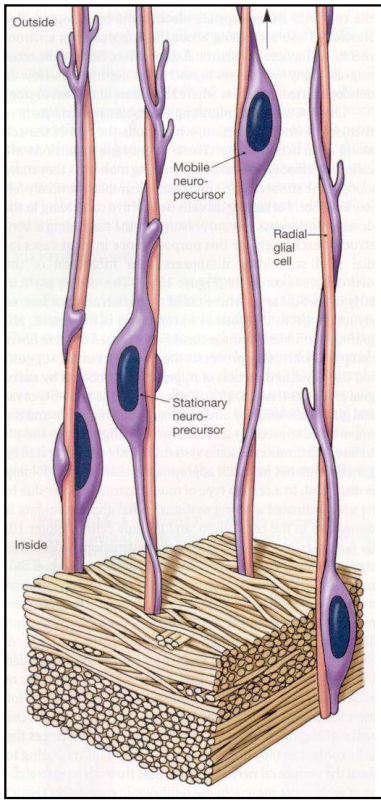



# Nervous System Development

# Early Embryonic Stages

Following fertilization, the embryo goes through several stages:

- zygote
- blastula
- gastrula

By this time, you already have the 3 layers

- endoderm, mesoderm, and ectoderm

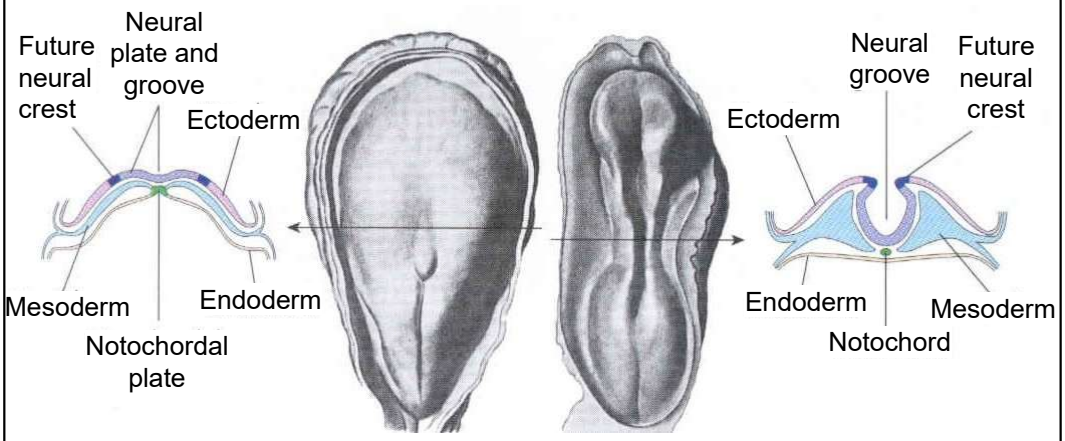
Then you finally get to the most exciting part:

Neurulation

# Steps in Neurulation

Day 18:

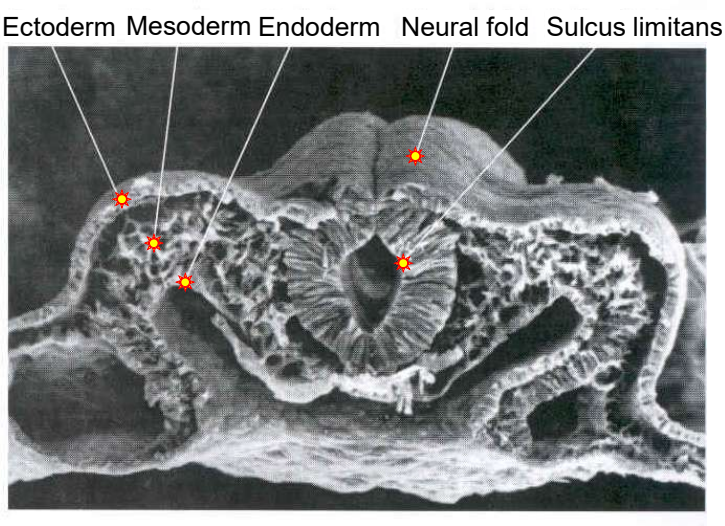
Chemical signals from mesoderm induce thickening of overlying ectoderm to form **neural plate**




Day 20:

Plate folds in along central axis to form **neural groove**

# Picture of early tube closure



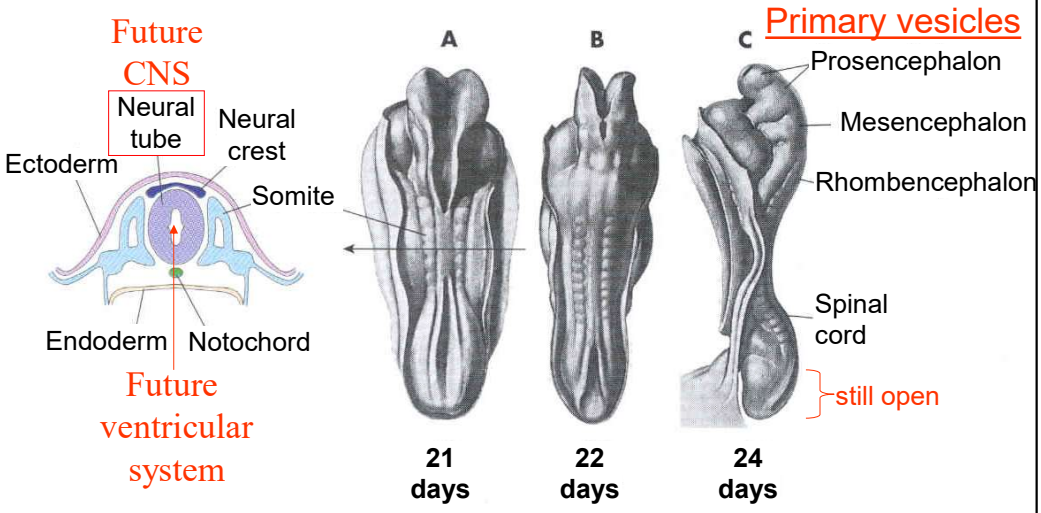

Note that neural folds are just touching, and tube has not yet separated from rest of ectoderm

# Soma and Viscera

- Soma
  - Body wall
  - structures derived from embryonic ectoderm
    - epidermis, CNS
  - mesodermal connective tissue of soma
    - dermis, skeletal muscle, bone, outer body cavity lining
  - Innervated by somatic nerves

- Viscera
  - structures derived from embryonic intermediate mesoderm
  - urinary system, gonads, gut, lungs, liver
  - Innervated by visceral nerves

# Fusion starts at cervical level and quickly proceeds rostrally and caudally



# Movies




Movie credit: David Shook

Movie 1: Xenopus laevis Vegetal View of Gastrulation & Neurulation: (15.0 hours elapsed, 48 minutes/second). View from vegetal pole, dorsal is up. Gastrulation takes about 8.5 hours, neurulation about 6.5 hours. Initally, only dorsal bottle cells are apically constricted; apical constriction (& bottle cell formation) spread laterally and then ventrally around the blastopore. Involution begins dorsally. Blastopore closure follows. Neural fold formation and closure follow. Beginning of brachial neural crest migration is apparent at end of movie. Refer to figures 1 & 2 in Gastrulation in Amphibians chapter.

Movie shows gastrulation and neurulation viewed from the vegetal pole, the future dorsal side at the top. Note the dramatic involution of the IMZ, which forms an annulus or ring of cells surrounding the large central disc of vegetal endodermal cells at the center of the vegetal pole. The bottle cells, marking the initiation of involution, have already formed mid-dorsally as indicated by the black pigment accumulation. Note that the dorsal IMZ, region above these bottle cells rolls over the blastoporal lip and disappears inside; subsequently this involution proceeds laterally, on both sides, and finally at the midventral line. As the IMZ involutes, it also extends posteriorly and converges around the circumference of the blastopore, but does so inside, out of sight. As it does so, note that the posterior neural tissue likewise converges and extends in the same fashion, on the outside; together these convergent extension movements squeeze the blastopore shut and simultaneously elongate the anterior-posterior axis of the embryo, pushing the future tail away from the head. Note that the converging and extending neural plate simultaneously rolls up to form a neural tube. See Keller, 1975,1976; Keller et al., 1991.

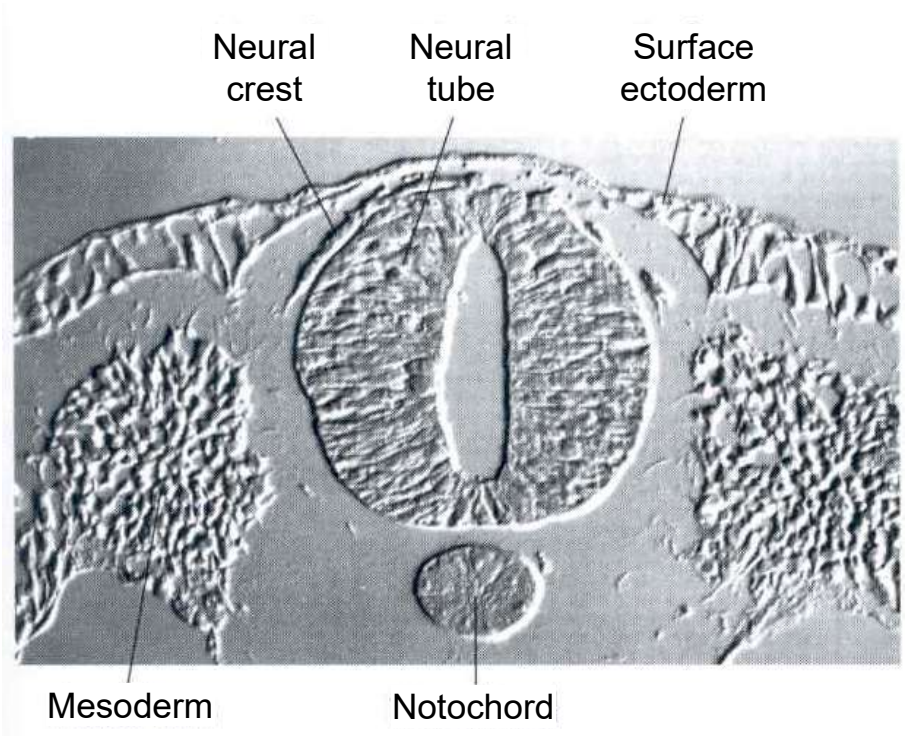
# Human neurulation movies

Human Neurulation Movie

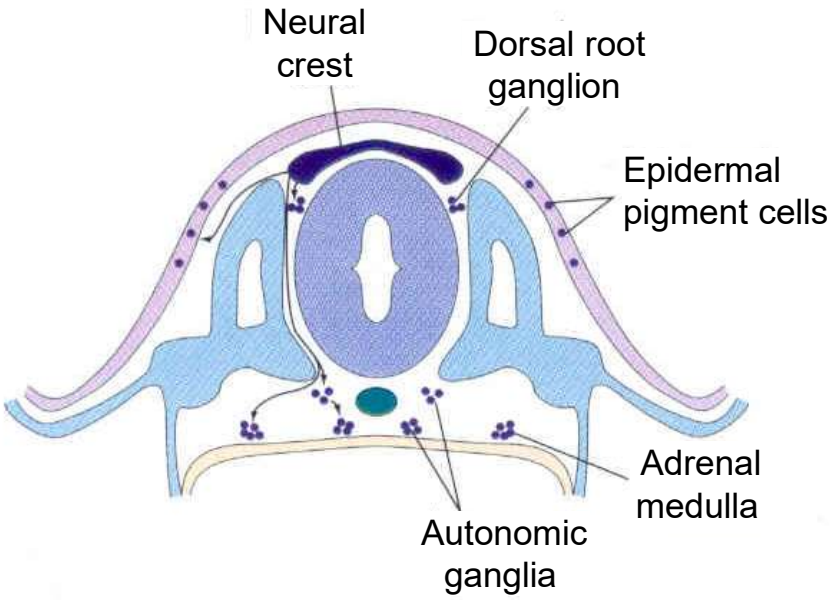
Human secondary Neurulation Movie

Movie credit: Mark Hill

http://embryology.med.unsw.edu.au/Movies/Humemb.htm

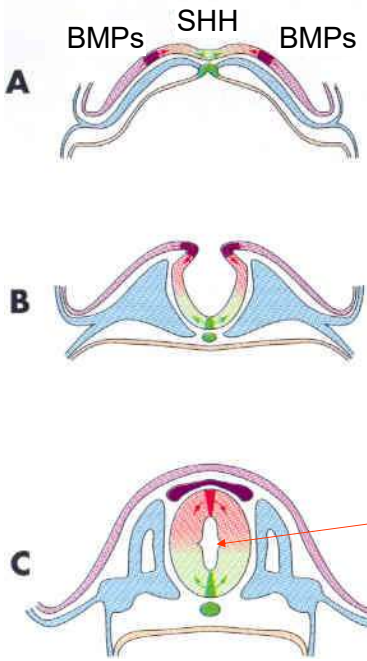

Neural crest
Neural tube
Surface ectoderm
Mesoderm
Notochord

# Neural crest derivatives



# Signals from ectoderm and notochord induce differentiation of dorsal and ventral neural tube

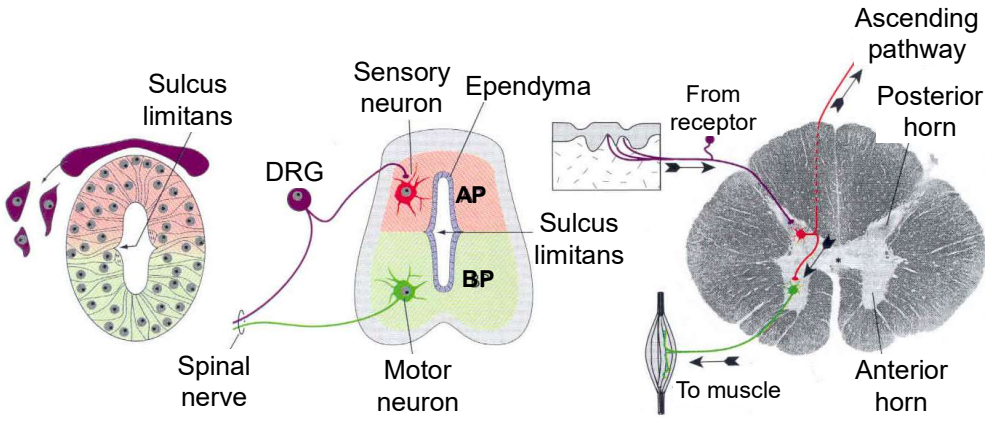
~Day 18




Bone Morphogenetic Proteins

Sonic Hedge Hog

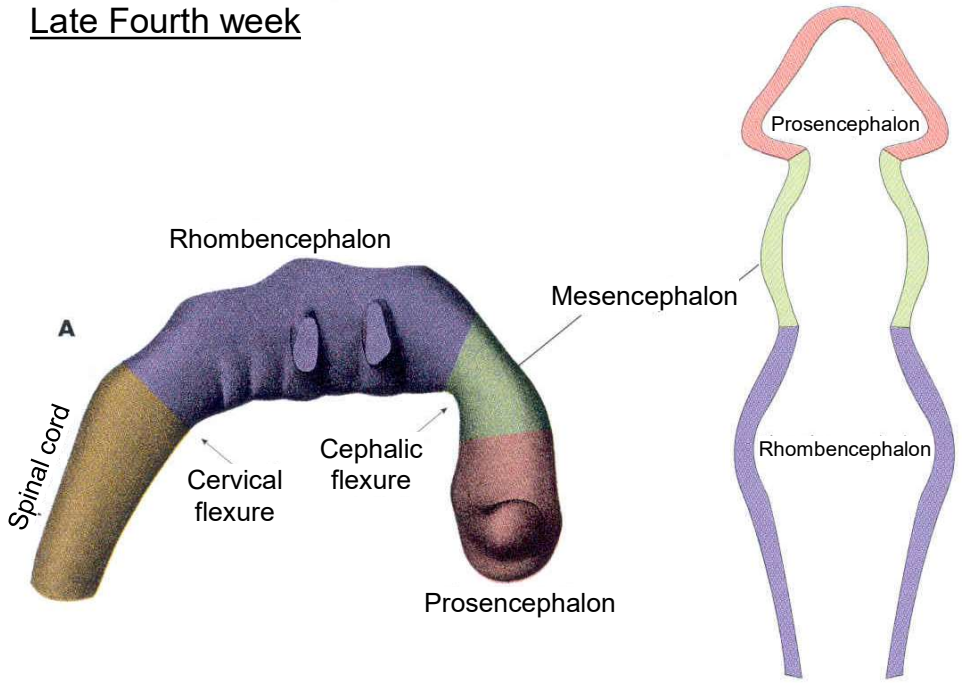
# Spinal cord development

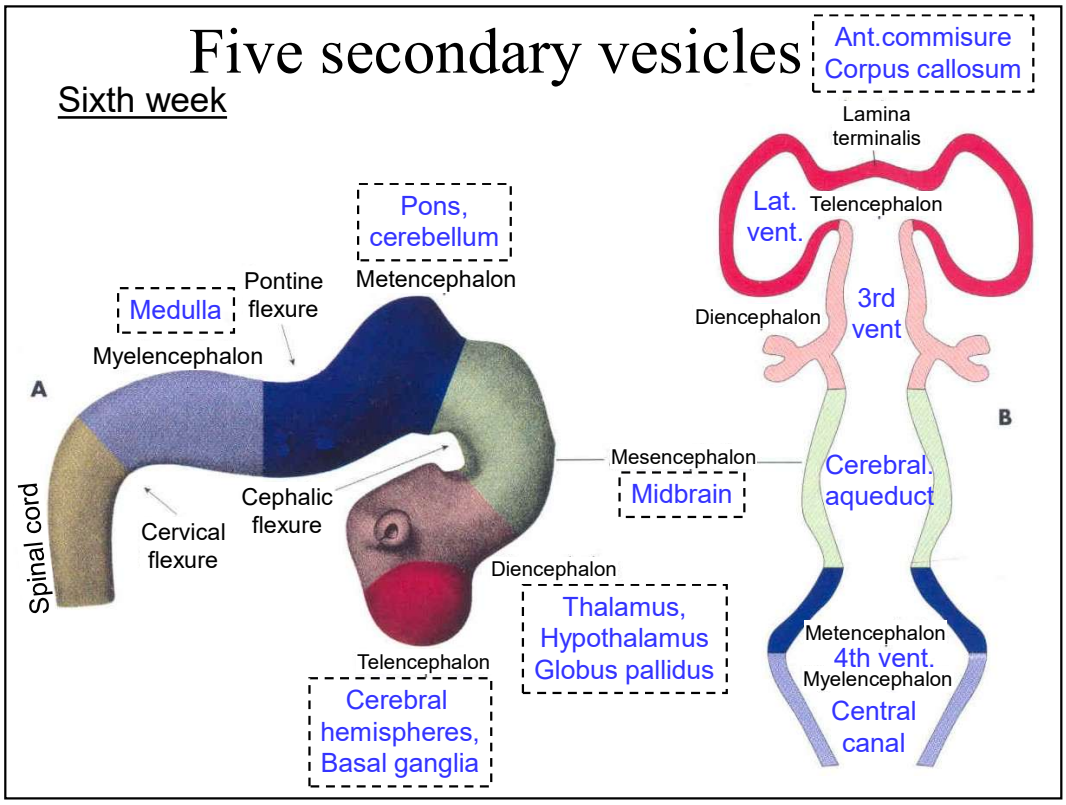



**AP = Alar plate**
**BP = Basal plate**

# Three primary vesicles

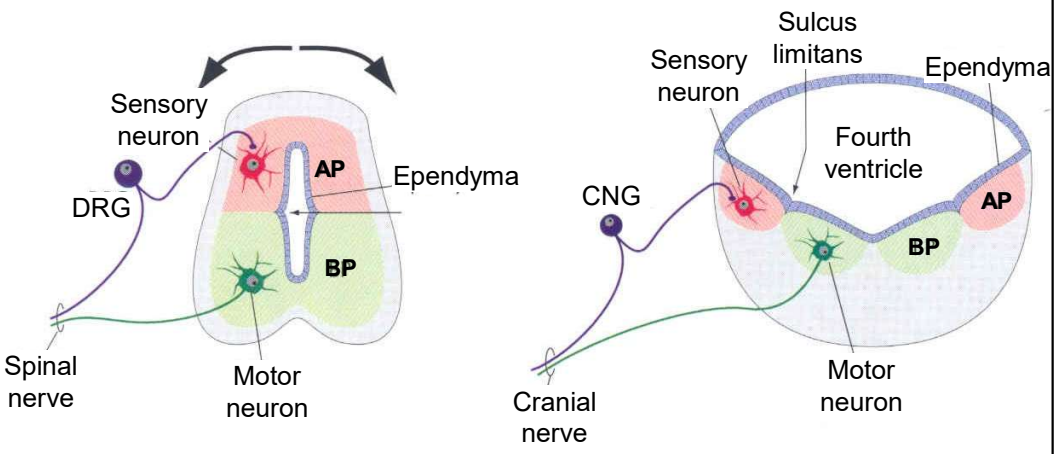
Late Fourth week





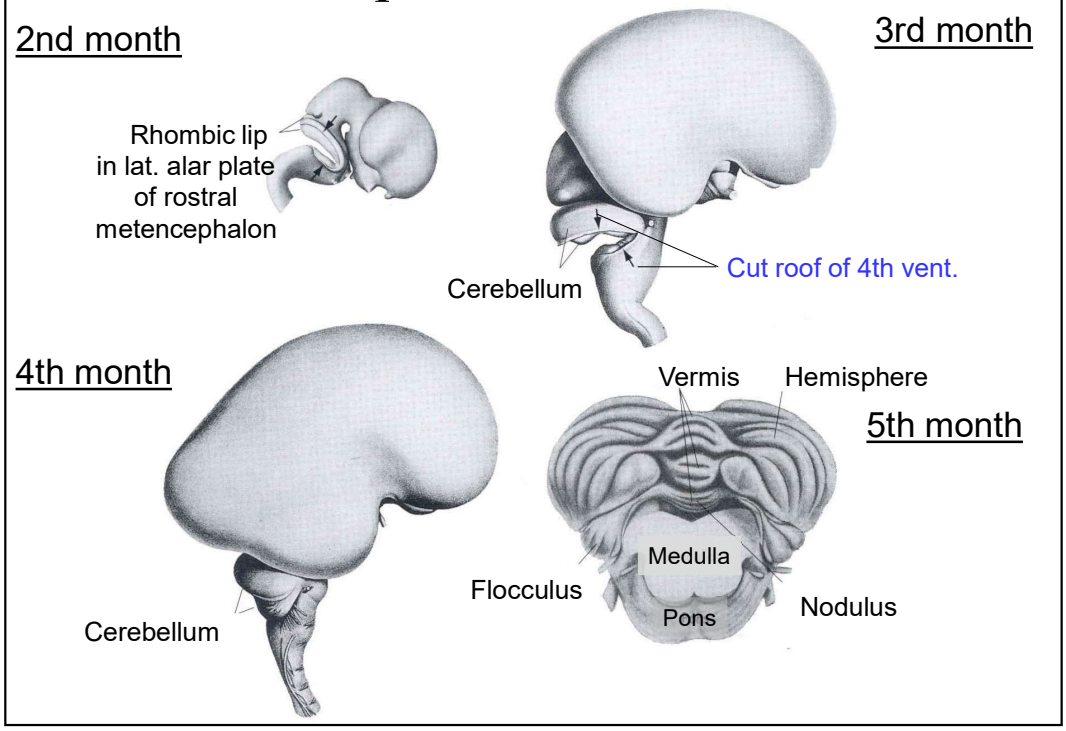

Note optic cup on side of diencephalon

# Floor of fourth ventricle

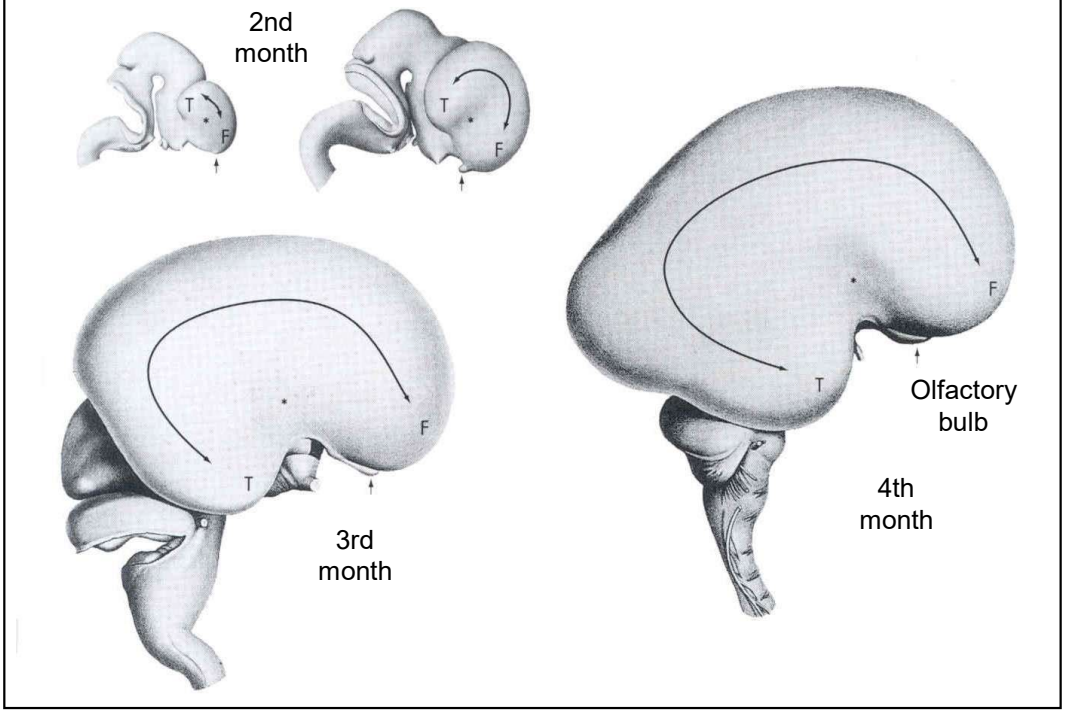



At level of Pontine flexure

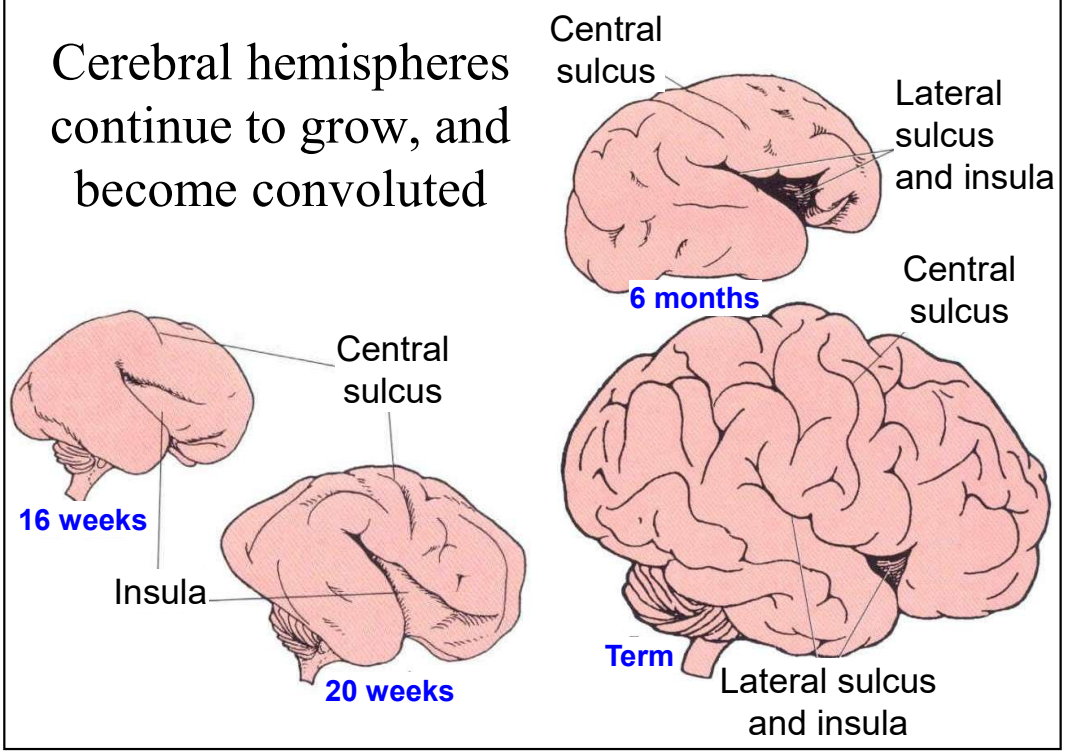
# Development of cerebellum



# Cerebral hemispheres

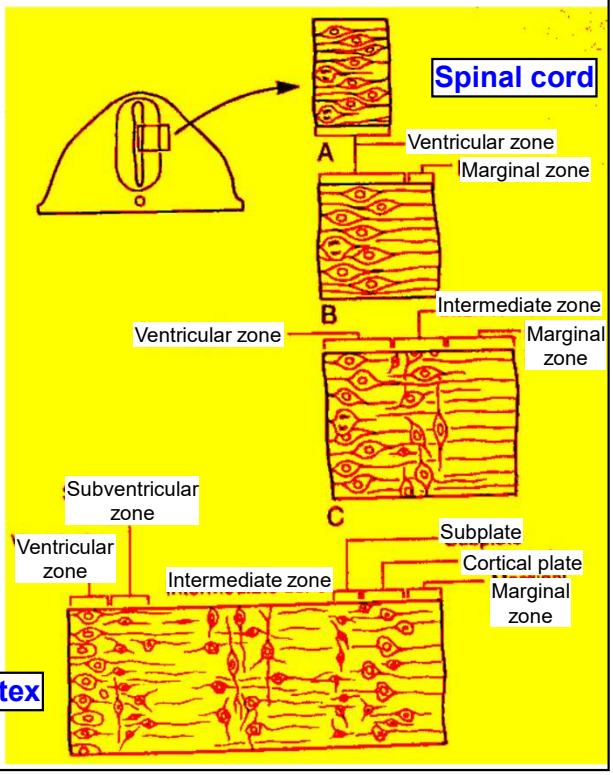


Cerebral hemispheres continue to grow, and become convoluted

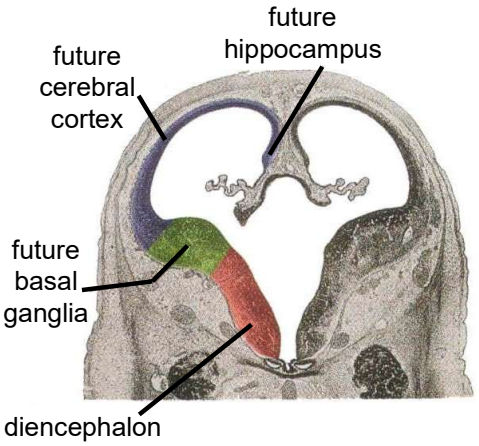


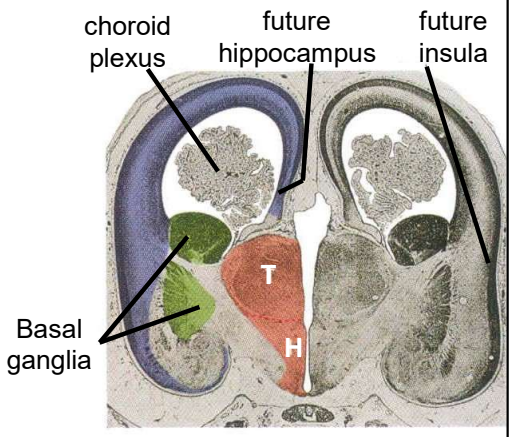
# Cells Proliferate and Migrate outwards along radial glia from the ventricular zone to form layers

- Variations in different parts of CNS
  - Cerebrum and cerebellum are more complex than spinal cord



# Cross section through telencephalon and diencephalon at 2nd and 3rd month



# What can go wrong?

•3% of births are associated with major malformations of the CNS, but most of these fetuses/infants do not survive

- •75% of spontaneously aborted fetuses and 40% of infants who die in 1st year have major CNS malformations

Defective closure of neural tube (= neural tube defect)

- •Incidence 1:1000
- •second most common type of congenital abnormality after congenital heart disease
- •Detect *in utero* by presence of α-fetoprotein
- •prevent with folic acid supplement

# Defective closure of neural tube

• Spina bifida: spinal cord open to skin

Meningocele: a bulge in the lumbosacral area consisting of a meningeal sac protruding through the bone defect.

Meningomyelocele: the sac contains malformed spinal cord tissue.

• Myelomeningocele: severe form of spina bifida including displacement of cerebellum and caudal brainstem

# Defective closure of neural tube

## Arnold-Chiari malformation

The lower part of the brain or cerebellum can be abnormally positioned so that it extends down through the foramen magnum

# Defective closure of neural tube

- Craniorachischisis: (fatal) CNS appears as an open furrow on dorsal surface of head and body

http://neuropathology-web.org/chapter11/chapter11bNTD.html

## Defective closure of neural tube

•Exencephaly:
The brain protrudes through a defect in the cranial vault

•Occipital Encephalocele

# Defective closure of neural tube

•Anencephaly: (rostral)

Cerebral hemispheres mostly absent, neural tube open to skin. Starts as exencephaly, gradually destroyed because of mechanical injury and vascular disruption.

Lateral and frontal views of anencephaly: Note associated cranial and facial abnormalities

# What can go wrong?

Defective secondary neurulation

- •Overlying skin surface may show dimpling, hairiness, or discoloration
- possible tethering of caudal spinal cord, cysts, and tumors

Other

- Holoprosencephaly: (rare, usually fatal) Partial or complete failure of the prosencephalon to separate into the diencephalon and telencephalic vesicles. Includes marked facial abnormalities (e.g., single midline eye with rudimentary nose above)
- Heterotopias: Ectopic patches of gray matter caused by defective migration - often very epileptogenic
- Lissencephaly: “Smooth brain” - absence of cortical folding
- Fetal alcohol syndrome: includes mild facial abnormalities and low IQ