Brain Development

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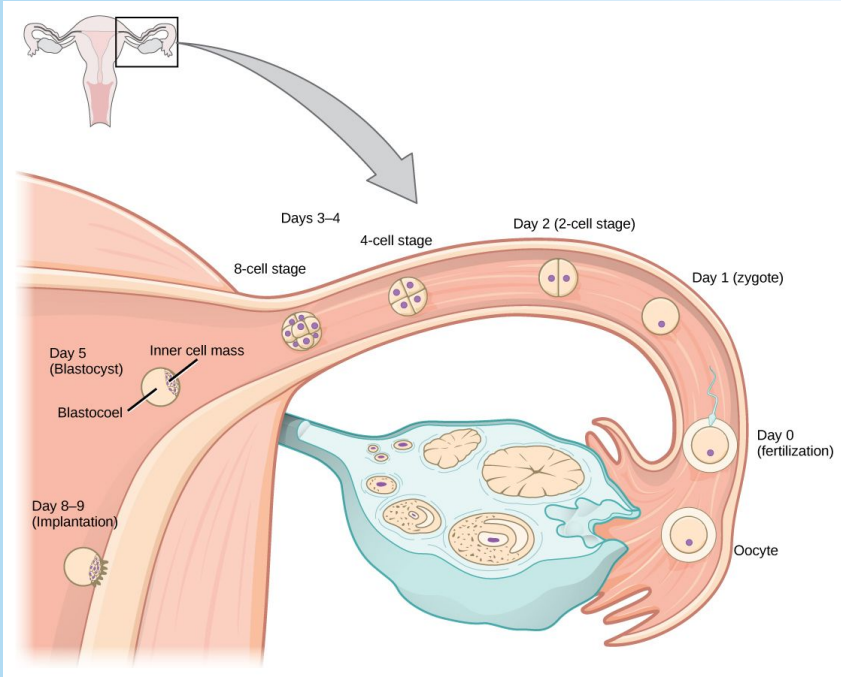
Prologue:

An oversimplified recap of how we got here

Day 0: Fertilization/conception

- Fertilization: when egg & sperm meet in the fallopian tube → form zygote
- Zygote → morula → blastocyst as travels down fallopian tube



https://open.lib.umn.edu/humanbiology2e/chapter/5-5-human-pregnancy-and-birth/ *credit: Ed Uthman*

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Day 6 - 14: Implantation & formation of fetoplacental unit

- Implantation: When blastocyst penetrates endometrium
- Blastocyst has 2 layers of cells
    - Outer trophoblasts: Penetrates the uterine wall
        - Trophoblast divides into syncytiotrophoblast & cytotrophoblast
            - Syncytiotrophoblast: development of placenta & secretion of b-HCG
            - Cytotrophoblast: forms chorionic cavity
    - Inner embryo-blasts: make the future fetus
        - Has bilayered embryonic disc: Epiblast & hypoblast

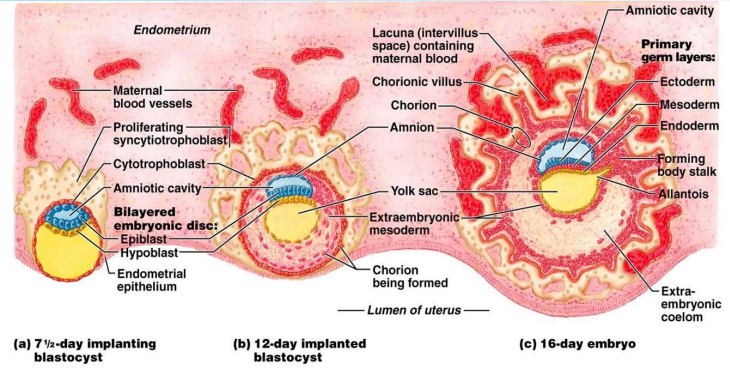
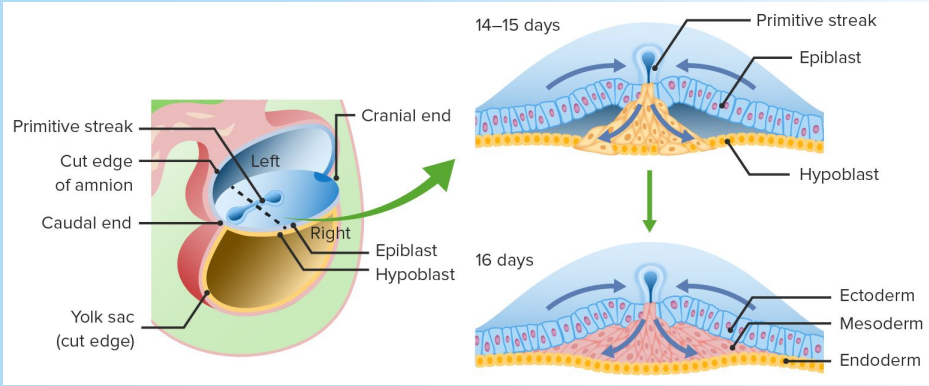


Image Source: Austin Community College District

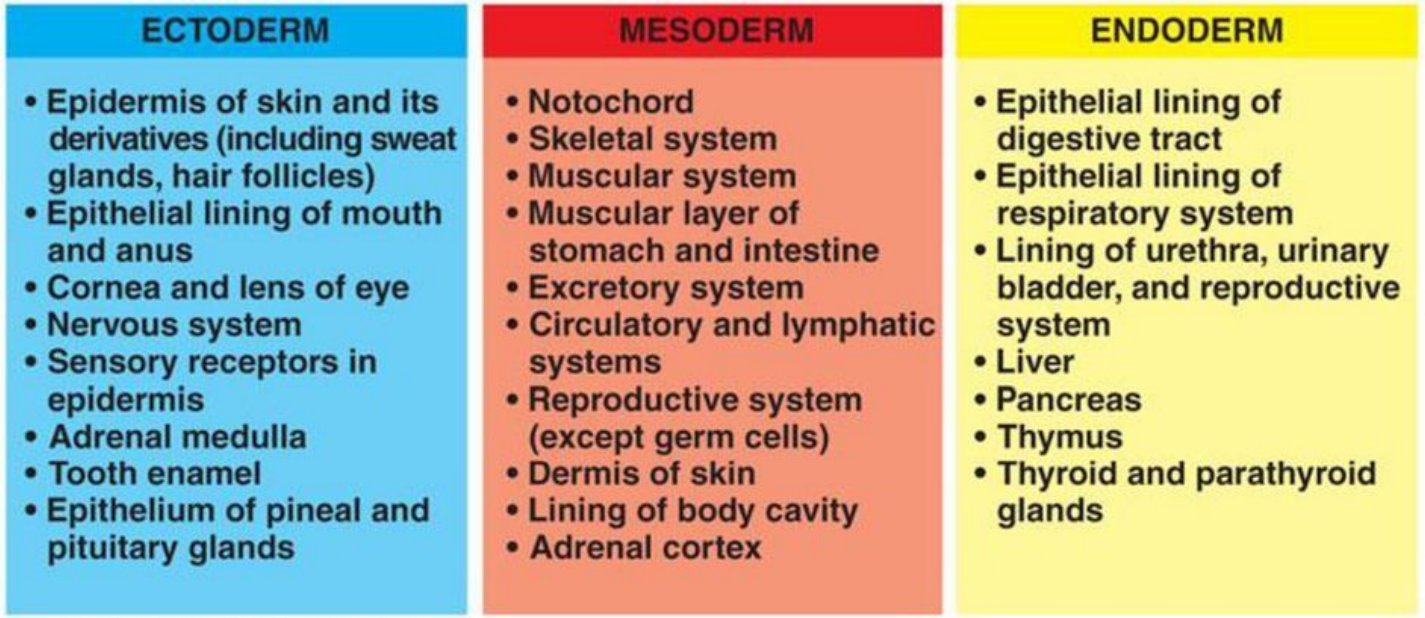
https://microbenotes.com/implantation-process-events-significance/

Week 3: Gastrulation

- Gastrulation: When the bilayered embryonic disc turns into a trilayered disc
  - How: Epiblast cells invade the primitive streak → replaces hypoblast and makes mesoderm
  - Makes the 3 germ layers: Ectoderm, endoderm, mesoderm
- The 3 germ layers give rise to all tissues and organs in the body



https://www.lecturio.com/concepts/gastrulation-and-neurulation/

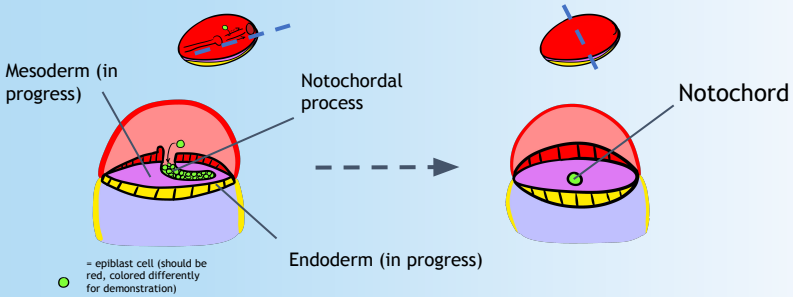


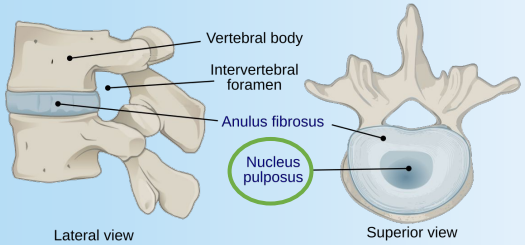
Notogenesis: Week 3

The formation of the notochord

Notogenesis

- Formation of the notochord:
  - How: Meanwhile gastrulation, epiblast cells invade the mesoderm and form a canal, eventually forming the notochord
- Notochord is responsible for inducing neurulation (formation of the neural tube)
- The nucleus pulposus of intervertebral disk is the remnant of the notochord



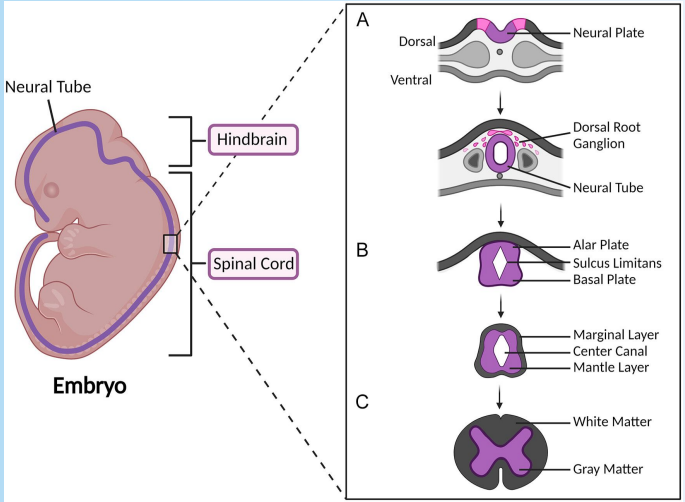


Neurulation: Week 3 - 4

Formation of the neural tube

Neurulation

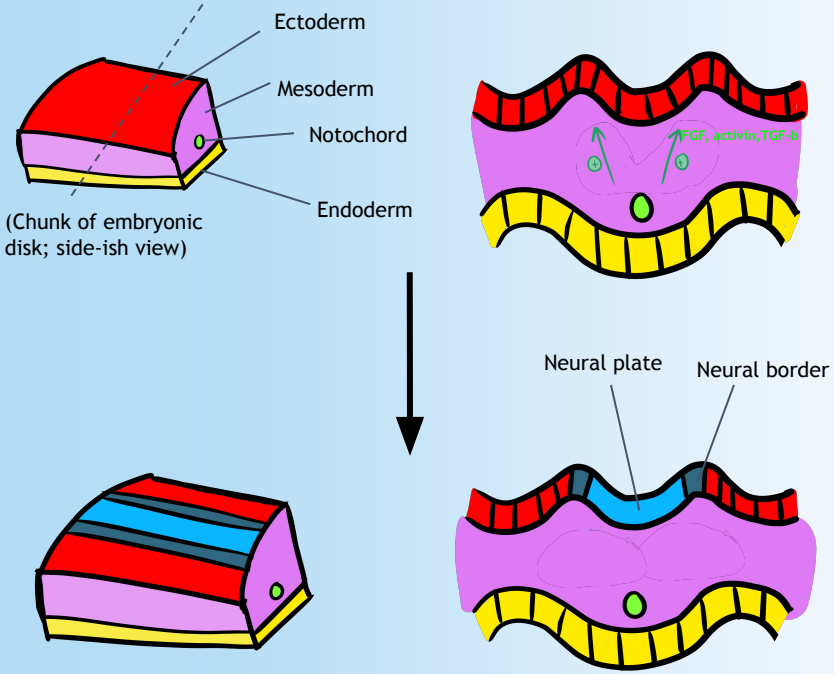
- Neurulation: Formation of the neural tube → future brain & spinal cord
- Occurs after notogenesis
- How?
  - **Step 1:** Notochord stimulation of ectoderm → neuroectoderm
  - **Step 2**: Neuroectoderm folding into the neural tube
  - **Step 3:** Migration of neural crest cells to different parts of the body



https://journals.sagepub.com/doi/10.1177/09636897241241998?icid=int.sj-full-text.similar-articles.9

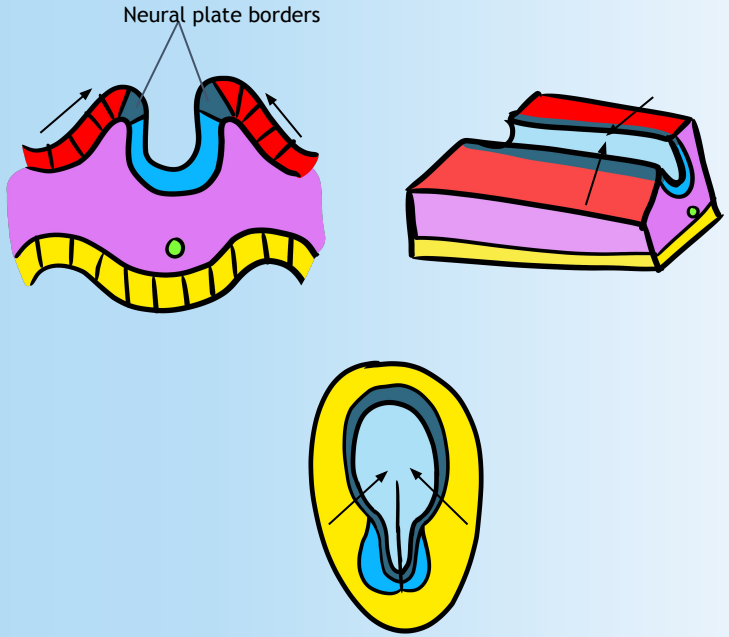
Step 1:

- The notochord releases fibroblast growth factor (FGF), activin, and transforming growth factor (TGF-b) to overlying ectoderm
- Overlying ectoderm → neuroectoderm (consists of a neural plate and 2 borders)



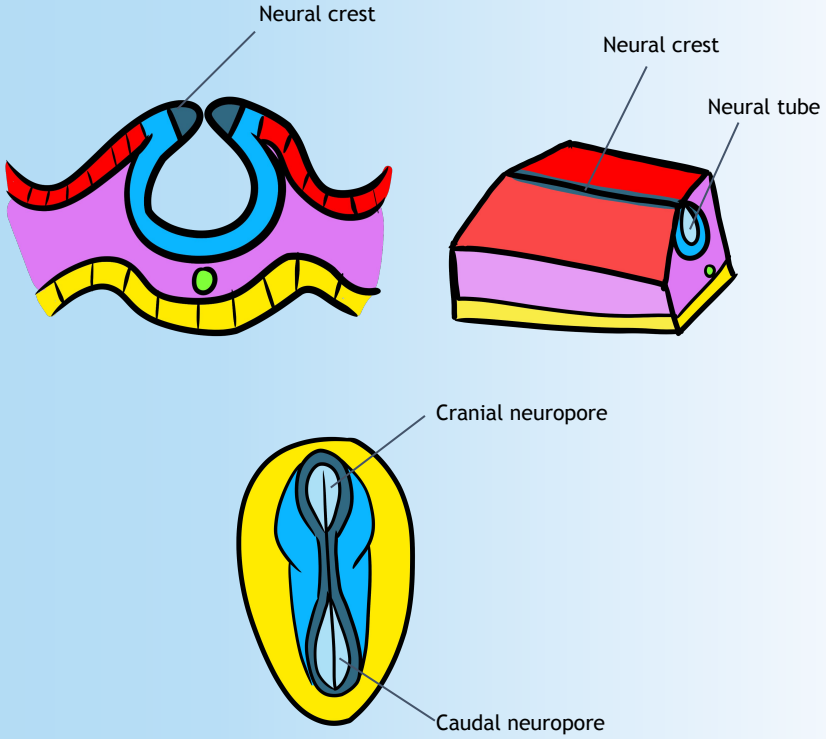
Step 2:

- The neural plate borders move inwards towards each other, causing the neuroectoderm to start folding into a tube



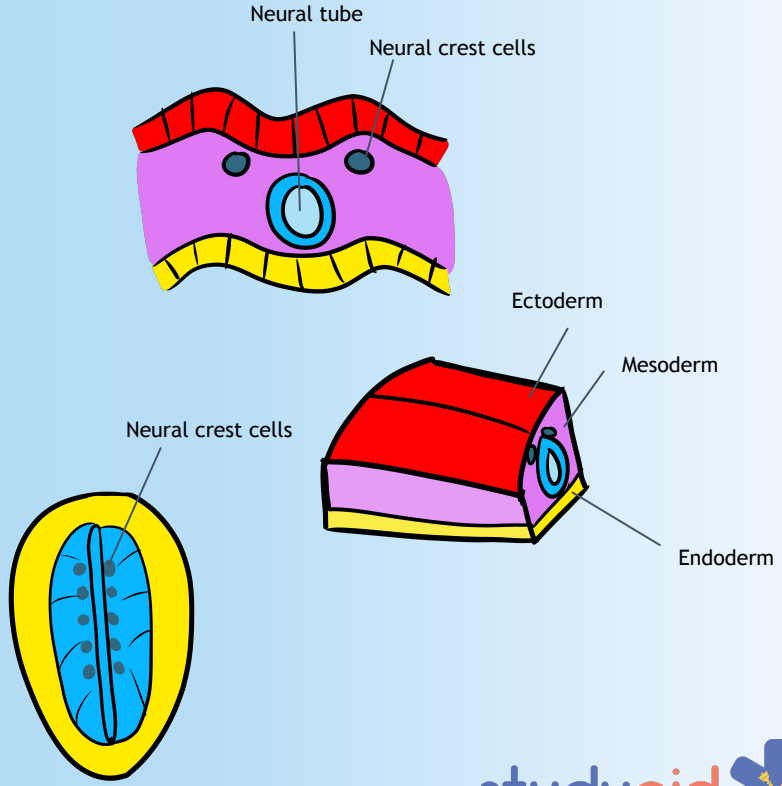
(Top view: ectoderm & mesoderm not shown)

- As the neuroectoderm continues to fold, neuropores are created
- Neuropores: openings in the neural tube
  - Rostral neuropore: towards the head
  - Caudal neuropore: towards the tail end
  - Failure or abnormality of neuropores to close will cause neural tube defects
- When the neural borders finally meet, they will create the neural crest



Step 3:

- Neural tube finally closes
- The neural crest releases neural crest cells which go to different parts of the body
    - Neural crest cells make:
        - Peripheral nervous system neurons
            - Schwann cells,
            - Dorsal root neurons
            - Autonomic ganglia
        - Melanocytes
        - Cranial bones
        - Adrenal medulla
        - And more…

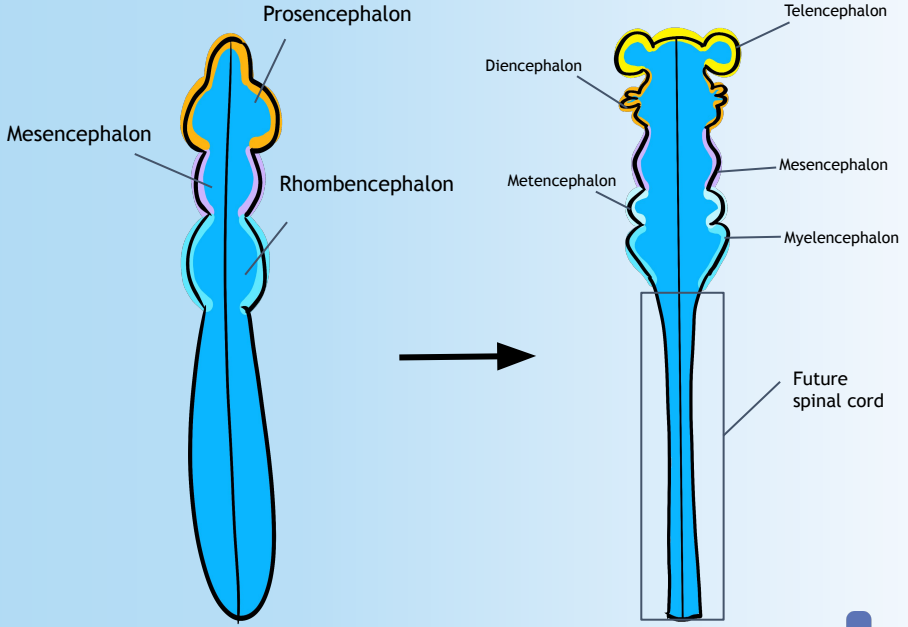


Cerebral vesicle differentiation & fetal spinal cord: Week 5

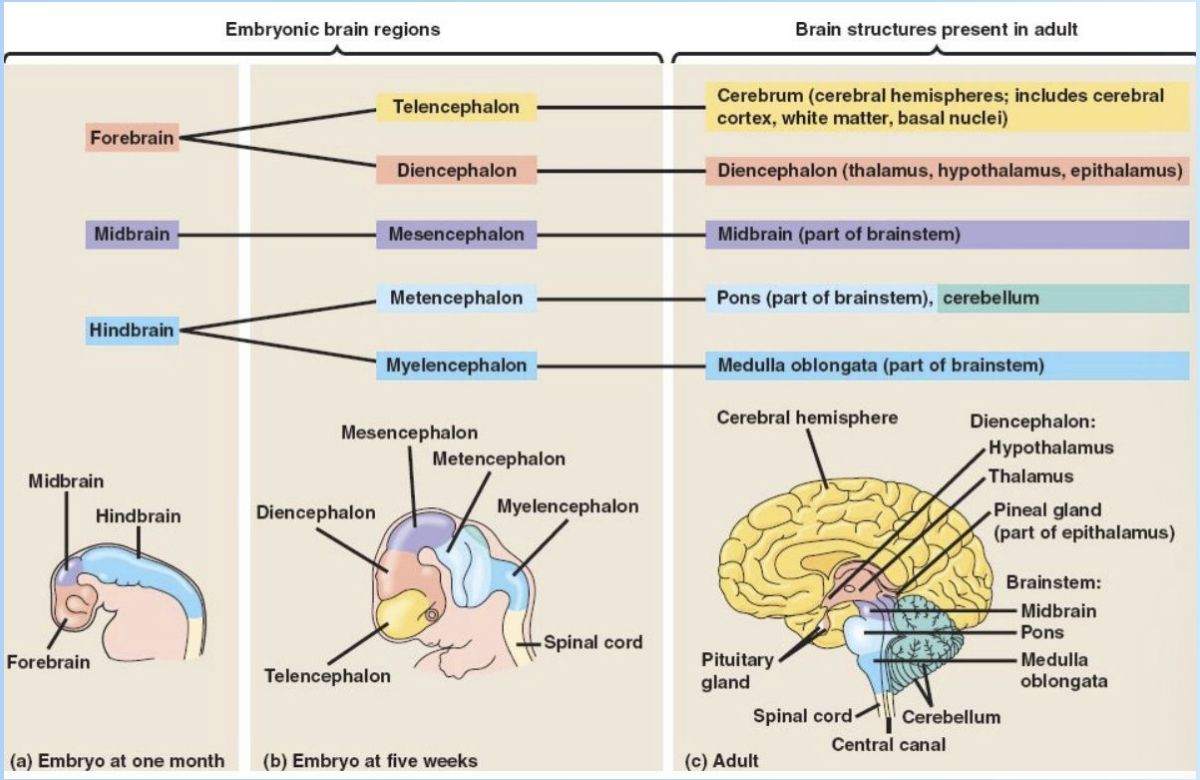
The formation of different structures of the brain and the spine

Cerebral Vesicle differentiation

- Gives rise to different brain structures
- Step 1: The rostral end of the neural tube differentiates into the prosencephalon, mesencephalon, and rhombencephalon
- Step 2: Continued differentiation
  - Prosencephalon → Telencephalon & diencephalon
  - Mesencephalon stays the same
  - Rhombencephalon → Metencephalon & myelencephalon



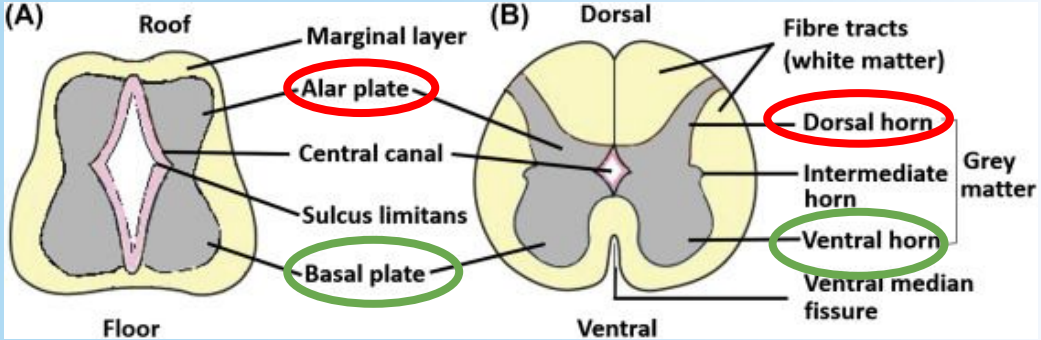
What do the five cerebral vesicles give rise to?



Pearson Education, Inc

Fetal spinal cord

- The fetal spinal cord:
  - Alar plate gives rise to the dorsal horn
    - Dorsal horn carries sensory tracts
  - Basal plate gives rise to the ventral horn
    - Ventral horn carries motor tracts

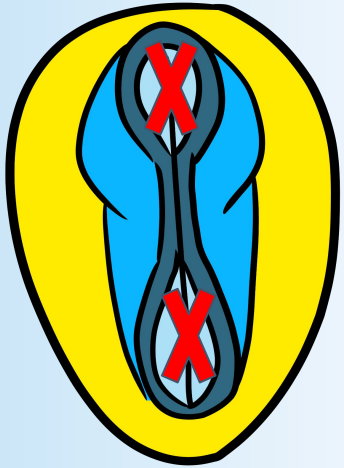


https://www.sciencedirect.com/science/article/abs/pii/B9780128052990000026

Clinical Correlation: Neural tube defects

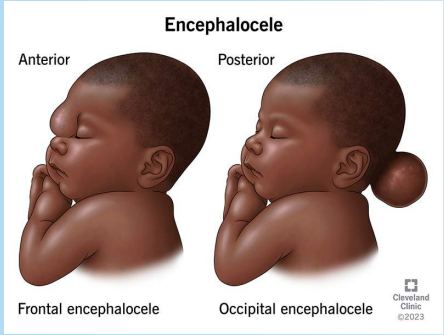
What are neural tube defects (NTDs)?

- Neuropores of the neural tube doesn’t close during neurulation
- Causes:
  - Folic acid (B9) deficiency
  - Genetics
- How to detect?
  - Screening: high AFP (alpha-fetoprotein) in maternal serum
    - Only in open NTDs (so not spina bifida occulta)
  - USG
  - Amniocentesis: high levels of AFP and AchE (acetylcholinesterase)
    - Only in open NTD

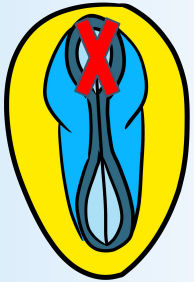


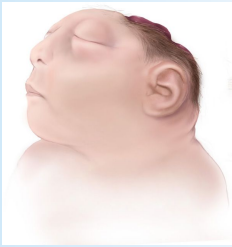
Failure of rostral neuropore closure

- Encephalocele:
  - Occipital or frontal bone defect → herniation of brain tissue
  - Covered by skin
  - Lethal in severe cases
- Anencephaly:
  - Complete absence of rostral neuropore closure → absence of forebrain and the skullcap
  - Incompatible with life



Encephalocele
https://my.clevelandclinic.org/health/diseases/encephalocele





Anencephaly
https://en.wikipedia.org/wiki/Anencephaly

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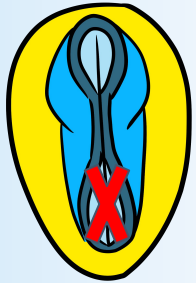
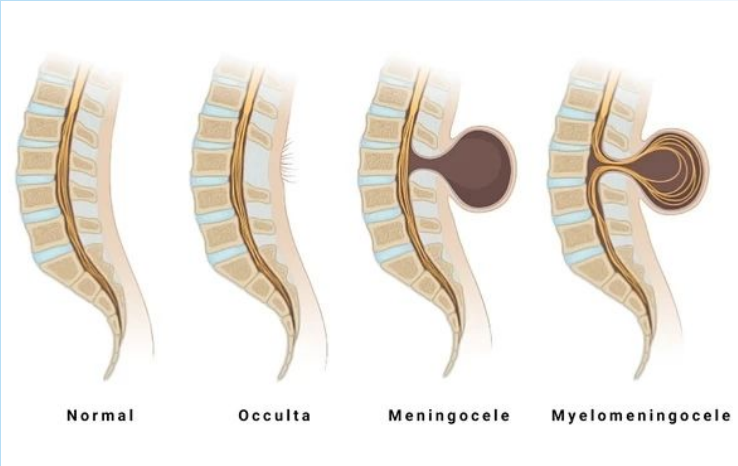
Failure of caudal neuropore closure



- Spina bifida occulta:
  - Most common closed NTD
  - Vertebral bone defect with everything else intact
  - Asymptomatic or mild signs
    - Hairy patch, dimple, or swelling where the vertebra is missing
- Meningocele:
  - Vertebral bone defect + herniation of meninges
- Myelomeningocele:
  - Most severe
  - Vertebral bone defect + herniation of meninges and spinal cord
  - Patients may have sensory deficits, bladder & bowel dysfunction, hydrocephalus (CSF accumulation in the brain) or motor deficits



https://storymd.com/journal/5mryynpuzj-spina-bifida/page/k8zg2lt55lv-what-are-the-types-of-spina-bifida

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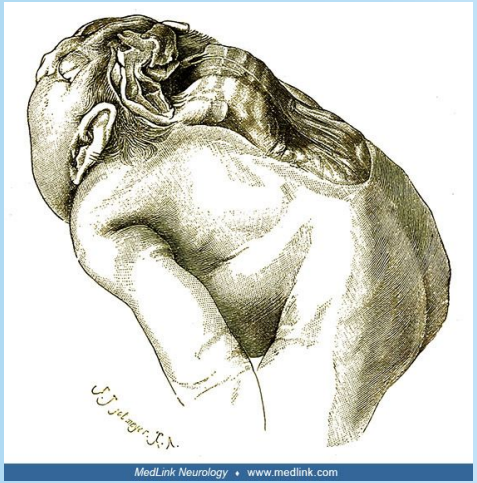
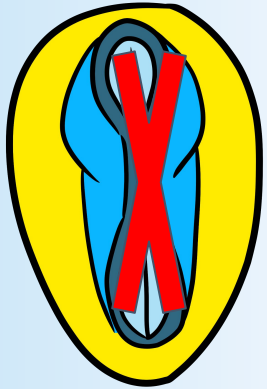
Failure of both neural pore closures

- Craniorachischisis
  - Ancepehlay + Spina bifida
  - Most severe NTD
  - Fatal



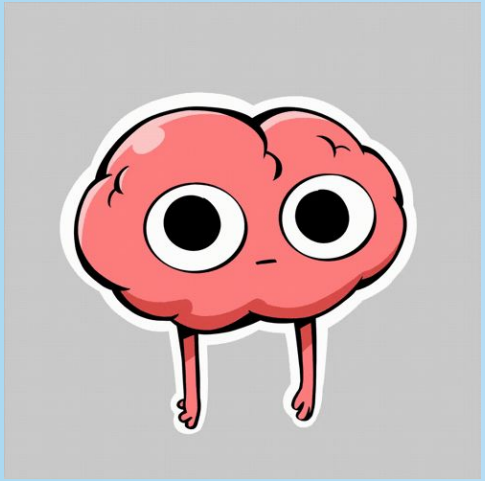


Recap

Embryological structure	Final form or remnant
Notochord	Nucleus pulposus of intervertebral disk (r)
Neural tube	Brain & spinal cord
Ectoderm	Nervous system, skin, hair, nails, adrenal medulla
Mesoderm	Skeletal system, muscular system, circulatory system, reproductive system, kidneys, lungs (epithelial layers), spleen
Endoderm	Endocrine system, GIT, liver, pancreas, urethra, bladder, lungs (inner layers)

Embryological structure	Final form / remnant
Neural crest cells	Peripheral nerve cells (Schwann cells, autonomic ganglia, dorsal root neurons), melanocytes, cranial bones, adrenal medulla
Telencephalon	Cerebral hemispheres (Cerebral cortex, white matter, basal ganglia)
Diencephalon	Epithalamus, thalamus, hypothalamus
Mesencephalon	Midbrain
Metencephalon	Pons & cerebellum
Myelencephalon	Medulla oblongata

Thank you!



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