Flexion and Neural Tube Formation

RECOMMENDED READING:

Larsen: Human Embryology 3rd edition

1. Review figures 2.4-2.6 and such text as necessary (pp 41-43 for source of definitive yolk sac and extra-embryonic coelom (cavity).
2. Pp 131-143. Text covers the formation of the intra-embryonic coelom and its division into peritoneal, pleural and pericardial cavities plus closure of the diaphragm.
3. Pp 57, Figure 3-4; pp 85-93. Text covers the transformation of the neural plate into the neural tube, the initial phases of differentiation of this tube and the origin of the neural crest. The multiple fates of neural crest derivatives will be given in other lectures.

LEARNING OBJECTIVES:

1. Review information on the formation of the extra-embryonic coelom from prior lecture.

Embryonic flexion and folding

2. Understand how the lateral plate mesoderm divides into somatopleure and splanchnopleure, which flex (fold) in the lateral plane and fuse ventrally. This results in the enclosure of some of the extra-embryonic coelom into the embryo.
3. Note that head/tail flexion is "driven" in part by rapid growth of the CNS and relative stiffness of notochord.
4. Understand the "accomplishments" of flexion and folding:
   a. Segregation of embryonic from extra-embryonic tissues except at umbilical cord.
   b. Enclosure the intra-embryonic coelom.
   c. Narrowing of the gut tube.
   d. Postioning of the buccopharyngeal membrane (future mouth) and cloacal membrane (future opening of urinary and gastrointestinal tracts) to a ventral position.
   e. "Movement" of the septum transversum and cardiogenic tissues ventrally.

Formation of and closure of the neural tube, division into primary brain vesicles and origin of neural crest.

5. Understand the morphological changes that transform the flat neural plate into the neural tube.
6. Understand the consequences of failure of the neural tube to close completely.
7. Understand the pattern of initial growth of the CNS in three primary vesicles.
8. Understand the origin and initial migration patterns of the neural crest.

GLOSSARY:

Flexion and folding

Cardiogenic area - the cardiogenic area first forms between cranial edge of the trilaminar germ disc and the neural plate on about day 19.
Central tendon of the diaphragm - A ventral vestige of the septum transversum.

Cephalic (also called, mesencephalic or cranial) flexure - On ay 22, the developing brain flexes sharply ventral in the region of the presumptive mesencephalon.
Cephalocaudal folding - On day 22 the relatively stiff dorsal midline structures (notochord, neural plate, and somites) overgrow the cranial end of the embryo and the yolk sac, resulting in the embryo folding sharply ventrally. A similar process occurs at the caudal end of the embryo beginning on about day 23.
Definitive pericardial cavity - The septum transversum (see below) descends to a level just superior to the yolk sac, partially separating the intraembryonic coelomic cavity into a superior primitive pericardial cavity and an inferior peritoneal cavity (future abdominal and pelvic cavities). During the fifth week, the primitive pericardial cavity is divided into an anterior definitive pericardial cavity and two posterior pleural cavities by two coronal pleuropericardial folds. These folds fuse at the midline and, with the esophageal mesoderm, to form the pericardial sacs.
Diaphragm - The diaphragm, chief respiratory muscle, is a composite of several embryological structures as outlined and diagramed in the text. The innervation depends on the origin of the muscle cells; the rim of the diaphragm is innervated by spinal nerves T7 - T12, while the musculature derived from the septum transversum is innervated by the phrenic nerve (C3 - C5).
Dorsal mesentery - In the fifth week, the GI tract is suspended in the peritoneal cavity from the presumptive intra-abdominal esophagus to the presumptive sigmoid colon by a thin membrane formed by reflections of peritoneum from the midline of the posterior wall of the peritoneal cavity.
Intraembryonic coelom - The cavities that develop between the splanchnopleuric and somatopleuric mesoderm on the left and right sides of the embryo at the end of the third week, coalesce during cephalocaudal and lateral folding to produce the single intra-embryonic coelomic cavity. This cavity gives rise to the definitive pericardial, left and right pleural, and peritoneal cavities.
Intraperitoneal - By convention, any organ suspended in the peritoneal cavity by a mesentery is called an intraperitoneal organ.
Lateral folding - Lateral folding of the embryo during the fourth and fifth weeks, results in fusion of the lateral edges of the ectoderm, somatopleuric mesoderm, presumptive coelomic cavities, splanchnopleuric mesoderm, and endoderm forming the cylindrical vertebrate body form with its presumptive integument, and gut tube.
Mesencephalic flexure - See cephalic flexure, above.
Pericardioperitoneal canals - Descent of the septum transversum partially separates the superior primitive pericardial cavity from the inferior peritoneal cavity. The two cavities, however, communicate through two posterio-lateral gaps on either side of the longitudinal axis. These are the pericardioperitoneal canals.
Peritoneal cavity - This cavity, derived from the region of the intraembryonic coelomic cavity, inferior to the developing diaphragm, will become the abdominal and pelvic cavities of the fetus.
Pleural cavities - The left and right pleural cavities are formed in the fifth week by the division of the primitive pericardial cavity by the pleuropericardial folds.
Pleuropericardial folds - These coronal folds of the lateral body wall mesoderm grow into the primitive pericardial cavity during the fifth week. As these evaginations of body wall mesoderm extend into the primitive pericardial cavity, meet at the midline and fuse with the mesoderm associated with the esophagus. This forms a left and right pleural cavity (enclosing the lung buds) and an anterior definitive pericardial cavity (enclosing the heart).

Pleuroperitoneal membranes - These membranes grow from the posterio-lateral (mesoderm) walls in the plane of the septum transversum during the fifth and seventh weeks, thus sealing off the pericardioperitoneal canals. These membranes acquire myoblasts from the septum transversum and form the muscular regions of the developing diaphragm. If one of these membranes does not develop (usually the left pleuroperitoneal membrane), then the abdominal contents may herniate into the pleural cavity; this is called a **diaphragmatic hernia.**
Primitive pericardial cavity - Descent of the septum transversum to a level just superior to the yolk sac partially divides the intraembryonic coelomic cavity into a superior primitive pericardial cavity, containing the heart and an inferior peritoneal cavity. The primitive pericardial cavity is divided into the left and right pleural cavities and the definitive pericardial cavity by the pleuropericardial membranes.
Retroperitoneal - This term refers to organs embedded within the sub-serous fascia of the peritoneum lining the body wall. Such organs may be embedded within the body wall in any location and include the bladder and umbilical ligaments (anterior body wall) and the ureters, and the kidneys (posterior body wall).
Secondarily retroperitoneal - These organs appear retroperitoneal (see above) but were initially intraperitoneal and became secondarily fused to the body wall. These include the pancreas, duodenum and ascending and descending colons.
Septum transversum - This most cranial block of mesoderm becomes apparent at the leading edge of the trilaminar germ disc on about day 22. As the cephalic end of the embryo begins to fold, it swings inferiorly and ventrally to a position just superior to the narrowing connection of the yolk sac and developing midgut. As it descends, it becomes innervated by cervical nerves C3, C4, and C5. It will form the central tendon of the diaphragm; its myoblasts will invade the pleuroperitoneal membranes to form diaphragmatic musculature.
Somatopleure - The embryonic somatopleure is associated with the embryonic ectodermal surface.
Splanchnopleure - The embryonic splanchnopleure is the mesoderm associated with endoderm forming the wall of the gut.
Umbilical cord - This composite structure is formed by the association of the connecting stalk (with its vasculature) and the neck of the yolk sac (the vitelline duct) as they become invested in amniotic membrane at the conclusion of embryonic folding in the 8th week.
Vitelline duct - As growth of the embryo overtakes that of the yolk sac, the connection between the yolk sac and the midgut of the GI tract narrows. By the end of the sixth week, the neck of the yolk sac has narrowed to a slim stalk, called the vitelline duct.

Neural plate development

Anencephaly - Failure of the cranial neuropore to close results in maldevelopment of the neural epithelium of the brain and its exposure at the forehead or crown.
Brain vesicles - The 3 primary brain vesicles (swellings): the prosencephalon (forebrain), mesencephalon (midbrain), and rhombencephalon (hindbrain) do not form until complete closure of the cranial neuropore but expansions of the neural plate that form each vesicle are apparent within the neural plate.
Caudal neuropore - Initial formation of the neural tube leaves two large openings, **cranial and caudal** neuropores. As the neural tube continues to close, the neuropores become progressively smaller. The cranial neuropore closes on day 24 and the caudal neuropore on day 26.

Chain ganglion (also sympathetic chain ganglion) - neural crest derivatives on both sides of the developing spinal cord. Neurons within the chain ganglia are peripheral neurons of the sympathetic nervous system.

Dorsal root ganglion (DRG) - Pairs of dorsal root ganglia are formed from neural crest cells that collect just lateral to the second cervical to first coccygeal segments of the spinal cord. These are the sensory component of peripheral nervous system.

Neural crest - These cells arise from the lateral lips of the neural folds. They detach from the neural plate in the cranial region before the cranial neuropore closes and as well as from more caudal regions of the neural tube. They take several different migratory routes to form dorsal root ganglia, chain and prevertebral ganglia (sympathetic nervous system), parasympathetic nervous system, melanocytes, elements of the facial skeleton, ciliary and pupillary muscles, dermis of the head and neck. See text for other derivatives.

Neural groove - Almost as soon as the neural plate appears (at about day 18), a thin longitudinal midline neural groove bisects it into presumptive right and left neural folds.

Neural plate - Beginning on day 19, the neural plate is "induced" by paraxial mesoderm and notochord from ectoderm that gives rise to neuroepithelium of the central nervous system.

Neurulation - Neurulation is the process of folding of the neural plate and closure of the cranial and caudal neuropores to form the neural tube. The neural tube below S2 arises from the caudal eminence by "secondary neurulation" (see text).

Neuroectoderm - This **neural epithelium** arises from the midline ectoderm within the neural plate.

Ventricular layer - This layer of neuroepithelium is located adjacent to the neural canal. It gives rise to neurons, supporting cells (glia) and ependyma of the CNS.