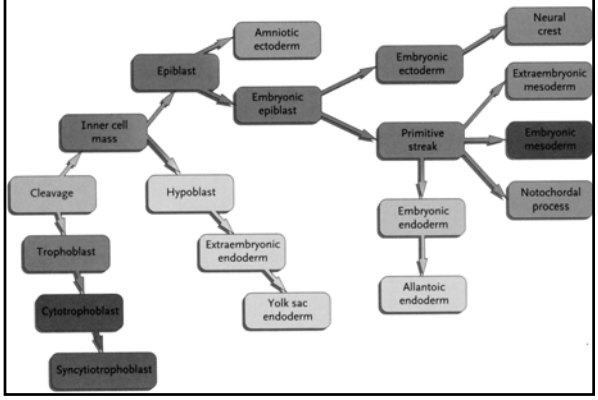
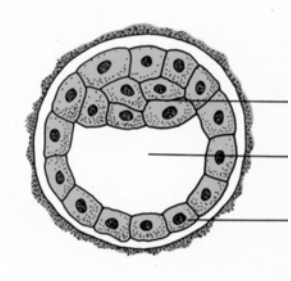
Gastrulation - Cell Lineages



Blastocyst

Embryo pole

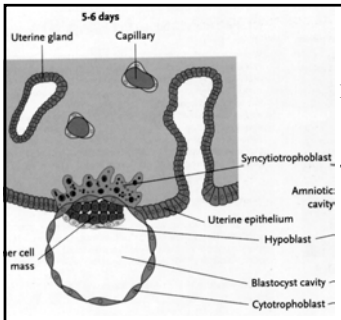


Inner cell mass (**embryoblast)**

Blastocoel

Outer cell mass (**trophoblast)**

abembryonic pole



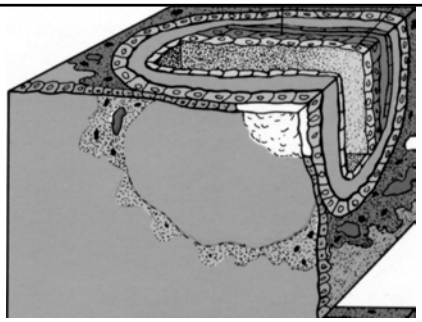
Day 6

Blastocyst adheres to endometrium at embryo pole

Trophoblast proliferation production of hCG (maintains corpus luteum)

Inner Cell Mass → Epiblast → Germ Layers

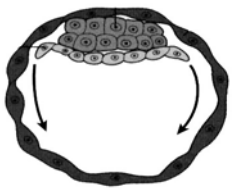
Inner Cell Mass → Hypoblast → Extraembryonic Endoderm/Mesoderm

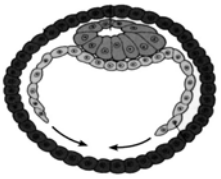


Bilaminar Disk – Epiblast and Hypoblast

Delamination – Separation of the Inner Cell Mass

Amnion





Amnion forms from epiblast

Cavitation – Formation of an internal space within a tissue

From BM Carlson, 1999

Gastrulation

Epiblast → Primary Germ Layers

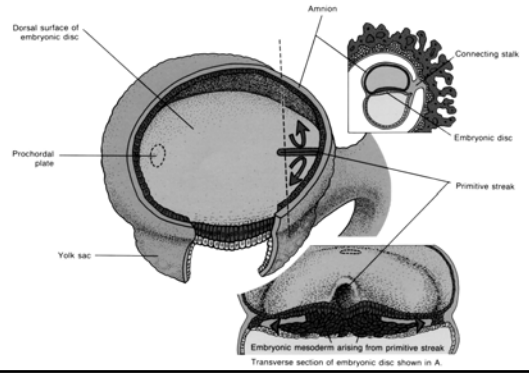
Ectoderm – outer layer – Skin, Nervous System, etc.

Mesoderm – middle layer – Muscle, Bones, etc.

Endoderm – Inner layer – Digestive Tract, Lungs, etc

Process – Morphogenetic Movements
Organized Cell Migration

Primitive Streak



Primitive Streak

Embryonic Day 15

Primitive groove – initiates gastrulation

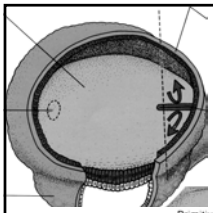
Primitive Streak – includes groove, node and pit

The Primitive Streak defines

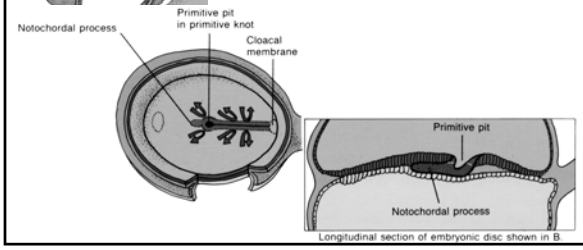
- Anterior – cranial
- Posterior – caudal
- Right and Left – lateral

Streak extends cranially then regresses caudally – depositing the notochordal process during regression.

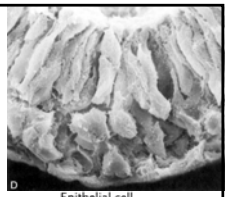
The tip of the regressing streak is the **Primitive Pit** and the **Primitive Node** (also called Hensen's Node)

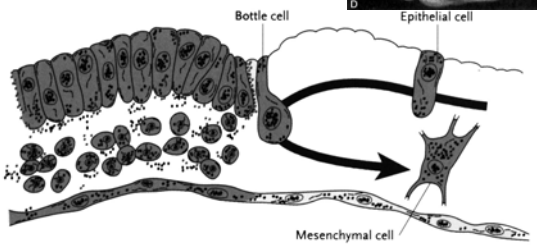


Primitive Node/Pit



Bottle Cells





Endoderm

First cells to go through the Streak form the Endodermal

These cells integrate and displace hypoblast cells

Mesoderm

Complex pattern of movements

Streak formation – Lateral Migration – Cardiac mesoderm

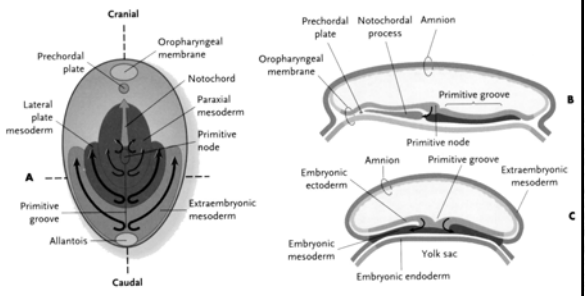
Streak regression - Lateral and Cranial Migration

- Lateral Plate Mesoderm
- Somitic Mesoderm

Streak Regression – Central and Cranial Migration

- Notochord – cellular rod, central long axis of embryo

Mesoderm



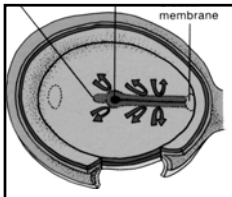
Ectoderm

Ectodermal cells don't enter the streak

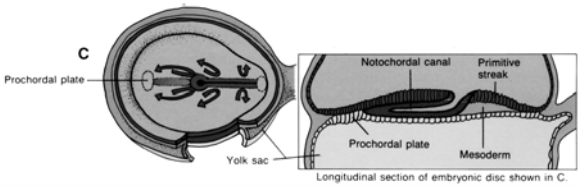
Cell layer expands as endodermal and mesodermal cells enter the streak

Cranial to the notochord – ectoderm and endoderm are in direct contact Oropharyngeal membrane

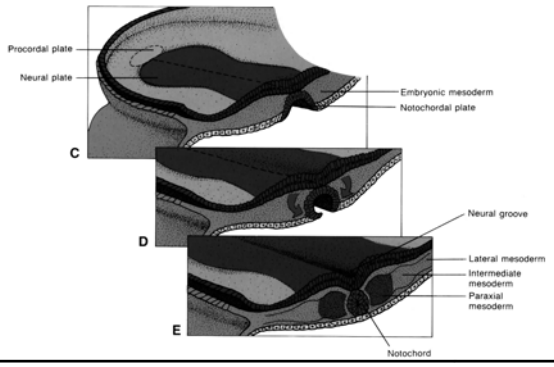
Between the Oropharyngeal membrane and the notochord is the pre-chordal plate – important for inducing the brain



Notochordal Process



Notochord



Embryonic Induction

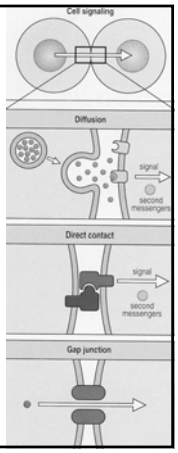
Definition: Signal from one group of cells influences the development of an adjacent group of cells

Inducing Tissue or Inducer

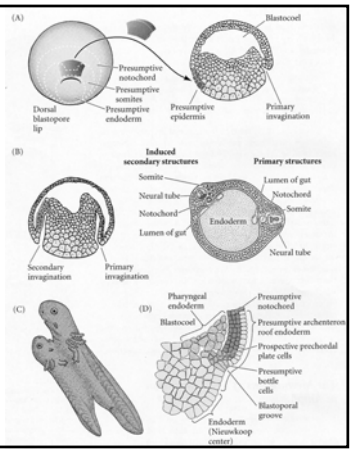
Inductive Signal - Morphogen

Responding Tissue
Competence

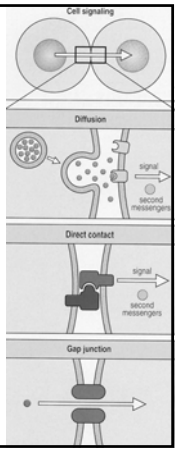
Expression of Target Gene



Primary Induction



Embryonic Induction



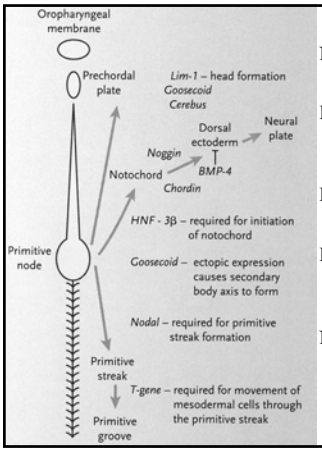
Definition: Signal from one group of cells influences the development of an adjacent group of cells

Inducing Tissue or Inducer

Inductive Signal – De-Repressor

Responding Tissue - Repressed Competence

Expression of Target Gene



Nodal – Required for primitive streak formation

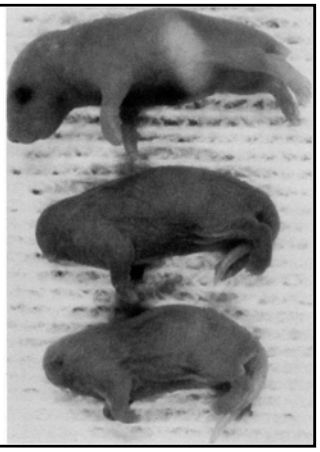
Lim1 – Homeobox containing; Node and pre-chordal plate Null - Headless

HNF3β – Hepatic nuclear factor; Notochord formation

BMP4 – Bone Morphogenetic Protein4; represses dorsal ectoderm

Noggin and Chordin – BMP4 inhibitors; de-represses ectoderm → neural tissue

Lim1 Mutant



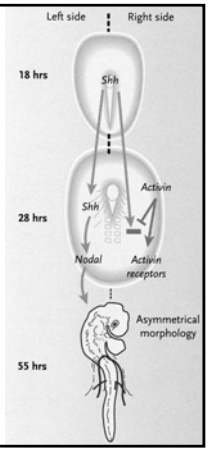
Left-Right Asymmetry

Node Signals:

SHH – Sonic Hedgehog – Left – induces Nodal

Activin – Right (inhibits SHH)

Reverse Asymmetry = situs inversus



Notochord as Inducer

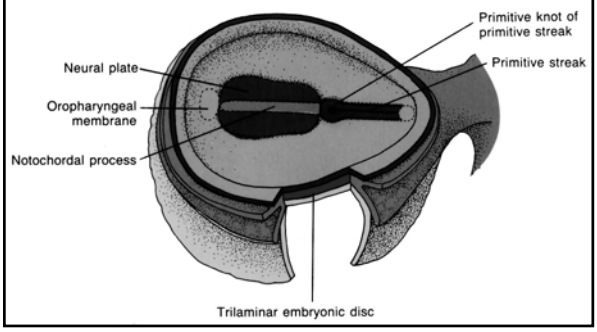
Induces overlying ectoderm → Neural Tissue (Neural Induction)

Specifies cell type in the Floor Plate of the Neural Tube

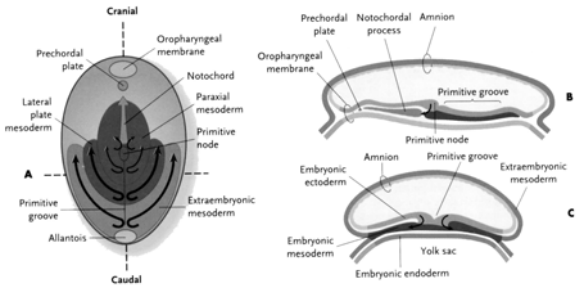
Transforms para-axial mesoderm (somite) into vertebral bodies

Stimulated early development of the dorsal pancreas

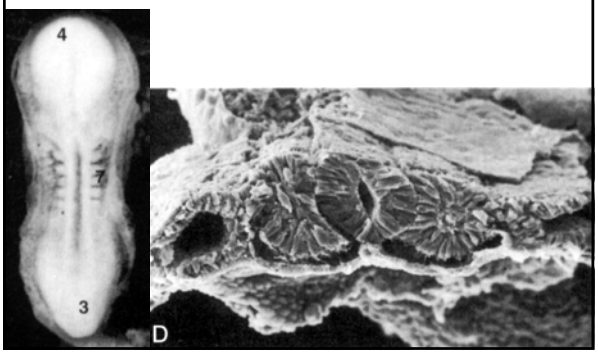
Neural Plate

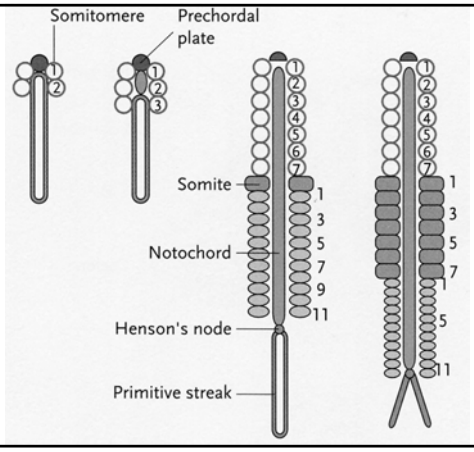


Mesoderm



Paraaxial Mesoderm - Somites





Somitogenesis

d18-d28 – Cranial to Caudal – 37 somites – form muscle, dermis, skeleton

Somitomeres 1-7 do not form somites – migrate to Pharyngeal Arches, muscles of face, jaw, throat

Somitomere 8 forms Somite; rate of 3-4 somites / day

Somite 1-4 – Occipital Region (skull, nose; ocular m., tongue

Somite 5-12 – Cervical Region (Cervical vertebrae, neck dermis)

Somite 13-24 – Thoracic Region (vertebrae, arms)

Somite 25-29 – Lumbar Region (abdomen, legs)

Somite 30-34 – Sacral Region (sacrum)

Somite 35-37 – Coccygeal Region (coccyx)

Segmentation of the Embryo

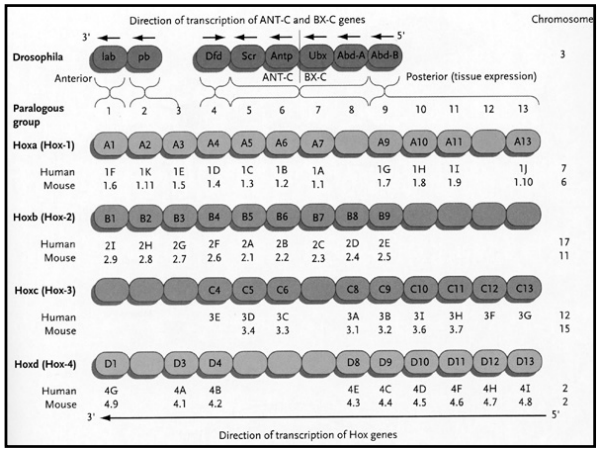
Segmentation occurs along the Anterior-Posterior Axis

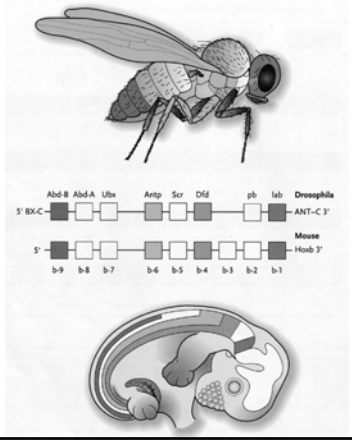
Each segment becomes an autonomous developing unit

Each segment can grow and undergo further segmentation

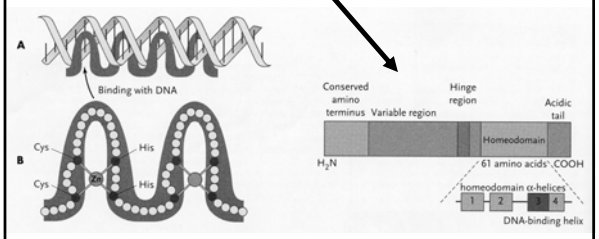
Molecular mechanisms are conserved

Genetic hierarchy	Functions	Representative genes	Effects of mutation
Maternal effect genes	Establish gradients from anterior and posterior poles of the egg	Bicoid Swallow Oskar Caudal Torso Trunk	Major disturbances in anteroposterior organization
Segmentation genes Gap genes	Define broad regions in the egg	Empty spiracles Hunchback Krüppel Knirps Tailless	Adjacent segments missing in a major region of the body
Pair-rule genes	Define 7 segments	Hairy Even skipped Runt Fushi tarazu Odd paired Odd skipped Paired	Part of pattern deleted in every other segment
Segment polarity genes	Define 14 segments	Engrailed Gooseberry Hedgehog Patched Wingless	Segments replaced by their mirror images
Homeotic genes	Determine regional characteristics	Antennapedia complex Bithorax complex	Inappropriate structures form for a given segmental level





Hox Genes Encode for Transcription Factors



Gastrulation Anomalies

Caudal Dysgenesis (Sirenomelia)
- Caudal defect
- Insufficient mesoderm formation
- Fused lower limbs, renal agenesis
- Genetic and Teratogenic
- Brachyury (T), Wnt

Holoprosencephaly
- Cranial defect
- Neuronal and craniofacial cell death
- Small forebrain, fused ventricles
- Teratogenic, e.g. alcohol

Neurulation

Readings:
- Chapter 5
- Chapter 10
  - P. 208-214
  - P. 218-219 (Peripheral Nerve)
  - p. 239-240 (Cranial Nerve)

Neurulation

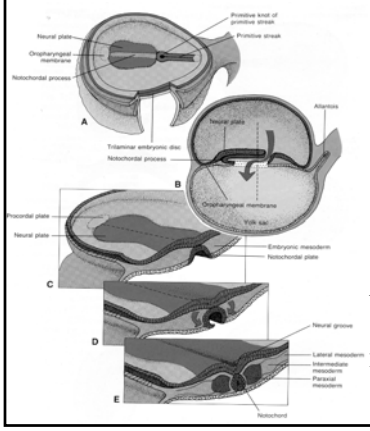
Induced by Notochord – Noggin/Chordin

Neural Plate → Neural Groove → Neural Tube

Regionalization – Subdivisions of the Central Nervous System (CNS)

Noggin, chordin → Anterior Neural Tissues Forebrain

FGF8 – Fibroblast Growth Factor 8 → Posterior neural tissues, i.e. spinal cord



Middle of third week: Neural Plate

Notochord induces overlying ectoderm → neural plate –

Thickening of cell layer

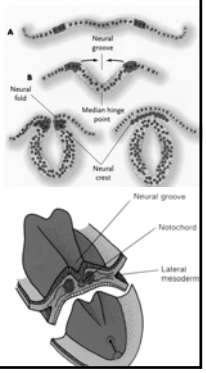
Anterior Inducer: Noggin/ Chordin

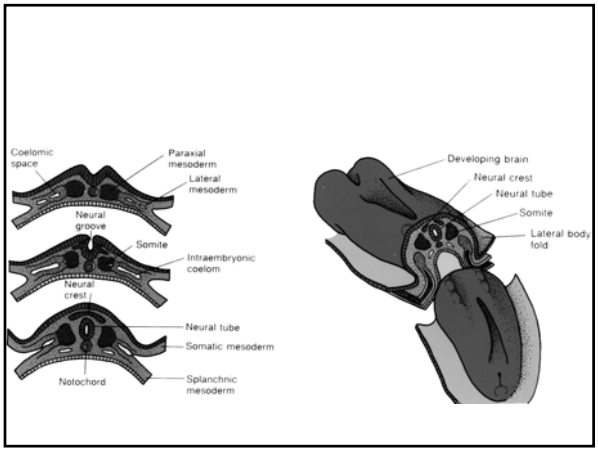
Posterior Inducer: FGF-8,

Neural Plate → Neural Tube

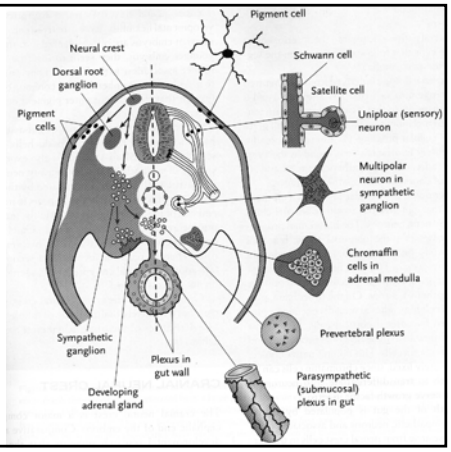
Four Stages of Neural Tube formation:

1) Thickening of the Neural Plate
2) Establishing the contours of the Neural Plate: Cell shape changes and rearrangement of cells
3) Lateral Neural Folds elevate to form the Neural Groove – medial hinge acts as an anchor, Cell shape changes apically, expanding lateral epidermis forces elevation
4) Apposition and fusion of the Neural Folds to form the Neural Tube

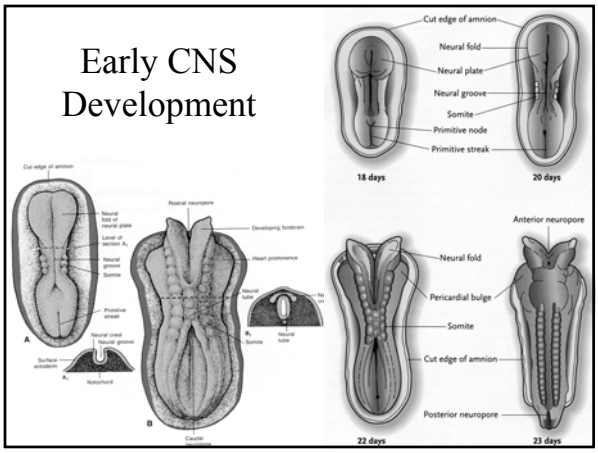




Neural Crest



Early CNS Development



Neural Tube Formation

Anterior Neuropore

Anterior

Central Fusion

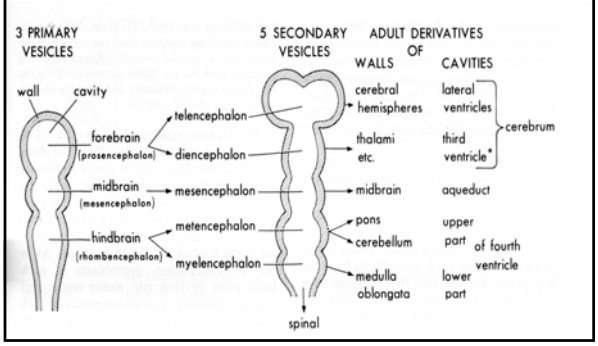
Posterior

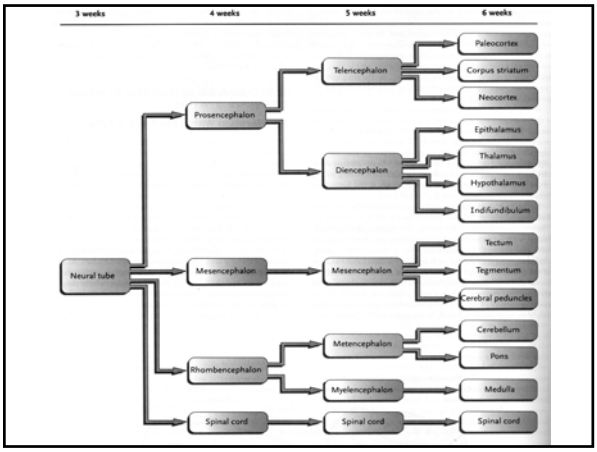
Posterior Neuropore

Completion – Closure of Neuropores

Secondary Neurulation – Posterior to the neuropore – Mesenchymal condensation to form a rod that undergoes cavitation – secondary fusion with primary neural tube.

Segmentation of the Neural Tube





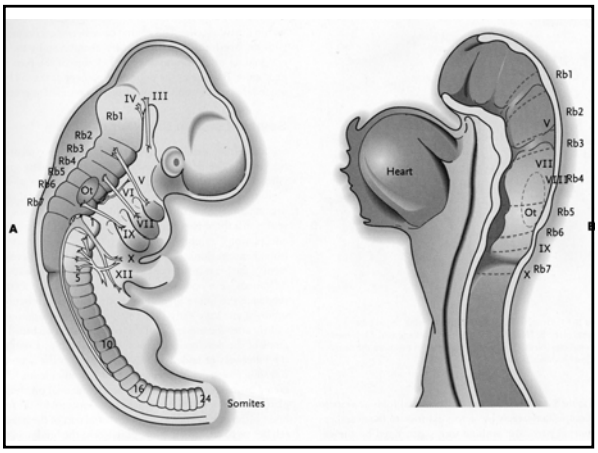
Segmentation of the Rhombencephalon

Neuromeres – Transient regularly spaced segments, also called Rhombomeres

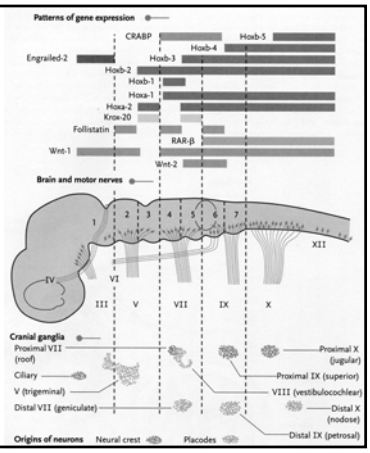
7 pairs – each an isolated compartment

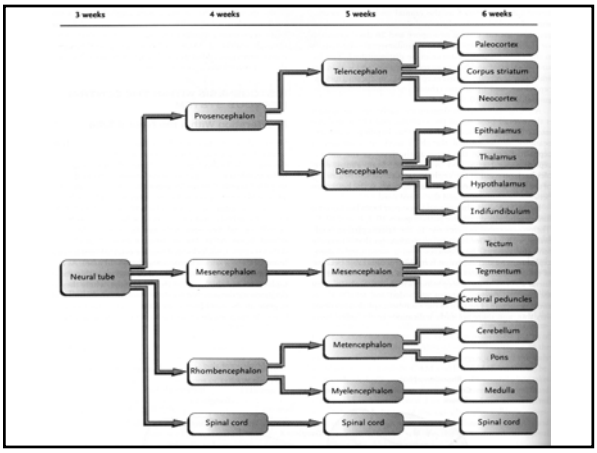
Alternating cell adhesive characteristics; alternating rhombomeres intermingle freely

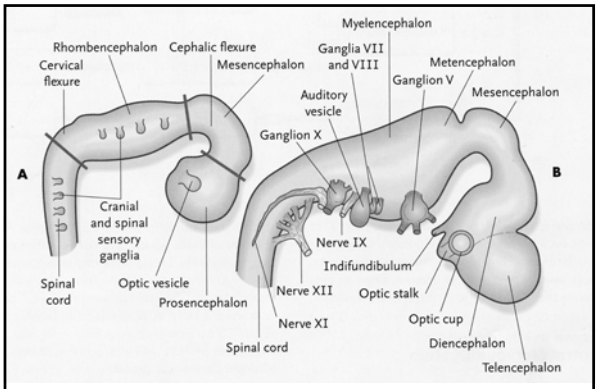
Segmental organization gives rise to specific cranial nerves



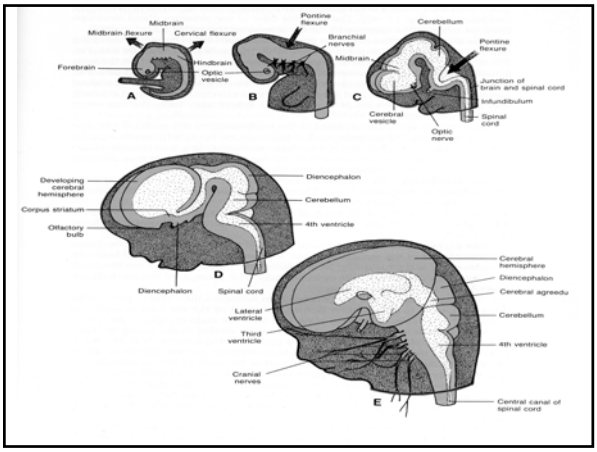
Specification and Position-Specific Gene Expression

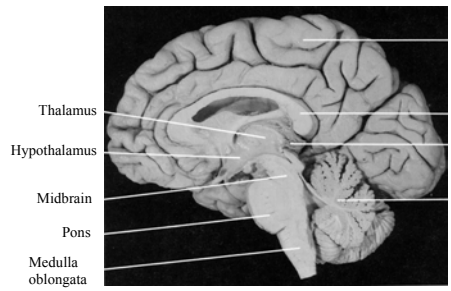




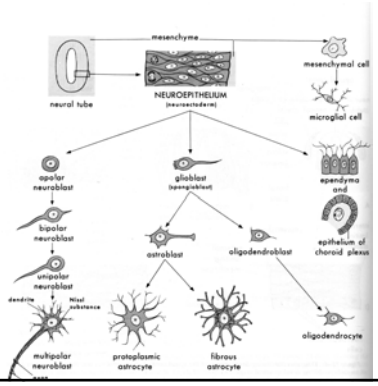


Cephalic flexure, Cervical flexure, Pontine flexure





Histogenesis of CNS cells



Cell Types

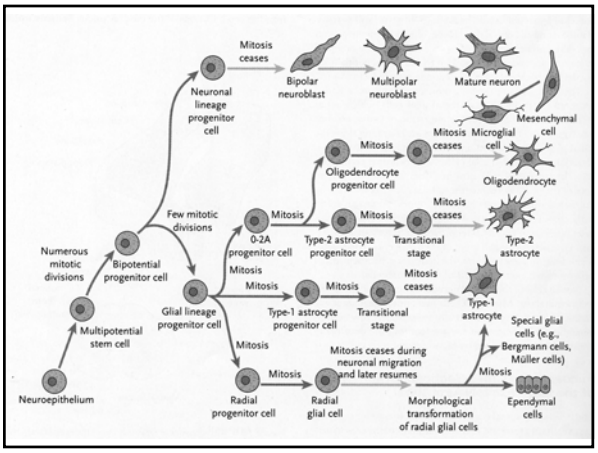
Neuroepithelium – Multipotential Stem Cell

Bipotential Progenitor Cell

Neuronal vs. Glial Cell Lineage

Neuronal Lineage (neurofilament expression):
Bipolar neuroblast, Multipolar neuroblast, Neuron

Glial Lineage (glia fibrillary acidic protein, GFAP):
Radial glia, Type-1 Astrocyte, Type-2 Astrocyte, Oligodendrocyte



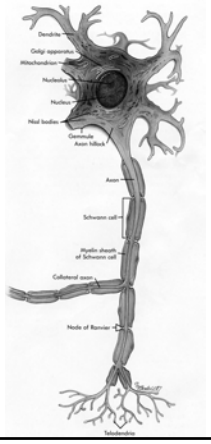
Dendrite

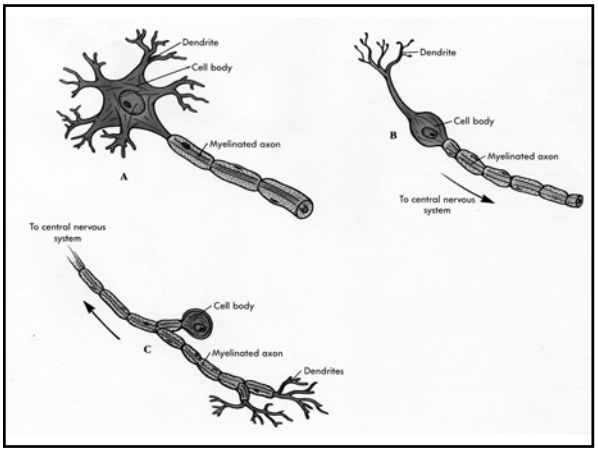
Cell Body

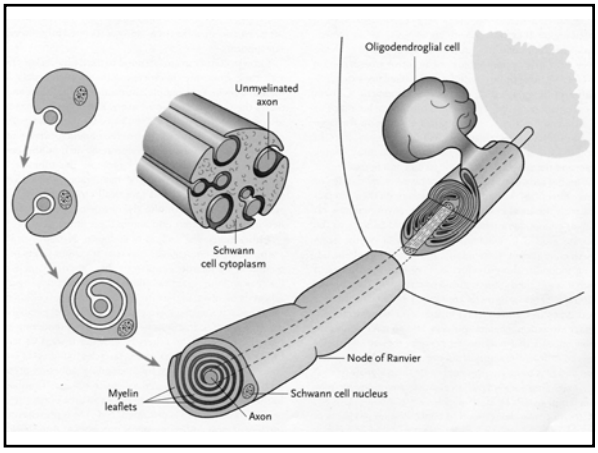
Axon

Schwann Cell

Myelin Sheath







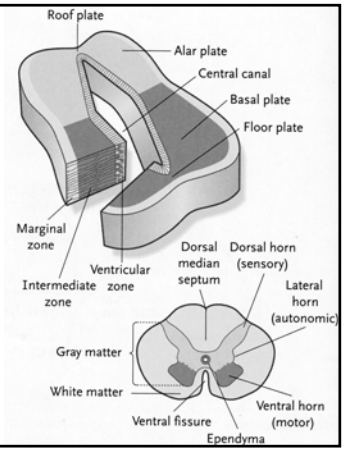
Spinal Cord

Central Canal – Lumen

Ventricular Zone – Cells lining the Central Canal becomes Gray matter

Intermediate Zone

Marginal Zone – neuronal cell processes; no cell bodies, becomes White matter



6 Parts of the Spinal Cord

2 Alar Plates (Left and Right)

Sulcus Limitans separates Alar and Basal plates

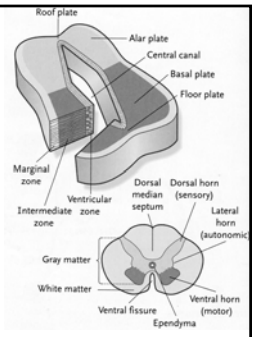
2 Basal Plates (Left and Right)

Roof Plate connecting Alar plates

Floor Plate connecting Basal plates

Basal plates → Motor – Ventral Horn

Alar plates → Sensory – Dorsal Horn

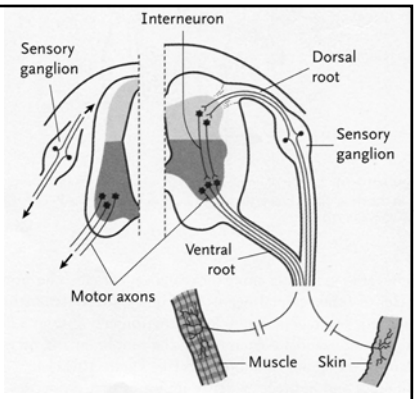


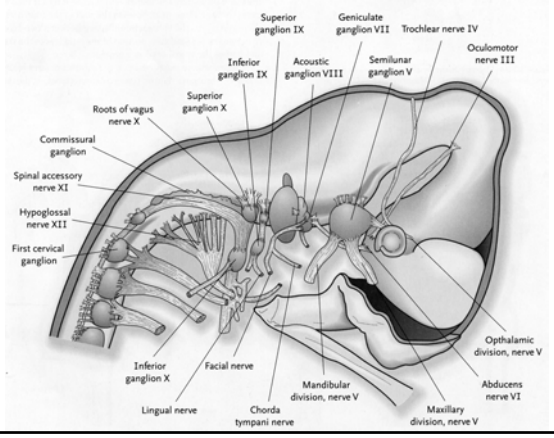
Nerves

Motor

Sensory

Autonomic
Sympathetic
Parasympathetic





Cranial Nerves

I – Olfactory; Telencephalon; No Ganglion; Sensory

II – Optic; Diencephalon; No Ganglion; Sensory

III – Oculomoter; Mesencephalon; Cilary Ganglion; Motor and Parasympathetic

IV – Troclear; Metencephalon; No Ganglion; Motor

V – Trigeminal (semilunar); Metencephalon, trigeminal placode; Trigeminal Ganglion; Sensory and Motor

VI – Abducens; Metencephalon; No Ganglion; Motor

VII – Facial; Metencephalon; 4 Ganglia – Superior, Inferior (Geniculate), Sphenopalatine, Submandibular; Motor, Sensory, Parasympathetic

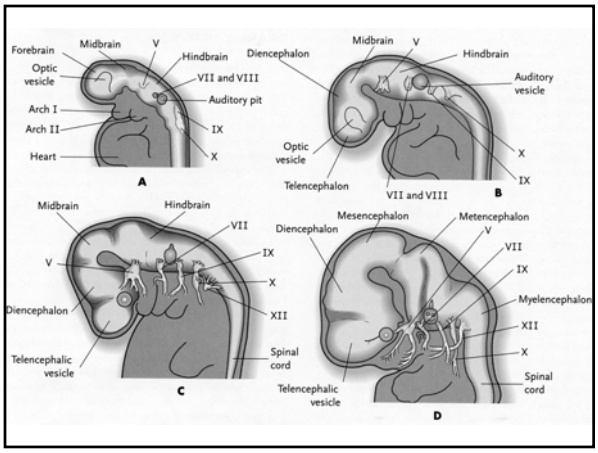
VIII – Vestibulocochlear; Metencephalon, 2 Ganglia – Acoustic, Vestibular; Sensory

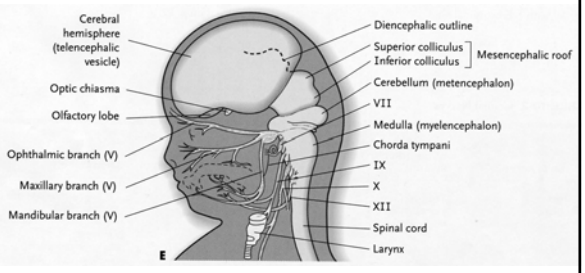
IX – Glossopharnygeal; Myelencephalon; 3 Ganglia – Superior, Inferior (Petrosal), Otic; Motor, Sensory, Parasympathetic

X – Vagus; Myelencephalon; 3 Ganglia – Superior, Inferior (Nodose), Vagal parasympathetic; Motor, Sensory, Parasympathetic

XI – Accessory; Myelencephalon; No Ganglia; Motor

XII – Hypoglossal; Myelencephalon; No Ganglia; Motor





Anomalies

Defective Neural Tube Closure
- Spinal Cord – Rachischisis
- Brain – Craniochisis (lethal)

Spina Bifida – Defective closure of anterior or posterior neuropore – lacking neural arch, bulging membranous sac called a Cele, containing cerebral spinal fluid +/- neural tissues

Spina bifida occulta – Defect in Neural Arch – mildest form

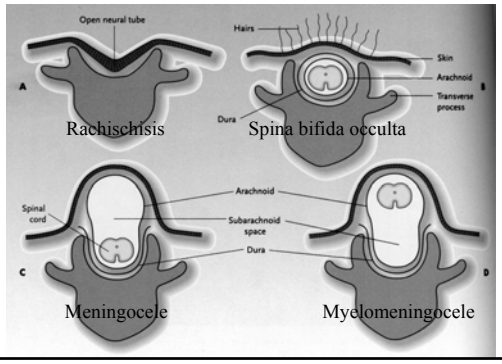
Meningocele – protruding dura and arachnoid tissues

Meningomyelocele – protruding spinal tissues

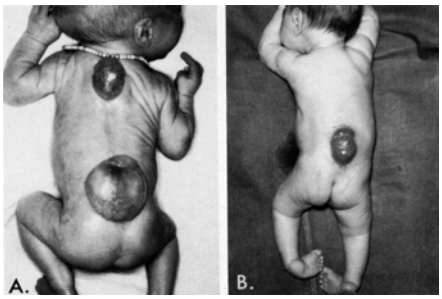
Meningoencephalocele – protruding brain tissues

Meningohydroencephalocele – protruding brain and ventricular tissues

Anomalies – Spinal Cord



Spinal Abnormalities



Spina bifida

Brain Abnormalities

microcephaly

holoprosencephaly

hydrocephaly

Early Heart Development

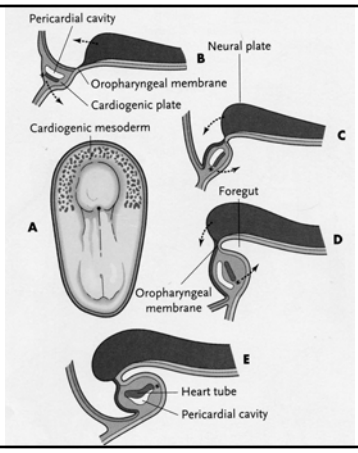
Precardiac mesoderm – horseshoe shaped extending back on both sides of the foregut

Endoderm induces early heart tissue

Mesoderm splits → somatic and splanchnic, cardiogenic plate is splanchnic and anterior to the oropharyngeal membrane

Space between somatic and splanchnic mesoderm will form pericardial cavity

180o rotation of the anterior embryo places the heart posterior to the oropharyngeal membrane



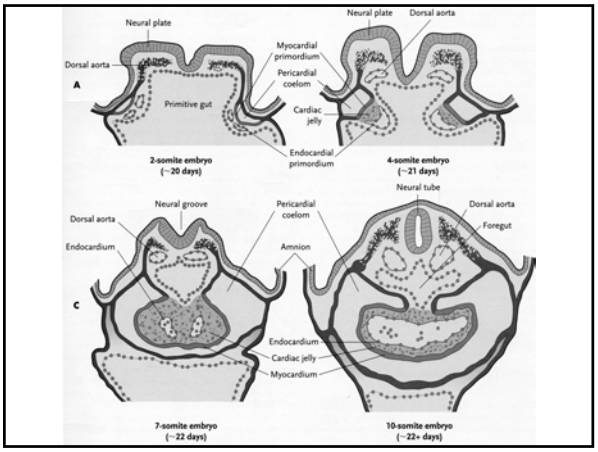
Heart Formation

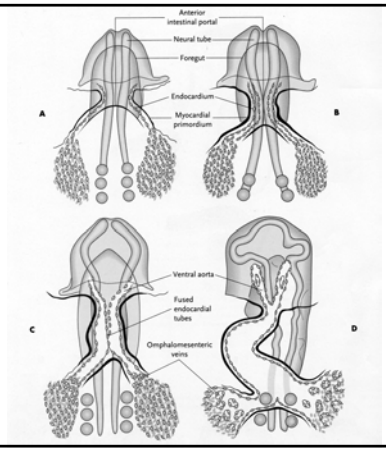
Vesicles in the pre-cardiac splanchnic mesoderm fuse to form paired endocardial primordia on both sides of the foregut

Endocardial primordia fuse along the midline to form the primitive tubular heart

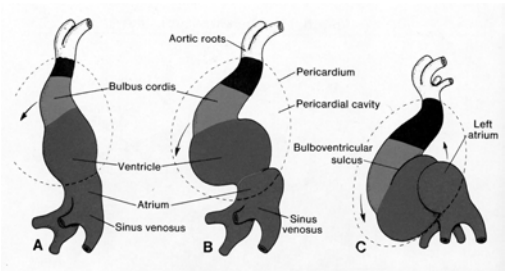
Inner endocardial lining becomes the endocardium, surrounded by matrix called cardiac jelly

Myocardium surrounds the cardiac jelly

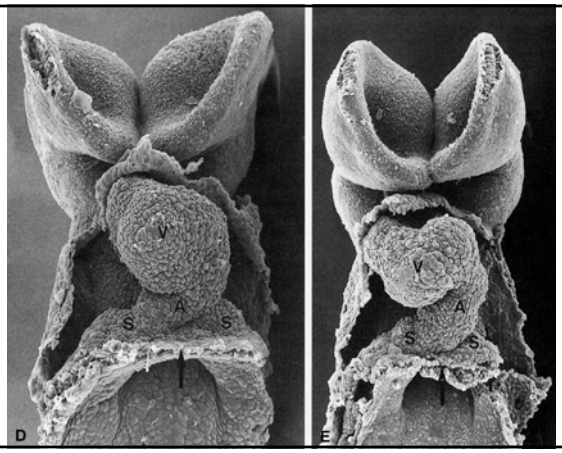


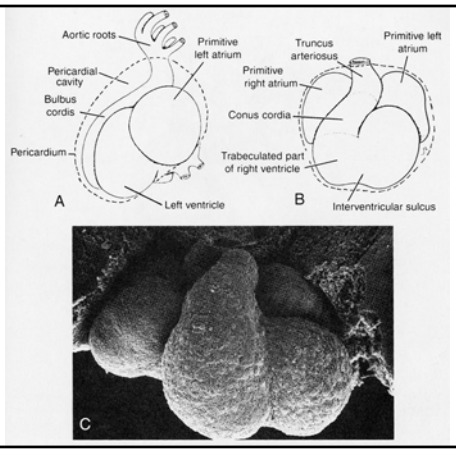


Heart Formation



Tubular heart forms an S-shaped loop





Blood and Vessels

Blood forms from blood islands in the Yolk Sac
Extraembryonic splanchnic mesoderm
Induced by extraembryonic endoderm
Stem cell = hemangioblasts in the blood islands
Blood-forming cells = hemocytoblasts
Vessel forming cells = endothelial cells