BHARATHIDASAN UNIVERSITY

Program: M.Sc., Biomedical Science

Course Title : Neurobiology

Neurodevelopment

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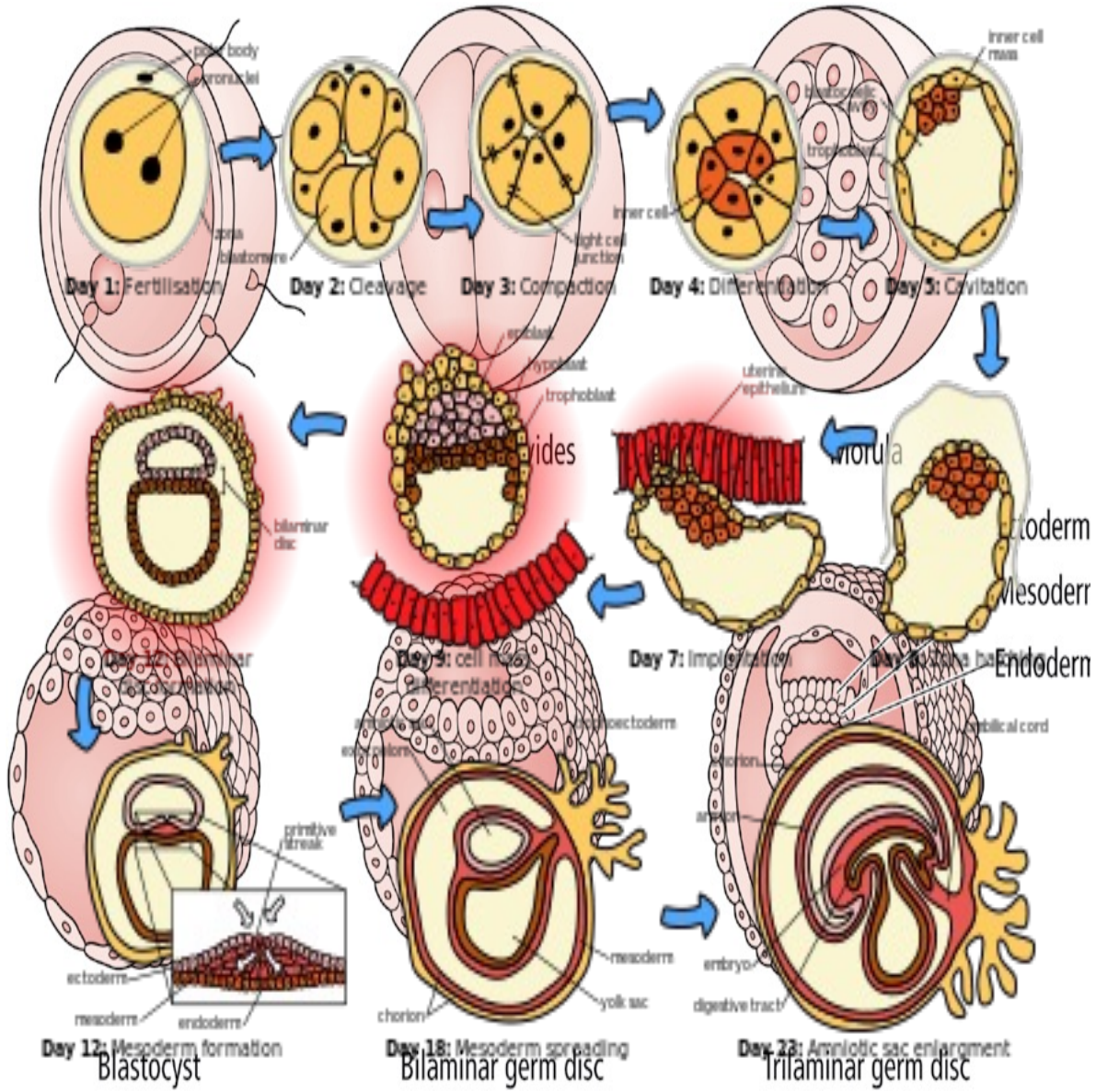
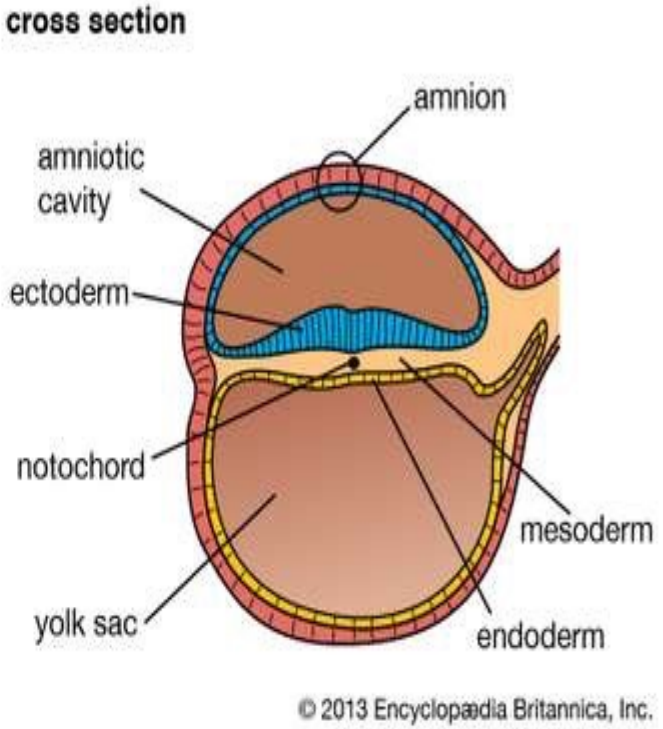
Neurodevelopment

- Fusion of the (male and female gametes) spermatozoon and the oocyte→Zygote→ mitotic activity, **cleavage→ morula (mulberry)** as the cells proliferate, trigger the expression of different genes on different cells, required for normal development.
- morula secrete a viscous fluid that creates a central cavity by pushing the cells to the periphery until a hollow ball of cells is formed - **Blastocyst** (blast= immature, **Cyst-**fluid filled ball like)


Day 1: Fertilisation
Day 2: Cleavage
Day 3: Compaction
Day 4: Differentiation
Day 5: Cavitation
Day 7: Implantation
Day 12: Bilaminar germ disc formation
Day 18: Mesoderm spreading
Day 23: Amniotic sac enlargement
Blastocyst
Bilaminar germ disc
Trilaminar germ disc
ectoderm
mesoderm
endoderm
yolk sac
chorion
embryo
amnion
umbilical cord
primitive streak
bilaminar disc
trophoblast
inner cell mass


cross section
amnion
amniotic cavity
ectoderm
notochord
mesoderm
yolk sac
endoderm
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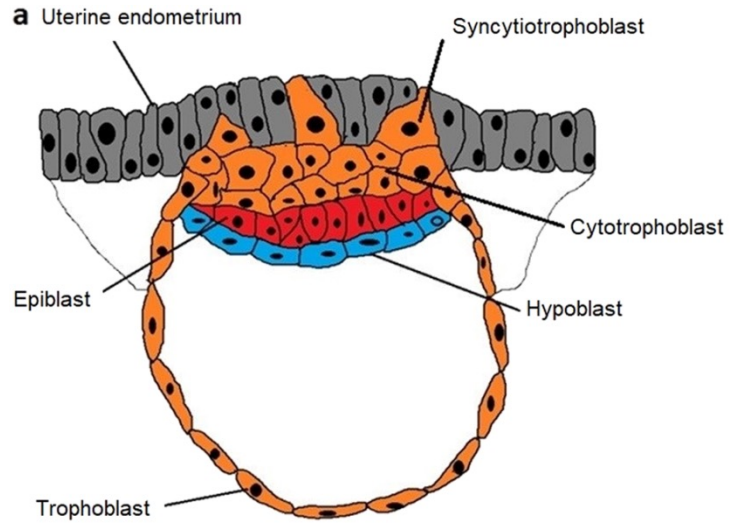
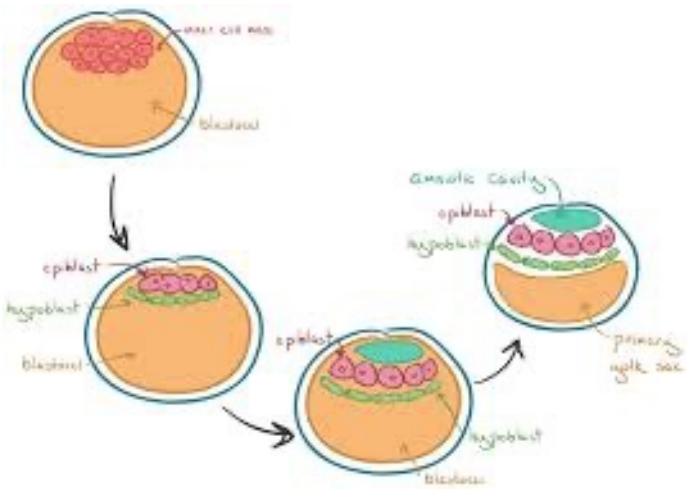
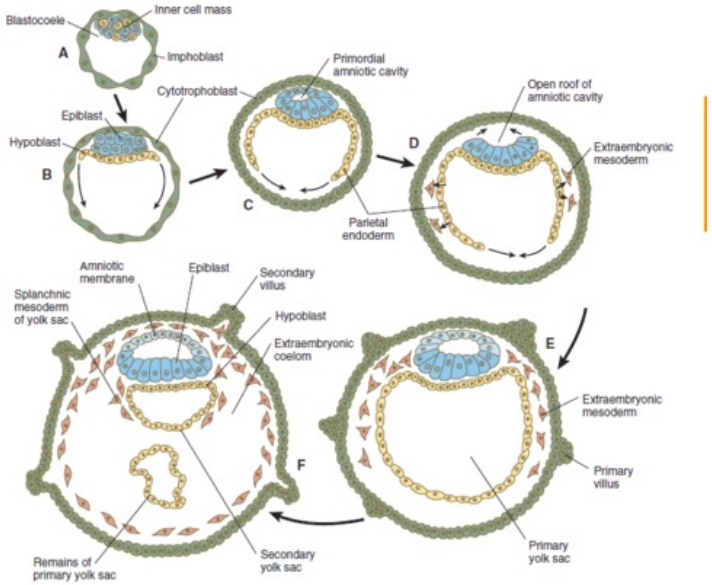
- most of the cells of the blastocyst are peripherally positioned cells are the trophoblasts.(trophe-nourishment) give rise to placenta.
- a few of the cells are trapped inside, adhering to upper pole of this hollow ball of cells are the embryoblasts, give rise to embryo.
- Trophoblasts express signaling molecule known as L-selectin, (a cytokine), that binds to receptors located on the surface of the mother's uterine endometrium.(implantation)



Bilaminar germ disc

- cells of embryoblasts rearrange themselves to form two layers, the epiblasts (epi- above) and the hypoblasts (hypo-under), and the embryo becomes known as the bilaminar germ disc.





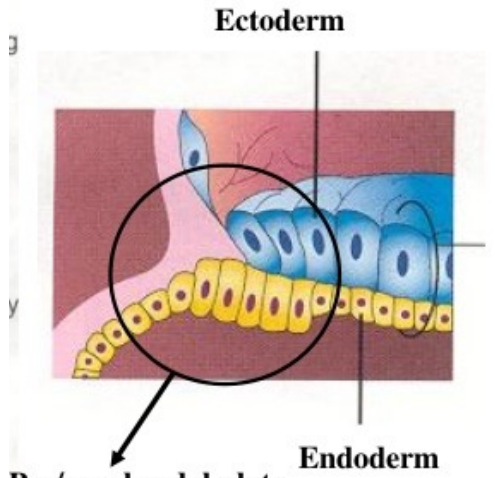
- epiblast is closer to the trophoblast cells than is the hypoblast,

Trilaminar germ disc

- Anterior end of the bilaminar germ disc, forming the prochordal plate,
- few cells of the epiblasts form desmosomal (desm-bond or bundle) contacts with a few cells of the underlying hypoblast, forming the prochordal plate (pro-supporting, chord-rope or string)

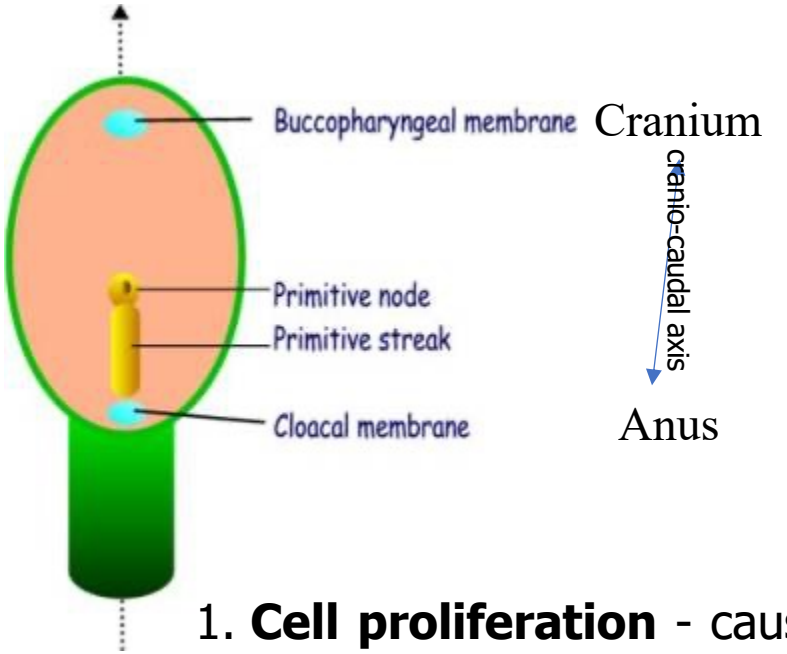
When viewed from above, the epiblast appears as an oval disc.

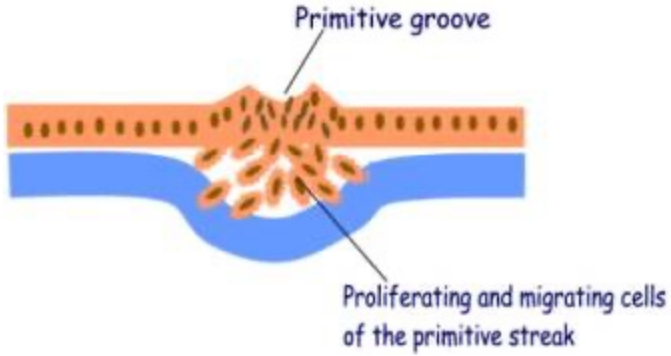
The connecting stalk marks the caudal end of the embryo. A structure of cells called primitive streak appears in the caudal (Tail end) half of the epiblast.



Firm union between ectodermal and endodermal cells occur at prechordal plate

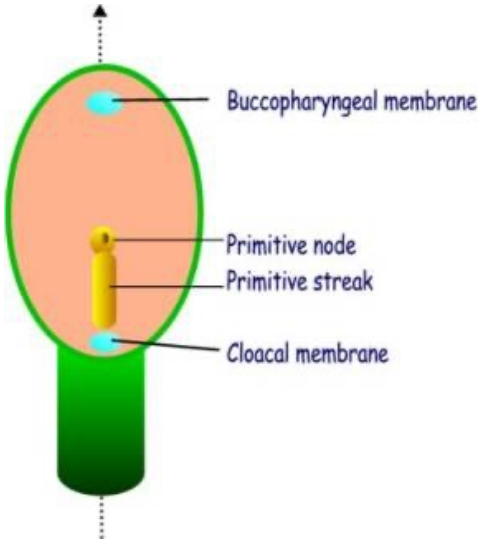
Three important processes occur at the primitive streak

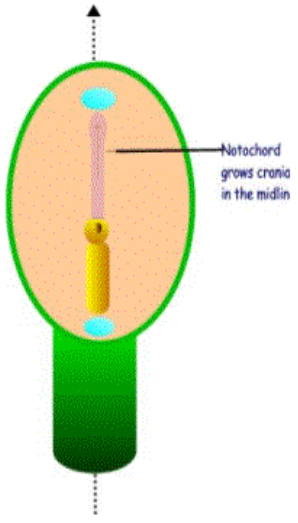


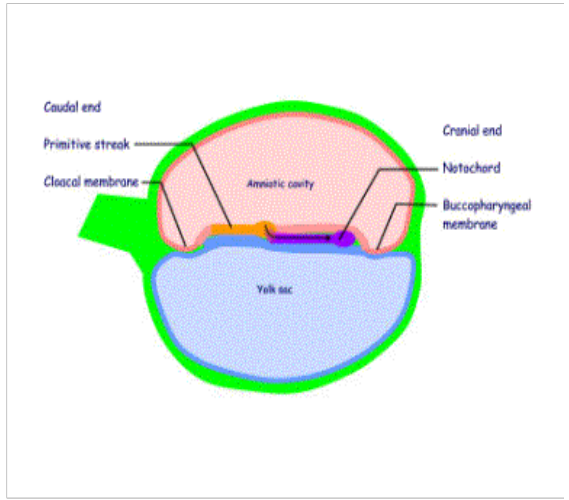


1. **Cell proliferation** - causes heaping up of the cells and is the source of a new layer of cells
2. **Cell migration** by amoeboid movement – the cells insinuate themselves between the epiblast and hypoblast
3. **Cell determination** - the cells arising from the primitive streak are determined to give rise to different rudiments

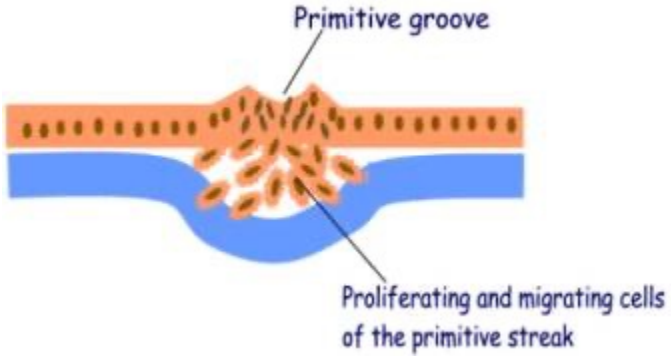
- The **notochordal process** grows out from the primitive node grows as a rod of cells that migrate cranially in the midline. Its growth is limited by the buccopharyngeal membrane. The most cranial part of the notochord is termed the **prochordal plate**.







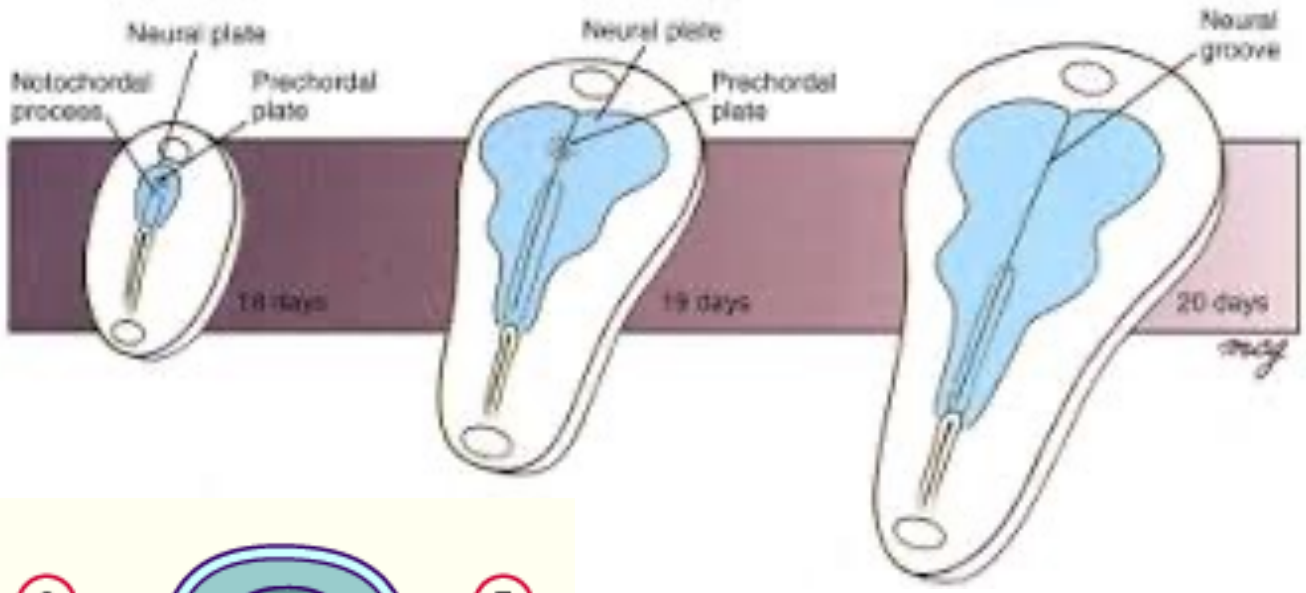
Formation of ectoderm, mesoderm, and endoderm

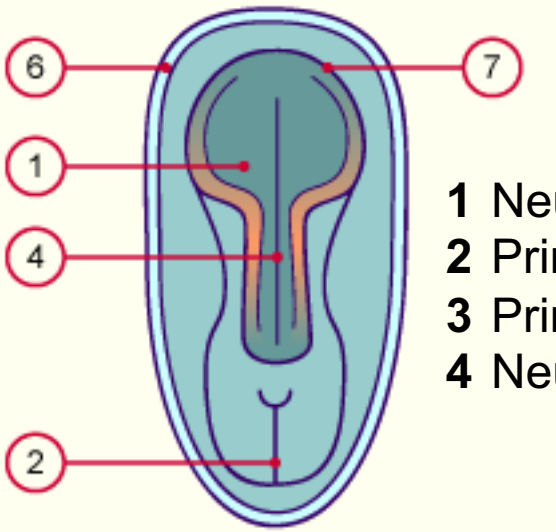


- epiblast undergo active mitosis along most of its surface and the newly formed cells migrate to the primitive streak, because primitive streak synthesis and release **fibroblast growth factors** (**FGF**)-8, (FIBR/O means fibrous tissue) this FGF-8 attract these newly proliferated epiblast cells.
- newly formed epiblast cells enter the primitive groove and pass into the space between the epiblasts and the hypoblast, thus forming a new intermediate layer of cells, the mesoderm.

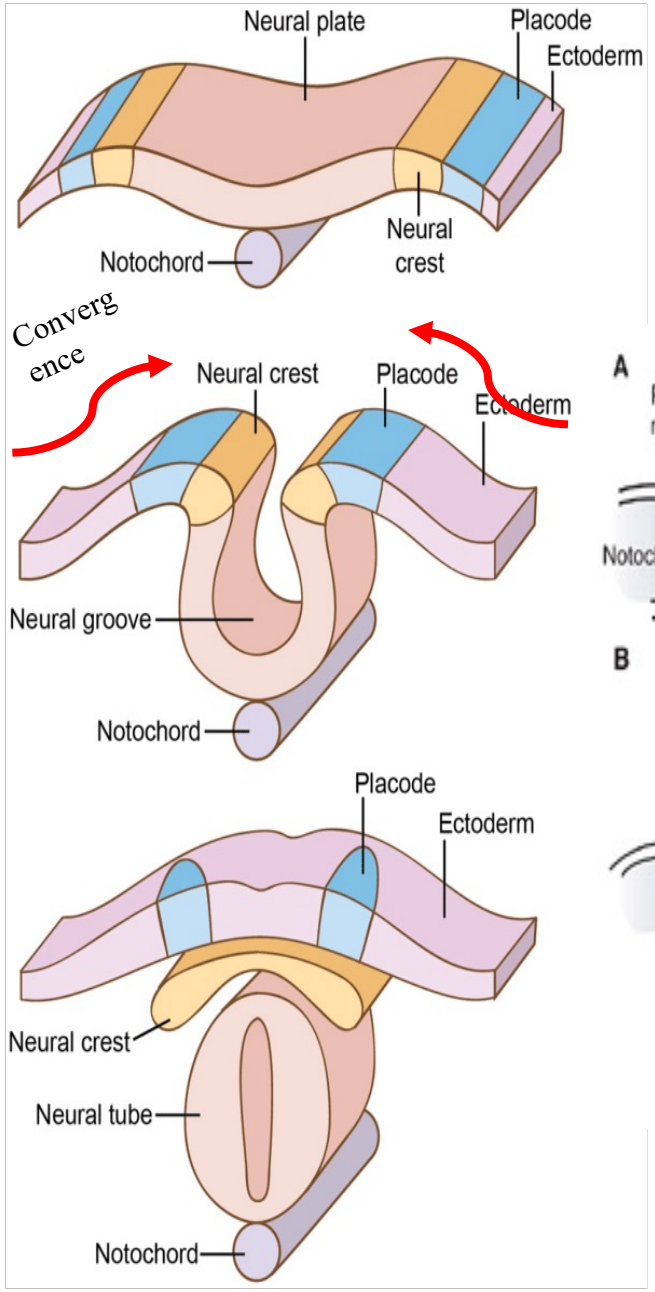
Some of these cells do not stop in the mesoderm space, but displace most of the original cells of the hypoblast, pushing the original cells of the hypoblast laterally. As this process is occurring, the epiblast is renamed the ectoderm and the new cell layer that replaces the hypoblasts is referred to as the endoderm.

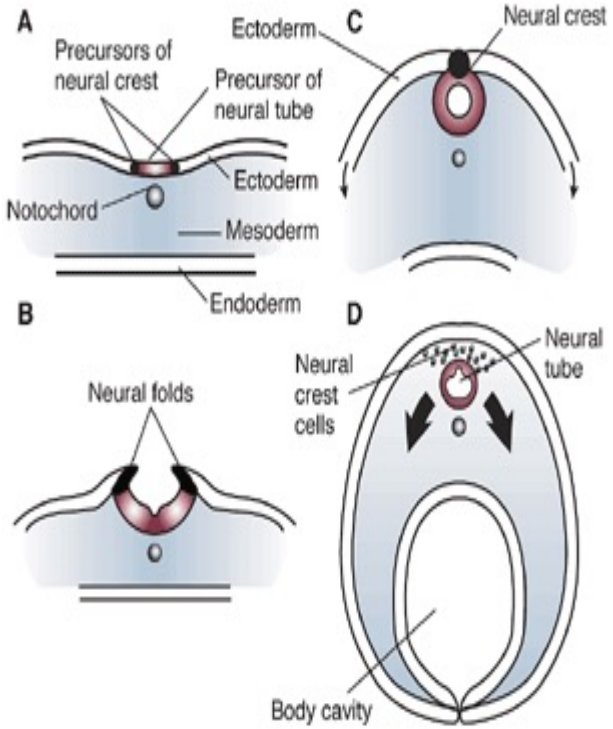
Neural plate

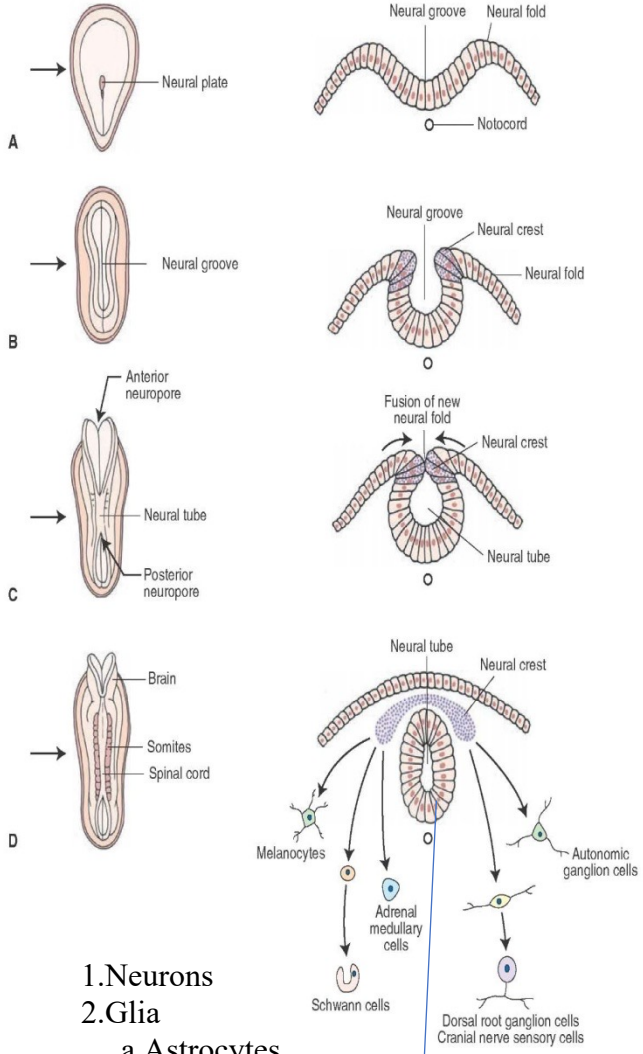




1 Neural plate
2 Primitive streak
3 Primitive nodes
4 Neural groove







1.Neurons
2.Glia
  a.Astrocytes
  b.Oligodendrocytes
  c.Ependymal cell

Neural plate

- a sheet of neuroectoderm called the neural plate and runs most of the length of the embryo.
- neural plate invaginates or to form a midsagittal groove, called neural groove.
- lateral edges of the neural plate encircle/converge/fuse form neural tube.
- a group of motile cells at the edges of the fold do not fuse into the tube and become neural crest cells to develop neural crest & migrate to specific locations throughout the body and head of the embryo.
- Neural tube: give rise to

Neuronal cells

- Neurons and
- macroglia
- of the CNS derive

non-neuronal cells

- choroid epithelium (lining the brain's ventricles)
- pineal gland
- septum pellucidum

Nervous System develops from 3 regions of ectoderm

- The most superficial germ layer of the embryo, called ectoderm, cells in dorsal region ectoderm, become neural cells and neural progenitor cells.

- 3 regions of ectoderm give rise to neurons, macroglia, and non-neuronal tissues
    1. **Neural tube**
    2. **Neural crest**
    3. **Placodes**

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Neural Fold

- The formation of the neural fold is initiated by notochord cells synthesis and release the signaling molecule called sonic hedgehog (SHH).
- As the neural plate begins to fold its cells also secrete SHH which continues to facilitate the process of neurulation.
- process of fusion starts at the midcervical level and proceeds anteriorly (rostrally) and posteriorly (caudally)
- two lips of the neural tube that contact each other expressing N-cadherins and neural cell adhesion molecules (N-CAMs) that permit the opposing lips to contact and adhere to each other thus forming the neural tube.

Neurulation

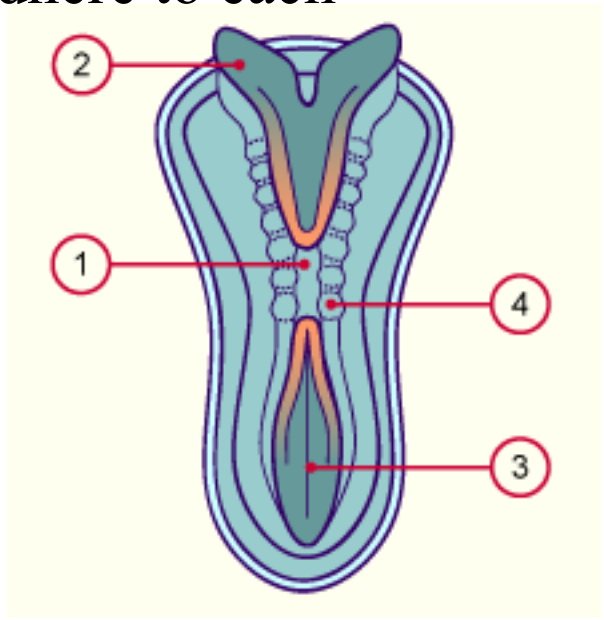
- Neurulation is a process of lateral edges of neural plate encircle to from neural tube is called Neurulation.
- Neurulation is the process whereby the embryo internalizes its developing nervous system
    - 1^{o} & 2^{o} neurulation
- Simply neural tube closure, termed neurulation
    - 1^{o} neurulation starts at a site in the rostral embryo that will become the neck, hours later
    - 2^{o} neurulation, initiates at a second site, located at the very rostral end of the neural tube.
    - some human populations, neural tube closure initiate at a third site, at the junction of the future hindbrain and midbrain.

neurulation

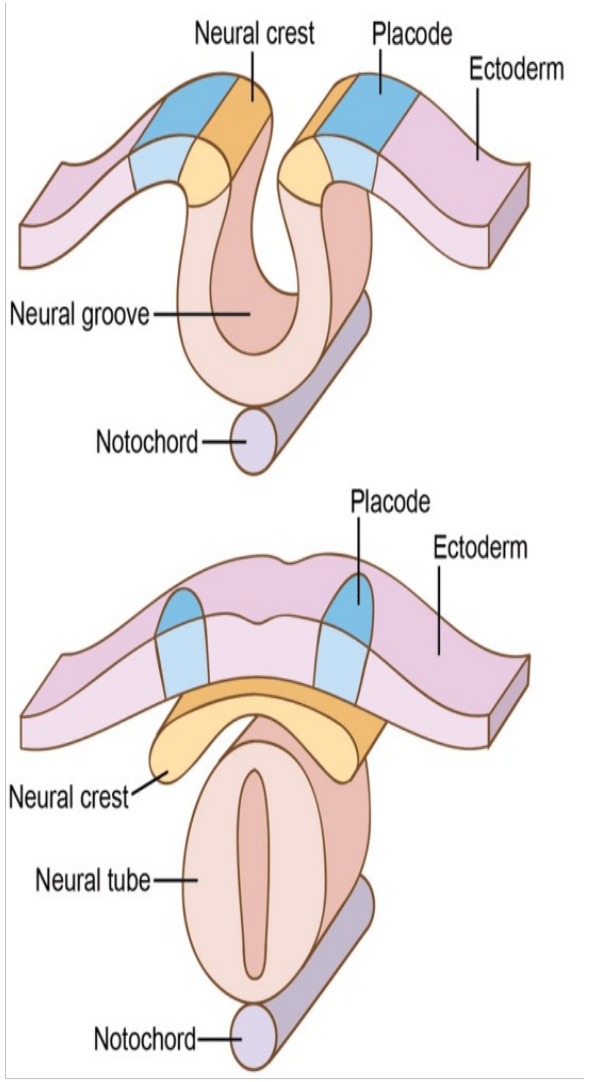
process of fusion starts at the midcervical level and proceeds anteriorly (rostrally) and posteriorly (caudally)

two lips of the neural tube that contact each other expressing N-cadherins and neural cell adhesion molecules (N-CAMs) that permit the opposing lips to contact and adhere to each other thus forming the neural tube.

1 Neural tube
2 Neural fold
3 Neural groove
4 Somites

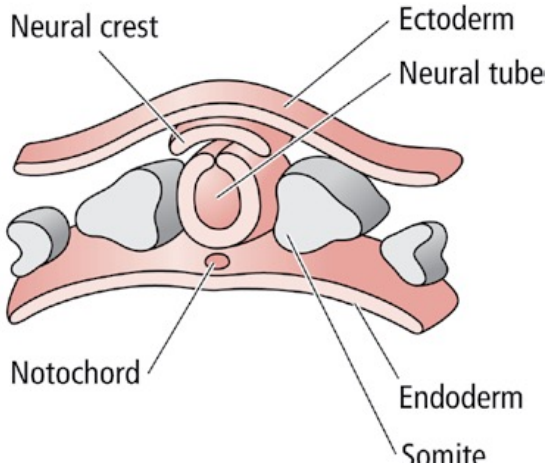


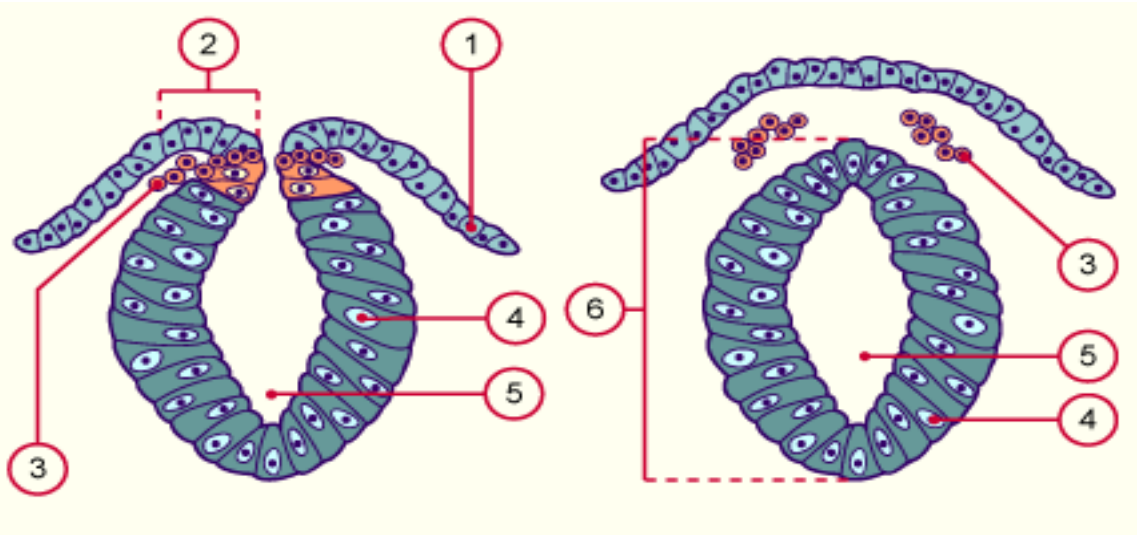
- closure proceeds bidirectionally
- tube closure initiates closer to the anterior than to the posterior end of the neuroectoderm
- the anterior opening or neuropore closes first
- the posterior opening or neuropore closes after 2 days of anterior neuropore closure.
- primary neurulation is complete when neural tube between the anterior and posterior neuropores is closed,
- The final regions of the neural tube to be closed are the anterior and posterior neuropores.
- The simultaneous fusions permit a separation of the neural tube from the overlying ectoderm, and complete internalization of the nervous system



Neural crest

- The neural crest is a narrow strip of cells at either edge of the developing neural plate.
- As the edges of the neural folds meet each other, some of their cells do not participate in the formation of the neural tube instead they form a narrow strip of cells, the **neural crest**
- The transformation of neural tube cells into neural crest cells depends on intermediate concentration of BMP(bone morphogenetic protein)4 from notochord. (high conc BMP4 give rise to neural tube).
- In addition to BMP4, the transcription factors **FOXD3** (**fork head box 3D protein**) and the zinc finger transcriptional repressor protein **Snail** (Snail because it was first isolated in snails) are required to commit these cells to becoming neural crest cells.





Failure of neural tube closure is a common birth defect.

- This birth defect is called Neural Tube Defects (NTDs).
- Some embryos with NTDs never come to term, get aborted in the 1st trimester.
- other cases, the neural tube forms but remains open but not always a severe one.