Neuroembryology I

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COPH G210
The primitive node & streak help to establish the body axis during gastrulation & is dependent upon *Nodal* expression.
Partial duplication of the primitive streak occurs in all phyla.
Duplication of the anterior aspect of the primitive streak during early gastrulation can lead to the duplication of the notochord with subsequent induction of overlying ectoderm to develop two neural tubes. The extent of the duplication can be variable. The transcription factor, Goosecoid, plays an important role in normal head development.
The notochord induces the ectoderm above it to develop into the neural plate. The neural plate then starts to fold on the lateral edges to form the neural groove.
The neural folds come together in the cervical region and fuse; closure then proceeds in a rostral and caudal direction.

Primary Neurulation

This process requires folate and must occur for proper nervous system development. The neural tube must be closed off from CSF.

Ant. Neuropore: E25
Post. Neuropore: E27
Secondary Neurulation

On E20, a mass of mesenchyme (caudal eminence) condenses, hollows out and then joins with the neural tube formed by primary neurulation by E40. Secondary neurulation forms the sacral and coccygeal spinal segments. In humans, most of the coccygeal spinal segments regress.
Primary vs. Secondary Neurulation

Primary:
1. Starts from ectoderm
2. Folds to form a tube

Secondary:
1. Starts from mesenchyme
2. Condenses, then hollows
3. Undergoes an epithelial transition
Insufficient mesoderm within the caudal eminence results in “Caudal Dysgenesis (Caudal Regression Syndrome)”. Pelvic & lower extremity hypoplasia with failure of sacral spinal cord development. Extreme cases result in “sirenomelia”. Assoc. with maternal diabetes.
Neural Tube Regions

1. Neuroepithelial Layer
   (Proliferative, Ventricular Layer):
   Highly mitotic & gives rise to neurons and macroglia

2. Mantel Layer:
   Will form s.c. gray matter

3. Marginal Layer:
   Will form s.c. white matter

Neuroepithelial layer forms ca. 250K neurons/minute! More neurons are born than survive. Once all neurons & macroglia are formed it differentiates into ependymal cells that line the ventricular system.
Neurons & macroglia are born at very specific times and migrate to very specific regions.

Neuroblasts migrate to pial surface then “retract” back to their proper position.

Each successive wave of neuronal proliferation has to pass through previously born neurons. This gives opportunity for synaptic contacts.
Neuroepithelial Cell Differentiation

Note: Gliablasts give rise to macroglia. Microglia do not arise from the neural tube, but migrate into & out of the CNS.
Failure of Neuronal Migration

Lissencephaly

Note smooth surface

Occurs during 3rd to 5th month of gestation.
Schizencephaly (Porencephaly) results from either an early vascular accident or a mutation in the homeobox gene $EMX2$. 
The mantel layer in the dorsal & ventral aspects of the neural tube form the alar & basal plates, respectively, that once fully developed are called the dorsal & ventral horns.

Alar = Sensory
Basal = Somatic motor

Intermediate horn = Sensory & Motor aspects of spinal ANS.
The sulcus limitans separates the alar & basal plates throughout the neuraxis.

Note the collection of neurons next to the basal plate that lie outside of the CNS. These are pseudounipolar neurons of the DRG whose central processes form the dorsal root & will enter the alar plate.

Note the axons arising from motoneurons of the basal plate forming the ventral root. ANS axons also exit the CNS via the ventral root.
Spinal Nerve Development

The dorsal root is formed from DRG axons & the ventral root is formed from axons of somatic & ANS motor neurons. The Spinal Nerve is where the dorsal & ventral roots join for a brief time before splitting into dorsal & ventral primary rami.
The Spinal Nerve is very short.

1 = Spinal Nerve  
2 = Dorsal Primary Ramus  
3 = Ventral Primary Ramus

The separation of sensory from motor information occurs in the roots.

The Ventral Primary Rami innervate the vast majority of mm.
The alar & basal plates extend throughout the neuraxis, but appear “modified” due to the developmental processes occurring in the neural tube that forms the CNS rostral to the spinal cord.

Brainstem:
Sensory functions are lateral
Motor functions are medial
Rostral to the spinal cord, the neural tube forms the brainstem and “brain”. Segmentation controlled by Hox genes.
During development, the neural tube folds on itself at several places to help conserve space. (Details in Neuro course.)
The neurocele will develop into the ventricular system and will be filled with CSF. Expansion of the telencephalic vesicle causes the characteristic “C” shape of the lateral ventricles that remain connected to the midline 3rd vent via the interventricular foramen.
The cerebral aqueduct is the most narrow part of the ventricular system & connects the third & fourth ventricles.
Cerebral aqueduct stenosis is the most common cause of hydrocephalus. Choroid plexus continues to make CSF even though it can not enter the subarachnoid space for reabsorption into the venous system.
Differential growth of the vertebral column & the spinal cord makes it appear as if the spinal cord ascends in the vertebral canal.

Note the stretching of the roots during development.
Neural crest cells are ectodermal & are found along the length of the neural tube. They start to migrate when the neural folds touch to form the neural tube. Any neuron outside of the CNS is of neural crest origin.
Some neural crest cells form ganglia that are visible to the naked eye; others form microscopic ganglia in the viscera.
Neural crest differentiates into a wide variety of cells.

Neural crest abnormalities found in one region may indicate there are defects in other regions as well.