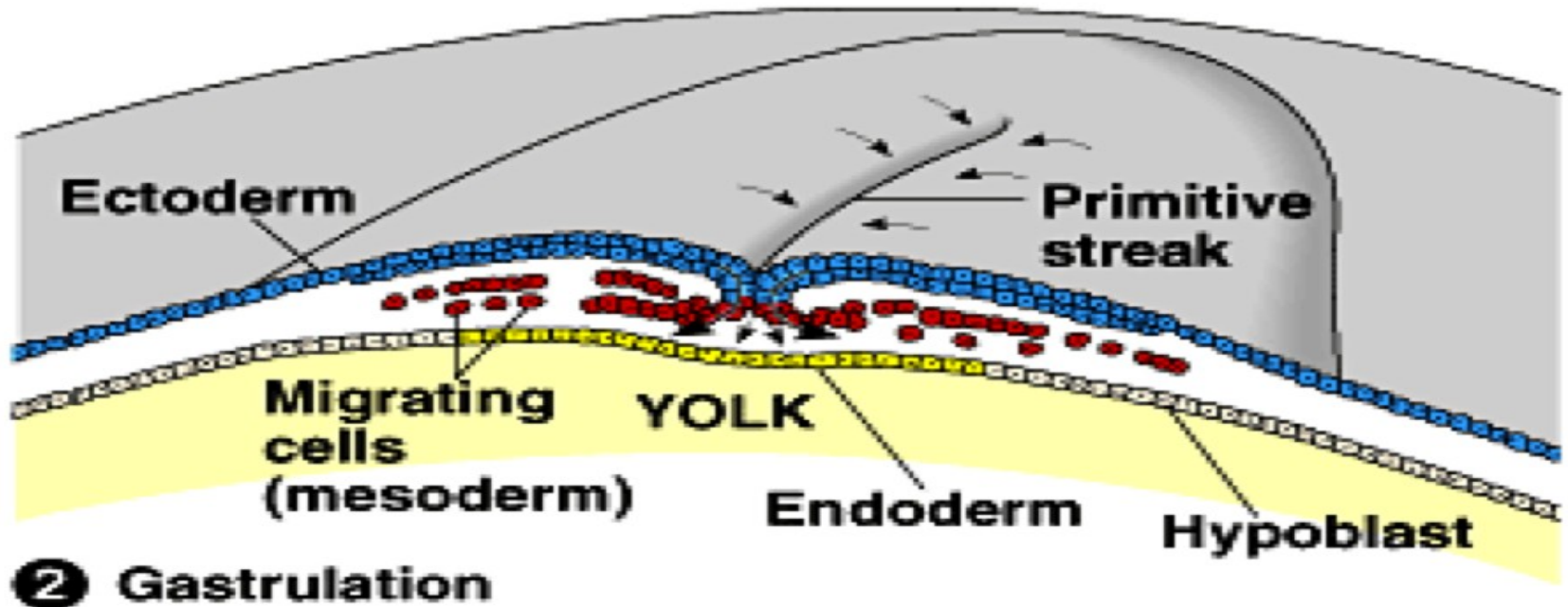
PRIMITIVE STREAK

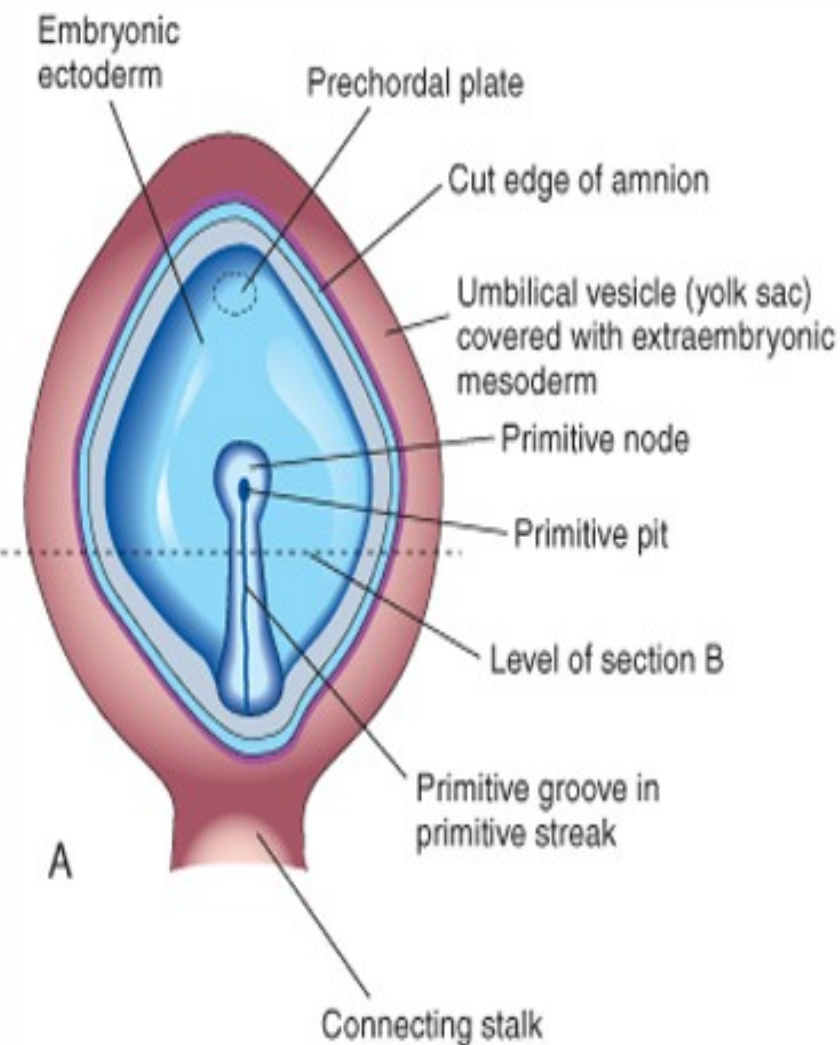
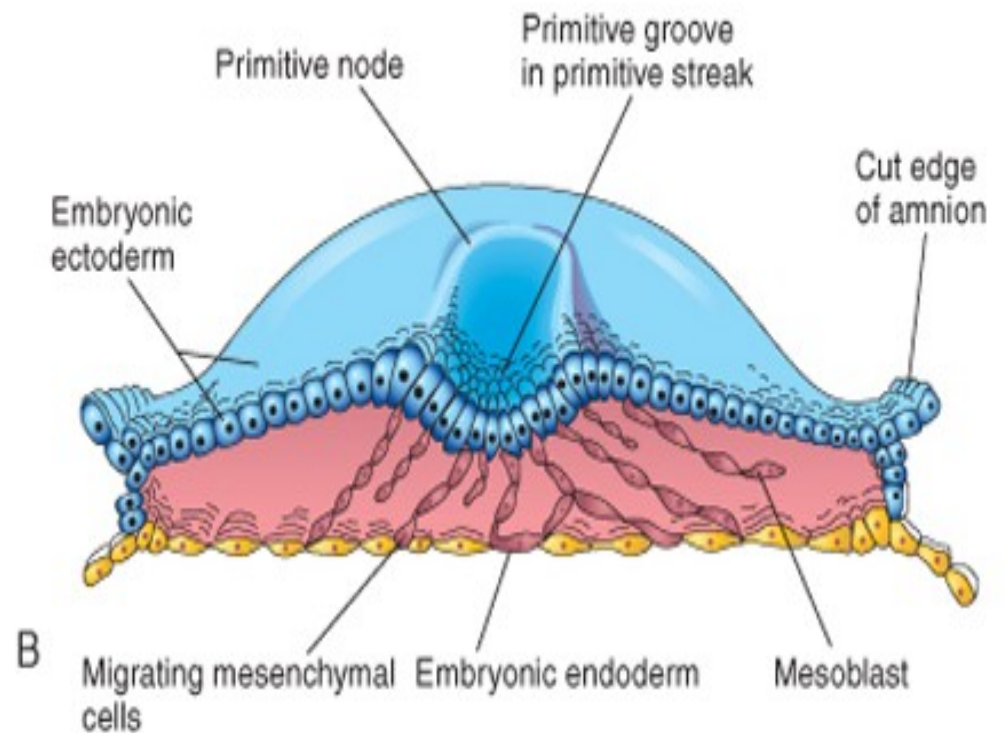
- The primitive **groove and pit** result from the invagination (inward movement) of epiblastic cells.
- Shortly after the primitive streak appears, cells leave its deep surface and form **mesenchyme**, a tissue consisting of loosely arranged cells suspended in a **gelatinous matrix**.
- **Mesenchymal cells** are ameboid and actively phagocytic.

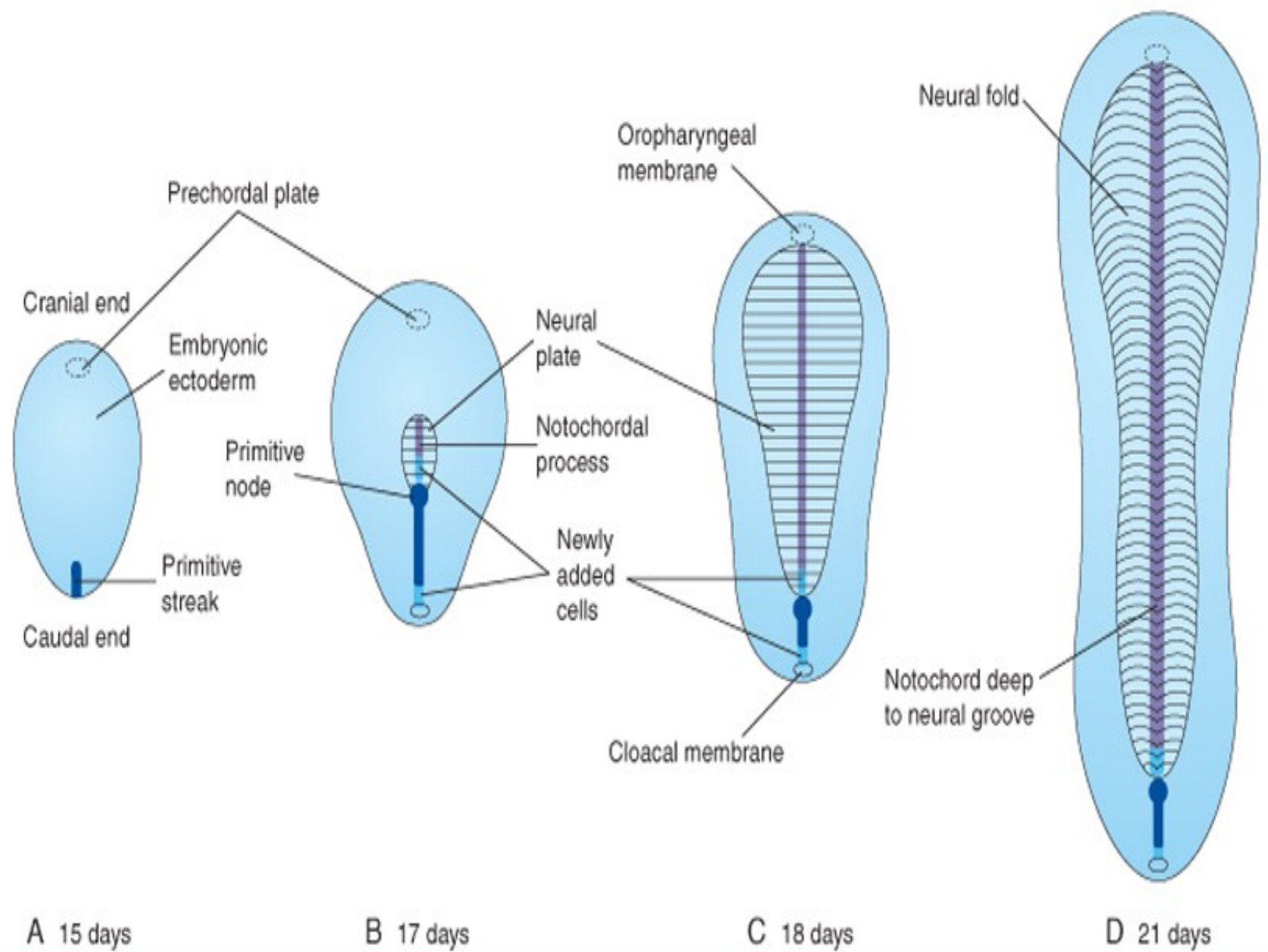
- With the elongation of the embryonic disc it becomes linear.
- The cranial end cells proliferate to form a globular swelling –
PRIMITIVE (Hensen's) NODE OR KNOT.



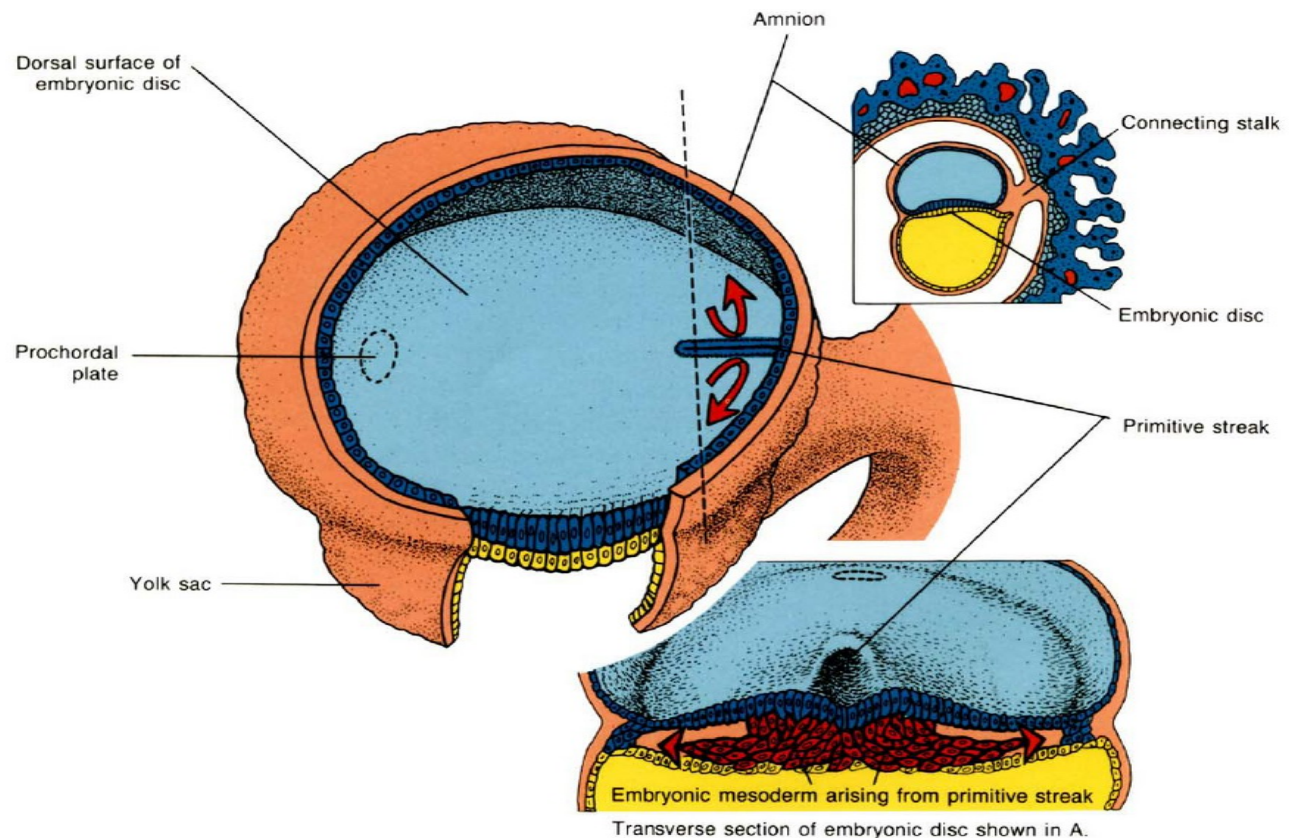
- The proliferating epiblastic cells upon reaching the primitive groove become flask shaped.
- They now invaginate through the groove & spread between epiblast & hypoblast.
- Some of them will replace the hypoblast & forms **EMBRYONIC ENDODERM**.



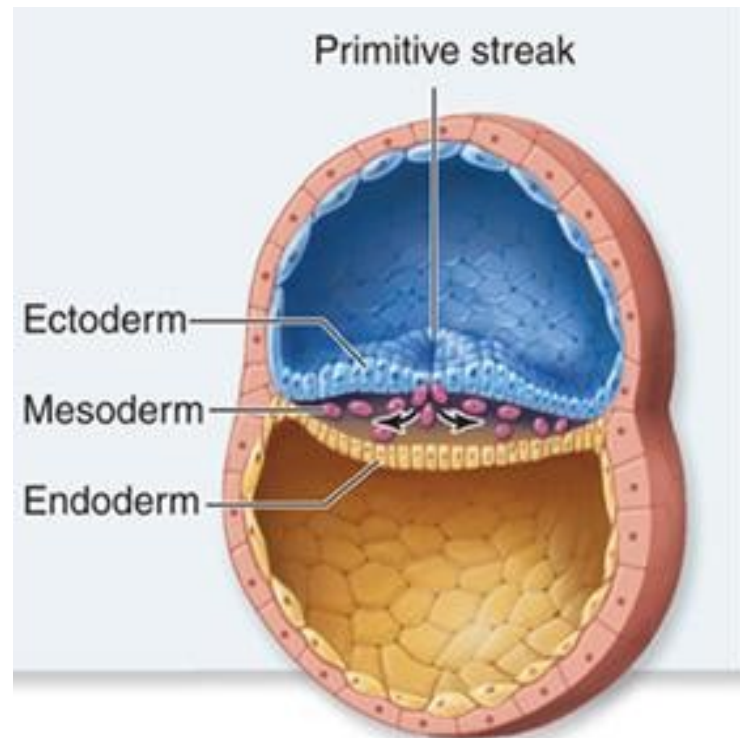




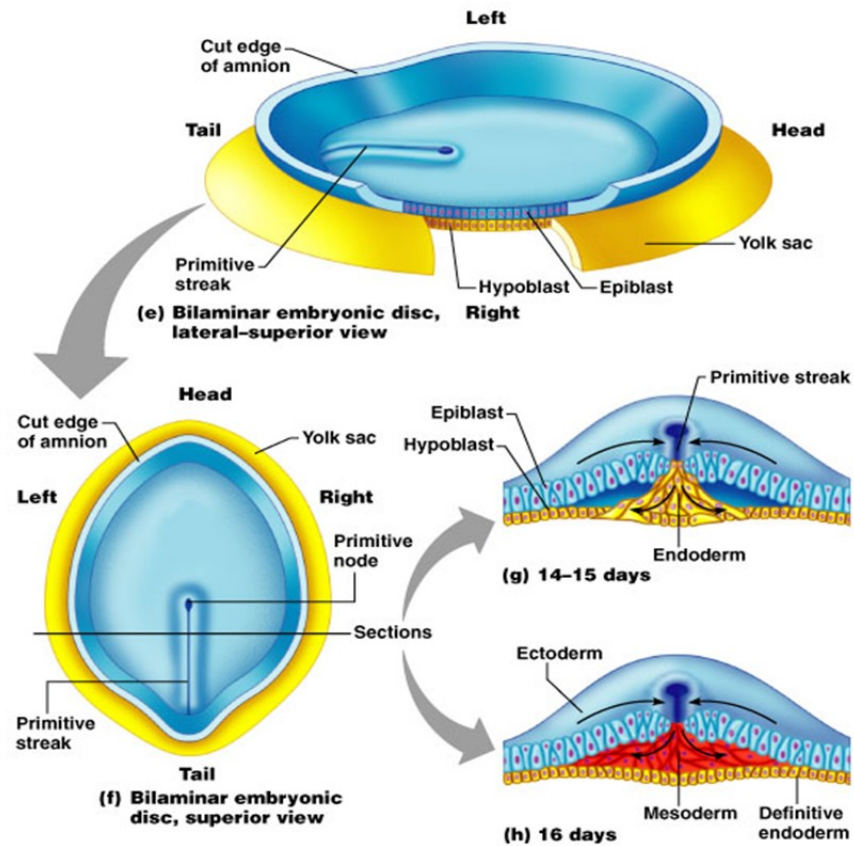
- Others spread between epiblast & newly formed endoderm to form a new germ layer
INTRA EMBRYONIC MESODERM.



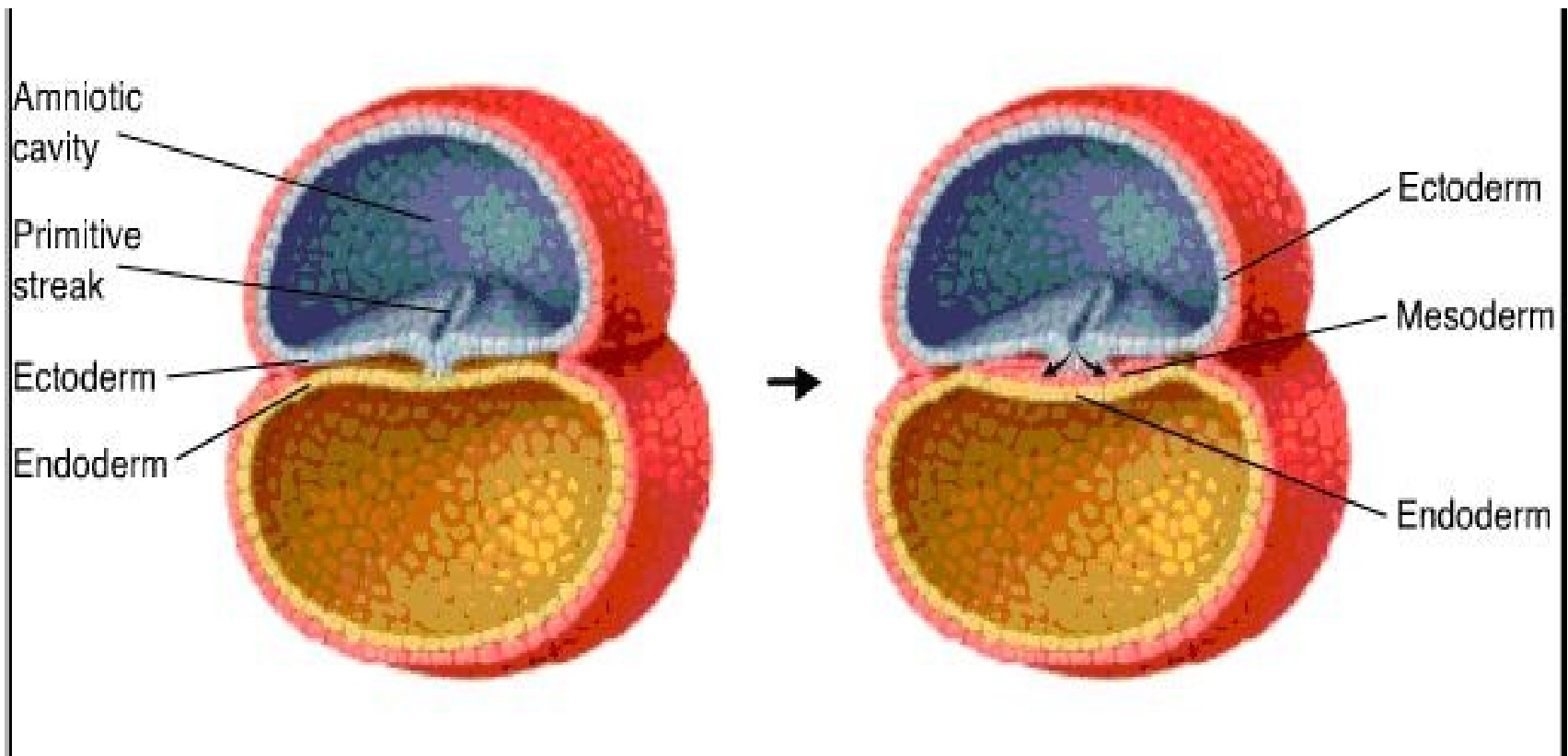
- The remaining cells of the epiblast will persist as **EMBRYONIC ECTODERM**.
- So all three germ layers are derived from epiblast ultimately.
- This process of invagination of epiblast cells through the primitive streak & formation of three germ layers is called – **GASTRULATION**



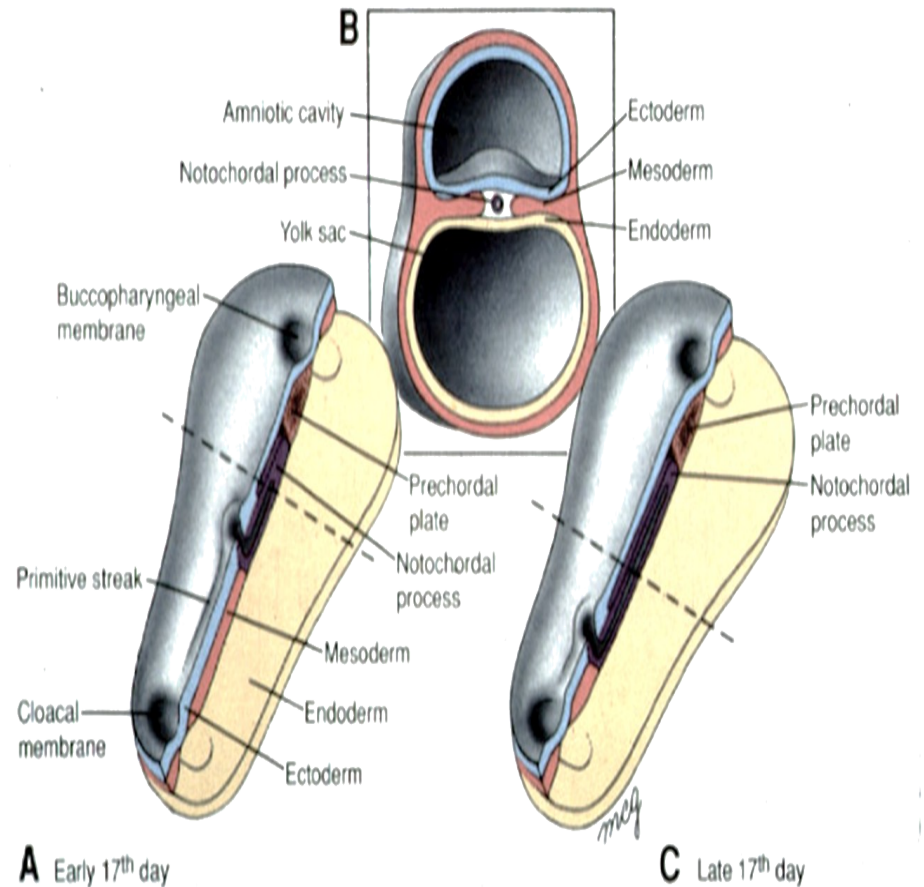
Gastrulation



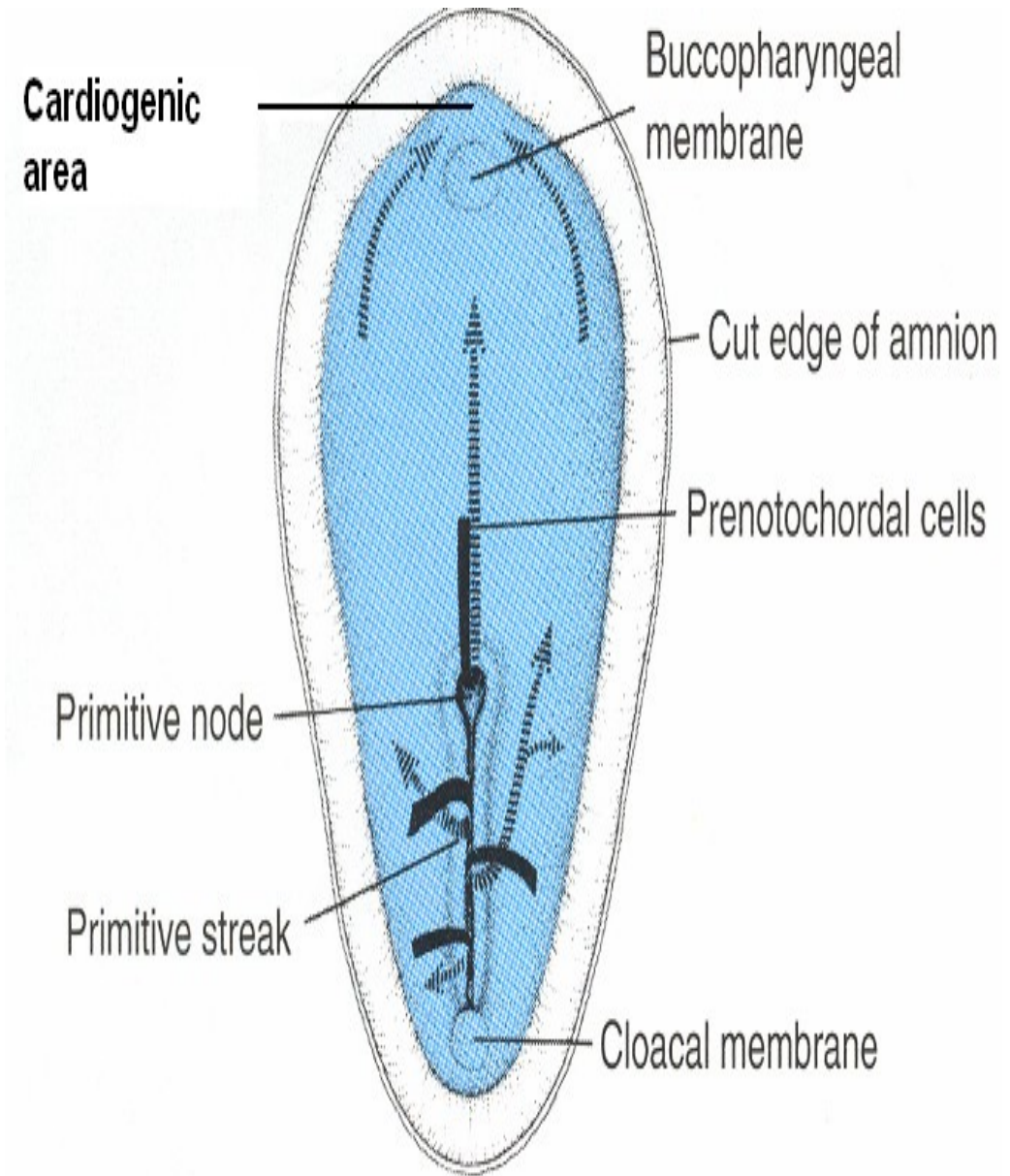
- The mesodermal cells spread between the endoderm below & ectoderm above in all directions.
- Gradually they migrate beyond the margin of the disc & merge with splanchnopleuric extra embryonic mesoderm.



- However in the region of prochordal plate it does not spread between ectoderm & endoderm.
- Here the ectoderm & endoderm are still in contact with each other – *BUCCOPHARYNGEAL MEMBRANE*.
- This later ruptures & forms the opening of future mouth.



- The IE mesoderm spreads cranial to prochordal plate & become continuous across the midline with opposite side.
- This mesoderm forms the **CARDIOGENIC AREA**.
- At the caudal end also behind the primitive streak the mesoderm does not spread between ectoderm & endoderm – **CLOACAL MEMBRANE**.
- This ruptures & forms the future anal opening.



- The primitive streak actively forms mesoderm upto 4th week.
- Thereafter the primitive streak gradually diminishes in size, becomes insignificant & disappears by the end of the fourth week.
- The embryonic disc now containing three germ layers namely ectoderm, mesoderm & endoderm is called – **TRILAMINAR GERM DISC.**

Fate of the Primitive Streak

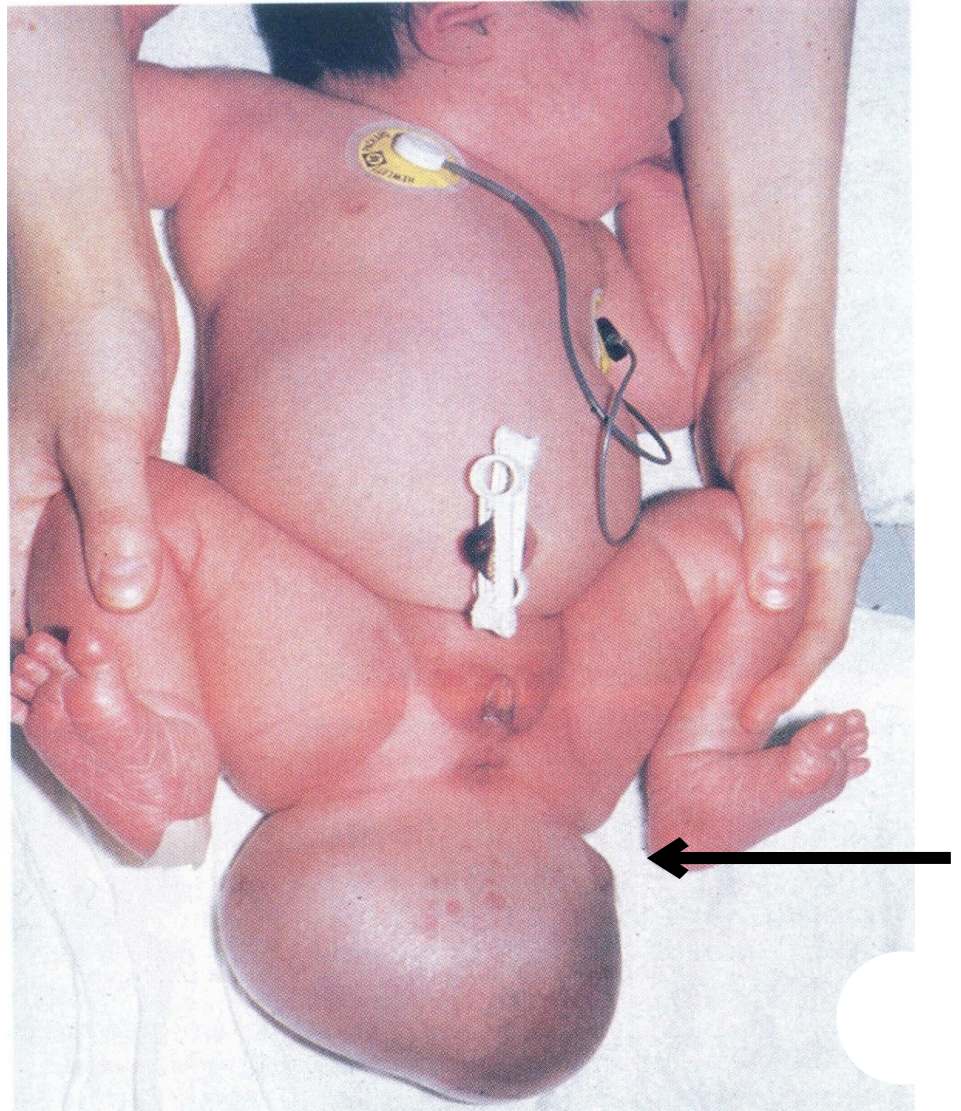
- The primitive streak actively forms mesoderm by the ingression of cells until the **early part of the fourth week**; thereafter, production of mesoderm slows down.
- The primitive streak diminishes in relative size and becomes an insignificant structure in the **sacroccygeal** region of the embryo.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

Sacroccygeal Teratoma

- Remnants of the primitive streak may persist and give rise to a **sacroccygeal 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.
- **Sacroccygeal teratomas** are the most common tumor in newborns and have an incidence of approximately one in 35,000; most affected infants (80%) are female.
- **Sacroccygeal teratomas** are usually diagnosed on routine antenatal ultrasonography, and most tumors are benign.
- These tumors are usually surgically excised promptly, and the prognosis is good.

SACROCOCCYGEAL TERATOMA

- Persistence of primitive streak that proliferates and forms new growth at the sacrococcygeal area



NOTOCHORD FORMATION

NOTOCHORDAL PROCESS AND NOTOCHORD

- Some mesenchymal cells that have ingressed through the streak and, as a consequence, acquired mesodermal cell fates 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.
- Prechordal mesoderm is a mesenchymal population rostral to the notochord and essential in forebrain and eye induction.

NOTOCHORDAL PROCESS AND NOTOCHORD

- The prechordal plate is the primordium of the **oropharyngeal membrane**, located at the future site of the oral cavity and may also have a role as a signaling center for controlling development of cranial structures.
- Mesenchymal cells from the primitive streak and notochordal process migrate laterally and cranially, among other mesodermal cells, between the ectoderm and endoderm until they reach the margins of the embryonic disc.
- These cells are continuous with the extraembryonic mesoderm covering the amnion and umbilical vesicle .

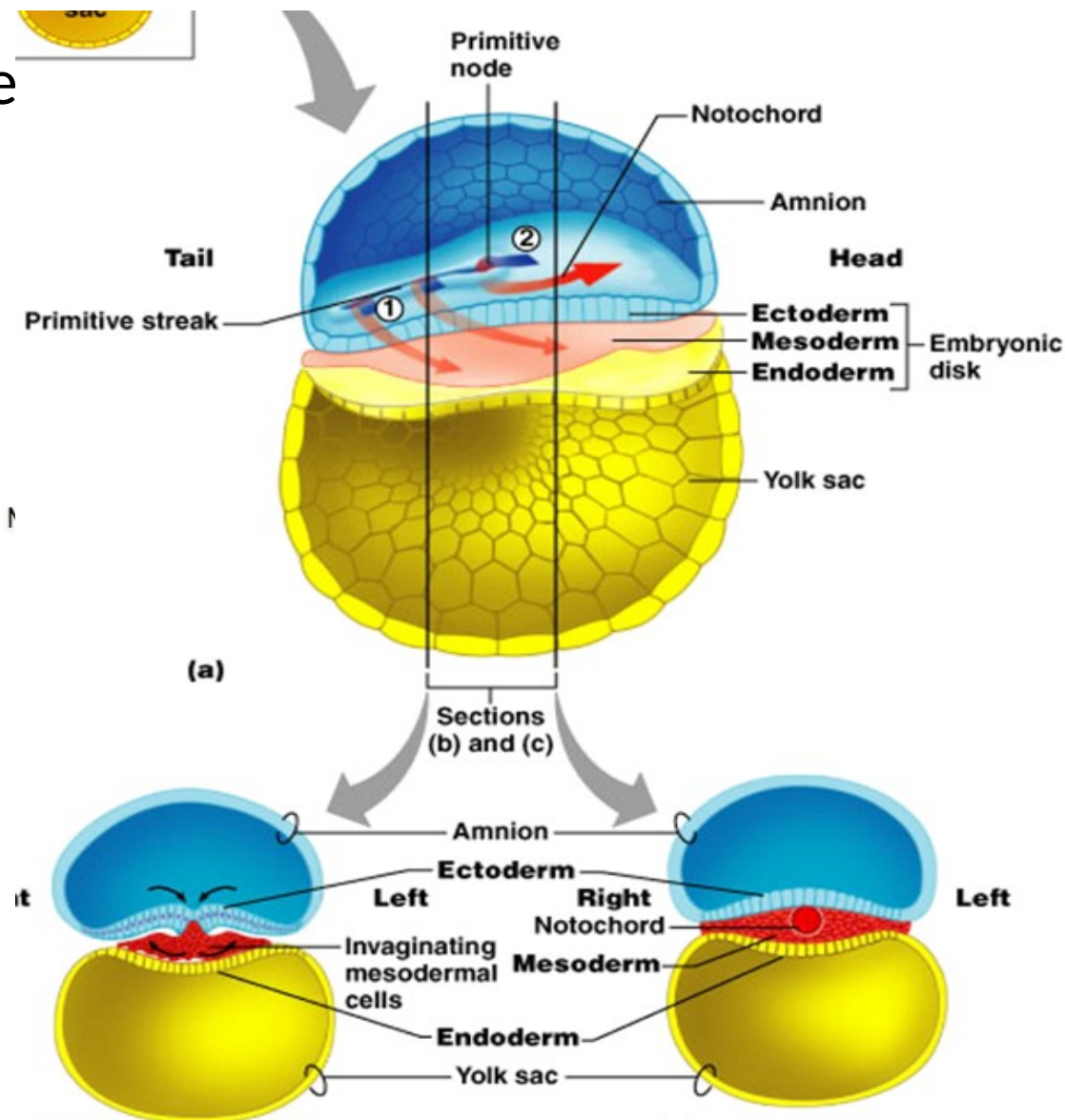
NOTOCHORDAL PROCESS AND NOTOCHORD

- Some mesenchymal cells from the primitive streak that have mesodermal fates migrate cranially on each side of the notochordal process and around the prechordal plate.
- Here they meet cranially to form cardiogenic mesoderm in the **cardiogenic area** where the **heart primordium** begins to develop at the end of the third week .
- Caudal to the primitive streak there is a circular area-the **cloacal membrane**, which indicates the future site of the anus .
- The embryonic disc remains bilaminar here and at the **oropharyngeal membrane** because the embryonic ectoderm and endoderm are fused at these sites, thereby preventing migration of mesenchymal cells between them .

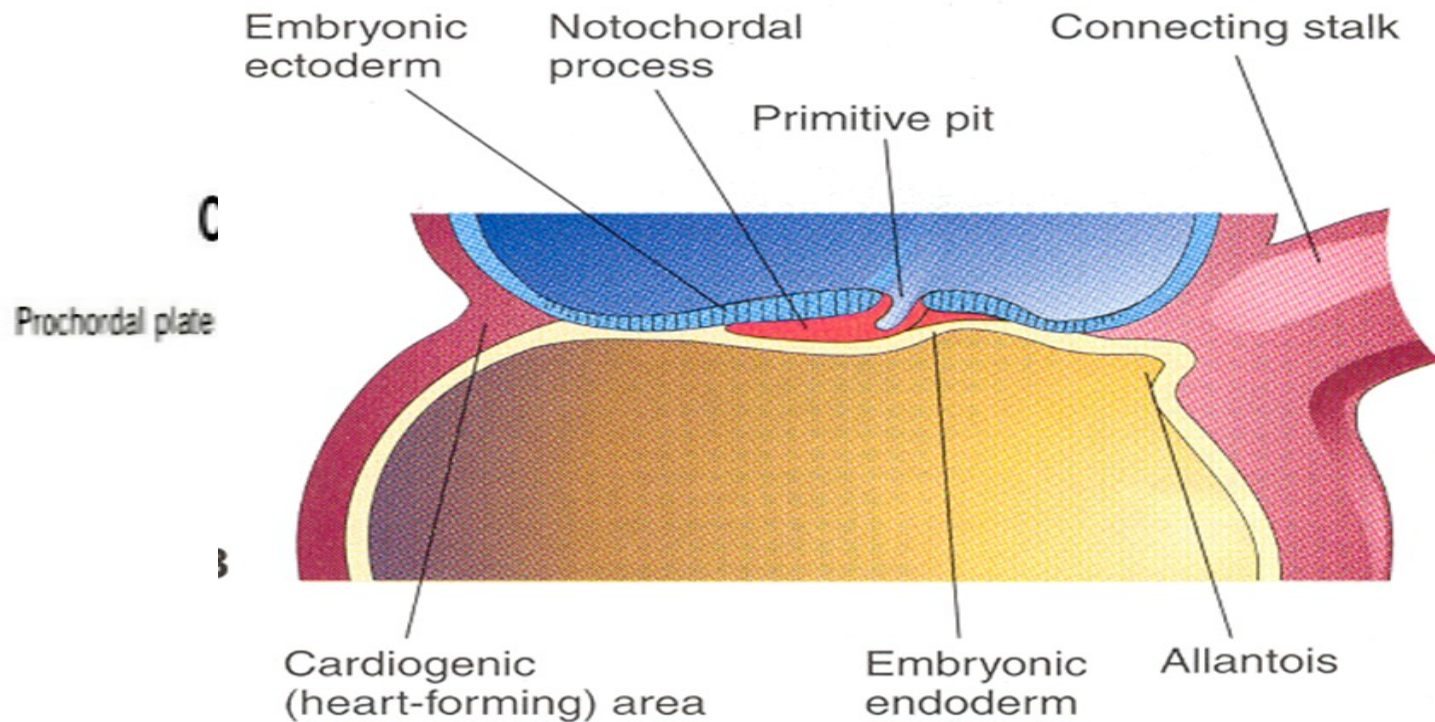
NOTOCHORDAL PROCESS AND NOTOCHORD

- By the middle of the third week, intraembryonic mesoderm separates the ectoderm and endoderm everywhere except
 - At the oropharyngeal membrane cranially
 - In the median plane cranial to the primitive node, where the notochordal process is located
 - At the cloacal membrane caudally
- Instructive signals from the primitive streak region induce notochordal precursor cells to form the **notochord**, a cellular rodlike structure.

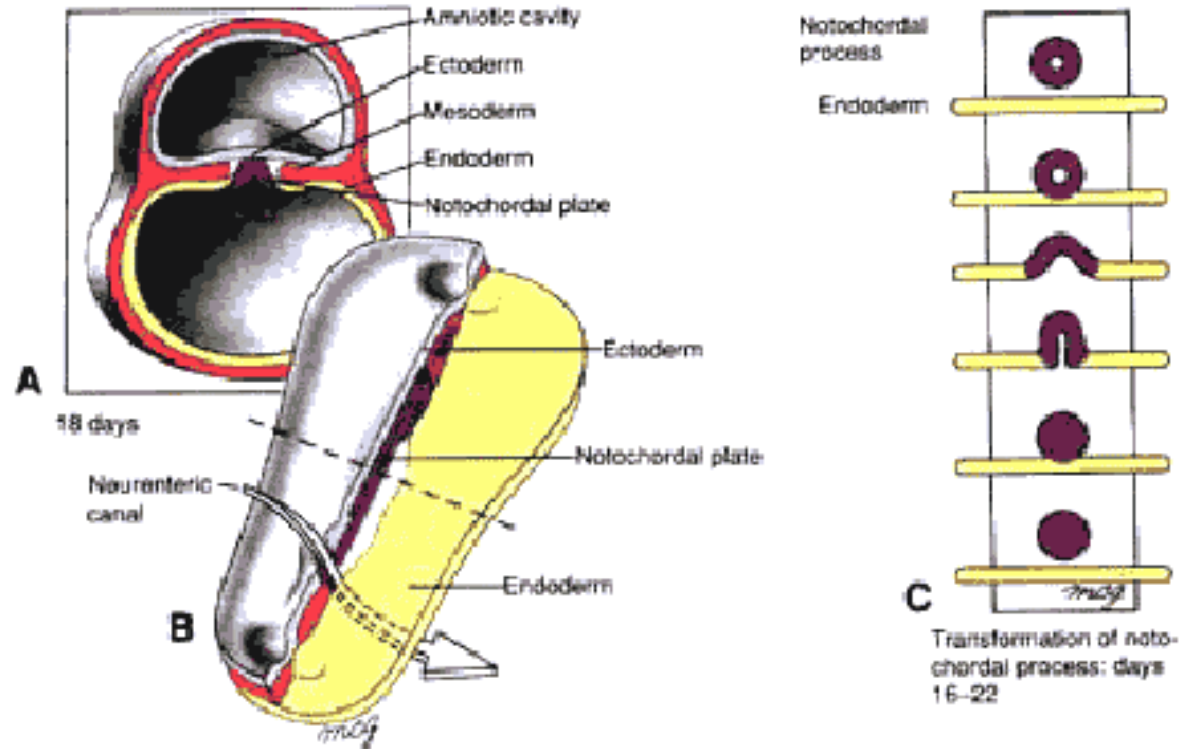
- Some mesenchymal cells migrate cranially from the primitive node towards the prechordal plate in the median plane.
- This solid cords of cells formed in the median plane – NOTOCHORDAL PROCESS.
- The cells are called as – **PRENOTOCHORDAL CELLS.**



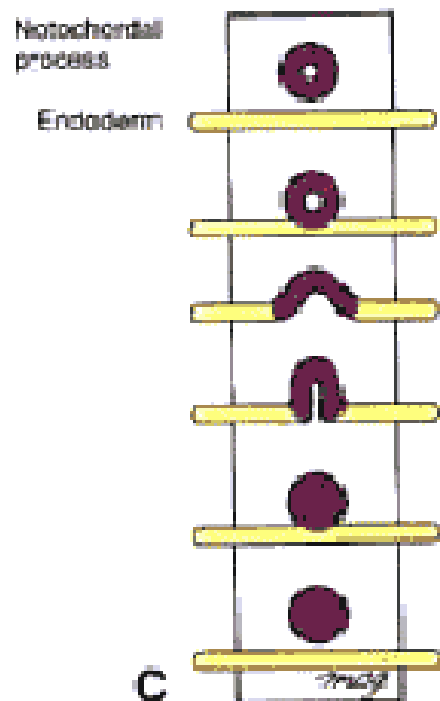
- This process soon acquires a lumen by the extension of the primitive pit.
- Thus it is converted into a tubular structure – **NOTOCHORDAL CANAL**.



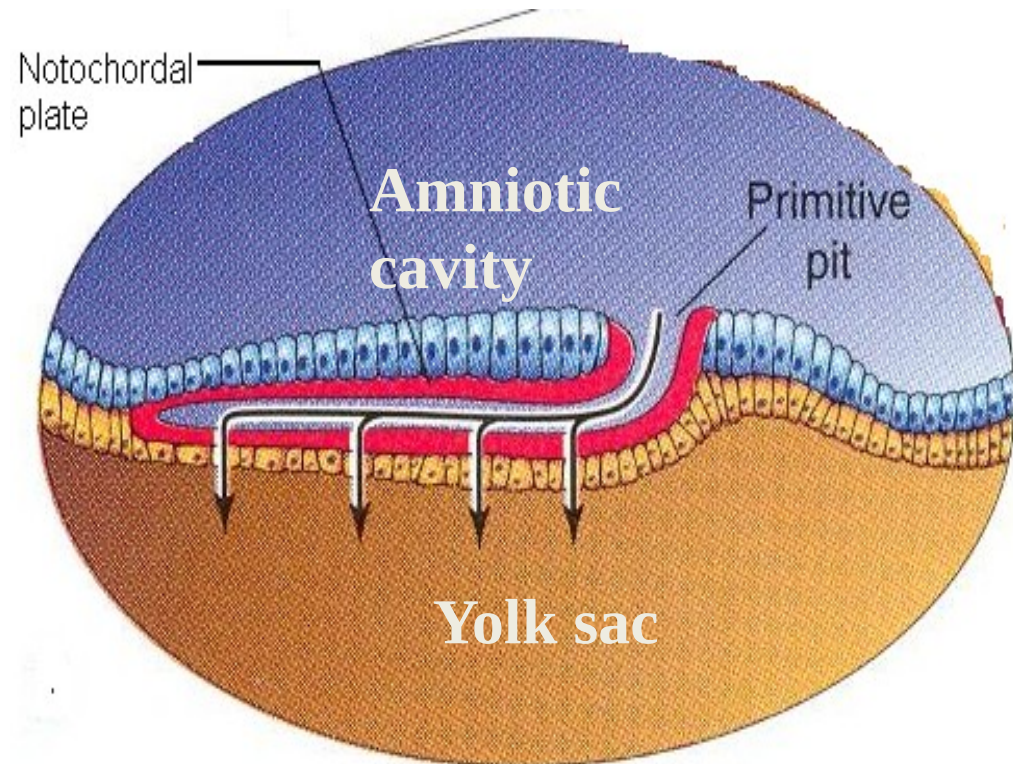
- The cells in the floor of the notochordal canal soon fuses with the endoderm.
- However at first the canal is separated from the yolk sac.



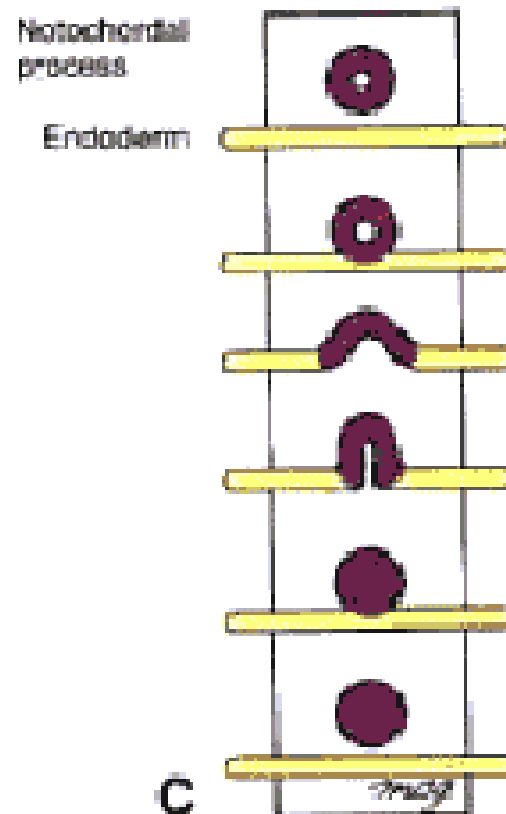
- But soon the fused layers degenerate.
- Openings are formed which communicates the notochordal canal with the yolk sac.



C
Transformation of notochordal process: days 16-22

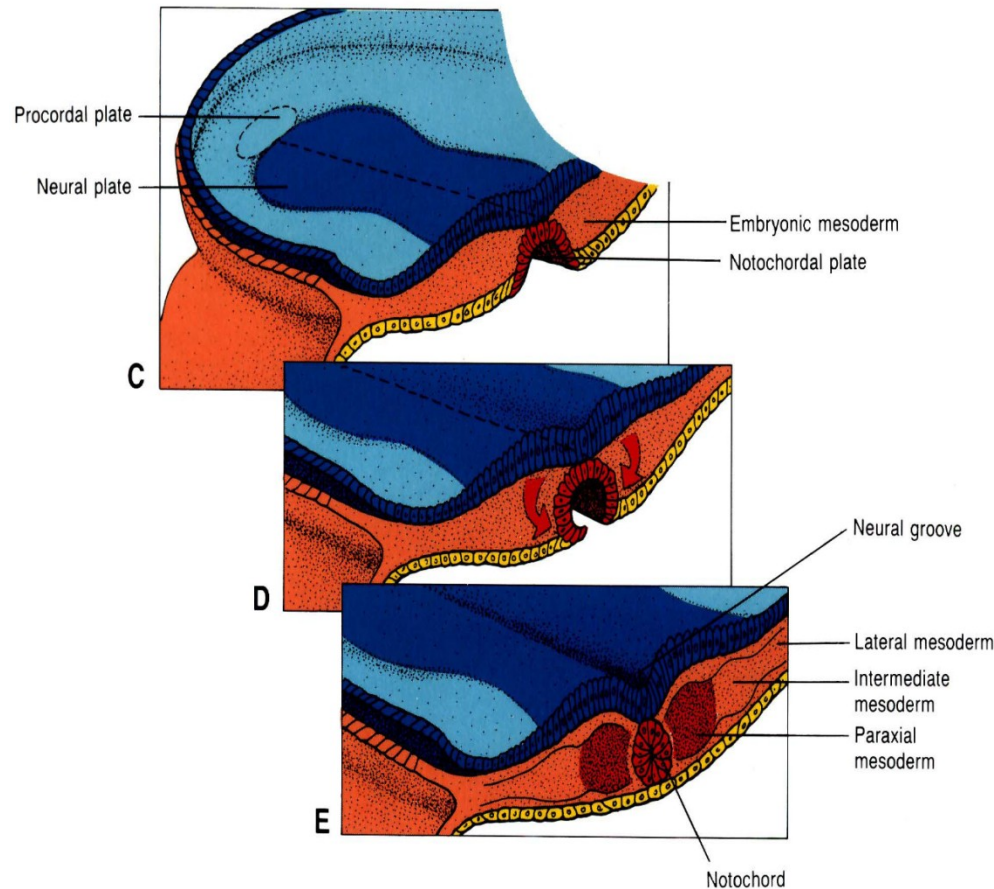
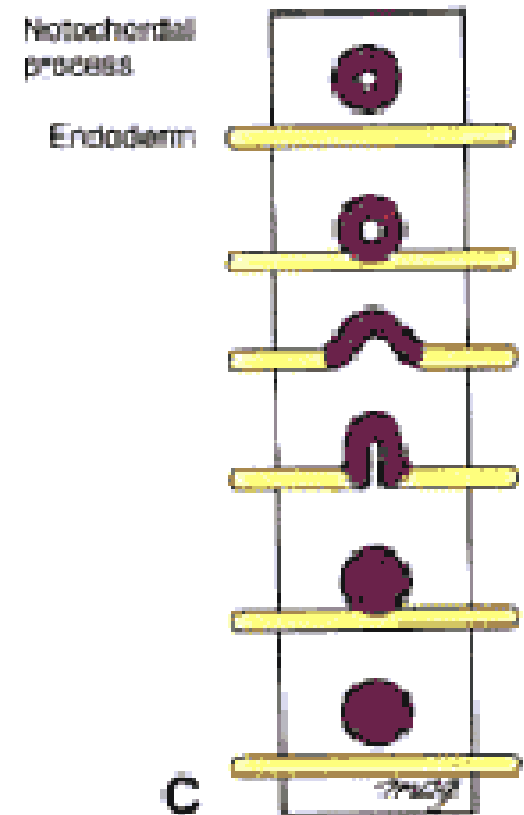


- The openings become confluent & the floor of the canal completely disappears.
- The canal is converted into a grooved notochordal plate.



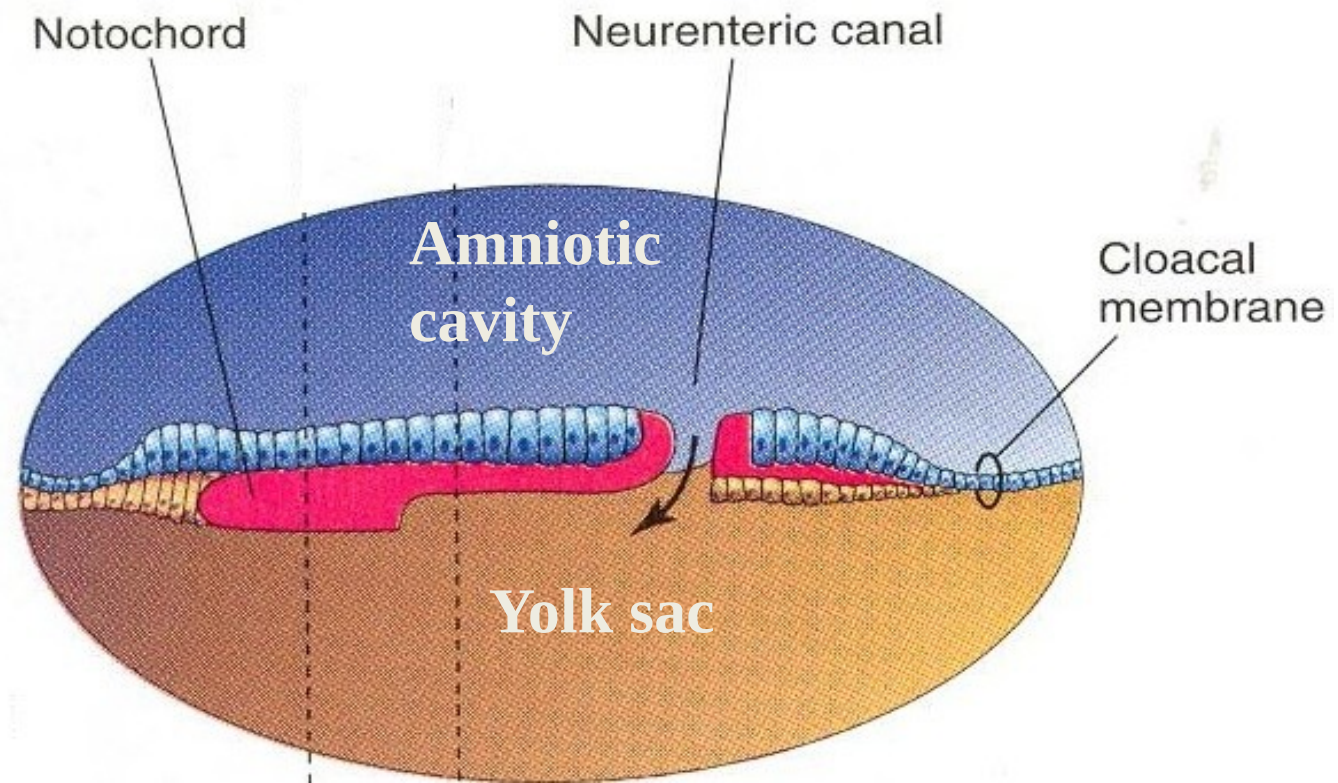
Transformation of notochordal process: days 16-22

- After sometime the flat notochordal plate soon becomes curved & tubular.
- The edges fuse & the notochordal tube is reformed.

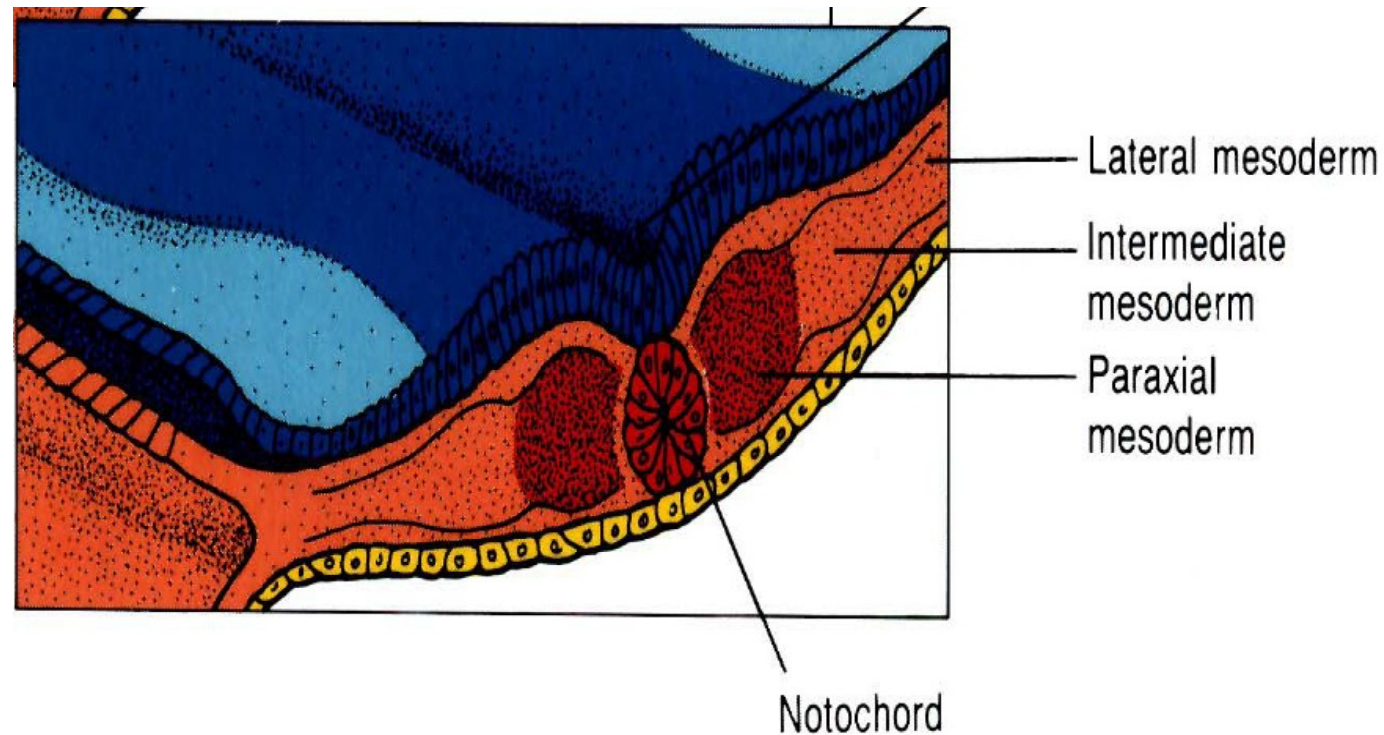


Transformation of notochordal process: days 16-22

- Cells of notochordal canal proliferate from the cranial end of the embryo & convert the tube into solid cords of cells.
- However the lumen persists temporarily at the caudal end near primitive pit – **NEURENTERIC CANAL**.
- Thus a transitory communication is still present between the yolk sac & amniotic cavities.

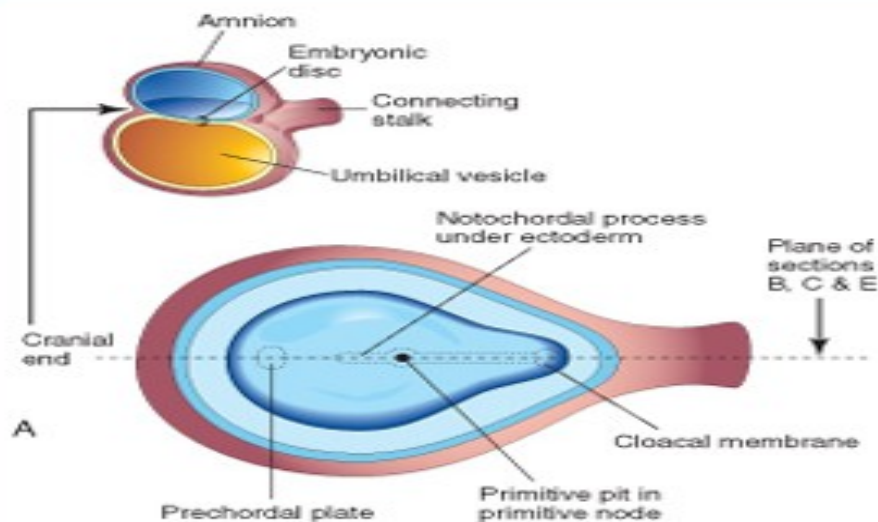
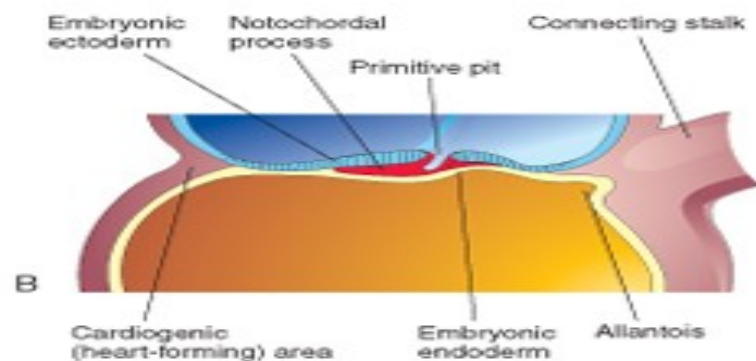
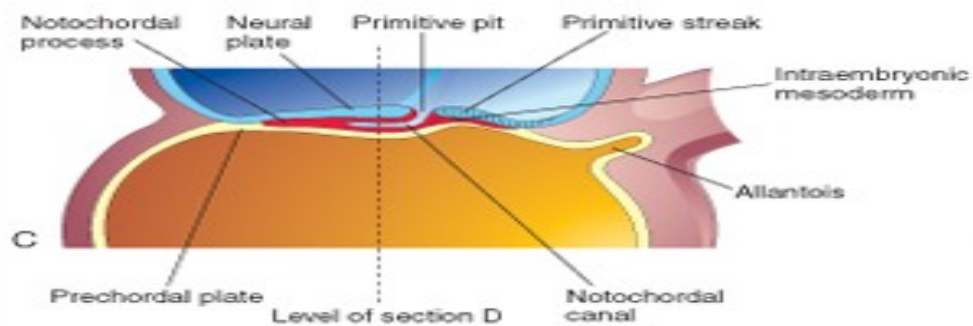
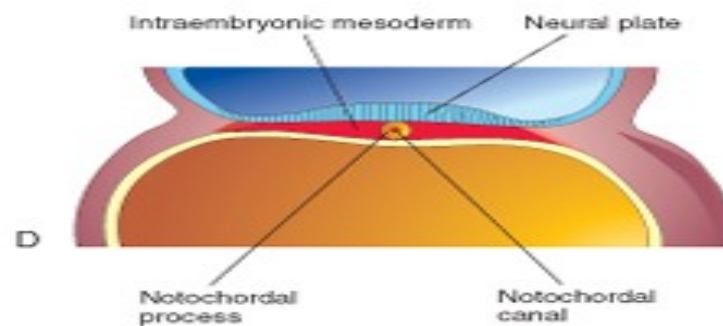
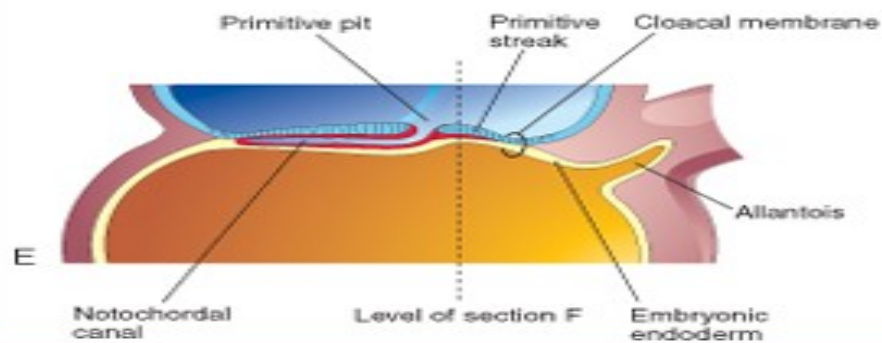
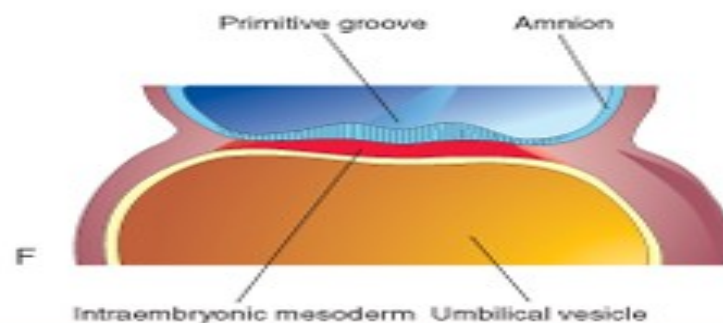


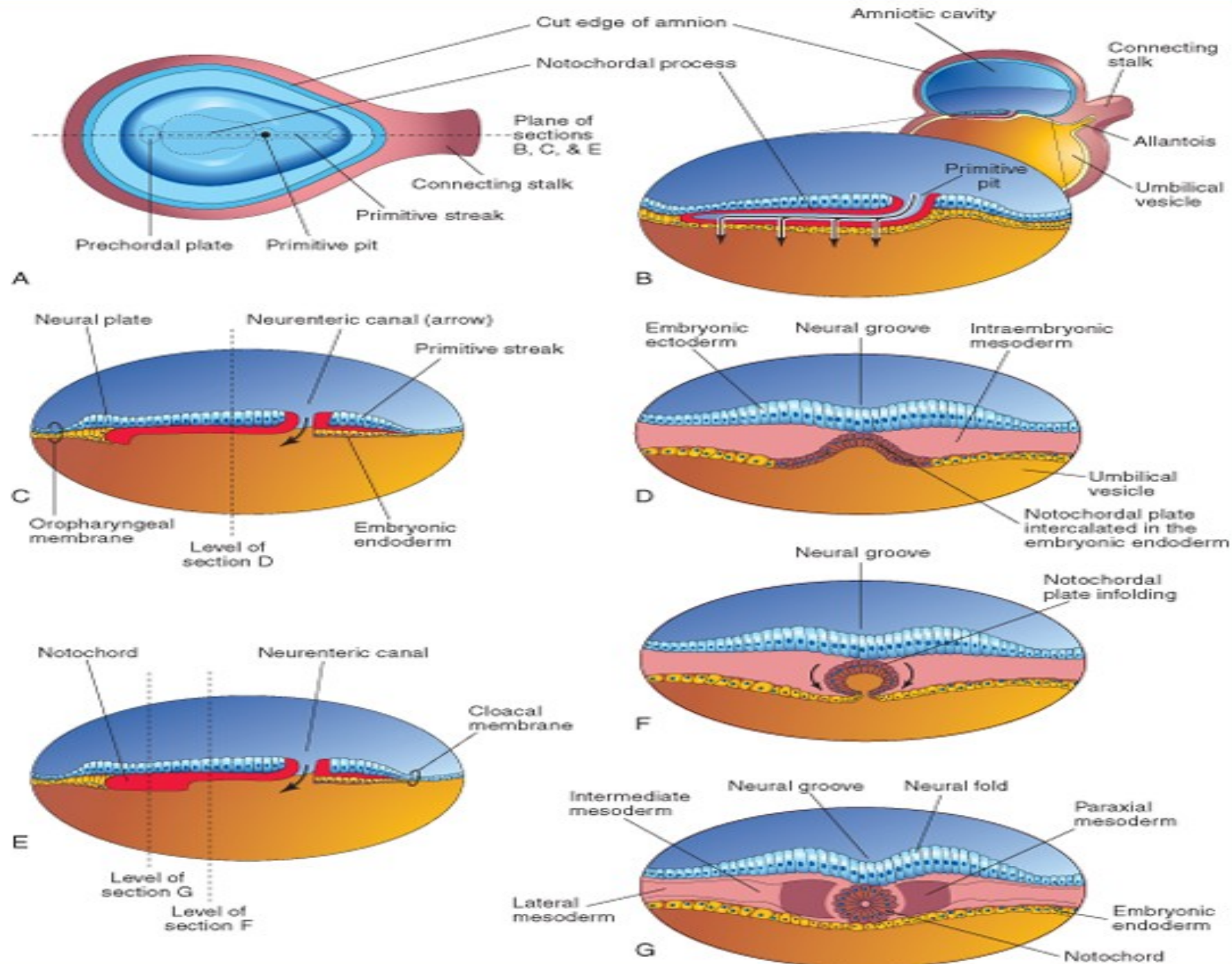
- With further proliferation of cells the neurenteric canal disappears.
- The notochord gets detached from the endoderm – **DEFINITIVE NOTOCHORD**.
- The endoderm becomes a continuous layer.



The notochord

- Defines the primordial longitudinal axis of the embryo and gives it some rigidity
- Provides signals that are necessary for the development of axial **musculoskeletal structures and the central nervous system**
- Contributes to the intervertebral discs





The notochord develops as follows:

- The **notochordal process** elongates by invagination of cells from the primitive pit.
- The primitive pit extends into the notochordal process, forming a **notochordal canal**.
- The notochordal process is now a cellular tube that extends cranially from the primitive node to the prechordal plate.
- The floor of the notochordal process fuses with the underlying embryonic endoderm.

The notochord develops as follows

- 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 .
- The openings rapidly become confluent and the floor of the notochordal canal disappears; the remains of the notochordal process form a flattened, grooved **notochordal plate**.

The notochord develops as follows:

- Beginning at the cranial end of the embryo, the notochordal cells proliferate and the notochordal plate infolds to form the **notochord** .
- The proximal part of the notochordal canal persists temporarily as the *neurenteric canal* , which forms a transitory communication between the amniotic and umbilical vesicle cavities.
- When development of the notochord is complete, the neurenteric canal normally obliterates.
- The notochord becomes detached from the endoderm of the umbilical vesicle, which again becomes a continuous layer .

FATE OF NOTOCHORD

- It degenerates & disappears as the vertebral column is formed.
- But its remnants persist in the intervertebral discs as **NUCLEUS PULPOSUS**.

FUNCTIONAL SIGNIFICANCE OF NOTOCHORD

1. Defines the primordial axis of the embryo.
2. Gives some rigidity to the embryo.
3. Serves as the basis for the development of axial skeleton.
4. Indicates future site of vertebral column.
5. Acts as the primary inductor in the formation of neural tube which forms the future nervous system

Remnants of Notochordal Tissue

- Both benign and malignant tumors (**chordomas**) may form from vestigial remnants of notochordal tissue.
- Approximately **one third of chordomas** occur at the base of the cranium and extend to the **nasopharynx**.
- Chordomas grow slowly and malignant forms infiltrate bone.

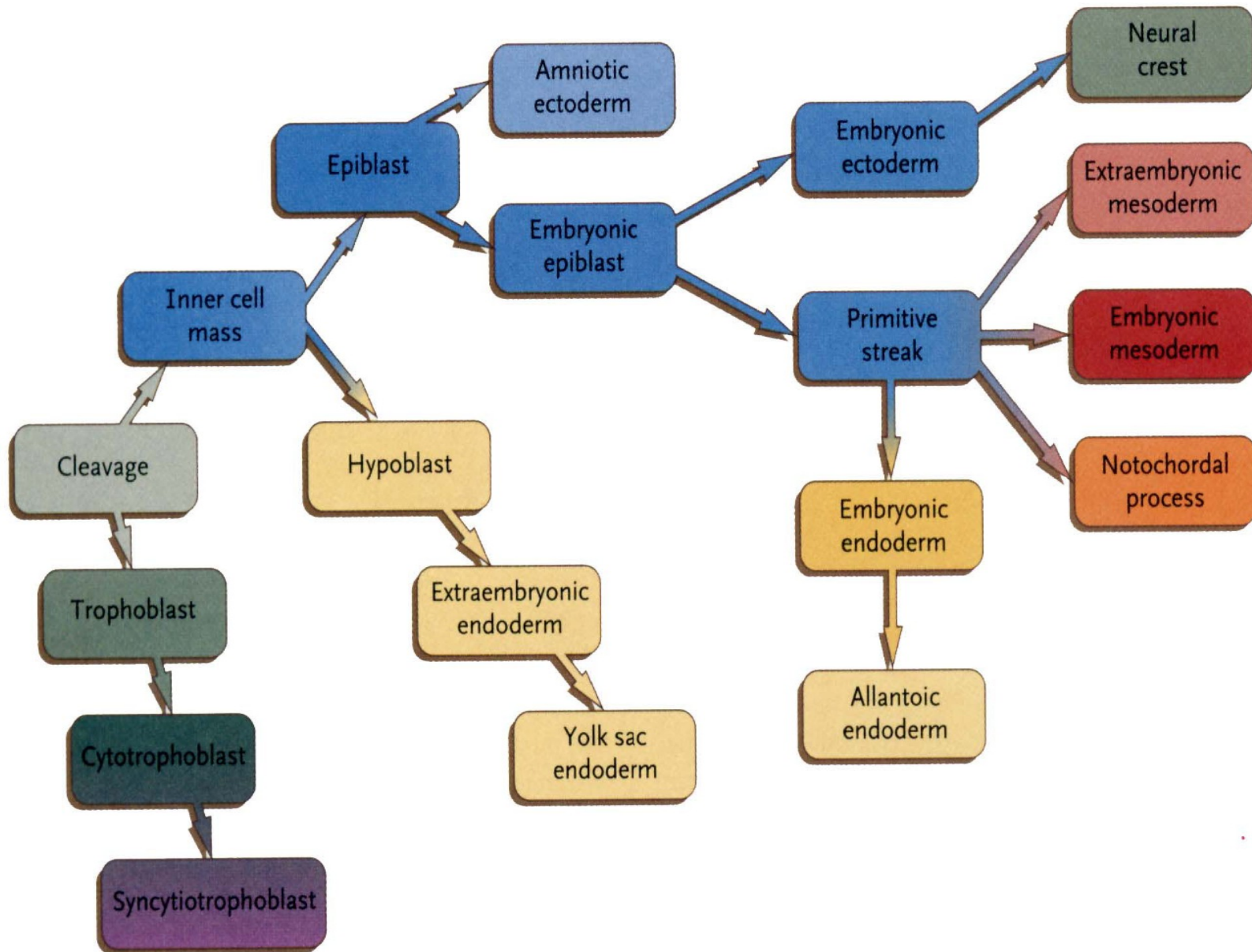
Embryonic inducers

- Signal from a group of cells develops other cells
- Inducer – inducing tissue
- Inducting signal
- Responding tissue
- Target gene

The notochord develops as follows

- The notochord extends from the oropharyngeal membrane to the primitive node.
- The notochord degenerates as the bodies of the vertebrae form, but small portions of it persist as the *nucleus pulposus* of each intervertebral disc.
- *The notochord functions as the **primary inductor** (signaling center) in the early embryo.*
- The developing notochord induces the overlying embryonic ectoderm to thicken and form the **neural plate**, the primordium of the central nervous system (CNS).

Summary



THE ALLANTOIS

- The allantois (Greek [Gr.] *allas*, sausage) 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 embryos of reptiles, birds, and most mammals, this endodermal sac expands to occupy most of the space between the chorion and the amnion.
-
- In those species, it has a respiratory function and/or acts as a reservoir for urine during embryonic life.

THE ALLANTOIS

- 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 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**.
- The blood vessels of the allantoic stalk become the umbilical arteries.
-
- The intraembryonic part of the umbilical veins has a separate origin.

Allantoic Cysts

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

Thank You