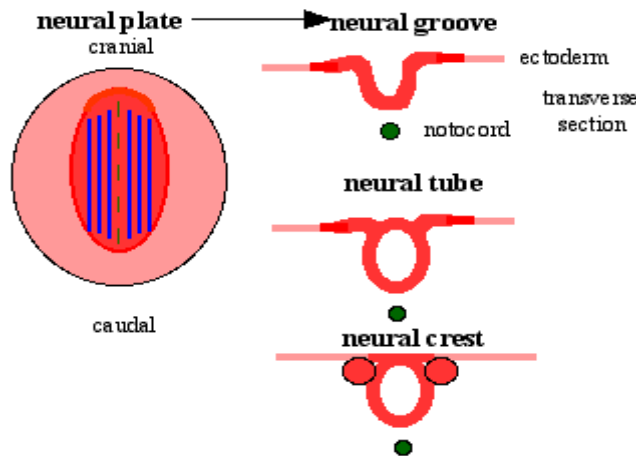


**Fourth week** of embryonic development is the beginning of organogenesis, (specific tissues and systems are beginning to differentiate) from the trilaminar embryo. On the embryo surface sensory placodes and limb buds appear. Sensory placodes (otic, lens, nasal) will form specific components of the ear, eye and nose. Limb buds form from ectoderm and mesoderm (somite) components and are the "paddle-like" projections from the trunk which will form all the upper and lower limb components. Within the embryo, this period of organogenesis is usually extended to cover until 8 weeks of development. Folding of the embryo continues and the earliest functioning organ is the heart. Other systems such as the circulatory, digestive, urogenital and nervous system begin to take shape.

### **Notochord development(Notogenesis):**

The notochord forms during gastrulation (3<sup>rd</sup> week) and induces the formation of the neural plate. The notochord is a cellular rod derived from cells migrating from the primitive node and pit it forms the first longitudinal midline axis around which the vertebral bodies are organized and is the basis for the axial skeleton. (*around notochord layered concentrations of cells appear, representing the primordia of the future vertebral bodies*) It will later regress.

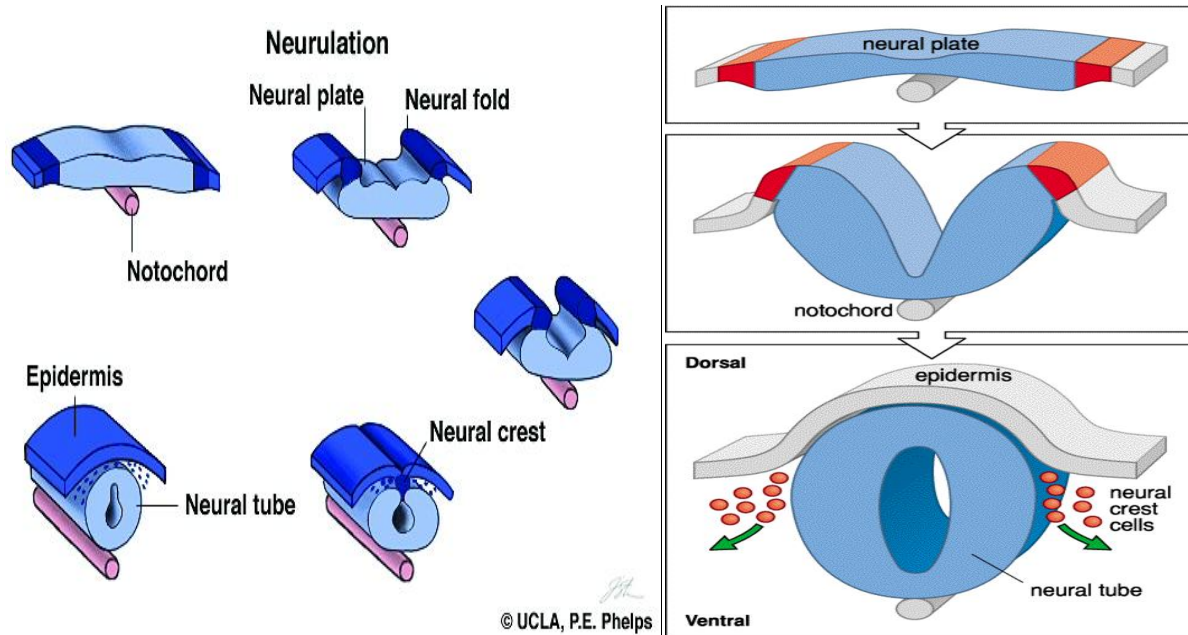


## *Neurulation*

Refers to the folding process in vertebrate embryos, which includes the transformation of the neural plate into the neural tube. The embryo at this stage is termed the neurula.

- The process begins when the notochord induces the formation of the central nervous system (CNS) by signaling the ectoderm germ layer above it to thicken and form the neural plate.
- Cells of the plate make up the neuroectoderm, and their induction represents the initial event in the process of neurulation.
- Lengthening of the neural plate and body axis by *phenomenon of convergent extension*, whereby there is a lateral to medial movement of cells in the plane of the ectoderm and mesoderm.
- As the neural plate lengthens, its lateral edges elevate to form neural folds, and the depressed midregion forms the neural groove. Gradually, the neural folds approach each other in the midline, where they fuse (forming the neural tube).
- The neural tube will later differentiate into the spinal cord and the brain, eventually forming the central nervous system.
- Until fusion is complete, the cephalic and caudal ends of the neural tube communicate with the amniotic cavity by way of the anterior (cranial) and posterior (caudal) neuropores respectively.
- Closure of the cranial neuropores occurs at approximately day 25 (18- to 20-somite stage), whereas the posterior neuropore closes at day 28 (25-somite stage).
- Neurulation is then complete, and the central nervous system is represented by a closed tubular structure with a narrow caudal portion, the spinal cord,

and a much broader cephalic portion characterized by a number of dilations, the brain vesicles .

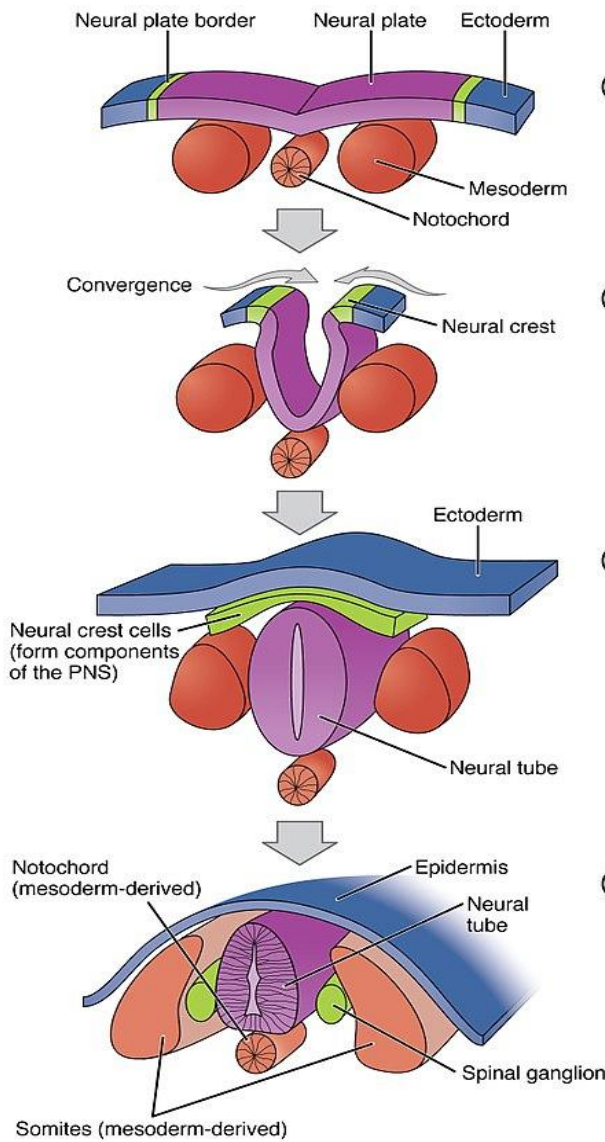


### Neural crest cells

As the neural folds elevate and fuse, cells at the lateral border or crest of the neuroectoderm begin to dissociate from their neighbors. undergo an epithelial-to-mesenchymal transition as it leaves the neuroectoderm by active migration and displacement to enter the underlying mesoderm. Neural crest cells also form and migrate from cranial neural folds, leaving the neural tube before closure in this region These cells contribute to the craniofacial skeleton as well as neurons for cranial ganglia, glial cells, melanocytes, and other cell types . Neural crest cells are so fundamentally important and contribute to so many organs and tissues that they are sometimes referred to as the fourth germ layer, give rise to :

- The dorsal root ganglia ,
- Schwann cells
- The autonomic nervous system
- Meninges

- Sensory ganglia
- Bones of the face
- Teeth
- Lens of the eyes
- Melanocytes
- Adrenal medulla & many glands.



① Neuroectodermal tissues differentiate from the ectoderm and thicken into the neural plate. The neural plate border separates the ectoderm from the neural plate.

② The neural plate bends dorsally, with the two ends eventually joining at the neural plate borders, which are now referred to as the neural crest.

③ The closure of the neural tube disconnects the neural crest from the epidermis. Neural crest cells differentiate to form most of the peripheral nervous system.

④ The notochord degenerates and only persists as the nucleus pulposus of the intervertebral discs. Other mesoderm cells differentiate into the somites, the precursors of the axial skeleton and skeletal muscle.